Journal of High School Science

Pulmonary tuberculosis deaths in high-burden India: replacing manual X-ray readouts with computer vision systems.

Ozvardar M.E[1], Otiono J[2]

Submitted: September 17, 2024, Revised: version 1, October 27, 2024, version 2, November 10, 2024
Accepted: November 12, 2024

Abstract

Tuberculosis (TB), caused by the bacterium *Mycobacterium tuberculosis*, is present in its latent form in a quarter of the world's population, but only a small fraction of those infected develop it. Ageing and an associated immunodeficient state is one of the triggers of the onset of active TB. India is currently the world's highest-burden country, having had unchecked transmission of the disease for decades. With an increasing and aging population, the growing number of cases of TB is putting a strain on the health system. First-line diagnosis of presumptive cases of pulmonary TB, the type of TB associated with the lungs, is discovered via a chest X-ray and its analysis, or reporting, relies on a radiologist. The shortage of radiologists in India, coupled with a predominantly rural population, has led to a significant number of Indians with active pulmonary going undiagnosed, leading to an unnecessarily high death toll over the years. This study explores the potential of computer vision systems as the first and only readers of chest X-rays to replace radiologists for diagnosing active pulmonary TB. We make the case that existing computer vision systems have advanced sufficiently and that their roll-out stands to expedite efforts to contain the disease. We further argue that such a roll-out is the most expedient and cost-effective way to reduce the disease's mortality and calculate to a first approximation, the impact of a full-scale roll-out on reducing the number of deaths in India.

Keywords

Pulmonary Tuberculosis, TB, TB in India, Computer vision systems, WHO, Artificial Intelligence, Radiology, Radiologist shortage, End TB strategy, Image recognition

[1]Corresponding Author: Melis Ela Ozvardar, Hisar School, Gokturk Merkez, İstanbul Caddesi, No:3, Eyupsultan, Istanbul, 34077, Turkiye. melis.ozvardar@hisarschool.k12.tr
[2]Jennifer Otiono, Cornell University, Department of Information Science, 236 Gates Hall, 107 Hoy Road, Ithaca, NY 14853, United States. jco66@cornell.edu

Introduction

Tuberculosis (TB) is an infectious disease primarily associated with the lungs. It is caused by the bacterium *Mycobacterium tuberculosis* and is spread from person to person *via* airborne droplet nuclei. About a quarter of the world's population is estimated to have contracted the TB bacteria. However, only 5 to 10 per cent of those infected are expected to develop the disease during their lifetimes. In 2022, an estimated 10.6 million people developed the disease, 7.5 million were diagnosed, and 1.3 million died from it (1.18 to 1.43 million at 95% confidence), down from approximately 2.0 million deaths in 2010. In 2019, the latest year for which the World Health Organization (WHO) published estimates of global causes of death, TB was the leading cause of death from an infectious disease and the 13th overall. Without treatment, approximately 50% to 60% of those infected with TB die. TB can generally be cured if treated with a course of drugs recommended by WHO. Case Fatality Ratio (CFR), the ratio of people who die of the disease, primarily due to late diagnosis or other confounding factors such as being diagnosed with drug-resistant TB or living with HIV, was 12.3% in 2022 (1).

There has been only an 8.7% reduction in the incidence rate between 2015 and 2022, compared to WHO's goal of reducing the rate by 50% between 2015 and 2025. WHO's goal is to reduce the number of TB deaths by 75% between 2015 and 2025, whereas the reduction between 2015 and 2022 was only 19%. Therefore, the results of current efforts are far off target from meeting WHO's goals of reducing the incidence rate and the number of deaths from TB.

We hypothesize that the most expedient way to reduce deaths from TB in high-burden India is through the full-scale deployment of computer vision systems as the first and only reader of chest X-rays. To achieve this, we show that the scale of the problem is likely to grow as the Indian population continues to grow and age. At the same time, we assert that the significant shortage of radiologists, who currently analyze and report on most X-rays, is unlikely to be resolved soon. Further, we argue that computer vision systems have advanced sufficiently to be utilized as the only reader of chest X-rays for diagnosing TB. Adopting computer vision systems as the only reader should address the limitations caused by the shortage of radiologists.

While studies assess the performance of computer vision systems in diagnosing TB and recommend their use in high-burden settings, we found no study that quantifies what such deployment means in terms of the number of lives that can be saved. In our research, we perform quantitative analysis of existing TB-related statistics from WHO and performance statistics of best-in-class commercially available computer vision systems to estimate the number of lives that can be saved by the full-scale deployment of such a system in India.

Literature review

This literature review seeks to build a case for using computer vision systems as the first and only reader in diagnosing TB in India. To achieve this goal, this review examines the demographic trends likely to contribute to an increased TB burden in India in the coming years, accepted active TB diagnosis methods, the radiologist's role in diagnosing active TB, the significant shortage of radiologists in India and identification and treatment of latent TB to prevent incidents of active TB. This review also examines the emergence of, and recent advances in computer vision

systems, the current uses of such systems in diagnosing diseases, including TB, and an analysis of the cost of rolling out such systems. Through this review, we aim to build support for our hypothesis that the full-scale deployment of best-in-class commercially available computer vision systems is the most expedient and cost-effective way to reduce the number of TB fatalities in India before using quantitative methods to estimate its impact on mortality.

Overview of TB globally

Aging population and the associated increase in medical conditions

Aging is associated with decreased physical and mental well-being, including a decline in lung function (2). Decline in lung function, adverse changes in lung physiology, and an impaired immune response are associated with advanced age and particularly with the risk of developing TB (3-5). In fact, aging is assessed to be a "*very significant risk factor for developing TB*" (6).

The United Nations expects the world population to grow from about 7.9 billion by the end of 2022 (7) and reach a peak of 10.3 billion by the middle of the 2080s (8). At the same time, the share of the total population over the age of 65 passed 10% in 2022, nearly double its share in 1960. The rate of growth of this age group has also accelerated since 2010 (9). WHO projects that the number of people over 60 will double from 1 billion in 2020 to 2.1 billion by 2050, while the number of people over 80 will triple during the same period to 426 million. Some high-income countries have already experienced such population aging; Japan is an example where 30% of the population is already aged 60 and over. WHO asserts that low and middle-income countries are experiencing the fastest aging of their populations and are expected to be home to two-thirds of the world's population of over 60 years of age by 2050 (2).

Diagnosing TB

TB can affect all parts of the body, although the primary location for infection of the bacterium is the pulmonary parenchyma, a part of the lung. A chest X-ray may not diagnose all cases of active TB and may be categorized as normal or only show findings that cannot be explicitly attributed to a case of active TB. Such findings may also indicate diseases such as lymphoma and sarcoidosis (10). However, a chest X-ray is, nevertheless, the first tool used to diagnose TB (11). It is even considered "*essential*" (12). Furthermore, in India, the National Tuberculosis Elimination Programme (NTEP) recommends chest X-ray and sputum testing for patients exhibiting signs of TB. These signs are stated as coughing and having a fever for more than two weeks, significant weight loss and hemoptysis; the medical term for coughing up blood. Sputum testing involves the analysis of the thick mucus, also known as phlegm, coughed up from the lungs. Analyzing and reporting on chest X-rays is a crucial aspect of diagnosing TB. Given India's size, population, and dispersion - where over 64% of the population lived in rural areas as of 2022 (7) - this undertaking requires ensuring that presumptive patients have access to local health facilities equipped with the necessary imaging equipment. Even with access to sufficient equipment, diagnosis needs radiologists, doctors specializing in diagnosing and treating medical conditions *via* medical imaging equipment, to interpret the images taken and report on them.

Impact of TB in India

Prevalence

In 2022, India is estimated to have accounted for 27%, or 2.82 million, of the total number of TB cases and 26%, or 342,000, of the number of deaths globally from TB. Both numbers are the highest for any one country in the world. WHO also estimates that of the 3.1 million people estimated to have been infected by TB but not diagnosed, 18% or ~ 418,000 were in India (13).

In 2022, India, with a population of 1.42 billion, overtook China as the country with the world's largest population. By 2050, India's population is expected to reach 1.67 billion. The share of persons over 60 years of age is expected to increase from 10.8% in 2022 to 20.8% in 2050, corresponding to a net increase of 195 million people to 348 million. During the same period, the share of persons over 80 years of age is expected to triple from 1.1% to 3.3%, or a net increase of 41 million to reach 55 million (14). WHO's expectations of the change in the age demographics of India's population align with its expectations of the global trend.

India has made significant advances in the prevention and treatment of TB in recent years. The quality of the health statistics used has also improved. In 2010, India was estimated to have had 3.4 million cases of TB, with an uncertainty interval between 1.4 million and 6.3 million. The incidence rate of TB, measured as new cases for a population of 100,000, fell from 276 in 2010, with a 95% confidence interval of 114 to 508 in 2010, to 199 in 2022, with a 95% confidence interval of 169 to 231. Even so, the point estimate rate of 199 remains significantly above the global point estimate incidence rate of 133 (124 to 143 at a 95% confidence interval) (13).

In March 2017, India's Ministry of Health and Family Welfare developed the National Strategic Plan 2017 – 2025 for TB Elimination by 2025 (15). This strategic plan called for the TB incidence rate to be reduced to 77 and the mortality rate to just 6 in 2023. WHO's 2022 point estimates for India for both rates remain significantly above the targets set forth for 2023 in the strategic plan (15). While the onset of the COVID-19 pandemic has adversely affected the diagnosis and treatment of TB and led to higher cases of illness and death (16), it remains the case that the incidence and mortality rate in India remains on track to be significantly higher than the targets set out in the country's strategic plan to eliminate the disease by 2025. Furthermore, the Ministry of Health and Family Welfare estimated in 2017 that decades of unchecked transmission have left hundreds of millions of Indians with latent TB. Latent TB has a higher risk of becoming active as people age (15). Such a large population with latent TB is likely to lead to an increase in cases of TB in India as the population ages as projected.

Radiologist shortage in India

Reporting on chest X-rays is primarily done by (human) radiologists in India. This creates a limitation in the availability and speed of diagnosing and, therefore, treating TB patients. A commonly cited statistic is that India has one radiologist for every 100,000 people, equating to approximately 14,000 active radiologists (17, 18). The presence of 14,000 radiologists indicates an increase of 4,000 radiologists since 2008. The country's population has also grown at a similar rate since then, which suggests that there has not been any improvement in the number of radiologists per unit of population (19). In contrast, in Europe, there were 13.5 radiologists for a population of 100,000 in 2022 (20). In the United States, there were estimated to be 31,960 radiologists (21) for a

population of 334 million (22) in 2023, corresponding to 9.6 radiologists for a unit of a population of 100,000.

