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Evaluating the cost-effectiveness of Cy-Tb for LTBI in India: a comprehensive economic modelling analysis

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Background: Latent tuberculosis infection (LTBI) remains a significant challenge, as there is no gold standard diagnostic test. Current methods used for identifying LTBI are the interferon-γ release assay (IGRA), which is based on a blood test, and the tuberculin skin test (TST), which has low sensitivity. Both these tests are inadequate, primarily because they have limitations with the low bacterial burden characteristic of LTBI. This highlights the need for the development and adoption of more specific and accurate diagnostic tests to effectively identify LTBI. Herein we estimate the cost-effectiveness of the Cy-Tb test as compared with the TST for LTBI diagnosis.

Methods: An economic modelling study was conducted from a health system perspective using decision tree analysis, which is most widely used for cost-effectiveness analysis using transition probabilities. Our goal was to estimate the incremental cost and number of TB cases prevented from LTBI using the Cy-Tb diagnostic test along with TB preventive therapy (TPT). Secondary data such as demographic characteristics, treatment outcome, diagnostic test results and cost data for the TST and Cy-Tb tests were collected from the published literature. The incremental cost-effectiveness ratio was calculated for the Cy-Tb test as compared with the TST. The uncertainty in the model was evaluated using one-way sensitivity analysis and probability sensitivity analysis.

Results: The study findings indicate that for diagnosing an additional LTBI case with the Cy-Tb test and to prevent a TB case by providing TPT prophylaxis, an additional cost of 18 658 Indian rupees (US$223.5) is required. The probabilistic sensitivity analysis indicated that using the Cy-Tb test for diagnosing LTBI was cost-effective as compared with TST testing. If the cost of the Cy-Tb test is reduced, it becomes a cost-saving strategy.

Conclusions The Cy-Tb test for diagnosing LTBI is cost-effective at the current price, and price negotiations could further change it into a cost-saving strategy. This finding emphasizes the need for healthcare providers and policymakers to consider implementing the Cy-Tb test to maximize economic benefits. Bulk procurements can also be considered to further reduce costs and increase savings.

Keywords: cost-effectiveness analysis, Cy-Tb, diagnostic tool, latent tuberculosis infection, TB control, tuberculin skin test.

Introduction

Latent tuberculosis infection (LTBI) is an asymptomatic non-transmissible clinical state. People with LTBI can progress to active TB, with a higher risk of reactivation that is greatly increased in those with immunocompromising conditions.[1] When the immune system reacts to exposure to the *Mycobacterium tuberculosis* antigen without causing an illness, it is classified as LTBI. Most individuals with LTBI have no signs or symptoms of TB and will never develop the disease. The risk of developing active TB following LTBI depends on age, gender, lifestyle characteristics and comorbidities.[2] Globally, LTBI prevalence has been estimated to be around 33%.[3] According to the World Health Organization (WHO) Global TB Report 2023, 4 million children <5 y of age with household contact with TB patients were targeted for LTBI treatment between 2018 and

2022. However, only 55% (2.2 million) were treated during that period.[4] Because of the risk factors, including malnutrition, comorbidities, alcohol and smoking, a significant percentage of the population is susceptible to developing active TB illness from LTBI.

Asymptomatic and non-transmissible, LTBI is a clinical condition. The risk of progress to active TB increases in people with immunocompromising diseases. People with LTBI may proceed to active TB or experience reactivation. Identifying and treating LTBI cases remains an important strategy in the fight against TB. Interferon-γ release assays (IGRAs) and/or tuberculin skin tests (TSTs) have been widely used to confirm the diagnosis of LTBI. While the TST is simple to use, it has a higher false positive rate among Bacille Calmette–Guérin (BCG)-vaccinated individuals and those who have a non-tuberculous mycobacterial infection. While the IGRA detects the release of interferon-γ (IFN-γ) in response to specific *M. tuberculosis* antigens, the TST uses a delayed-type hypersensitivity response to determine *M. tuberculosis* sensitization. While the WHO suggests using the IGRA in high-income countries, in low- and middle-income countries the TST is widely used.[5] IGRAs are whole blood tests that assess the immune system's reaction to antigens produced by *M. tuberculosis* and they are useful to distinguish between LTBI and active TB.[5]

To overcome the limitations of the TST and IGRA, the highly specific Cy-Tb skin test (Statens Serum Institute, Copenhagen, Denmark) was developed for the diagnosis of LTBI. The Cy-Tb test is based on the antigens ESAT-6 and CFP-10, which are also present in the IGRA, and it is administered and read similarly to the TST. The Cy-Tb test relies on an extensive 5-mm cut-point induration due to its great specificity, regardless of the presence of human immunodeficiency virus (HIV), BCG or both.[6] In order to diagnose LTBI, the Cy-Tb test combines the convenience and cost-effectiveness of the TST with the specificity of the IGRA. The Cy-Tb test is also unaffected by BCG vaccination. This test showed excellent results in a phase 3, double-blind, randomised trial that was published in 2017.[7] It demonstrated 94% agreement with the IGRA findings and comparable induration sizes to those of the TST.

Most of the high TB burden countries currently use the TST with pure protein derivative (PPD RT 23) as the standard diagnostic test. The necessity for adopting newer, more specific tests has been brought to light by the periodic shortage of PPD, the low specificity of the test in the population vaccinated with BCG and the time-consuming training required for the TST.[8] Thus new LTBI diagnostic tools are being introduced that require evaluation in terms of cost-effectiveness, acceptability and feasibility before being integrated into the public health system. The current study aims to examine the cost-effectiveness of the newly introduced Cy-Tb LTBI diagnostic test as compared with the TST.

