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Review and cost-effectiveness analysis of rapid tuberculosis screening: Implementing the sputum pooling method in Indonesia

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ABSTRACT

Background: Indonesia continues to face significant challenges in meeting its tuberculosis (TB) case detection targets, partly due to the underutilization of diagnostic resources like Rapid Molecular Tests (RMTs). Innovative, cost-effective strategies are urgently needed to scale up screening efforts.

Objectives: This study aims to review the diagnostic accuracy, cost-effectiveness, and implementation considerations of the pooling sputum strategy to assess its potential for enhancing TB screening in Indonesia.

Materials and methods: This study was conducted using publicly available data from the Indonesian Ministry of Health and findings from existing literature. The projected impact was analyzed by implementing a 4-sample pooling sputum method for RMT (Xpert MTB/RIF Ultra) compared to the current individual testing strategy.

Results: The analysis projects that the pooling sputum strategy could increase RMT screening capacity fourfold. The national average monthly tests per RMT unit could rise from 120 to 480 individuals screened. Consequently, the projected time required to screen 100,000 individuals per province could decrease from an average of 5.5 months to 1.4 months. The strategy offers potential cost savings averaging 36.71% (±14.97%). A review of diagnostic data from previous studies shows high accuracy (sensitivity 97.35%; specificity 99.25%).

Conclusion: The pooling sputum method presents a viable and powerful strategy to significantly enhance the efficiency of TB screening in Indonesia. This approach can substantially increase RMT utilization, accelerate case detection, and reduce costs, thereby helping Indonesia progress towards its 2030 TB elimination targets. A pilot study is recommended to validate these findings within the Indonesian healthcare context.

Introduction

The Indonesian Ministry of Health has set ambitious targets to reduce tuberculosis (TB) incidence and mortality, aiming for a decrease to 65 new cases and 6 deaths per 100,000 people, respectively.[1] To meet these goals, the Ministry has prioritized TB screening as a key strategy. Since 2021, following the Director General of Disease Prevention and Control's Circular Letter (No. HK.02.02/III.I/936/2021), the Rapid Molecular Test (RMT) has become the primary diagnostic tool for TB in Indonesia. Under this directive, individuals suspected of having TB are first examined using the RMT.[2]

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By 2022, Indonesia had deployed 2,167 RMT devices, surpassing the National Strategy for TB Control's target of 2,133 units for 2020-2024. Each RMT unit, when functioning optimally, can conduct up to 200 tests per month. However, despite the increase in the number of devices, the utilization rate of RMTs has not seen a corresponding rise. In 2022, the average utilization rate of these devices was only 60%, equating to just 120 tests per month per unit. Furthermore, in 23 provinces, the RMT utilization rate was below 60%, with some areas reporting as low as 13%. This is significantly below the national target of 80% utilization.[1,3]

The underutilization of RMTs has serious implications. In 2022, 23% of TB suspects, approximately 832,351 individuals, did not undergo laboratory testing. This gap is concerning, especially as the proportion of TB cases diagnosed through RMTs is increasing, reaching at least 12% in 2022.[1]

Transmission of TB remains a critical public health issue. Individuals with active TB can infect 10-15 others annually.[4] Research by McCreesh and White (2018) published in Nature highlights the significant role of household, repeated, and non-repeated contacts in TB transmission.[5] The Indonesian Ministry of Health aims to achieve a 90% TB case detection rate by 2030, aligning with global targets for 2030.[1,2] Given TB's high transmissibility, optimizing RMT usage is crucial for identifying new cases and curbing the disease's spread.

Globally, the World Health Organization (WHO) estimated 10.6 million TB cases in 2021, with 39.7% remaining undiagnosed. In Indonesia, about one-third of TB cases are missed or not reported, often due to delayed, missed, or unattempted diagnoses. The government's current strategy primarily targets symptomatic individuals for testing. However, the 2022 Joint External Monitoring Mission (JEMM) recommended expanding screening to high-risk populations to enhance TB detection.[6]

Financial constraints pose another challenge. Indonesia's national strategy for TB control requires IDR 47.3 trillion for 2020-2024, but only IDR 15.7 trillion is available. Annually, the WHO estimates that Indonesia needs IDR 8.1 trillion for TB prevention, diagnosis, and care, yet it receives only IDR 1.7 trillion in funding. Since 2009, Indonesia has consistently met just 41% of its annual TB program funding needs, hindering efforts to detect new cases.[7,8]

To address this challenge, this study provides a review of pooling sputum and a cost-effectiveness analysis of its potential implementation in Indonesia to provide evidence-based support for health policy decisions.