Numerous reasons are cited for the shortage of radiologists in India, ranging from an insufficient number of training programs, trained radiologists leaving India for better pay opportunities overseas, and a workload of over 100 scans per day leading to high attrition rates (17, 18, 23). Another major issue affecting presumptive TB patients' access to radiological services is the skewed geographical distribution of radiologists in the country. Approximately 30% of beds and 50% of healthcare facilities in India are in rural areas (24), where over 60% of the population lives. However, radiologists prefer to live and work in "Tier 1" cities, where the market share of radiologic services is estimated at 40 to 50% (25). At the same time, there is a shortage in 'Tier 2' and 'Tier 3' cities and no radiologists in rural areas (17). The shortage of radiologists and the significant geographical mismatch between the distribution of the Indian population and the provision of radiological diagnostic services is a factor explaining what the Ministry of Health and Family Welfare, Government of India calls "*more than a million 'missing' cases [of TB] every year*" that are either undiagnosed or "*unaccountably and inadequately diagnosed*" (15). It is worth noting here that the "*more than a million 'missing' cases*" that the Government of India is referring to in their National Strategic Plan 2017-25 published in March 2017 is estimated to have been reduced to 418,000 in 2022. Given the high mortality rate of TB when left untreated or if treated late, the absence of the diagnosis of many TB cases should be considered as one of the reasons for the high mortality rate from TB per unit of population in India.

Efforts to alleviate the shortage in radiology services

Providing rural populations access to more diagnostic imaging equipment is part of the effort to reduce the number of undiagnosed cases of TB. India's imaging equipment market is expected to grow at a compounded annual growth rate (CAGR) of 12-15 % between 2023 and 2028, significantly higher than the global rate of 5% (26, 27). Private healthcare providers play a significant role in the diagnostic sector, which covers pathology and radiology, with radiology accounting for two-thirds of the sector by expenditure. In 2020, the private sector accounted for 60% of the total value of services provided. At the same time, the small and independent, mainly non-hospital laboratories comprise the unorganized part of the sector, which, at 80%, accounted for the vast majority of the private diagnosis services sector (25). With a large portion of the Indian diagnosis services sector already being driven by private sector enterprises, it is unsurprising that the most significant growth in the diagnostic imaging equipment market is expected in Tier 2 and Tier 3 cities rather than in rural areas (25).

Teleradiology reporting is a way with which rural communities can access radiology services, including for the diagnosis of presumptive TB patients (27). X-rays can be taken with portable hand-held X-ray devices, provided as part of public-private partnerships (PPP) in areas where diagnosis services are not available. Teleradiology then allows radiologists in cities to assess X-rays taken of patients in areas where diagnosis services are unavailable. Even with such increased access to radiologists, Mr. Pranav Rajpurkar, Assistant Professor at Harvard University's Department of Biomedical Informatics, states that this shortage of

radiologists has meant that chest X-rays "*are not even reported by radiologists*" (28, 29).

To become a radiologist in India, a student must first earn a Bachelor of Medicine, Bachelor of Surgery (MBBS) degree. To earn an MBSS degree, the student must undergo 4.5 years of classroom study and complete one additional year as an intern. The student must then complete a 3-year postgraduate program in radiology to qualify as a medical doctor (MD) radiologist. Alternatively, the student may complete a 2-year diploma program in medical radiodiagnosis (30). In Indian medical institutions, there is approximately one radiology seat for every 15 clinical seats, whereas closing the shortage of radiologists would require this ratio to be 1:4-5, indicating that there are not enough training programs in the country to eliminate the shortage.

Despite the efforts to expand the size of diagnostic imaging services available to populations living outside of major cities, the increasing number of active TB cases due to a growing and aging population with a large cohort living with latent TB, the existing significant shortage of radiologists in India, the scarcity of training programs and the length of time it requires to train a radiologist extensively have, in recent times, led to discussions on the use of advanced technologies, including Artificial Intelligence (AI), in connection with teleradiology to address the shortfall (17, 18, 23, 24, 27).

Identification and treatment of latent TB to prevent incidents of active TB

The National TB Prevalence Survey in India 2019-21 estimates that 31%, or approximately 430 million Indians, were infected with *Mycobacterium tuberculosis* as of 2021 (31). WHO recommends using the tuberculin skin test (TST), one of the two tests used to diagnose latent TB along with Interferon gamma release assay (IGRA), a blood test, for low to middle-income countries with a high TB burden only in people with HIV and for children under the age of 5 (32). The recommendation by the Indian authorities is broader, with either test recommended for those on immunosuppressants, anti-TNT alpha drugs, dialysis, silicosis, those preparing for an organ transplant and household contacts (HHC) with cases of active TB over the age of 5 (33). TST involves the injection of tuberculin into the forearm and measuring the maximum diameter of the resulting induration after 48 to 72 hours. The size of the resulting induration determines the likelihood that a person carries the disease, and the threshold for the maximum size of the induration to conclude a positive diagnosis depends on the risk profile of the person, such as their age, history of certain medical conditions, immunosuppressive status, lifestyle, HIV status and history of known recent TB contacts (34).

In their research paper, Hashim, Z. *et al*. argue that the definition of HHC in the Indian guidelines would result in "*roughly half a billion people*" qualifying for treatment. They further state that, while no data exists for India, worldwide studies indicate that treatment's preventative effect lasts several years after discontinuing treatment and that numerous other aspects, such as risk factors other than transmission to developing active TB, cost, limitations on the effectiveness of treatment protocols should be taken into account when considering any effort to diagnose and treat latent TB on a large scale. They conclude that HIV patients and those in the pediatric age group offer the most potential for preventative screening and

treatment of latent TB rather than the wider risk group as defined in the India guidelines (35). A further limitation of preventative tests is that a positive result indicates that the person has been exposed to TB but does not inform whether the disease is latent or active (36).

The traditional method of administering TST requires the presumptive patient to visit a healthcare facility twice: once to be administered the test and a second to measure the resulting induration using a pen and a ruler. The second visit must not be more than 72 hours after the administration of the test, as the result becomes invalid then, and the test must be re-administered. The large volume of presumptive patients that qualify for the test under the definition of HHC in the Indian guidelines is cited as one of the obstacles to rolling out a more comprehensive testing program for latent TB in India (33). However, studies have shown that measuring the induration from pictures taken by the presumptive patient on their mobile telephones and sent to the healthcare facility is a viable alternative to a second visit. In their study, Naraghi *et al.* find that a 3D photogrammetric reconstruction of the mobile telephone image using a purpose-built application and the subsequent measurement of the induration provides greater accuracy than the traditional pen and pencil measurement method (37). Further support is found by San Pedro and Barfeh, who developed an algorithm to measure the maximum size of an induration from digital images and found their results to be 91.5% accurate when compared to a healthcare professional's measurement (38). The smart mobile telephone penetration rate in India was 71% in 2023 and is projected to reach 96% in 2040 (39). Developing image processing software and implementing it in healthcare facilities could, therefore, be a path to alleviating some of the cited hurdles associated with the roll-out of TST to a broader risk group in India. Catching more latent TB cases before the patients develop the disease would consequently complement the efforts to lower the number of undiagnosed active TB cases.

Computer Vision

Emergence of computer vision

Computer vision or object detection and image classification systems are among "*neurally-inspired technologies*", taking their inspiration from the workings of the unit of the brain and the nervous system, the neuron (40). Contrary to the common shape of a typical cell in the human body, nerve cells, or neurons, are made up of a cell body and elongated extensions called axons for sending electrical impulse signals and branches called dendrites for receiving such electrical impulses (41). They work by receiving impulses from other neurons through their dendrites, and if the combined stimulus received is strong enough, the neuron triggers an impulse of its own through its axons. Nothing happens if the stimulus received is below the threshold required to trigger an impulse. Therefore, the neuron's output is binary: it either fires or does not, and the intensity of the signal put out is determined by its frequency. The connections of each of the dendrites with the axons of other neurons, called synapses, have different strengths, called synaptic weights, and the synaptic weight determines how much influence the firing of one neuron has on whether the receiving neuron fires or not. Hence, in a very simplistic way, what determines whether a neuron fires or not is whether it receives impulses through its dendrites, the strength of such incoming impulses, if any, and a minimum value, or threshold, that the

combined strength of the incoming impulses must exceed for the neuron to send an impulse of its own (42). This process has led to the emergence of computer vision or object detection and image classification systems, such as the subject of this research paper and other AI applications (40).

The notion of artificial neural networks was introduced in 1943 by McCulloch and Pitts (43). In 1957, Rosenblatt invented the Mark I Perceptron at the Cornell Aeronautical Laboratory, a simple example of a computer vision machine with one input layer of artificial neurons, one output layer of neurons and no hidden layers in between. In his book, "*Principles of Neurodynamics. Perceptrons and the Theory of Brain Mechanisms*" (1962), Rosenblatt put forward ideas for machines that incorporated layers of neurons and a convergence theorem, where he theorized that by changing the synaptic weight of each pair of artificial neurons or training them, would lead to a vector, which is a series of weights between neurons, that would lead to the correct classification of an object in a finite amount of time (44). In 1969, Minsky and Papert demonstrated that a single-layer neural network, such as the one used in the Perceptron, could only compute linear functions, had a closed solution and that there was no need for machine learning to make such a machine work (45). This insight led to decreased interest in neural networks and was widely credited with starting what is commonly referred to as an AI winter (46).

In the 1960s and 1970s, the first neural networks incorporating hidden layers, layers between the input and output layers, were introduced, although they needed more data to train them. Such neural networks incorporating hidden layers are called deep neural networks (47). Scientists also had to overcome the challenges of training such deep neural networks by developing two essential methods, gradient descent and backpropagation, short for backward propagation of errors. Gradient descent is a method of adjustment of the weights in a neural network in small steps by iteratively correcting the weights until a local minimum value for the loss of a neural network is achieved. Here, the loss of a neural network, or the error rate, refers to the probability that the neural network will give an incorrect answer, either in the form of a false positive or a false negative, while recognizing an image or object. While Widrow and Hoff of Stanford University designed ADELINE in 1959, which was the first instance of the incorporation of gradient decent as a method of error correction, their system only had a single layer and the adoption of gradient decent in a deep neural network became possible after scientists developed a more 'smoothing varying' threshold function, which determines when a neuron fires, as opposed to the step-function type of threshold function utilized previously (47). Although Rosenblatt introduced the notion of backpropagation, it was first implemented by Hinton, Williams and Rumelhart in 1986. It used the chain rule in derivatives to allow for the piecemeal adjustment of weights iterating backwards from each layer to the previous one (48).