Methods

Study setting

India has the highest number of LTBI cases, with almost 300–400 million individuals infected.[9] Among these it is estimated that 2.6 million are likely to develop active TB every year. The government of India set a goal to end TB by 2025, as per India's National Strategic Plan (2017–2025). TB preventive therapy (TPT) is one of the core 'prevent' pillars for elimination of TB.[9] Thus the management of LTBI is crucial to efforts to curb the TB burden not only in India, but in many other high-burden countries around the world. Yet there is no gold standard test to diagnose LTBI or predict development of TB among LTBI patients. As per the National TB Elimination Programme (NTEP) diagnostic algorithm, testing for LTBI using the TST or IGRA is not required for initiating TPT in people living with HIV or children <5 y of age who are in contact with pulmonary TB patients.[10] Still, there is no ideal approach for diagnosing and testing LTBI. For LTBI treatment over the past decades, isoniazid preventive therapy (IPT) and chemoprophylaxis for 6 months (6H) has been the most widely used regimen under programmatic conditions. The WHO recommends multiple TPT options that are equivalent to 6H, newer regimens such as rifapentine and isoniazid (3HP) for 3 months and 1 month daily rifapentine and isoniazid (1HP).[11] Since the treatments of LTBI and active TB work in concert to lower the incidence of TB, the NTEP advises active case identification and case holding efforts for both TB and LTBI in areas with a high prevalence of TB. In light of this, increasing the TPT could speed up India's efforts to 'end TB' and reduce the incidence of TB.

Study design

A decision analytic method was used for assessing the cost-effectiveness of the Cy-Tb test for diagnosing LTBI and to prevent TB in household contacts. The health system's costs were taken into account when creating this cost-effectiveness model, which covered expenses such as screening household contacts, treating LTBI patients with isoniazid preventive medication for 6 months and managing adverse drug reactions (ADRs) brought on by isoniazid. This study estimates the additional costs associated with implementation of the Cy-Tb test as an intervention for the diagnosis of LTBI in India and assesses the cost-effectiveness of this approach in preventing the progression of LTBI to active TB.

Study perspective

A health system perspective was used for this cost-effectiveness evaluation, which considered only the expenditures that the health system undertakes, such as the cost of diagnosing LTBI, isoniazid preventive medication for LTBI, major and minor ADRs due to LTBI treatment and diagnosis and treatment of active TB.

Intervention and comparator

The next-generation skin test for LTBI detection, the Cy-Tb test, is regarded as an intervention for LTBI diagnosis. The comparator is for LTBI is the TST. The Mantoux technique is used to do TSTs, injecting 0.1 ml of 2 TU/5 TU PPD intradermally into the volar portion of the forearm. The transverse diameter of the TST induration is measured after 48–72 h. If the induration diameter is >5 mm, the outcome is deemed positive. The Cy-Tb test reads precisely like the TST.

