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The Accessibility, Affordability, and Early Detection of Tuberculosis

Tanvi Kadiri[1], Kathryn Wilwohl[#], Virgel Torremocha[#] and Jothsna Kethar[#]

[#]Advisor

ABSTRACT

Tuberculosis (TB) stands as the leading cause of death from an infectious agent worldwide, with a high fatality rate. It is primarily transmitted through the airborne *Mycobacterium tuberculos*is (M. tb) from an infected patient to a healthy individual. Annually, millions of people go undiagnosed for TB at an early stage and lose the opportunity for timely treatment, making early TB diagnosis a high priority. Prevalence surveys also have shown that many individuals with lab-confirmed TB disease lack symptoms and do not seek diagnosis or care. Moreover, delays in initiating treatment are commonly observed even after TB diagnosis, heightening the risk of disease transmission in the community. This research paper aims to address these challenges by analyzing the impact of various socioeconomic, policy, and healthcare factors on the accessibility of TB diagnosis. Furthermore, it aims to analyze current effective tuberculosis diagnosis techniques, assessing their strengths and weaknesses. Despite the presence of promising new drugs in the clinical trial stage offering hope for patients with extensively drug-resistant tuberculosis (XDR-TB) or very drug-resistant TB, the primary challenge remains the timely and species-specific detection of Tuberculosis. In addition to the detection of disease, identifying its drug resistance patterns and ensuring the availability of highly active short-course drug treatments are imperative, ideally lasting just a few weeks. This is essential to support the World Health Organization's (WHO) Global efforts to "END TB" by 2030, to reach 90% of people primarily through early diagnosis, innovative treatments, and vaccine development.

Introduction

Despite many medical tech advances, TB diagnosis methods are scarce in many communities because certain diagnostic tools and techniques are expensive. As a result, impoverished communities cannot afford them. Therefore, more research is needed to develop a cheap and widespread alternative to traditional diagnostic techniques. Also, many advanced diagnostic methods need machines and trained staff. This may be a challenge in low-resource regions. This is especially true in India, Indonesia, China, the Philippines, and Pakistan. Also, if collected, samples would have to travel far to viable facilities, which may incur large added costs. This challenge shows the need for a simple, local diagnosis method that works across the world. It may also be beneficial to understand the stigma tied to TB and how socioeconomic factors block detection (Yenet et al., 2023).

According to WHO (2023), a quarter of the global population is estimated to carry bacteria from the *Mycobacterium tuberculosis* complex, which causes tuberculosis. Annually, over eight to ten million new tuberculosis cases emerge globally, resulting in around three million deaths around the world. Moreover, infections in immunocompromised patients, as well as multi-drug-resistant bacterial strains have magnified the problem. Early detection of tuberculosis and drug resistance significantly enhances survival rates and aids in identifying contagious cases, facilitating contact tracing and public health interventions. Standard diagnostics still rely on methods developed in the last century, being both slow and inaccurate. For example, sputum culture, smear microscopy, and GeneXpert PCR machines are expensive, require specific infrastructure, are time-consuming, and cannot detect drug-resistant strains. As a result, in rural communities, timely detection of TB is a problem. However, methods such as the use of AI to detect tuberculosis in posteroanterior chest radiographs, artificial intelligence, and the use of sound analysis to identify TB with smartphones, could prove useful in low-income countries. International programs, such as the END TB Strategy, are promising, including three major pillars of success: integrated patient-centered care and prevention, supportive policies, and intensified research and innovation. The third pillar is widely successful, however is often not reachable by underprivileged communities. Therefore, it is vital to assess both the accessibility and reliability of these solutions. With more than half of the world's population lacking access to healthcare services, causing 100 million people to be pushed into poverty, the need for an affordable, accessible solution to early TB detection is pressing. Despite the challenges associated with TB detection, continuous improvements in diagnosis have led to better access to treatment for individuals affected by the disease. As a result, overall mortality from all forms of TB has shown a significant reduction from 2000 to 2022, as depicted in the graph below.