In 2009, Fei-Fei Li, a professor at Stanford University, launched ImageNet, a database of images. The premise of ImageNet was that increasing the amount of labelled data in the dataset is critical to developing more accurate computer vision systems (49). Today, ImageNet includes 15 million images of 22,000 classes of objects (50). In 2010, Li launched the ImageNet Large Scale Visual

Recognition Challenge (ILSVRC), where participants developed algorithms for detecting and classifying a list of 1,000 classes of images to achieve the lowest error rate. In 2012, in a moment that Li recently described as a "*watershed moment for AI's evolution*" and "*the beginning of ... deep learning revolution*" (50), a team led by Krizhevsky from the University of Toronto won the ILSVRC with their neural network architecture named AlexNet, achieving an error rate of 15%, 10.8 percentage points lower than the nearest algorithm (53). AlexNet was unique because it incorporated eight layers and was trained on two Graphics Processing Units, or GPUs, instead of the traditional Central Processing Unit, or CPU. Although AlexNet was not the first computer vision system to be trained using GPUs (51), it was the first demonstration that the use of multiple layers, significant compute power and an extensive database for training – AlexNet used 1.2 million images as its training set (52) – would be sufficient to achieve significant advances in computer vision. During the eight years ILSVRC ran between 2010 and 2017, the top-5 error rate, the percentage of times the target label did not appear among the five highest-probability predictions, of the most accurate system fell from 28.2% to 2.7%. For comparison, the error rate of a human is 5% (49, 53).

Although GPUs have primarily been used for graphics-intensive applications like computer games, their potential for training computer vision and other AI models was recognized due to the success of systems trained by GPUs, such as AlexNet. GPUs made the task of training and running such AI systems significantly faster and less resource-intensive since they were built for parallel processing by design, which was very useful as such parallel processing could handle the linear algebra computations required in matrix multiplications necessary in AI training and use easier (50). GPUs are deemed to be 10 to 20 times faster in training speech recognition systems (54), and Raina, Madhavan, and Ng found that large models could be trained up to 70 times faster using GPUs than by using CPUs (55). The 2023 edition of Stanford University's Human-Centered Artificial Intelligence's annual report on Artificial Intelligence Index Report states that GPU performance has "*since 2003 ... increased by roughly 7,000 times*" and the median FLOP/s per U.S. Dollar of GPUs, a measure of the price of GPU computing power, is "*5600 times greater than in 2003*", corresponding to a doubling in price performance every 1.5 years (56).

The results of ILSVRC showed that computer vision neural networks could outperform humans in certain areas. The improvement in the efficacy of computer vision architectures should continue in conjunction with the improvement in the power of GPUs, leading to more and more complicated networks being trained with ever-expanding datasets. This is likely to result in an expansion in the use of computer vision technology in diverse areas, including that for medical diagnosis and treatment.

Computer vision systems in medical diagnosis

Computer vision systems are increasingly aiding medical professionals in diagnosing conditions and diseases. A prominent such application is Mammography Intelligent Assessment (MIA), a computer vision system approved for use on patients by the European Union. MIA has been deployed in the United Kingdom and Hungary with positive results in identifying cases of breast cancer that would have otherwise gone undiagnosed

when mammograms were reviewed only by radiologists. In fact, MIA has halved the number of missed diagnoses (57). In addition, the process of radiologists checking mammograms is very labor-intensive. It can result in delays if a sufficient number of trained medical professionals are not available to review the mammogram images (58). By using longitudinal data on patients and training the systems on biopsies and results of other follow-up procedures, MIA complements the capabilities of radiologists by flagging an image for further review, thus making it an efficient tool to double-check an initial diagnosis. The system has a Convolutional Neural Network (CNN) architecture, a type of neural network architecture suitable for recognizing patterns in images. MIA has been trained on over 3 million images from multiple sites (58).

Another application of computer vision systems is Healthy.io, a home test kit designed for patients rather than medical professionals. This innovative AI-powered tool benefits individuals with diabetes and high blood pressure by enabling them to conduct tests at home. The tool transforms urine ACR testing, one of the most frequently used diagnostic tests to detect infections, into a self-administered test kit with the necessary equipment. A mobile telephone application contains guidance videos, audio and text, thus making it easy for patients to perform the test and learn their results (59, 60). Evidence from an observational study suggests that this new ACR testing technology can help improve ACR test compliance and engage patients with a new experience, thus allowing them to form a preference for home testing. Additionally, according to the York Health Economics Consortium, if Healthy.io's solution was to roll out nationally, this new approach could save more than 11,000 lives and save the National Health Service, the UK's public health system, "*at least £660 million over 5 years*" (59).

Although not deployed in a real-world setting, a study reported by Shibata and colleagues demonstrated the comparison between the performance of their trained deep learning residual algorithm and the performance of three residents in ophthalmology in diagnosing glaucoma, a group of irreversible eye diseases that can cause blindness. Using fundus photography with and without glaucoma indications, the team developed a learning algorithm known as Deep Residual Learning for Image Recognition (ResNet) and analyzed its accuracy with statistical interpretations before setting the algorithm for testing. A testing dataset consisting of the images of 60 eyes of glaucoma patients and 50 images of the eyes of normal subjects was presented to the algorithm and the residents. The deep learning algorithm produced a significantly higher diagnostic performance, with an accuracy rate of 96.5%, while the three residents performed at accuracy rates of between 72.6% and 91.2% (61). Although the number of residents used in this study to determine a benchmark for human diagnostic performance was only three, this example illustrates the possibility of learning algorithms performing with higher efficacy than trained doctors.

Another computer vision system not currently deployed in a real-world setting is SkinLesNet, developed by Azeem et al. to identify malignant skin lesions and track melanoma cancer, a type of skin cancer, using a multi-layered CNN. The team trained SkinLesNet on a dataset of labeled images, achieving an accuracy rate of 96% from one testing dataset and 92% and 90% from two

others (62). They also compared two benchmark CNN models, VGG16 and ResNet50, to the proposed SkinLesNet model to identify the highest efficacy rate amongst the three. SkinLesNet had the highest accuracy and lowest loss, or error.

Despite the high efficacy rate of computer vision systems such as MIA, these deep learning algorithms are still mainly used as "*the second reader in the workflow*" (58), allowing humans to remain the first reader of the images in question. In the case of MIA, the model is used as a double-checking tool rather than as the first point of assessment or the first reader of an image. The AI technology allows a second screening, thus freeing up radiologists' time and generally speeding up the diagnosis process (58). During the screening, a second human makes the final decision when MIA and a radiologist return different opinions. Whether MIA is used as an independent reader or a concurrent reader, a radiologist always checks the results (63). The system can make a determination in seconds. Still, those results may be held back to allow doctors to check them before making a final decision. In this instance, the computer vision system is used to flag images rather than make an assessment. Therefore, it plays a different role than a clinician; the system's unique competencies can be utilized as a complementary tool to improve diagnostic performance rather than as a potential replacement trying to compete with clinicians (57).

Despite the efficacy of computer vision systems in diagnosing certain diseases and conditions, the possibility of deploying such systems as the first reader in the diagnostic workflow comes with numerous concerns, such as privacy, security of patient data and the inherent biases a computer vision system may have because of its training dataset (64). Their use as a first reader also comes with moral and even legal implications: what happens when a computer vision system incorrectly classifies an image it is reviewing as 'normal' when the presumptive patient had the disease or the condition and suffers injury as a result? Can the patient pursue redress in such a case even though tort laws are typically designed for natural persons and laws governing medical malpractice or negligence may also not be applicable (65)? A search among 62 commentaries, surveys, presentation abstracts, narrative reviews, and one social media study found patients and the public did not know how to address potential errors that an AI system can make and that that radiologists believe that they should be in the loop when it comes to responsibility (66).

There are also human factors to overcome to achieve wider acceptance of AI systems in medical diagnosis. A survey conducted in the Department of Radiology at Bispebjerg-Frederiksberg Hospital in Copenhagen, Denmark, found that, at 6.8%, the participants had lower acceptable error rates for AI systems, and in this specific case for a low-risk AI system designed to diagnose knee osteoarthritis, than for humans (at 11.3%), prompting the researchers to raise the questions as to whether AI should have lower acceptable error rates than humans (67). Another survey of 1,041 radiologists and residents found that basic AI-specific knowledge was associated with a higher degree of fear of replacement and intermediate and advanced AI-specific knowledge was inversely related to fear of replacement (68). Yang *et al.* demonstrated that medical students, residents and radiologists believed that "*there is a lack of AI education during medical school and residency*" (66). The results of these surveys

and searches show that educating medical students and professionals on AI systems could alleviate the fear of such technologies and lead to their wider acceptance.

Computer vision systems in the diagnosis of active TB

Similar to the development of computer vision systems for other medical conditions discussed in the previous section, there have also been advancements in computer vision systems specifically for diagnosing TB. Scientific studies have trained, validated and tested existing CNNs with their own datasets (69, 70), developed their own computer vision models and trained, validated and tested on their own datasets (71, 72), tested a single commercially developed computer vision system in a front line setting such as an active case-finding program or on tertiary hospital (73, 74) and compared the performances of multiple commercially developed computer vision systems (75-77) Some commercially developed computer vision systems, such as Mumbai, India-based Qure.ai's qXR, have also published case studies on the performance of their system when deployed in the field (78).

A case study examined the effect of one such deployment in the Philippines. Here, qXR was utilized in four mobile vans with portable chest X-ray equipment and was used as the only reader in the workflow, bypassing the radiologist's traditional role. It returned a reading in less than a minute (78). Presumptive patients whose chest X-rays were flagged by qXR were administered sputum testing immediately, which allowed for same or next-day diagnosis. In the traditional workflow, it took approximately one week for a radiologist to examine and report on a chest X-ray, and a patient identified as potentially TB-positive was then asked to come back for sputum testing, which could take up to two weeks. This meant that some of the presumptive TB-positive cases would never return for sputum testing, thereby delaying a positive diagnosis and treatment, leading to further spread of the disease and a higher fatality rate (79). What was unique about this deployment of the qXR computer vision system was that it is used as the first and only reader in the workflow and eliminated the traditional role of a radiologist. The qXR system has been deployed in over 50 countries, including 150 sites in 24 states in India, even though it has yet to be deployed at scale, and in the case of the state of Kerala, at only one site (80).