Materials and methods

Study design and data sources

This study employed a strategic literature review framework. A comprehensive search was conducted across multiple electronic databases, including PubMed, Scopus, and Google Scholar, to identify relevant articles published up to 2024. The search strategy utilized a combination of keywords: ("pooling sputum" OR "pooled testing") AND ("tuberculosis" OR "TB") AND ("Xpert MTB/RIF" OR "Xpert Ultra") AND ("cost-effectiveness" OR "diagnostic accuracy"). Additionally, official reports and technical guidelines from the Indonesian Ministry of Health (2022-2023)[1,3] and the World Health Organization (WHO)[6] were manually searched to gather data on the Indonesian context, RMT utilization, and programmatic costs.

Inclusion and exclusion criteria

Studies were included if they met the following criteria: 1) evaluated the pooling of sputum samples for TB diagnosis, 2) utilized Xpert MTB/RIF or Xpert Ultra assays, 3) reported quantitative data on diagnostic accuracy (sensitivity, specificity), or 4) provided data on cost-effectiveness or cost savings. Only full-text articles published in English were considered. Studies were excluded if they were editorials, case reports without systematic data, or qualitative studies not focused on diagnostic performance or cost.

Data extraction and synthesis

Data from the included studies were extracted into a standardized template. Key information extracted included: author, year, country of study, study design, number of samples, pooling ratio (e.g., 4-to-1), and reported outcomes (sensitivity, specificity, and percentage of cost savings). The data extracted on diagnostic accuracy (Table 1) and cost savings (Table 2, Table 3) were descriptively synthesized and summarized. A qualitative summary of implementation challenges, such as the dilution effect and logistical hurdles, was also compiled from the literature.[9]

Table 1. Diagnostic accuracy data from previous studies on pooling sputum.

References	All Negative		Positive*	
	Detected (%)	Not detected (%)	Detected (%)	Not detected (%)
13	0	77 (100)	32 (100)	0
12	0	16 (100)	19 (95)	1
14	0	6 (100)	95 (96)	4
15	NR	NR	87 (100)	0
10	1	34 (97.1)	61 (95)	3
Total	1	133	294	8
Sensitivity	97.35% (95% CI: 94.85-98.85%)			
Specificity	99.25% (95% CI: 95.91-99.98%)			

Note: *positive: classified by ct<38, NR: not reported

Table 2. Theoretical cost savings of a pooling sputum method for 4 samples in 1 Xpert cartridge using Xpert MTB/RIF Ultra.

Reference	Country	Total of the sample	Individual suspected TBC (%)	Percentage of cost savings	Test sensitivity (%)	Test specificity (%)
18	Nigeria	738	115 (16)	31	NR	NR
10	Brazil	396	95 (24)	12.4	95	97.1
13	Lao	436	199 (45)	46	100%	100%
19	Cameroon	4156	274 (6.6)	48	99.4%	NR
20	Cambodia	584	91 (15,6)	27	NR	NR
17	Lao	3076	NR	35.6	97.6	97
12	Brazil	1280	320 (25)	57	94	100
Cost saving average based on references (%±SD)					36.71±14.97	
Cost saving maximum (%)					57	
Cost saving minimum (%)					12.4	

Note: *NR: not reported.

Table 3. Theoretical cost savings of a pooled testing strategy using 4 pooled samples.[14]

Study setting (disease prevalence)	No. of pooled tests + No. of individual tests required[a]	Cost of pooled testing strategy ($)	Cost savings with pooled testing strategy ($)	Percentage of cost savings (%)
Community (11%)	185+276	4,600.78	2,764.46	59.6
District hospital (26%)	185+520	7,035.90	329.34 (4)	4.7
Total population (16%)	185+372	5,558.86	1,806.38 (25)	32.5

Results

The pooling sputum design method: A technical overview

In the original scheme, TB screening was reserved for individuals suspected of TB by collecting personal sputum for further examination using the RMT instrument. In this innovation, the pooling sputum method is a strategy where sputum samples from multiple individuals are combined into a single tube for a single diagnostic test.[17] This approach is designed to increase testing throughput and reduce costs, particularly for screening high-risk populations.