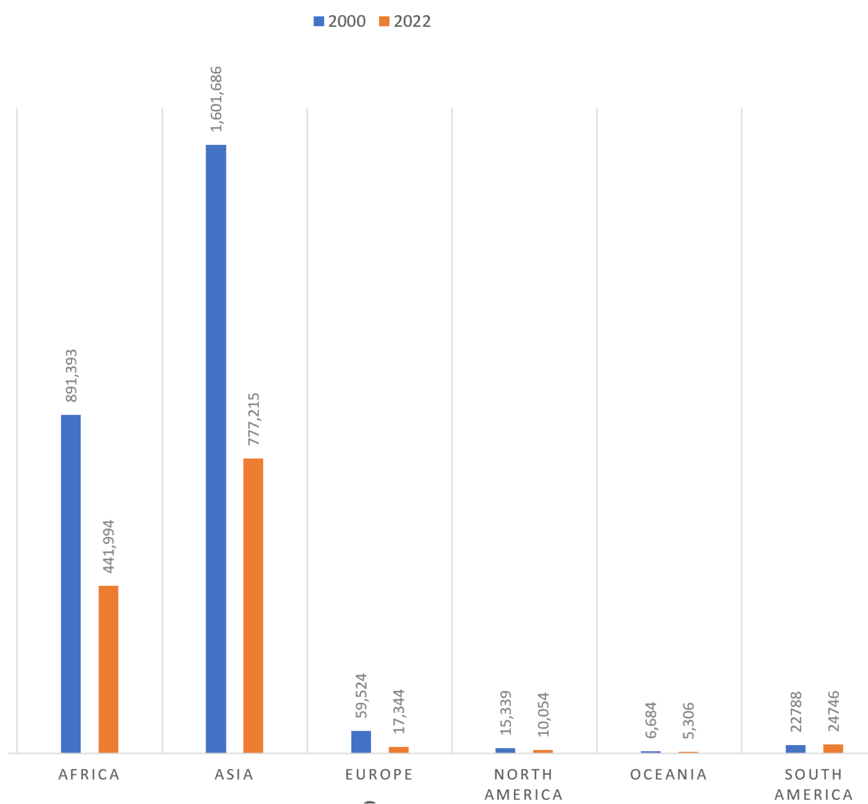


Figure 1. Estimated Tuberculosis Mortality Rate by Region (Tuberculosis Deaths based on the 2023 WHO report). This image demonstrates the significant reductions from 2000 to 2022 (Graph created by Kadiri, 2024).

As reported by the Centers for Disease Control (CDC), due to domestic TB control activities, the United States has one of the lowest TB case rates in the world (*Mission Statement and Activities | About Us | TB | CDC*, n.d.). Efforts to increase TB diagnosis effectiveness in the US have generally been successful, with advanced technology being available to clinicians, particularly due to the country's first-world status and vigorous government programs. However, high healthcare costs have discouraged those infected from diagnosing and treating the disease. Available care plans may include high insurance deductibles, which limit access to medical technologies, such as CAT scans, bronchoscopy, and tissue biopsies. The implementation of the Patient Protection and Affordable Care Act (ACA) in U.S. public health policy, successfully granted access to healthcare to millions, allowing for greater TB diagnosis and treatment efforts (Rosenbaum, 2011). However, the act is imperfect, placing poor individuals, whose incomes are greater than Medicaid eligibility standards, out of the qualification bracket. Furthermore, the act excludes childless adults and undocumented immigrants (Roby, 2020). As per CDC statistics for the year 2021, 4% of U.S. TB cases occurred among children younger than 15. Children ages 5–14 years had the lowest TB incidence rate (0.4 cases per 100,000 persons). Adults 65 years of age or older had the highest TB incidence rate in 2021 (4.0 cases per 100,000 persons). This lack of access only accentuates the need for more affordable testing regimes that target high-risk populations regardless of insurance coverage.

According to a study conducted by the Texas Medical Association, Texas remains the uninsured capital of the US, housing more than 4.3 million people without health insurance. This handicapped much of the population, especially the 1.6 million undocumented immigrants in the state. With many of these immigrants passing along the Mexico-Texas border, they are often subjected to poverty, overcrowding, stress from immigration, and lack of access to healthcare, all of which largely contribute to the continued spread of TB (*The Uninsured in Texas*, n.d.).