A study by Nxumalo et al. conducted in conjunction with scientists from Qure.ai found that "*qXR software was sensitive and specific in categorizing chest radiographs as consistent with […] TB, and can potentially aid in the earlier detection and management of these diseases.*" Their analysis was a statistical observational study conducted in one tertiary hospital in South Africa. One of the study's primary goals was to test the efficacy of the qXR system on the existing infrastructure found in local hospitals in the country. Their results indicated that using existing X-ray equipment, the system achieved a sensitivity of 90% (with a 95% confidence interval of 87 - 93%), specificity of 79% (with a 95% confidence interval of 73 - 84%) and negative predictive value of 85% (with a 95% confidence interval of 79 - 91%) (81). The sensitivity ratio indicates the percentage of clinically proven positive cases of TB the system identified as positive for TB, and the specificity ratio indicates the percentage of clinically proven negative cases of TB the system identified as negative for TB. The negative predictive value indicates the ratio of cases the system identified as

negative that were also clinically proven negative.

The predictive success of computer vision systems in diagnosing active TB is not confined to one system by one supplier. Codlin *et al*. independently assessed 12 computer vision systems against the performance of "*Expert Reader*" level radiologists and "*Intermediate Reader*" level radiologists (77). Calculating the Area Under Curve (AUC) of a Receiver Operating Characteristics (ROC) curve at varying threshold values for positive TB identification, which allowed them to calculate the ratio of true clinically-proven positive identifications to total positive identifications by the system, they demonstrated that six systems developed by Qure.ai, Delft Imaging, Lunit, DeepTek, JF Healthcare and OXIPIT performed as well as an Expert Reader level radiologist. The range of point estimate for the ROC AUC for these six systems was 0.73 - 0.82. The three systems by Qure.ai, Delft Imaging, and Lunit, at point estimates for the ROC AUC of 0.82, performed "*significantly better*" than the Intermediate Level radiologist and a system by Infervision, at a point estimate for the ROC AUC of 0.76, performed as well as an Intermediate Reader level radiologist only. They also showed that the quality of the X-ray equipment affected the systems' performance. Overall, they concluded that there is now a "*wide selection of quality CAD [Computer-Aided Detection] software solutions*" available for implementation in TB programs.

In their 2016 summary of current recommendations and guidance, WHO stated that studies were conducted on one commercially available computer vision system and that those studies had methodological limitations and lacked generalizability. As a result, WHO did not provide any recommendations for using computer vision systems to detect TB. Instead, WHO recommended the use of such systems for research purposes (82). However, in the face of rapid advances in computer vision technology and the evidence outlined in recently published studies it has reviewed, in December 2020, WHO issued a rapid communication, acknowledging that "*the diagnostic accuracy and the overall performance of CAD software were similar to the interpretation of digital chest radiography by a human reader, in both the screening and triage contexts*" and "*CAD may be used as an alternative to human reader interpretation of plain digital CXR for screening and triage for TB*" for presumptive patients over the age of 15 (83). This major policy shift is perhaps the highest endorsement of the potential benefits of computer vision systems as first readers in presumptive TB patients' diagnosis and treatment workflow. This is especially true in high-burden countries and even more applicable in the case of India.

Cost-effectiveness of computer vision systems in diagnosing active TB

Bashir *et al*. performed a study in which they estimated the cost of rolling out four computer vision systems, namely CAD4TB, InferRead, Lunit and qXR, to 80 per cent diagnostic coverage in Pakistan over a four-year period. In their study, they assumed that the rollout would involve a combination of implementation in facilities and active case finding through mobile vans equipped with portable X-ray devices. They found that implementing the rollout with human readers would cost USD 23.97 million, whereas deploying a computer vision system would cost between USD 2.65 to USD 19.23

million, depending on the system used. Their analysis included the cost of the equipment required for image analysis, such as X-ray machines, mobile vans, fixed and variable facility costs, the cost of using the computer vision systems, including software, storage support and maintenance, installation and training, as well as radiologist staff costs. They concluded that "*integrating CAD software in implementation strategies for case finding could be an economical way to attain the intended programmatic goals*". They further stated that in high TB-burden countries with limited availability of trained radiologists, "*CAD would be the only option for implementation of CXR for ACF at scale in many* settings" (84).

Differences in the characteristics of the two countries should limit the extent to which the results of their study can be applied to India, even after accounting for the difference in population sizes. Pakistan has a higher incidence rate of TB and a lower percentage of incident cases entering treatment. On the other hand, both countries are lower-middle income countries with a high TB-burden, a shortage of trained radiologists, and similar TB mortality rates and percentages of their populations living in rural areas (85-87, 92).

An India-specific study on the cost of implanting computer vision systems in diagnosing TB is a 2024 study by the Indian Institute for Public Health in Gandhinagar. In their study, the authors calculated the Incremental Cost-Effective Ratio (ICER), a commonly used summary measure of the economic value of a medical intervention, of qXR from Qure.ai and Genki from Deeptek, another provider of computer vision systems for the diagnosis of TB. The study found that the qXR system had an ICER of 9,865 INR per case screened/interpreted, corresponding to only 0.05 x the GDP per capita of India, and was, therefore, cost-effective when compared to the manual reading of chest X-rays. While more expensive, Genki was also found to be cost-effective (88).

Methods

This study analyzed the hypothetical impact of the roll-out of a best-in-class computer vision system at scale as the only reader of chest X-rays for diagnosing pulmonary TB on deaths from the disease in India. The analysis used WHO-published datasets for 2022 and the sensitivity ratio performance of best-in-class commercially available computer vision systems as calculated in research studies. Since some of the data in both WHO-published datasets and research studies on computer vision systems contained a degree of uncertainty in the form of confidence intervals, we used established statistical methods such as the transformational properties of expected value and variances, approximations using Taylor series expansions of functions and the results of Monte Carlo simulations to calculate similar degrees of uncertainty around our point estimates.

In our analysis, we used the following parameters and point estimates with 95% confidence intervals of the following statistics: *WHO statistics and parameters for incidence and mortality rates from TB in India for 2022.*

Table 1. WHO statistics and parameters, Thousands=K, Million = M

	Code	Estimate / Parameter	Point Estimate / Parameter Value	95% CI lower bound	95% CI upper bound	Standard Error
Number of incident cases (all forms)	INALL	Estimate	2.82 M	2.39 M	3.28 M	219 K
Incidence (all forms) per 100,000 population	INALLR	Estimate	199.0	168.6	231.4	15.5
Total of new and relapse cases and cases with unknown previous TB treatment history	P1	Parameter	2.26 M	n/a	n/a	n/a
thereof pulmonary	P2	Parameter	0.75	n/a	n/a	n/a
Previously treated patients, excluding relapse cases (pulmonary or extrapulmonary, bacteriologically confirmed or clinically diagnosed)	P3	Parameter	146 K	n/a	n/a	n/a
Number of laboratory-confirmed TB cases with drug-resistant TB	P4	Parameter	64.4 K	n/a	n/a	n/a
Incidence of TB cases who are HIV-positive	INHIV	Estimate	48 K	40 K	55 K	4.1 K
Number of deaths from TB in people who are HIV-positive	FATHIV1	Estimate	11 K	8 K	14 K	1.5 K
Number of deaths from TB (all forms, excluding HIV)	FATHIV0	Estimate	331 K	237 K	440 K	48.0 K
Number of deaths from TB (all forms)	FATALL	Estimate	342 K	248 K	450 K	48.0 K
TB case fatality ratio	FATALLR	Calculated	0.12	0.08	0.17	0.02
TB treatment success for those started drug-resistant TB (2020 data)	TSDR	Parameter	0.69	n/a	n/a	n/a
Case detection rate (all forms) [also known as TB treatment coverage]	TRCOV	Estimate	0.85	0.73	1.00	0.06

and, *Sensitivity rate of best-in-class computer vision systems*. Even though studies show that there are several options for deployment (76, 77), we took qXR by Qure.ai as the best-in-class computer vision system due to the availability of several studies by the company and conducted independently on its efficacy as well as the prevalence of the system under deployment, both in India and in other countries. We were interested in the sensitivity ratio in our analysis as this rate is the detection rate of a true positive case of pulmonary TB, conditional on the presumptive patient having active TB and can, therefore, be used to estimate what per cent of undiagnosed cases of active TB can be caught using the system. The point estimate of the sensitivity ratio and the standard error of p_{SR} was calculated as

$$\hat{p}_{SR} = \frac{TP}{TP + FN} = p\left(TP \middle| Active\ TB\right) \quad (1)$$

$$SE_{p_{SR}} \approx \sqrt{\frac{\hat{p}_{SR}(1-\hat{p}_{SR})}{n}}. \quad (2)$$

In our analysis, we used $\hat{p}_{SR}$ and $SE_{p_{SR}}$ for the qXR system as reported by Nxumalo *et al* (74) where $\hat{p}_{SR}=0.90$ and $SE_{p_{SR}}=\frac{0.03}{1.96}=0.0153$. With a sample size of 382, we calculated the variance of their sample set as 0.09, which also equals the theoretical variance of a Bournelli random variable with p = 0.90. The point estimate reported in this study is similar to that of Qin *et al* (76), who reported 0.9081 with a standard error of 0.00245. For prudence, we used the point estimate, standard error and variance reported by Nxumalo *et al.*

Results

Impact of deployment of computer vision systems for the diagnosis of TB in India

Using the transformational properties of expected value and variances, we derived the number of undiagnosed cases of TB in India (Code: UDALL) in 2022 with the following point estimate and 95% confidence interval

$$E(UDALL)=E(INALL)-P1-P3 \quad (3)$$
$$\overline{INALL}-P1-P3 \quad (4)$$
$$2\,820\,000-2\,255\,641-146\,383 \quad (5)$$
$$417\,976 \quad (6)$$

We assumed all the estimated values and confidence intervals calculated by WHO were part of the same dataset. Therefore, the same n, or sample size, was applied to calculate all standard errors.

$$SE_{UDALL}=\frac{\sigma_{UDALL}}{\sqrt{n}}=\frac{\sigma_{INALL-P1-P2}}{\sqrt{n}}=\frac{\sigma_{INALL}}{\sqrt{n}}=SE_{INALL}=234\,694 \quad (7)$$

Therefore, UDALL, or the number of undiagnosed cases of TB in India, was calculated to have a 95% confidence interval between 0 and 847976. Please note here that, due to the transformational properties of variances, the relatively large confidence interval calculated by WHO in estimating the total incidence cases of all forms (INALL) carried over to our estimation of the number of undiagnosed cases and resulted in a confidence interval with the lower limit being 0. It should be noted here that the standard of error in WHO's estimates for incident cases of all forms decreased significantly over time. It is now only 20% of its value 20 years ago, but it remains too high to be able to make more precise estimates in our study.