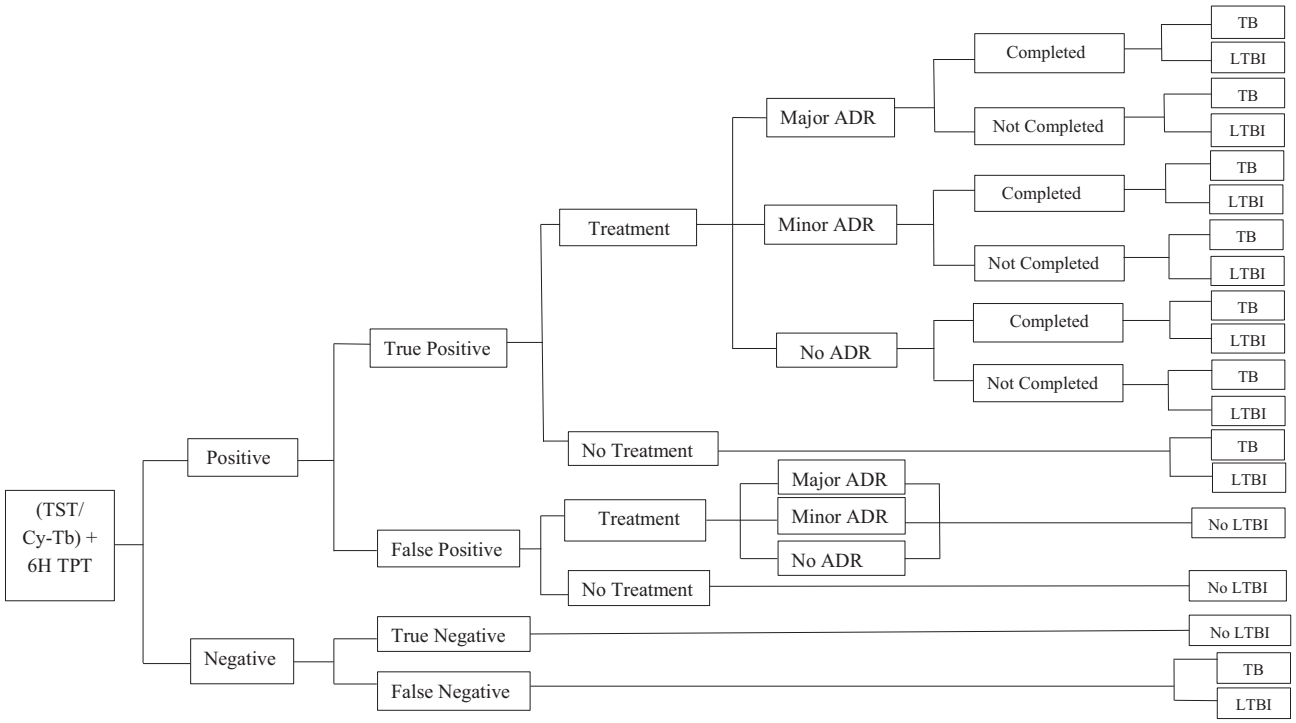

Figure 1. Decision tree to estimate the cost-effectiveness of the Cy-Tb test compared with the TST for LTBI diagnosis.

Model description

In Excel (Microsoft, Redmond, WA, USA), a deterministic decision tree model for cost-effectiveness analysis was created to assess the test's sensitivity and specificity in diagnosing LTBI in household contacts of index TB patients. Two tests were investigated for the analysis, one diagnosed by TST and the other diagnosed by the Cy-Tb test. Data from secondary sources, including published papers, systematic reviews and primary data sources were used to parameterize the model.

Decision tree

The clinical pathway for screening close contacts of infectious TB index cases is represented as a decision tree (Figure 1). The decision tree's branches represent the probability of testing positively or negatively and, among tested positives, the likelihood of identifying the true positives and false positives. The probability of initiating preventive therapy among test-positive cases and associated toxicity (no, minor and major ADRs) are added in the decision tree. The last two branches of the decision tree represents LTBI treatment completion status and further breakdown of TB and LTBI cases. Further, the false positive cases who had isoniazid treatment are branched to three types of ADRs. The false negative cases are broken down to TB and LTBI. The TST and Cy-Tb test were included in the decision tree separately. This decision tree is sourced and adapted from a previous cost-effectiveness study on different screening strategies for the diagnosis of suspected LTBI.[12]

Model input parameters

The key input parameters included in the model for the cohort population are given in Table 1. With a hypothetical cohort of 100 000, this model considers the study population as individuals >18 y of age who had at least one household contact and were not on antitubercular medication or had a history of TB in the 6 months prior. The key input parameters used in this model are demographic characteristics, an epidemiological parameter (prevalence of LTBI), the diagnostic accuracy of the TST and Cy-Tb test (sensitivity and specificity), cost data for the TST and Cy-Tb test and effectiveness parameters such as TPT outcomes.

Cost data

This model employed an ingredients-based costing methodology, in which the cost of each unit was multiplied by the resource amounts to determine the overall costs. We derived the unit cost of each diagnostic strategy. The cost of the test kit, consumables (vial, syringe and needle), equipment and human resource time are included in the direct costs of diagnosing LTBI.[13] The cost of the Cy-Tb test kit was taken from MyLab.[14] The time spent by human resources testing the patient was converted into procedure costs, which were gathered from the published literature.[15] The other costs, such as TPT (6H) costs, major ADR costs and minor ADR costs, are taken from a cost-effectiveness study.[16] The cost was converted to US dollars ($) based on the exchange rate at the time of study (US$1 = 83 Indian rupees (₹).

Table 1. Input parameter for cost-effectiveness of the Cy-Tb test as compared with the TST for LTBI diagnosis and treatment

	Input parameters	Base case	Lower	Upper	Distribution	Source
Demographic value	Cohort population	100 000	100 000	100 000	NA	Assumption
Prevalence	LTBI HH contacts in India	0.526	0.421	0.631	Beta	20
Diagnostic accuracy*	Cy-Tb positive	0.415	0.332	0.498	Beta	6
	Cy-Tb negative	0.585	0.468	0.702	Beta	6
	TST positive	0.319	0.255	0.383	Beta	19
	TST negative	0.681	0.545	0.817	Beta	19
	Cy-Tb true positive	0.989	0.791	1.000	Beta	6
	Cy-Tb false positive	0.011	0.009	0.014	Beta	6
	Cy-Tb true negative	0.802	0.642	0.963	Beta	6
	Cy-Tb false negative	0.198	0.158	0.237	Beta	6
	TST true positive	0.807	0.646	0.968	Beta	19
	TST false positive	0.193	0.154	0.232	Beta	19
	TST true negative	0.606	0.485	0.727	Beta	19
	TST false negative	0.394	0.315	0.473	Beta	19
TPT 6H treatment outcomes	No ADR	0.956	0.765	1.000	Beta	21
	Minor ADR	0.030	0.024	0.036	Beta	21
	Major ADR	0.014	0.011	0.017	Beta	21
	Start INH treatment	0.307	0.246	0.368	Beta	23
	No INH treatment	0.693	0.554	0.832	Beta	23
	Treatment completed	0.188	0.150	0.226	Beta	23
	Treatment not completed	0.812	0.650	0.974	Beta	23
	Developed TB HH contact	0.100	0.080	0.120	Beta	22
	Remain LTBI HH contact	0.900	0.720	1.000	Beta	22
Cy-Tb	Sensitivity of Cy-Tb	0.780	0.624	0.936	Lognormal	6
	Specificity of Cy-Tb	0.990	0.792	1.000	Lognormal	6
TST	Sensitivity of TST	0.770	0.616	0.924	Lognormal	19
	Specificity of TST	0.590	0.472	0.708	Lognormal	19
Cost data in ₹ (US$1=₹83)	Cy-Tb HR	250	200	300	Gamma	15
	TST HR	250	200	300	Gamma	15
	TST kit	169	135	203	Gamma	13
	Cy-Tb kit	376	301	451	Gamma	14
	TPT 6H treatment	1888	1510	2266	Gamma	16
	Major ADR	8361	6689	10 033	Gamma	16
	Minor ADR	2963	2370	3556	Gamma	16
	Diagnosis cost of TB	1602	1282	1922	Gamma	16
	Treatment of active TB	7903	6322	9484	Gamma	16
WTP threshold	WTP threshold (GDP per capita) (in ₹)	216 590	216 590	216 590	NA	24