The need for affordable and accessible TB testing is becoming increasingly necessary, with new advancements in technologies such as AI, computer-aided detection software with digital chest X-rays, and Government programs. However, these advancements only benefit the privileged, excluding impoverished populations. As a result, TB continues to remain undiagnosed among these groups of people, spreading undetected to unassuming populations. With the help of my research, we will be able to gain insight into the various alternatives to popular TB detection methods, and the advantages and disadvantages of each.

Methodology

While conducting my research, I explored the various technological options that are effective in increasing the accessibility and accuracy of TB diagnosis. My primary goal was to identify the drawbacks and advantages of diagnosis options. Some of these options included [Rapid Sputum Tests for Tuberculosis and cough sound analysis using AI algorithms, …] Furthermore, I analyzed the effectiveness of these techniques using relevant data, compiling my findings into a comprehensive research paper.

The paper analyzes the impact of various factors on accessibility, including how impacts such as cost and infrastructure affect the availability of Tuberculosis diagnostic tools and techniques. The paper also details the drawbacks and advantages of several current diagnosis methods to assess their strength in tackling inaccessibility. In particular, it advocates for the use of the TB rapid sputum test and recognizes the potential for the use of AI in diagnosis efforts. By utilizing AI, we can greatly reduce the costs associated with the analysis and possible transportation of samples associated with traditional detection methods: sputum culture, smear microscopy, and GeneXpert PCR.

Diagnosis Options for Early Detection

Rapid Sputum Tests for Tuberculosis (TB)

A sputum culture can be used to find infection-causing pathogens. The test is conducted by adding a sample of sputum to a solution. The growth of bacteria indicates a positive test; the patient has tuberculosis. Unlike normal sputum cultures which take 1 to 8 weeks to provide results, a rapid sputum test can tell if a person has TB within 24 hours. (*Rapid Sputum Tests for Tuberculosis (TB) | Kaiser Permanente*, n.d.) A final study was conducted comparing the performance of the TB-rapid test to the LJ culture method using a sample of 56 patients, 7 of whom are HIV positive. With the culture test serving as the study's control, the rapid detection test was determined to have an accuracy rate of 92.70% (Aliannejad et al., 2016).

	Standard Culture Test					
Rapid Test		Positive	Negative	Sensitivity (%)	Specificity (%)	Accuracy (%)
	Positive	17	4	100%	89.60%	92.70%
	Negative	0	35			

Figure 2. Presented is a comparative matrix of test results for the rapid sputum test versus the standard culture test conducted on a total of 56 samples. The results from rapid sputum test yielded positive results in 17 samples and negative results in 4 samples. The sensitivity of the rapid sputum test was 100% , specificity was 89%, and accuray rate was 92% accuracy, when compared to the Standard culture method. Created and copyrighted by Tanvi Kadiri (Aliannejad et al., 2016).

Analysis of *Mycobacterium tuberculosis* Using Artificial Intelligence

AI has increasingly become prevalent in the medical industry, allowing for easier diagnosis methods. However, though efficient, the technology may pose some problems. For, example, while TB-AI demonstrates high sensitivity in identifying bacilli, its ability to differentiate between pathogenic and contaminant bacilli remains relatively weak. This discrimination relies on recognizing morphological changes induced by specific histological reactions, such as caseous necrosis, granuloma formation, and inflammation. As of now, TB-AI lacks the knowledge to make definitive diagnoses, still needing external confirmation by physicians. TB-AI is designed to automatically detect acid-fast stained TB bacilli and exhibits high sensitivity and moderate specificity. With this technology, pathologists don't need to manually search for bacilli under a microscope, reducing the risk of misdiagnosis. In practical application, positive results from TB-AI require confirmation by pathologists, while negative results should undergo review to ensure accuracy (Xiong et al., 2018).