To estimate the breakdown of undiagnosed cases of TB and pulmonary TB by HIV status and drug-resistant TB status and the rest of the undiagnosed population, we followed the following procedure.

1] We used WHO's point estimate and confidence interval for incidences of TB who were HIV-positive and used the reported number of new and relapse cases and cases with unknown previous TB treatment history who were HIV positive (P4) to calculate a point estimate and confidence interval for the

number of undiagnosed cases (UDHIV). 2] We assumed that the proportion of undiagnosed cases that were drug-resistant was the same as the proportion of such cases (NTFDRD) among the reported number of new and relapse cases and cases with unknown previous TB treatment history (P1) and that, therefore, drug-resistant TB status was independent of a person's chances of remaining undiagnosed, and 3] the percentage of pulmonary cases among all incident cases (P2 = 75% (13)) was the same as the percentage of pulmonary cases among the reported number of new and relapsed cases and cases with unknown previous TB treatment history (P1) and therefore whether a person had pulmonary or extrapulmonary TB was independent of a person's chances of being diagnosed. Using our assumptions and the transformational properties of expected values and variances, we calculated the breakdown of undiagnosed cases of TB and pulmonary TB by HIV status and drug resistance status and the rest of the undiagnosed population, shown in Table 2.

Table 2. Point estimate and confidence interval for distribution of undiagnosed cases of TB, Thousands =K, Million = M

	Code	Estimate / Parameter	Point Estimate / Parameter Value	95% CI lower bound	95% CI upper bound	Standard Error
Number of incident cases (all forms)	INALL	Estimate	2.82 M	2.39 M	3.28 M	235 K
Number of undiagnosed cases of TB	UDALL	Estimate	418 K	0	878 K	235 K
thereof HIV- and with no drug-resistant TB	UDNOR	Estimate	396 K	0	831 K	222 K
thereof pulmonary	UDNORP	Estimate	297 K	0	623 K	167 K
thereof HIV+	UDHIV1	Estimate	10 K	2 K	18 K	4 K
thereof pulmonary	UDHIV1P	Estimate	8 K	2 K	14 K	3 K
thereof with drug-resistant TB	UDDR	Estimate	12 K	0	25 K	7 K
thereof pulmonary	UDDRP	Estimate	9 K	0	19 K	5 K

For the treatment success rate of diagnosed cases in India, we used data from WHO (13) as shown in Table 3.

Table 3. TB treatment success rates in India

	Code	Treatment Success Rate	Note
New and relapse cases and cases with unknown previous TB treatment history	NTFD	0.87	Cases registered in 2021
thereof HIV- and with no drug-resistant TB	NTFDHIV0NRD	0.88	Cases registered in 2021
thereof HIV+	P4	0.78	Cases registered in 2021
thereof with drug-resistant TB	NTFDRD	0.64-0.69 (WA=0.68)	Started second line treatment in 2020

We used WHO-published parameters to assess the mortality rates among undiagnosed or untreated cohorts. WHO states that "*without proper treatment, … nearly all HIV-positive people with TB will die*" (89), and we therefore used a mortality rate of 99% for such cases. For the mortality rate of non-HIV-positive cases, the same source states an average mortality rate of 60%, and this is the rate we used for the mortality rate for all non-HIV-positive cases of TB.

Table 4. Mortality rate of TB if left untreated

	Code	Mortality Rate
Cases of TB with HIV- status and with no drug-resistant TB	NTFD	0.60
Cases of TB with HIV+ status	NTFDHIV0NRD	0.99
Cases of drug-resistant TB	P4	0.60

We found evidence that the in-hospital mortality rates among pulmonary and extrapulmonary cases of TB did not differ (90). Based on this finding, we assumed that treatment success rates in India and the disease's mortality rate, if left undiagnosed or untreated, would apply to both pulmonary and extrapulmonary TB cases.

We now have four estimated variables with expected values and standard errors: qXR sensitivity (QRXSR), the number of undiagnosed people with pulmonary TB who are also HIV-positive (UDPHIV1), the number of undiagnosed people with pulmonary drug-resistant TB (UDPDR) and the number of undiagnosed people with pulmonary TB who are HIV-negative and do not have the drug-resistant form of the disease (UDPNOR). We also have the following six parameters: the mortality rates for people with TB and HIV, people with drug-resistant TB and all others with TB if left untreated (P:UDHIV1:MR, P:UDDR:MR and P:UDHIV0NRD:MR, respectively) and the mortality rates for people with TB and HIV, people with drug-resistant TB and all others with TB if treated by the Indian health system (P:DHIV1:MR, P:DDR:MR and P:DHIV0NRD:MR, respectively).

We could therefore express the number of lives that qXR could save (LS100), if rolled out to full coverage in India as a function of these four variables.

$$LS100 = f(QRXSR, UDPHIV) + g(QRXSR, UDPDR) + h(QRXSR, UDPNOR) \quad (8)$$

where,

$$f(QRXSR, UDHIV1) = QRXSR \times UDPHIV1 \times (P:UDHIV1:MR - P:DHIV1:MR) \quad (9)$$

$$= LS100\ HIV1 \quad (10)$$

$$g(QRXSR, UDDR) = QRXSR \times UDPDR \times (P:UDDR:MR - P:DDR:MR) \quad (11)$$

$$= LS100\ RD \quad (12)$$

$$h(QRXSR, UDNOR) = QRXSR \times UDPNOR \times (P:UDHIV0NRD:MR - P:DHIV0NRD:MR) \quad (13)$$

$$= LS100\ HIV0NRD \quad (14)$$

The variables representing the number of lives saved by the roll-out of computer vision systems for each of the three sub-groups of previously undiagnosed patients are each a function of the product of two variables. The expected values of $f(QRXSR, UDHIV\,1)$, $g(QRXSR, UDDR)$ and $h(QRXSR, UDNOR)$ can be approximated by using the first order Taylor series expansion of each such product. With this approach, the expected value of a function of two variables can be approximated to be the same function of the means of the variables in question

$$E(f(X,Y)) = E\left(f(\theta) + f'_x(\theta) \times (X - \mu_x) + f'_y(\theta) \times (Y - \mu_y) + R\right),$$
$$about\ any\ \theta = (\theta_x, \theta_y) \quad (15)$$
$$\sim E(f(\theta)) + E(fx'(\theta) \times (X - \mu x)) + E(fy'(\theta) \times (Y - \mu y)) \quad (16)$$
$$E(f(\theta)) + f'_x(\theta) \times E(X - \mu_x) + f'_y(\theta) \times E(Y - \mu_y) \quad (17)$$
$$E(f(\theta)) + 0 + 0 \quad (18)$$
$$f(\mu_x, \mu_y) \quad (19)$$

Therefore,

$$E(f(QRXSR, UDHIV\,1)) = E(QRXSR) \times E(UDPHIV\,1) \times (P:UDHIV\,1:MR - P:DHIV\,1:MR) \quad (20)$$
$$0.90 \times 7\,817 \times (0.99 - 0.22) \quad (21)$$
$$5\,417 \quad (22)$$

= expected number of lives saved from previously undiagnosed pulmonary TB patients with HIV (or LS100HIV1)

$$E(g(QRXSR, UDDR)) = E(QRXSR) \times E(UDPDR) \times (P:UDDR:MR - P:DDR:MR) \quad (23)$$
$$0.90 \times 8\,952 \times (0.60 - 0.32) \quad (24)$$
$$2\,263 \quad (25)$$

= expected number of lives saved from previously undiagnosed pulmonary TB patients with drug–resistant TB (or LS100RD)

$E(h(QRXSR, UDNOR) = E(QRXSR) \times E(UDPNOR) \times$ (P: UDHIV0NRD: MR - P: DHIV0NRD: MR) (26)
$$0.90 \times 296\,714 \times (0.60 - 0.12) \quad (27)$$
$$127\,305 \quad (28)$$

= expected number of lives saved from previously undiagnosed pulmonary TB patients without HIV or drug–resistant TB (or LS100HIV0NRD)
and using the transformational properties of expected values,

$$E(LS\,100) = E(LS\,100\,HIV\,1) + E(LS\,100\,RD) + E(LS\,100\,HIV\,0\,NRD) \quad (29)$$
$$5\,417 + 2\,263 + 127\,305 \quad (30)$$
$$134\,985 \quad (31)$$

To calculate the variability of our point estimates, we used the variability in our estimates for *UDPHIV*1, *UDPDR* and *UDPNOR* based on the variability of the underlying datasets in Table 2 and the variability in the true positive detection rates of the qXR system, or *QRXSR*. *QRXSR*, is binomial and, for $n=1$, follows a Bernoulli Distribution. From the study by Nxumalo *et al.*, *QRXSR* is expected to have an estimated variance of $\hat{p}_{SR} \times (1-\hat{p}_{SR})=0.09$. We assumed that qXR's specificity performance was independent of a patient's potential HIV status and whether they harbor a drug-resistant form of TB and that, therefore, the same detection rate and variability applied to all three of our sub-datasets. To calculate the variance of the number of detections for each of the three sub-datasets, we ran Monte Carlo simulations with 100,000 iterations for each sub-dataset. At repeated 100,000 iterations, the calculated number of true positive detections was, in most cases, within 1.25% of the expected number of true positives, which itself was an approximation calculated using the first-order Taylor series expansion of the multiplication of two variables. We, therefore deemed the number of iterations to be sufficiently large to approximate the true distribution of the number of detections for each sub-dataset. The results are presented in Table 5.