Effectiveness parameters

The sensitivity and specificity of the Cy-Tb test were taken from a randomized controlled trial conducted in South Africa.[17] This study was sourced from a reference of a systematic review and meta-analysis done by the WHO consolidated guidelines on TB.[18] The clinical effectiveness of the TST was taken from a systematic review published by Pai et al.[19] The prevalence of LTBI in household contacts in India was taken from a clinical trial conducted in South India.[20] The total positive, total negative, true positive, false positive, true negative and false negative cases with the Cy-Tb test and TST were estimated using the sensitivity, specificity and prevalence of LTBI. The following formulae were used to estimate true positive, true negative, false positive, false negative, total positive and total negative cases.

$$\text{True positve (TP) cases} = \text{Sensitivity} \times \text{Prevalence} \quad (1)$$

$$\text{True negative (TN) cases} = \text{sensitivity} \times (1 - \text{prevalence}) \quad (2)$$

$$\text{False positive (FP) cases} = (1 - \text{specificity}) \times (1 - \text{prevalence}) \quad (3)$$

$$\text{False negative (FN) cases} = (1 - \text{sensitivity}) \times \text{prevalence} \quad (4)$$

Table 2. Incremental cost-effectiveness of the Cy-Tb test for diagnosing LTBI as compared with TST

	Total		Incremental		
Strategy	Cost	TB cases prevented	Cost	TB cases prevented	ICER
Cy-Tb and TPT 6H	₹215 097 159	36 925	₹8 832 873	473	₹18 658
TST and TPT 6H	₹206 264 287	36 452	–	–	–

Table 3. Diagnostic accuracy of the Cy-Tb test and TST for LTBI diagnosis

Test	TP	FP	TN	FN	Sensitivity	Specificity	PPV	NPV
Cy-Tb	0.99	0.01	0.80	0.20	0.78	0.99	0.99	0.80
TST	0.68	0.32	0.70	0.30	0.77	0.59	0.68	0.70

TP: true positive; FP: false positive; TN: true negative; FN: false negative; PPV: positive predictive value; NPV: negative predictive value.

$$\text{Total positive cases} = \text{True positive} + \text{False positive} \quad (5)$$

$$\text{Total negative cases} = \text{True negative} + \text{False negative} \quad (6)$$

The effectiveness parameters include the ADR by 6H TPT, which was categorized into minor, major and no ADRs, and was collected from a cost-effectiveness study based in southern India.[21] The efficacy of the 6H TPT was collected in terms of the total number of LTBI patients and the distribution of active TB cases following the results of the 6H TPT from a systematic review and meta-analysis conducted by Moonan et al.[22] Information on the proportion of persons starting and completing LTBI treatment was collected from the NTEP report.[23]

Model outcome parameters

The outcomes of the model were expressed in terms of the number of cases prevented from progression to TB from LTBI and the overall costs incurred for both the Cy-Tb test and TST. This economic model compared the incremental cost and incremental cases of the Cy-Tb test and TST. The incremental cost effectiveness ratio (ICER) is calculated to compare the effectiveness of the Cy-Tb test. It was calculated as the difference in cost (total cost to test and treat LTBI) divided by the difference in outcome (number of active TB cases prevented).

Willingness to pay (WTP)

The WTP threshold for 2023 is a one-time gross domestic product (GDP) per capita of ₹216 590 (US$2595). The ICER is compared with the threshold to determine whether the Cy-Tb test is a more cost-effective way to diagnose LTBI.[24]

Sensitivity analysis

Using one-way sensitivity analysis (OWSA), the robustness of the model was evaluated by adjusting the input parameters 20% above and below normal values if the probability was >1 and it adjusted to 1. It was also used to determine how changes in input parameters impacted the results of the model. Additionally, factors that impact the ICER more strongly were determined. With the use of a tornado diagram, the uncertainty in the result factors and their impact on the ICER were demonstrated. Probabilistic sensitivity analysis (PSA) was used to validate the model by using 1000 iterations of Monte Carlo simulations with their 95% confidence intervals. We also assessed the feasibility of the two tests qualitatively based on expert opinion.

Cost threshold analysis

The price of the Cy-Tb test was taken from a single company's quotation for the current cost-effectiveness analysis. However, the cost of purchasing the Cy-Tb vials is a significant factor in determining the total cost of LTBI screening, and we did not have a market price. To find the optimum Cy-Tb test price at which it is most cost-effective, we used threshold analysis through OWSA.

Study oversight

This article was reviewed and approved by the manuscript review committee and research integrity committee of the Indian Council of Medical Research–National Institute for Research in Tuberculosis. Since the study used secondary data from the published literature, this study did not require institutional ethics committee approval.