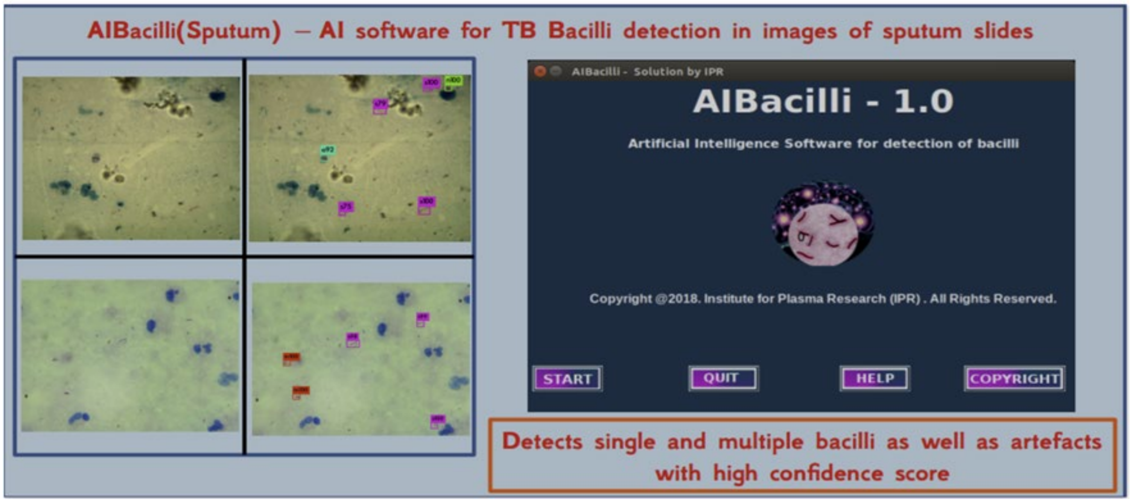


Figure 3. AIBacilli: Automated detection of single and multiple bacilli in sputum smear tests, using an AI software developed at the Institute of Plasma Research. AI-based technique of Object Detection is used by this software , where the work was conducted at Civil Hospital, Ahmedabad. The software can run on CPU/GPU/ARM devices (*Robotics, AI & ML*, n.d.-b).

AI-Assisted Chest X-Rays

The use of modern digital radiography machines, coupled with computer-aided detection, could serve as an essential tool to increase the efficiency of TB diagnosis. Labor-intensive manual inspection methods require experience in this particular field to provide precise conclusions. However, AI greatly accelerates the screening process (Acharya et al., 2022). To analyze the accuracy of this technology, a study uses a database of 3500 TB infected and 3500 normal chest X-ray images. Using ChexNet, our findings concluded that the accuracy, precision, and sensitivity in the detection of tuberculosis using X-ray images were 96.47%, 96.62%, and 96.47%, respectively. However, though being more efficient, the technology is expensive and requires constant access to electricity. Therefore, the method is not currently viable for impoverished communities (Rahman et al., 2020).

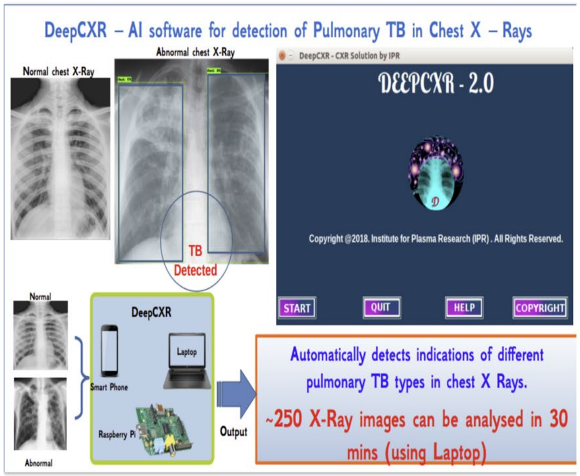
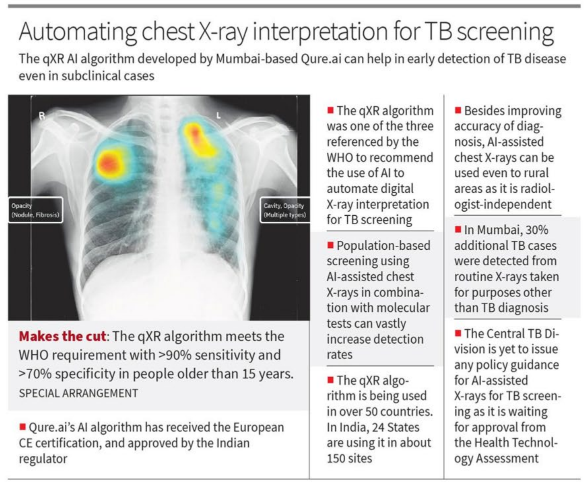


Figure 4. AI Software for Fast Automated Screening of TB using Chest X-Ray Images, in collaboration with ICMR headquarters, Delhi (*Robotics, AI & ML*, n.d.-b).