Table 5. Mean and variability of undiagnosed cases of pulmonary TB that are detected by the qXR system

		Simulated with 100,000 iterations		
	Expected Value	**Mean**	**Error Rate of Mean**	**Standard Deviation**
System detected number of undiagnosed cases of pulmonary TB – HIV+	7 035	7 040	0.07%	2 408
System detected number of undiagnosed cases of pulmonary TB – drug-resistance TB	8 056	8 125	0.85%	4 381
System detected number of undiagnosed cases of pulmonary TB – HIV- and with no drug-resistant TB	267 042	269 572	0.95%	145 436

We used the standard deviations estimated from our simulation and the expected values calculated earlier to calculate a degree of uncertainty for the lives saved in each patient subgroup.

Based on 2022 TB statistics, we calculated that, a national roll-out of the qXR system, or systems of similar sensitivity ratio, India stands to save the lives of 5417 people (95% CI: 1783 – 9057) of HIV+ status with undiagnosed pulmonary TB, 2263 people (95% CI: 0 – 4675) with drug-resistant undiagnosed pulmonary TB and 127305 people (95% CI: 0 – 263198) of HIV- status without drug-resistant undiagnosed pulmonary TB. As before, the relatively large confidence interval calculated by WHO in estimating the total incidence cases of all forms (INALL) carried over to our estimation of the number of lives that could be saved by the roll-out of computer vision systems and resulted in a wide confidence interval for each of the three groups of previously undiagnosed patients.

Finally, using transformation properties of expected values and variances, we calculated that

$$LS100 = LS100\,HIV\,1 + LS100\,RD + LS100\,HIV\,0\,NRD \quad (32)$$

with a 95% confidence interval of between 0 – 270947 around the point estimate of 134 985. Such avoidance of pulmonary TB deaths would have meant that in 2022, India's HIV-negative TB mortality rate per 100,000 would have been 14.2 (assuming a reduction in mortality in line with our point estimate) instead of WHO's point estimate of 23.4 and consequently, would have provided a significant boost to help WHO and the Government of India reach their respective mortality target rates for the mid-2020s.

Table 6. Estimated number of lives saved with computer vision systems of otherwise undiagnosed cases

	Code	Expected Value	95% CI lower bound	95% CI upper bound
Total number of lives saved: otherwise undiagnosed cases of pulmonary TB	LS100	134 985	0	270 947
thereof cases with HIV+ status	LS100HIV1	5 417	1 783	9 050
thereof cases with drug-resistant TB	LS100RD	2 263	0	4 675
thereof HIV- status and with no drug-resistance TB	LS100HIV0NRD	127 305	0	263 198

Another way the full roll-out of a best-in-class computer vision could reduce deaths from pulmonary TB would be by improving the quality and speed of diagnosis by reducing the number of cases lost to follow-up and not evaluated at all. At 87%, the treatment success rate in India is on par with the global average (91, 92). As qXR's deployment in the Philippines shows, by reducing the time it takes for a chest X-ray to be reported on by a radiologist to mere minutes and thereby allowing sputum testing to be administered immediately upon a chest X-ray being flagged, computer vision systems decrease the likelihood that a patient gets lost to follow-up and not enter treatment at all. In India, in 2022, of the 2.3 million new and relapse cases and cases with unknown previous TB treatment history, only 1.9 million patients entered treatment (13). Other factors may also explain this discrepancy, such as the lack of treatment facilities in high-burden rural areas or a period shift between the diagnosis and treatment start date of patients. Nevertheless, a speedier positive diagnosis and communication of the results to the patient is likely to reduce this gap, prevent deaths and hinder the spread of the disease by active TB patients who remain outside of the treatment cycle. Other factors may explain the discrepancy in the number of incidents and treated cases, such as people with active TB having access to, but choosing not to go to, healthcare facilities and, therefore, not entering treatment. Our calculations above do not consider such incidence cases and should hence be considered best-case estimates. We could not find a source of the estimated percentage of undiagnosed cases of TB in India due to patients' unwillingness to seek treatment in a health facility despite having access to one. However, for the sake of completeness, we restate the expected values of our results from Table 6 below using the transformational properties of expected values, assuming three

scenarios: that 10%, 20% and 30% of undiagnosed cases, respectively, will remain so regardless of the enhanced coverage due to the full-scale deployment of a computer vision system.

Table 7. Estimated number of lives saved with computer vision systems of otherwise undiagnosed cases – sensitivity to percentage of patients who choose not to use diagnostic services

	Expected Value	Expected Value	Expected Value	Expected Value
Percentage of undiagnosed cases who choose not to seek diagnosis	0%	10%	20%	30%
Total number of lives saved: otherwise undiagnosed cases of pulmonary TB	134 985	121 487	107 988	94 490
thereof cases with HIV+ status	5 417	4 875	4 333	3 792
thereof cases with drug-resistant TB	2 263	2 037	1 810	1 584
thereof HIV- status and with no drug-resistance TB	127 305	114 575	101 844	89 114

Having computer vision systems as readers of chest X-rays for presumptive TB patients should also alleviate the high workload and the stressful environment that has been partly blamed for burnouts, the exit of radiologists to seek working conditions abroad and the broader shortage of radiologists in India. Freeing their time should also allow speedier diagnosis of other diseases that radiologists report on, which should speed up the entry of patients with such diseases to treatment and ultimately improve their prognosis.

Discussion

India has advanced significantly in detecting and treating pulmonary TB in recent years. Between 2002 and 2022, the estimated number of cases of TB decreased by 20% despite a growing population, resulting in a decline of the estimated incidence rate from a point estimate of 320 per 100,000 population to 199 (13). During the same period, the number of undiagnosed or "*unaccountably and inadequately diagnosed*" cases has fallen by 82% but, at an estimated 418,000 cases, remains high. Despite the progress, the results fall significantly short of WHO's and the Government of India's targets. India experiences a significant shortage of radiologists to report on chest X-rays of presumptive TB patients. The problem of a lack of radiologists is unlikely to ease soon due to an insufficient number of training programs and the high turnover rate of radiologists. The continued increase in population and the predicted aging of India's population over the following decades, a significant proportion of whom have latent TB, is likely to put further pressure on the health system as an increasing number of people develop the disease later in life. Diagnosis and preventative treatment of latent TB is best suited for the highest-risk groups, such as those living with HIV, and WHO does not recommend its rollout to wider risk groups. Although the Indian health authorities include a broader definition for high-risk groups, a rollout at a large scale has significant challenges and has not been implemented to date. Diagnosis and preventative treatment of latent TB for the highest-risk groups can, nevertheless, complement the efforts to diagnose and treat active TB when battling the disease in India.

Given the insufficient number of training programs and the length of time it takes to train a radiologist, the shortage of radiologists in India will likely remain a limiting factor in the diagnosis and treatment of TB, especially in the face of a growing and aging population. Advances such as teleradiology to balance the workload of radiologists, combined with PPP initiatives to reach rural populations, have likely contributed to the decline in undiagnosed cases and the lowering of the incidence and mortality rates by controlling the spread of the disease. However, despite the decrease in incidences and deaths per unit of population, the sheer size of the problem means that deaths and the burden of the disease remain extremely high, with an estimated 342,000 people dying in India in 2022 alone from a disease that is mainly curable if diagnosed and treated early.

Computer vision systems have improved significantly in recent years in diagnosing several medical conditions, including TB. With radiologists in short supply, deploying such systems to report on X-rays has the advantage of bringing a scalable solution to the diagnosis of TB. While existing systems are not perfect, studies on the efficacy of commercially available systems have shown that several systems perform on par with or better than a radiologist. Also, a cost-benefit analysis on the rollout of computer vision systems for diagnosing active TB in India shows available systems offering a cost-effective solution. Such systems have been deployed in other countries, including India, although their deployment in the country is not at a large scale. The recent progress of computer vision systems has led WHO to recommend their use as first-reader in the diagnosis and treatment of TB in high-burden countries in 2020, reversing a decision from four years earlier.

Conclusion

Mass deployment of best-in-class computer vision systems in India as the first and only X-ray reader has the potential to contribute significantly to the country's efforts to decrease TB infection, especially when also implemented as part of teleradiology reporting solutions. We estimate that a complete roll-out of the system would save 135,000 lives annually and reduce the mortality of TB in India to 14.2 deaths per population of 100,000 (at the point estimate reduction in deaths) based on 2022 data, down from 23.4 currently. A partial, but still at scale, roll-out should have a proportional positive effect on reducing TB deaths. Although we do not attempt to quantify its impact on mortality rates, a quicker diagnosis of TB should decrease the instances of patients being lost to follow-up, thus reducing the spread of the disease within communities. Additionally, it should lessen the clinical severity for TB patients receiving treatment and allow radiologists more time to evaluate patients with other potential diseases. Finally, the high variability in our estimates should decrease as the quality of the data reported by WHO continues to improve, as it has in recent years.

References

1. World Health Organization, Tuberculosis. https://www.who.int/health-topics/tuberculosis#tab=tab_1

2. World Health Organization, Aging and health, 2022. https://www.who.int/news-room/fact-sheets/detail/ageing-and-health

3. Schaaf, H. S., Collins, A., Bekker, A., Davies, P. D. Tuberculosis at extremes of age. Respirology, 15(5), 747–763, 2010. https://doi.org/10.1111/j.1440-1843.2010.01784.x

4. Guerra-Laso, J. M., Gonzalez-Garcia, S., Gonzalez-Cortes, C., Diez-Tascon, C., Lopez-Medrano, R., Rivero-Lezcano, O. M. Macrophages from elders are more permissive to intracellular multiplication of *Mycobacterium tuberculosis*. Age, 35(5), 1235–1250, 2013. https://doi.org/10.1007/s11357-012-9451-5

5. Thomas, T. Y., Rajagopalan, S. Tuberculosis and aging: A global health problem. Clinical Infectious Diseases, 33(9), 1034–1039, 2001. https://doi.org/10.1086/322671

6. Olmo-Fontánez, A. M., Turner, J. Tuberculosis in an aging world. Pathogens, 11(11), 1101, 2022. https://doi.org/10.3390/pathogens11101101

7. World Bank Group, World development indicators. http://data.worldbank.org/data-catalog/world-development-indicators

8. United Nations, World population prospects 2024, 2024. https://www.un.org/development/desa/pd/

9. United Nations Population Division, World population prospects: 2022 revision, 2022. https://data.worldbank.org/indicator/SP.POP.65UP.TO.ZS

10. Cardinale, L., Nika, L., Teti, M., Dalpiaz, G., Larici, A. R., Rea, G. Pulmonary tuberculosis in diagnostic imaging: The great mime. Recenti Progressi in Medicina, 109, 220–225, 2018. https://doi.org/10.1701/2896.29193