Results

Base case analysis

The base case analysis for the hypothetical cohort of 100 000 showed that the total cost incurred for diagnosing an LTBI case and treating with 6H TPT for preventing the development of active TB disease is ₹215 (US$2.59) million for the Cy-Tb test and ₹206 (US$2.48) million for the TST (Table 2). The distribution of various health system costs for the Cy-Tb test and TST includes the kit cost (₹376 vs ₹169), human resources (₹250), 6H TPT (₹1888),

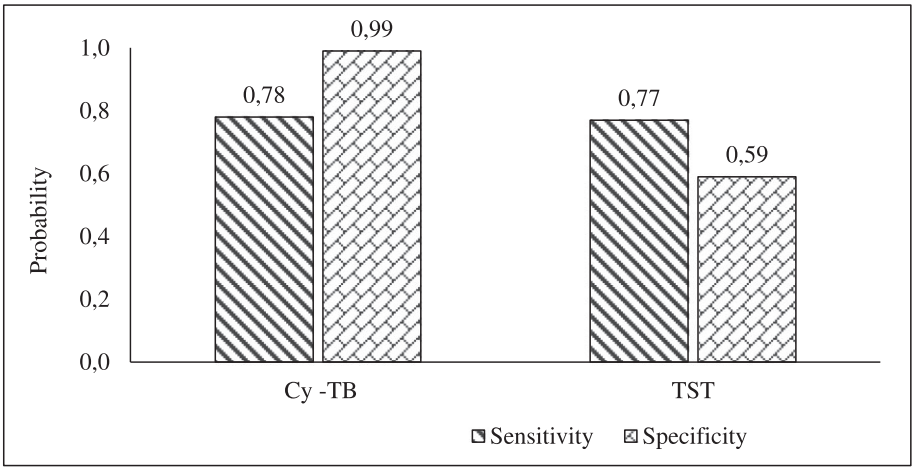

Figure 2. Sensitivity and specificity of the Cy-Tb test and TST for LTBI diagnosis.

minor ADRs (₹2963), major ADRs (₹8361), diagnostic cost of TB (₹1602) and treatment of active TB (₹7903). It was observed that the kit cost is higher for the Cy-Tb test compared with the TST. The human resources cost, 6H TPT cost, ADR cost, diagnostic cost and treatment cost of TB disease are considered the same for both tests. In terms of effectiveness, LTBI diagnosis by the Cy-Tb test followed by 6H TPT yields a higher prevention of TB cases (36 925 vs 36 452) compared with the TST with 6H TPT. The ICER was calculated using the incremental cost and the incremental TB cases prevented by the Cy-Tb test and TST along with 6H TPT. The ICER was ₹8 832 873/473 (₹18 658 [US$224.7]), which indicates that we have to spend an additional ₹18 658 for the Cy-Tb test with 6H TPT compared with the TST.

Diagnostic accuracy

Table 3 gives the diagnostic accuracy of the LTBI Cy-Tb test and TST, including the rates of true positive, false positive, true negative, false negative, sensitivity, specificity, positive predictive value and negative predictive value. The sensitivity and specificity are 0.78 and 0.99, respectively, for the Cy-Tb test and 0.77 and 0.59, respectively, for the TST. It was observed that both the sensitivity and specificity were higher in Cy-Tb test compared with the TST. Similarly, the true positive and true negative rates were found to be higher in the Cy-Tb test (0.99 and 0.80, respectively), while the true positive and true negative rates in the TST were 0.68 and 0.70, respectively. Figure 2 shows the difference in sensitivity and specificity between the Cy-Tb test and TST.

Qualitative analysis

Comparing these two tests qualitatively, the cost, specificity, accuracy, ease of administration, ease of use for patients, turnaround time, loss to follow-up, infrastructure and community implementation level were assessed. In Table 4, the score is given based on expert opinion. The overall score was high for the Cy-Tb test (17) followed by the TST (14).

Table 4. Qualitative analysis of the Cy-Tb test and TST for LTBI diagnosis

Factors	Cy-Tb	TST
Cost	+	+
Accuracy	++	+
Specificity	++	+
Ease of administration	++	++
Ease for patient	+	+
Turnaround time	++	+
Loss-to-follow-up	+	+
Infrastructure	+++	+++
Level of implementation at community	+++	+++
Overall score	17	14

Sensitivity analysis

To understand the uncertainty around the model, OWSA and PSA were performed. The OWSA showed that Cy-Tb negative, TST negative and Cy-Tb kit cost had a greater influence on the ICER value (Figure 3). The PSA highlighted that the joint incremental cost and effectiveness using TB disease prevented were 55% of the iteration values (Figure 4). The CEAC in Figure 5 highlights that diagnosis by a Cy-Tb test with 6H TPT has a 55% chance of being a more cost-effective intervention.