Automating chest X-ray interpretation for TB screening

The qXR AI algorithm developed by Mumbai-based Qure.ai can help in early detection of TB disease even in subclinical cases

Makes the cut: The qXR algorithm meets the WHO requirement with >90% sensitivity and >70% specificity in people older than 15 years. SPECIAL ARRANGEMENT

- Qure.ai's AI algorithm has received the European CE certification, and approved by the Indian regulator
- The qXR algorithm was one of the three referenced by the WHO to recommend the use of AI to automate digital X-ray interpretation for TB screening
- Population-based screening using AI-assisted chest X-rays in combination with molecular tests can vastly increase detection rates
- The qXR algorithm is being used in over 50 countries. In India, 24 States are using it in about 150 sites
- Besides improving accuracy of diagnosis, AI-assisted chest X-rays can be used even to rural areas as it is radiologist-independent
- In Mumbai, 30% additional TB cases were detected from routine X-rays taken for purposes other than TB diagnosis
- The Central TB Division is yet to issue any policy guidance for AI-assisted X-rays for TB screening as it is waiting for approval from the Health Technology Assessment

Figure 5. Shows Chest X-ray interpretation using AI published in - The Hindu Prasad (2023)

The qXR software, an AI tool, is designed to interpret chest X-ray (CXR) images for tuberculosis (TB) abnormalities. It has been endorsed by the World Health Organization (WHO) for use in TB screening and triage. The qXR algorithm analyzes the CXR image and promptly generates a TB abnormality score, ranging from 0.01 to 0.99, within a matter of seconds (John et al., 2023).

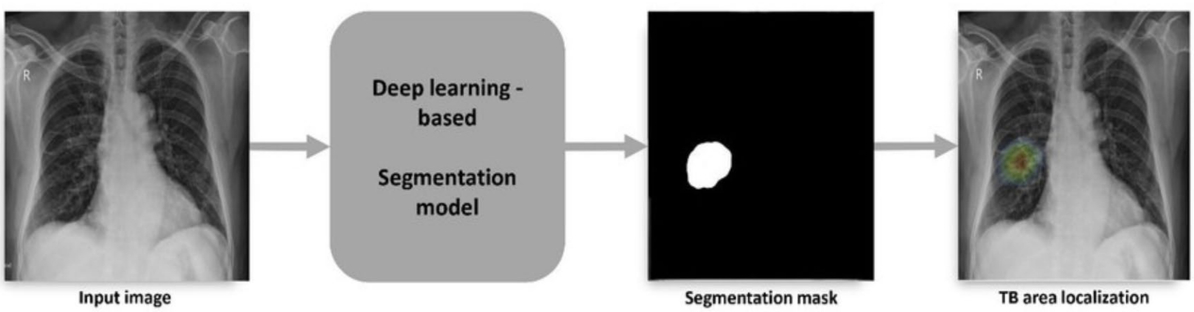


Figure 6. Utilizing AI in reading Chest X-rays for TB screening in Vietnam (*VinBrain and FIT Utilizing AI in Tuberculosis Screening in Vietnam*, n.d.)

Machine Learning Cough Sound Analysis

The use of cough analysis to detect TB is fairly new, and still in its developing stages. Symptom-based screening acts as a replacement in low-resource regions, where triage tools, such as chest-rays, are unavailable. Advancements in technology have led to improved tracking devices, making the process even easier. The technology analyzes both the frequency and the nature of cough sounds, converting the captured sound into spectrograms. An algorithm is then used to detect coughs as well as identify the cough. However, further research must be conducted to validate the various AI algorithms. Extreme verification of these algorithms is either limited, doesn't exist, or uses a small data set. The LCM, CayeCoM, and VitaloJak have been recognized for accurately measuring cough frequency, however, these devices are large and bulky, generally being obstructive to the common user. With the development of AI, however, smartphones with cough detection and recording applications can provide a more discrete and reliable alternative. (Zimmer, 2022) A study published by Cornell University aims to validate the credibility of smartphone collections using a dataset of 724,694 cough audio samples and 1,105 patients. A visual representation of the frequency and time characteristics of sounds can be achieved through various methods, including spectrograms and waveform displays.