11. Rea, G., Sperandeo, M., Lieto, R., Bocchino, M., Quarato, C. M. I., Feragalli, B., et al. Chest imaging in the diagnosis and management of pulmonary tuberculosis: The complementary role of thoracic ultrasound. Frontiers in Medicine (Lausanne), 8, 753821, 2021. https://doi.org/10.3389/fmed.2021.753821

12. Skoura, E., Zumla, A., Bomanji, J. Imaging in tuberculosis. International Journal of Infectious Diseases, 32, 87–93, 2015. https://doi.org/10.1016/j.ijid.2014.12.007

13. World Health Organization. Global Tuberculosis Report 2023, 2023. https://doi.org/10.1007/s12098-023-04264-8

14. World Health Organization, World Health Statistics 2024, 2024. https://data.who.int/countries/356.

15. Ministry of Health and Family Welfare, Government of India, National strategic plan for tuberculosis: 2017-25, elimination by 2017-2025. https://nhm.hp.gov.in/storage/app/media/National%20Strategic%20Plan%202017-25.pdf

16. United Nations General Assembly, Political declaration of the high-level meeting on the fight against tuberculosis, 2023. https://www.stoptb.org/un-high-level-meeting-tb/un-high-level-meeting-tb-2023#:~:text=The%20UN%20General%20Assembly%20(UNGA,equitable%20access%20to%20prevention%2C%20testing%2C

17. News18, India has just one radiologist for 100 scans a day. Here's how it can plug the shortage, 2023. https://www.news18.com/india/india-has-just-one-radiologist-for-100-scans-a-day-heres-how-it-can-plug-the-shortage-8619426.html.

18. Medical Buyer, India has alarming ratio of one radiologist per lakh people, 2023. https://www.medicalbuyer.co.in/india-has-alarming-ratio-of-one-radiologist-per-lakh-people/.

19. Kalyanpur, A. Commentary - Radiology in India: The next decade. Indian Journal of Radiology and Imaging, 18(3), 191–192, 2008. https://doi.org/10.4103/0971-3026.41869

20. Radiology Society of North America, Radiology facing a global shortage: Specialty affected by COVID-19, aging population and demand for imaging, 2022. https://www.rsna.org/news/2022/may/global-radiologist-shortage.

21. U.S. Bureau of Labor Statistics, Occupational employment and wage statistics. https://www.bls.gov/oes/current/oes291224.htm

22. United States Census Bureau, Happy New Year 2023, 2022. https://www.census.gov/library/stories/2022/12/happy-new-year-2023.html

23. The New Indian Express, Wanted: radiologists to meet growing healthcare needs, 2024. https://www.newindianexpress.com/xplore/2024/Apr/02/wanted-radiologists-to-meet-growing-healthcare-needs

24. Praxis Global Alliance, Rising opportunity of healthcare delivery in Tier 2+ cities of India, 2024. https://www.praxisga.com/insights/healthcare-and-lifesciences/rising-opportunity-of-healthcare-delivery-in-tier-2-cities-of-india

25. Choudhary, S. Growth of radiology market in tier 2 & 3 cities of India, 2024. https://www.linkedin.com/pulse/growth-radiology-market-tier-2-3-cities-india-dr-salil-choudhary/

26. HealthCareRadius, Trends in India's diagnostic imaging market, 2024. https://www.healthcareradius.in/diagnostic-radiology/trends-in-indias-diagnostic-imaging-

market#:~:text=The%20Indian%20diagnostic%20imaging%20market,is%20pegged%20at%20five%20percent.

27. Financial Express, Radiologist shortage issue continues to persist and worsen: Dr. Arjun Kalyanpur, Chief Radiologist & Founder CEO, Teleradiology Solutions, 2023. https://www.financialexpress.com/business/healthcare-radiologist-shortage-issue-continues-to-persist-and-worsen-dr-arjun-kalyanpur-chief-radiologist-founder-ceo-teleradiology-solutions-2997196/.

28. Rajpurkar, P. Profile. https://pranavrajpurkar.com.

29. Jha, A. AI and health part one: DrGPT will see you now. Economist Podcasts, The Economist, 2024. https://podcasts.apple.com/tr/podcast/economist-podcasts/id151230264?i=1000656423660.

30. Aster Medical Imaging. Scope of radiologist in India. https://www.astermedicalimaging.com/blog-inner/career-in-radiology/#:~:text=In%20India%2C%20one%20has%20to,diploma%20program%20in%20medical%20radiodiagnosis

31. National TB Prevalence Survey in India 2019 – 2021. https://tbcindia.mohfw.gov.in/2023/06/06/national-tb-prevalence-survey-in-india-2019-2021/

32. World Health Organization. Latent Tuberculosis Infection: Updated and Consolidated Guidelines for Programmatic Management, 2018. https://www.who.int/publications/i/item/9789241550239

33. Sterling, T. R., Njie, G., Zenner, D., Cohn, D. L., Reves, R., Ahmed, A., et al. Guidelines for the treatment of latent tuberculosis infection: Recommendations from the National Tuberculosis Controllers Association and CDC. MMWR Recommendations and Reports. 69, 1–11, 2020. http://dx.doi.org/10.15585/mmwr.rr6901a1

34. U.S. Centers for Disease Control and Prevention, Mantoux Tuberculin Skin Test. https://www.cdc.gov/tb/education/mantoux/pdf/Mantoux_TB_Skin_Test.pdf

35. Hashim, Z., Tyagi, R., Singh, G. V., Nath, A., Kant, S. Preventive treatment for latent tuberculosis from Indian perspective. Lung India 41(1), 47-54, 2024. https://doi.org/10.4103/lungindia.lungindia_336_23

36. U.S. Centers for Disease Control and Prevention, What You Need to Know About the TB Skin Test. https://www.cdc.gov/tb/media/What_You_Need_to_Know_About_the_TB_Skin_Test.pdf.

37. Naraghi, S., Mutsvangwa T., Goliath R., Rangaka M., Douglas T. Mobile phone-based evaluation of latent tuberculosis infection: Proof of concept for an integrated image capture

and analysis system. Computers in Biology and Medicine, 98, 76-84, 2018. https://doi.org/10.1016/j.compbiomed.2018.05.009

38. San Pedro, J. M. M., Yousefian Barfeh, D. P. Tuberculin Skin test checker using digital image processing, LPU–Laguna Journal of Engineering and Computer Studies, 4(1), 2018. https://lpulaguna.edu.ph/wp-content/uploads/2018/12/8-TUBERCULIN-SKIN-TEST-CHECKER.pdf

39. Statista. Smartphone penetration rate in India from 2009 to 2023, with estimates until 2040, 2023. https://proxy.parisjc.edu:8293/statistics/1229799/india-smartphone-penetration-rate/

40. Jha, A. Babbage: The science that built the AI revolution—part one. Economist Podcasts, The Economist, 2024. https://shows.acast.com/e421d786-ec36-4148-aa99-7a3b2928a779/65e8ae7343c1bc0016fc9fdc.

41. The University of Queensland Australia, Woodruff, A. Brain anatomy: What is a neuron? Queensland Brain Institute. https://qbi.uq.edu.au/brain/brain-anatomy/what-neuron#:~:text=Neurons%20(also%20called%20neurones%20or,at%20every%20step%20in%20between.

42. National Institutes of Health (US), & Biological Sciences Curriculum Study, NIH Curriculum Supplement Series: Information about the brain. Bethesda, MD: National Institutes of Health, 2007. https://www.ncbi.nlm.nih.gov/books/NBK20367/

43. McCulloch, W. S., Pitts, W. A logical calculus of the ideas immanent in nervous activity. Bulletin of Mathematical Biophysics, 5, 115–133, 1943. https://link.springer.com/article/10.1007/BF02478259#citeas

44. Rosenblatt, F. Principles of neurodynamics: Perceptrons and the theory of brain mechanisms. Spartan Books, 1962. https://books.google.com/books/about/Principles_of_Neurodynamics.html?id=7FhRAAAAMAAJ

45. Minsky, M., Papert, S. A review of perceptrons: Introduction to computational geometry. MIT Press, 1969. https://direct.mit.edu/books/monograph/3132/PerceptronsAn-Introduction-to-Computational

46. Crevier, D. AI: The tumultuous search for artificial intelligence. New York, NY, Basic Books, 1993. https://www.amazon.com/Ai-Tumultuous-History-Artificial-Intelligence/dp/0465029973

47. Jha, A. Babbage: The science that built the AI revolution - part two. Economist Podcasts, The Economist, 2024. https://embed.acast.com/e421d786-ec36-4148-aa99-7a3b2928a779/

babbage-the-science-that-built-the-ai-revolutionpart-two.

48. Rumelhart, D. E., Hinton, G. E., Williams, R. J. Learning representations by back-propagating errors. Nature, 323, 533–536, 1986. https://www.nature.com/articles/323533a0

49. Gershgorn, D. The data that transformed AI research—and possibly the world. Quartz. Atlantic Media Co, 2017. https://qz.com/1034972/the-data-that-changed-the-direction-of-ai-research-and-possibly-the-world

50. Jha, A. Babbage: The science that built the AI revolution - part three. Economist Podcasts, The Economist, 2024. https://embed.acast.com/e421d786-ec36-4148-aa99-7a3b2928a779/babbage-the-science-that-built-the-ai-revolutionpart-three.

51. Chellapilla, K., Puri, S., Simard, P. High performance convolutional neural networks for document processing. In Proceedings of the Tenth International Workshop on Frontiers in Handwriting Recognition . Université de Rennes 1, La Baule, France, 2006. https://inria.hal.science/inria-00112631/document

52. Krizhevsky, A., Sutskever, I., Hinton, G. ImageNet classification with deep convolutional neural networks. Neural Information Processing Systems, 25, 2012. https://proceedings.neurips.cc/paper_files/paper/2012/file/c399862d3b9d6b76c8436e924a68c45b-Paper.pdf

53. Russakovsky, O., Deng, J., Su, H., Krause, J., Satheesh, S., Ma, S., et al. ImageNet large scale visual recognition challenge. International Journal of Computer Vision, 115, 211–252, 2015. https://link.springer.com/article/10.1007/s11263-015-0816-y

54. LeCun, Y., Bengio, Y., Hinton, G. Deep learning. Nature, 521(7553), 436–444, 2015. https://www.nature.com/articles/nature14539

55. Raina, R., Madhavan, A., Ng, A. Y. Large-scale deep unsupervised learning using graphics processors. In Proceedings of the 26th Annual International Conference on Machine Learning (pp. 873–880), 2009. https://robotics.stanford.edu/~ang/papers/icml09LargeScaleUnsupervisedDeepLearningGPU.pdf

56. Human-Centered Artificial Intelligence, Artificial intelligence index report 2023. Stanford University, 2023. https://aiindex.stanford.edu/wp-content/uploads/2023/04/HAI_AI-Index-Report_2023.pdf

57. Jha, A. AI and health part one: DrGPT will see you now. Economist Podcasts, The Economist, 2024. https://podcasts.apple.com/tr/podcast/economist-podcasts/id151230264?i=1000656423660.