Cost Threshold Analysis

A cost threshold analysis was done to find the optimum price of the Cy-Tb test kit by changing the different costs for the kit. It was estimated that when the cost of the Cy-Tb kit is ₹376, the ICER is 18 658. The threshold analysis showed that when the cost decreases to ₹286, the Cy-Tb test becomes a cost-saving

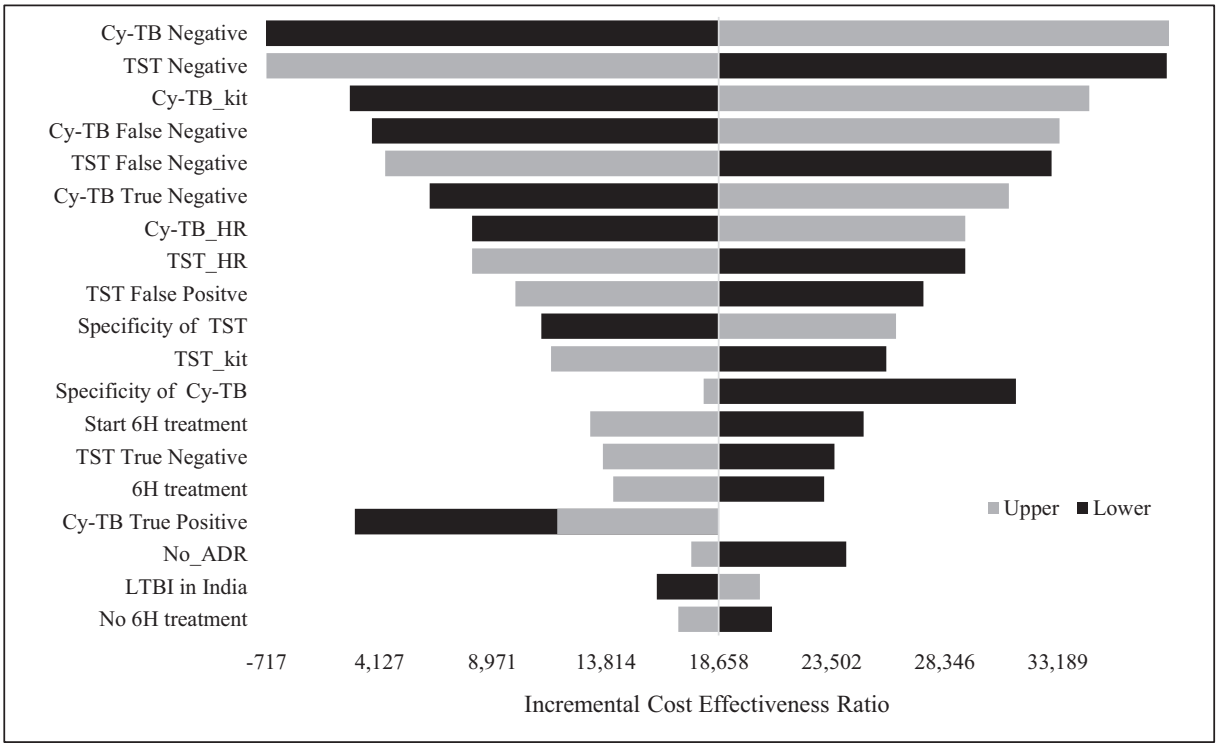

Figure 3. OWSA of different parameters affecting the ICER.

strategy with an ICER of −353. This indicates that if the cost of the Cy-Tb kit can be reduced to ₹286 from ₹376, one can save ₹353 to avoid getting active TB. The cost reduction and the ICER values are illustrated in the cost threshold analysis plane (Figure 6).

Discussion

The Cy-Tb test is an innovative method for diagnosing LTBI. When compared with other tests that are currently used for LTBI diagnosis, it is rapid and precise. The Cy-Tb test uses newer *M. tuberculosis* antigen-based skin tests like ESAT-6 and CFP-10, which combines the specificity of IGRA with a simpler skin test platform. Similar to the TST, the Cy-Tb test measures induration in millimetres and is obtained 48–72 h after intradermal antigen injection. The clinical effectiveness of the Cy-Tb test has been documented by a meta-analysis conducted by the WHO consolidated guidelines.[18] It was documented that the sensitivity, specificity, agreement and safety were considerably higher for the Cy-Tb test when compared with the other available tests.[17] For the first time, the current study provides evidence of other dimensions of cost-effectiveness of the Cy-Tb test for diagnosing LTBI.

Since LTBI patients may eventually develop active TB, a proper diagnosis and effective therapy are essential for the management of LTBI. Due to its ease of use, the TST has been the most widely utilized method for the diagnosis of LTBI. However, it has the drawback of being positive in those who have received the BCG vaccination. The key discovery was that, in terms of correctly classifying individuals with and without LTBI, the Cy-Tb test is more affordable than the TST. The Cy-Tb test is an easy and convenient skin test as compared with other screening tests to diagnose LTBI, utilizing a single, universal cut-off unaffected by BCG vaccination. The Cy-Tb test might become a useful instrument for point-of-care infection detection. The currently available LTBI tests are indirect and measure the immune response following exposure to TB, and these tests require the infected person to have an adequate immune response to obtain a reliable result. An alternate test for diagnosing LTBI in children and adolescents as well as in people living with HIV, with comparable specificity, greater cost-effectiveness and more dependable results, is the Cy-Tb test.[3]

India accounts for 28% of the global TB burden among the South East Asian countries with the highest TB burden. The national prevalence survey, which was conducted in India in 2021, found that 31% of people had LTBI. Between 5% and 10% of LTBI patients are expected to develop clinically active TB illness, and these cases may go on to infect many others.[25] It is commonly known that people with TB infection carry a potential risk of developing active TB. Therefore, the most important aspect of TB elimination is preventing active TB by identifying and treating TB-infected people and breaking the chain of transmission.[26] It was recommended by the *Lancet* Commission that the elimina-