An algorithm is then run to analyze the cough's features to identify TB. Ultimately, the study concluded the method has a 90% sensitivity and 70% specificity, therefore making it a good "first step," surpassing WHO's requirements for a triage test (Suda, 2023).

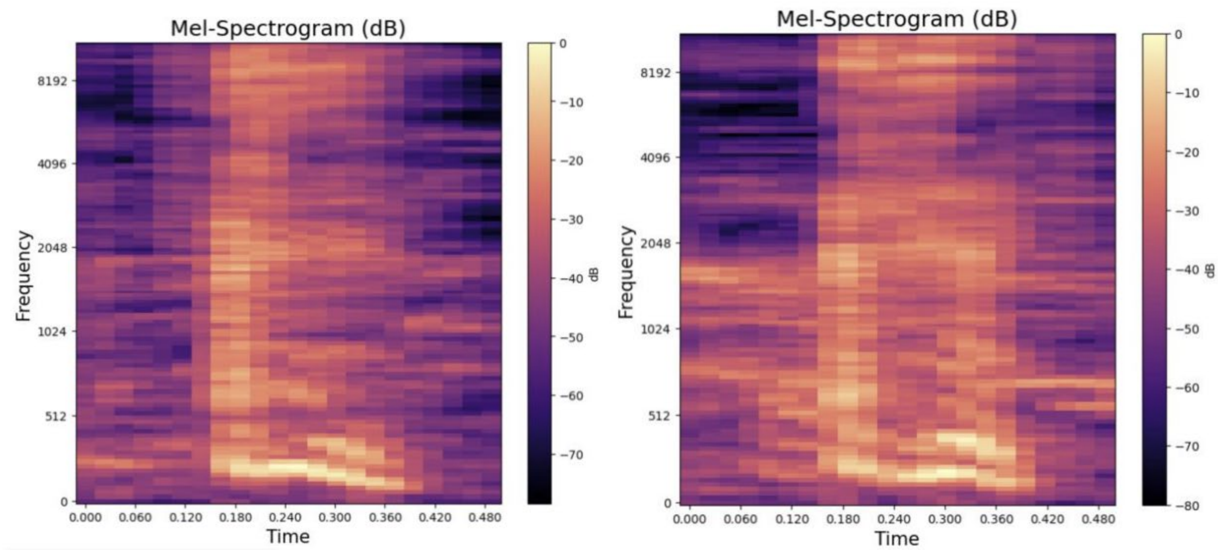


Figure 7. Example image of a TB Positive (right) and Negative (left) Mel Spectrogram (Suda, 2023).

The use of AI to diagnose tuberculosis is still developing and may have a place for error. A study was conducted to assess this margin of error, using a dataset with 33,000 passive coughs and 1600 forced coughs in a controlled setting with similar demographics (Sharma et al., 2024).

Collecting data using a smartphone model, it can be concluded that the device had a 95% confidence interval in subjects with a higher bacterial load or lung cavities. Another aspect of sound diagnosis is differentiating TB and other related respiratory illnesses. A study approached this question by presenting experiments based on a dataset of 1358 forced cough recordings obtained in a developing-world clinic from 16 patients with confirmed active pulmonary TB and 35 patients suffering from respiratory conditions suggestive of TB but confirmed to be TB negative. It was determined that the LR system yields the most accurate results using 5 machine learning classifiers, logistic regression (LR), support vector machines, k-nearest neighbor, multilayer perceptron, and convolutional neural networks (Pahar et al., 2021). A third study analyzed the detection of TB versus other respiratory diseases using a constant data collector. The study collected data, using the Hyfe Research application, by monitoring the coughs of patients in 5 different countries (Uganda, South Africa, the Philippines, Vietnam, and India) and compared patterns of cough between people with microbiologically confirmed TB, clinical TB, and other respiratory diseases. Participants were required to have a new or worsening cough and were excluded if they had taken TB or other antimicrobial medication. There are no conclusive results offered from the study (Huddart et al., 2023).