58. NHS England, Mia mammography intelligent assessment, 2021. https://transform.england.nhs.uk/ai-lab/explore-all-resources/understand-ai/mia-mammography-intelligent-assessment/

59. NHS England. Healthy.io: Smartphone albuminuria urine self-testing, 2021. https://transform.england.nhs.uk/ai-lab/explore-all-resources/understand-ai/healthyio-smartphone-albuminuria-urine-self-testing/

60. Healthy.io.,Healthy.io | Healthcare at the speed of life. https://healthy.io/eu/

61. Shibata, N., Tanito, M., Mitsuhashi, K., Fujino, Y., Matsuura, M., Murata, H., et al. Development of a deep residual learning algorithm to screen for glaucoma from fundus photography. Scientific Reports, 8, 14665, 2018. https://www.nature.com/articles/s41598-018-33013-w

62. Azeem, M., Kiani, K., Mansouri, T., Topping, N. SkinLesNet: Classification of skin lesions and detection of melanoma cancer using a novel multi-layer deep convolutional neural network. Cancers (Basel), 16(1), 108, 2023. https://doi.org/10.3390/cancers16010108

63. Kheiron Medical. MIA overview (UK). https://www.kheironmed.com/wp-content/uploads/2021/08/Kheiron_Mia_Product-One-Pager_UK_Vf1.pdf

64. Pillai, A. S. Utilizing deep learning in medical image analysis for enhanced diagnostic accuracy and patient care: Challenges, opportunities, and ethical implications. Journal of Deep Learning in Genomic Data Analysis, 1(1), 1–17, 2021. https://thelifescience.org/index.php/jdlgda/article/view/13

65. Lupton, M. Some ethical and legal consequences of the application of artificial intelligence in the field of medicine. Trends in Medicine, 18, 2018. https://www.oatext.com/some-ethical-and-legal-consequences-of-the-application-of-artificial-intelligence-in-the-field-of-medicine.php

66. Yang, L., Ene, I. C., Arabi Belaghi, R., Koff, D., Stein, N., Santaguida, P. Stakeholders' perspectives on the future of artificial intelligence in radiology: A scoping review. European Radiology, 32(6), 1477–1495, 2022. https://doi.org/10.1007/s00330-021-08214-z

67. Lenskjold, A., Nybing, J. U., Trampedach, C., Galsgaard, A., Brejnebøl, M. W., Raaschou, H., et al. Should artificial intelligence have lower acceptable error rates than humans? BJR Open, 5(1), 20220053, 2023. https://doi.org/10.1259/bjro.20220053

68. Huisman, M., Ranschaert, E., Parker, W., Mastrodicasa, D., Koci, M., Pinto de Santos, D., et al. An international survey on AI in radiology in 1,041 radiologists and radiology

residents part 1: Fear of replacement, knowledge, and attitude. European Radiology, 31(12), 7058–7066, 2021. https://doi.org/10.1007/s00330-021-07781-5

69. Lakhani, P., Sundaram, B. Deep learning at chest radiography: Automated classification of pulmonary tuberculosis by using convolutional neural networks. Radiology, 284(2), 574–582, 2017. https://doi.org/10.1148/radiol.2017162326

70. Chen, C.-F., Hsu, C.-H., Jiang, Y.-C., Lin, W.-R., Hong, W.-C., Chen, I.-Y., et al. A deep learning-based algorithm for pulmonary tuberculosis detection in chest radiography. Scientific Reports, 14, Article 65703, 2024. https://www.nature.com/articles/s41598-024-65703-z

71. Lee, S., Yim, J. J., Kwak, N., Lee, Y. J., Lee, J. K., Lee, J. Y., et al. Deep learning to determine the activity of pulmonary tuberculosis on chest radiographs. Radiology, 301(2), 435-442, 2021. https://doi.org/10.1148/radiol.2021210063

72. Wu, S. C., Wang, X. J., Ji, J. Y., Geng, G., Zhang, Z. H., Hou, D. L. A preliminary investigation on a deep learning convolutional neural networks based pulmonary tuberculosis CT diagnostic model. Chinese Journal of Tuberculosis and Respiratory Diseases, 44(5), 450-455, 2021. https://doi.org/10.3760/cma.j.cn112147-20210108-00026

73. Vijayan, S., Jondhale, V., Pande, T., Khan, A., Brouwer, M., Hegde, A., et al. Implementing a chest X-ray artificial intelligence tool to enhance tuberculosis screening in India: Lessons learned. PLOS Digital Health, 2(12), e0000404, 2023. https://doi.org/10.1371/journal.pdig.0000404

74. Nxumalo, Z. Z., Irusen, E. M., Allwood, B. W., Tadepalli, M., Bassi, J., Koegelenberg, C. F. N. The utility of artificial intelligence in identifying radiological evidence of lung cancer and pulmonary tuberculosis in a high-burden tuberculosis setting. South African Medical Journal, 114(6), e1846, 2024. https://doi.org/10.7196/samj.2024.v114i6.1846

75. Cao, X. F., Li, Y., Xin, H. N., Zhang, H. R., Pai, M., Gao, L. Application of artificial intelligence in digital chest radiography reading for pulmonary tuberculosis screening. Chronic Diseases and Translational Medicine, 7(1), 35-40, 2021. https://doi.org/10.1016/j.cdtm.2021.02.001

76. Qin, Z. Z., Ahmed, S., Sarker, M. S., Paul, K., Sikder Adel, A. S., Naheyan, T., et al. Can artificial intelligence (AI) be used to accurately detect tuberculosis (TB) from chest X-rays? An evaluation of five AI products for TB screening and triaging in a high TB burden setting. ArXiv, 2021. https://doi.org/10.48550/arXiv.2006.05509

77. Codlin, A. J., Dao, T. P., Vo, L. N. Q., Forse, R. J., Truong, V. V., Dang, H. M., et al. Independent evaluation of 12 artificial intelligence solutions for the detection of tuberculosis. Scientific Reports, 11, 23895, 2021. https://doi.org/10.1038/s41598-021-03265-0

78. Qure.ai, Tuberculosis crisis in underserved populations: The mobile radiology answer. https://qure-website-images.s3.ap-south-1.amazonaws.com/Case_Study_for_TB_page_Access_TB_Philippines_x_Qure_f5c8c8caad.pdf?updated_at=2023-10-09T09:28:55.572Z.

79. Tedla, K., Medhin, G., Berhe, G., Mulugeta, A., Berhe, N. Delay in treatment initiation and its association with clinical severity and infectiousness among new adult pulmonary tuberculosis patients in Tigray, northern Ethiopia. BMC Infectious Diseases, 20(1), 456, 2020. https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-020-05191-4

80. Timeline Daily, AI X-rays detect more TB cases, offering new hope for early diagnosis, 2023. https://timelinedaily.com/health/ai-X-rays-detect-more-tb-cases-offering-new-hope-for-early-diagnosis.

81. Nxumalo, Z. Z., Irusen, E. M., Allwood, B.W., Tadepalli, M., Bassi, J., Koegelenberg, C. F. N. The utility of artificial intelligence in identifying radiological evidence of lung cancer and pulmonary tuberculosis in a high-burden tuberculosis setting. South African Medical Journal, 114(6):e1846, 2024. https://doi.org/10.7196/samj.2024.v114i6.1846

82. World Health Organization, Global Tuberculosis Programme, Chest radiography in tuberculosis detection: Summary of current WHO recommendations and guidance on programmatic approaches, 2016. https://iris.who.int/bitstream/handle/10665/252424/9789241511506-eng.pdf?sequence=1

83. World Health Organization, Rapid communication on systematic screening for tuberculosis, 2023. https://www.who.int/publications/i/item/9789240016552

84. Bashir, S., Kik, S.V., Ruhwald, M., Khan, A., Tariq, M., Hussain, H., et al. Economic analysis of different throughput scenarios and implementation strategies of computer-aided detection software as a screening and triage test for pulmonary TB. PLoS ONE 17(12), e0277393, 2022. https://doi.org/10.1371/journal.pone.0277393

85. World Bank Group. World Bank Income Groups. https://ourworldindata.org/grapher/world-bank-income-groups

86. World Bank Group. Data: Rural population (% ot total population) – Pakistan. https://data.worldbank.org/indicator/SP.RUR.TOTL.ZS?locations=PK

87. Kamil, T., Radiology in Pakistan, 2023. https://www.linkedin.com/pulse/radiology-pakistan-taimoor-kamil/

88. Indian Institute of Public Health Gandhinagar, Regional Resource Centre for Health Technology Assessment. Reflecting on Six Years of Centre Progress 2018 – 2024. 2024.

https://iiphg.edu.in/images/pdfs/2024/A%20journey%20of%20six%20years%20of%20HTA%20RRC%20(2018-2024)%20at%20IIPHG.pdf

89. World Health Organization, Tuberculosis, 2023. https://www.who.int/news-room/fact-sheets/detail/tuberculosis#:~:text=TB%20is%20the%20leading%20cause,died%20of%20HIV%2Dassociated%20TB

90. Banta, J. E., Ani, C., Bvute, K. M., Lloren, J. I. C., Darnell, T. A. Pulmonary *vs.* extra-pulmonary tuberculosis hospitalizations in the US [1998–2014]. Journal of Infection and Public Health, 13(1), 131–139, 2020. https://doi.org/10.1016/j.jiph.2019.07.001

91. World Health Organization. Tuberculosis profile: India. (n.d.). https://worldhealthorg.shinyapps.io/tb_profiles/?_inputs_&entity_type=%22country%22&iso2=%22IN%22&lan=%22EN%22

92. World Health Organization, Global Tuberculosis Report 2022, 2022. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022