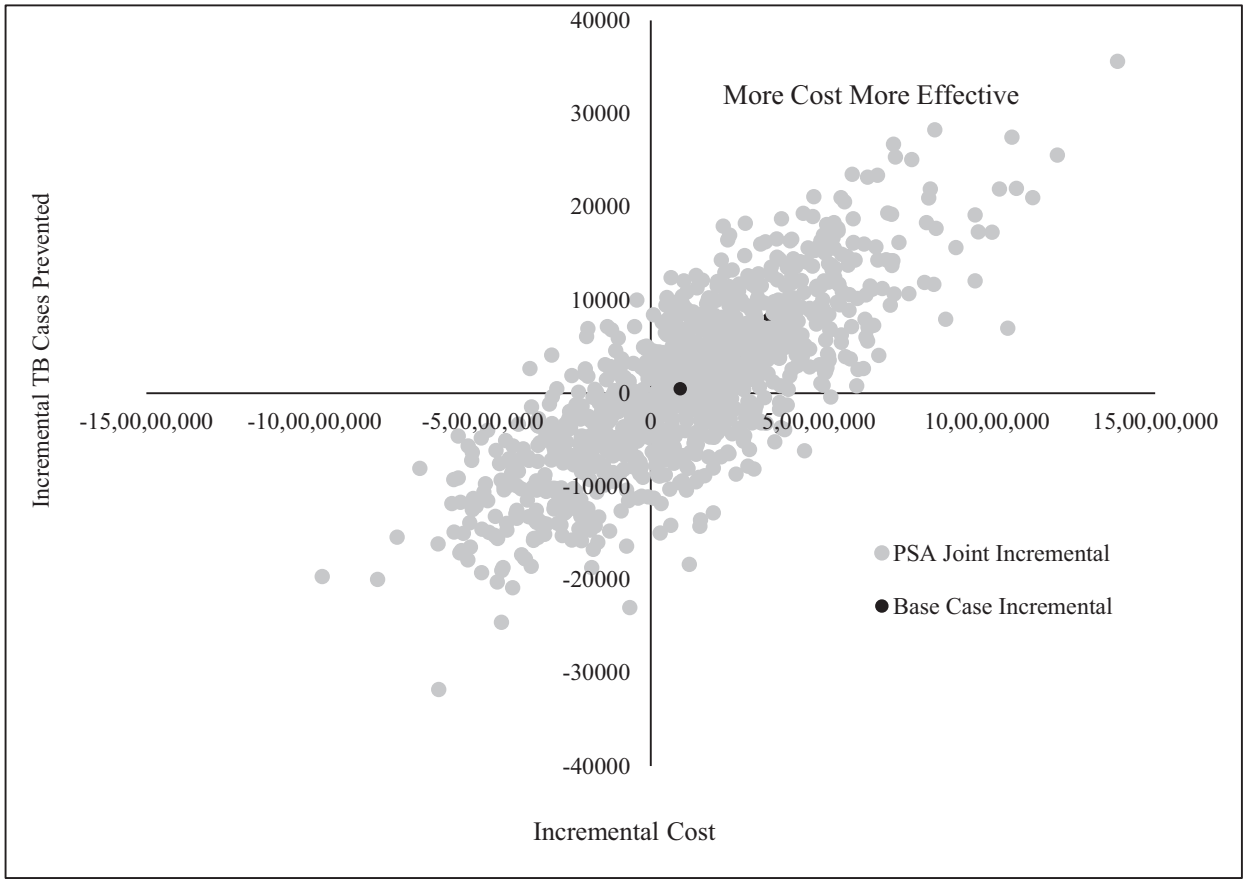

Figure 4. Cost-effectiveness plane (PSA).

tion of TB would be challenging unless TB preventive treatment is included in the strategy.[27] Therefore, it is imperative to put into practice proven interventions such as accurate diagnosis of LTBI (Cy-Tb) and a shorter newer regimen (1HP) targeting key populations. Our study demonstrated that implementation of a novel diagnostic tool, the Cy-Tb test, would be cost-effective in screening household contacts of TB patients for LTBI. Our findings will help to change the policy from a 'no test, treat only approach' to a 'test and treat approach', particularly in TB burden countries like India.

The main purpose of the Cy-Tb test design was to provide a high level of specificity in a field-friendly manner. In the context of high BCG coverage, it enhances the specificity of the TST. This implies that the Cy-Tb test may significantly reduce morbidity and medical costs if it is made widely available. The TST has been the accepted method of testing for LTBI since its introduction in 1908. Later, the IGRA test was developed to address the problems with the BCG vaccine and non-tuberculous mycobacteria infection that were observed with the TST in countries with a high TB burden and low BCG coverage. The Cy-Tb test may be a reliable, practical method for identifying LTBI, which is crucial for the control of TB. At present, the production of PPD used for the TST has been stopped. With the current scenario of high coverage of BCG vaccination in India, there are fewer possibilities to detect false positive cases if the Cy-Tb test is implemented to diagnose LTBI. The accurate detection of true positive cases will result in reduced costs from treating false positive LTBI cases. Our estimates show that at the current price for the Cy-Tb test quoted by the company, the test remains cost-effective. Even though the cost of the Cy-Tb test kit is currently high, it may be lowered with greater procurement volume and through price negotiations, which would improve the savings indicated in the cost threshold analysis.