Molecular Tests (GeneXpert Omni)

Traditional molecular TB tests have a high sensitivity, generally recommended for use. However, the technology is expensive and requires a laboratory facility with continuous power. When faced with rural and resource-limited areas, this challenge is unavoidable, with the added cost of the transportation of samples. However, with the development of the GeneXpert Omni, a portable molecular testing kit, this obstacle is overcome, offering an inexpensive, on-site diagnosis (Gill et al, 2022). Operating with a mobile and having a cloud connection, the device makes it easy to access and transfer data and is easy to transport.

Additionally, its ability to withstand dust, humidity, and high temperatures allows it to be used in various environments. A study was conducted to analyze the device's accuracy, using a sample size of 160 TB positive samples and 40 TB negative samples. The study's primary goal was to analyze the accuracy rate between GeneXpert (traditional molecular testing) and Omni in a controlled environment. The results indicated the sensitivity for rifampicin-resistant TB detection of MTB Ultra on Omni was estimated to be 0.7% higher than of MTB Ultra on GeneXpert (Georghiou et al, 2021).

		Omni		
		Positive	Negative	Total (%)
GeneXpert	Positive	158 (79.8%)	1^a (0.5%)	159 (79.9%)
	Negative	0 (0.0%)	40 (20.1%)	40 (20.1%)
	Total (%)	158 (79.4%)	41 (20.6%)	199 (100%)

Figure 8. Results from the study analyzing the accuracy of Omni in comparison to GeneXpert Omni. Created and copyrighted by Tanvi Kadiri (Georghiou et al., 2021)

Tuberculin Skin Test (TST)

Being an intradermal injection, the TST Tests skin hypersensitivity for mycobacterial antigens. This test is fairly accessible, being both low cost and having a high availability rate. However, its accuracy may vary, not differentiating latent infection from the disease, and it's important to note that if the individual is vaccinated with Bacille Calmette-Guérin (BCG) can potentially lead to a false positive reaction on a TB skin test (*Tuberculosis (TB) - Testing in BCG-Vaccinated Persons*, 2022). Some limitations of the test are that it can take weeks post-exposure for the immune system to react. In addition, two visits are required to analyze the TST results with the help of a trained medical professional. Furthermore, immunosuppressed individuals may not mount an immune response. This proves to be significant as many impoverished people's immune systems are damaged due to poor sanitation and living conditions. Therefore, the test would not be reliable for our target demographic.

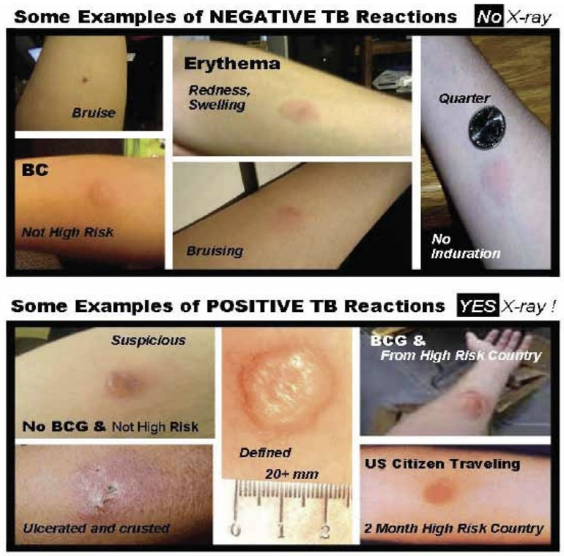


Figure 9. Some examples of Positive and Negative Skin test results for reference (DRP-TB-Study-Guide, 2021).

Conclusion

In conclusion, eradicating TB hinges on early detection, accessibility, and affordability. These factors play a crucial role in ensuring that individuals affected by TB receive prompt diagnosis and treatment, ultimately contributing to global efforts to eliminate this disease. This goal can be achieved through the application of the Rapid Sputum Test, and the GeneXpert Omni, a molecular test. Additionally, the use of machine learning sound analysis seems promising but may need further research. These methods all prioritize affordability and low resource consumption, therefore serving a greater demographic. In comparison, traditional TB testing methods, such as sputum culture, smear microscopy, X-rays, and GeneXpert PCR, require high monetary and energy costs, which may not be available for underdeveloped societies. By prioritizing early detection strategies, enhancing access to diagnostic services, and making treatments affordable, we can move closer to achieving the goal of eradicating TB worldwide.

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