Limitations

Our model considered the diagnosis of household contacts of TB patients in India for targeted LTBI screening of high-risk population such as diabetics, immunosuppressive patients, malnourished and indigenous population. The other limitation is that our model did not consider the issues related to challenges of implementation. However, there is a need to implement newer diagnostic tools for accurate and early diagnosis to achieve the global 'End TB' targets.

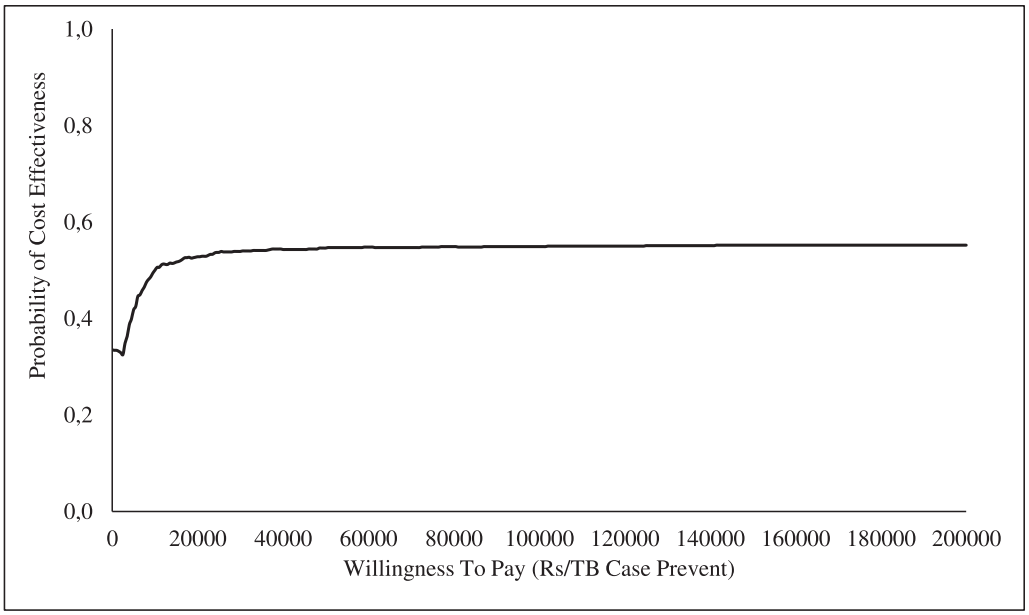

Figure 5. Cost-effectiveness acceptability curve.

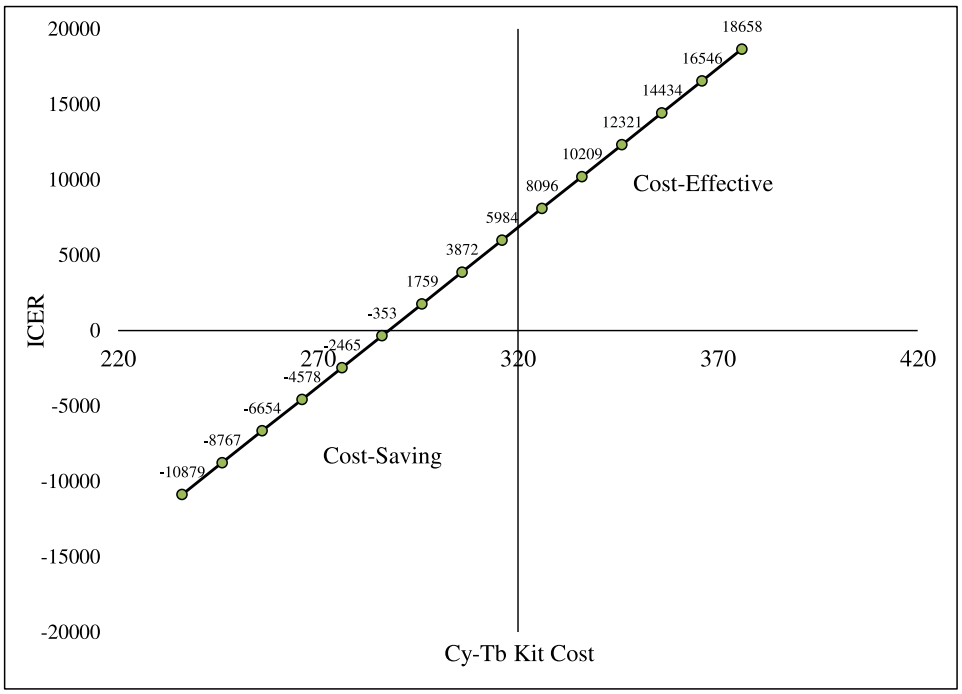

Figure 6. Cost threshold analysis of the Cy-Tb test.

Conclusions

Overall, this study demonstrated that implementing the Cy-Tb test for diagnosing LTBI among the household contacts of TB patients would be a most cost-effective strategy as compared with the TST. It indicates that using the Cy-Tb test in high-risk populations to detect and treat LTBI is a cost-effective intervention. We are re-emphasizing the recommendation of many researchers that the treatment of LTBI is a prerequisite for achieving TB elimination goals. The evidence presented in this study will help point the way towards implementation of a new diagnostic tool

for strengthening the programmatic management of LTBI in India and other high TB burden countries.[28,29] Research alone cannot stimulate the changes, these findings must be translated into sustainable policies and effectively implemented in practice.

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