Figures 1 and 2 represent a schematic of the innovation strategy to accelerate and improve new TB case finding using RMT, specifically for TB risk groups within households. Identity data of known active TB patients are traced to addresses and family members within a household. The most common approach, and the focus of this review, involves pooling samples from four individuals for testing with a single Xpert MTB/RIF Ultra cartridge.[17,10-12] In this scheme, 0.5 mL of sputum from each of four individuals is combined to create a 2 mL pooled sample. This pooled sample is then tested using only one new Xpert cartridge with Xpert MTB/RIF Ultra and processed in the village GeneXpert platform (Figure 1).

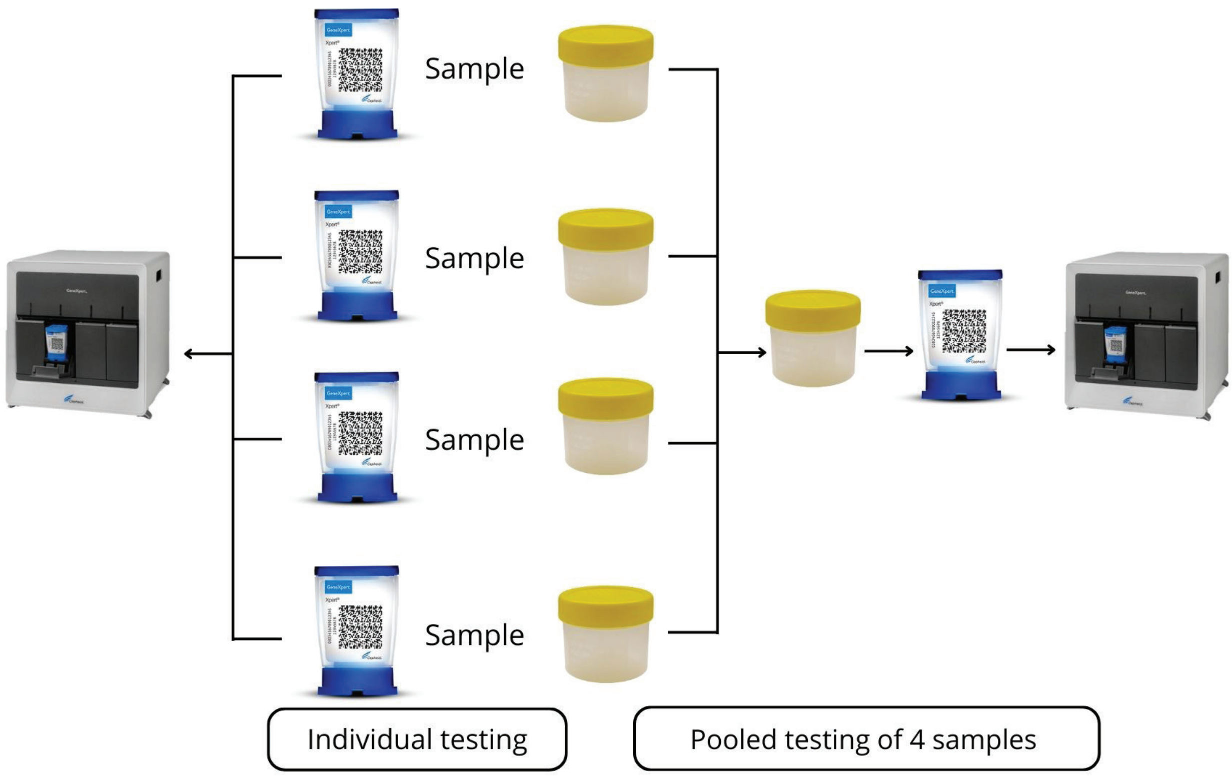

Figure 1. Innovative method of accelerating new TB cases-finding using the pooling sputum method (4 samples for 1 cartridge, a total of 16 samples for 1 test using Xpert MTB/RIF Ultra). *This figure illustrates the implementation of the pooling sputum method, wherein four individual sputum samples are combined into a single pooled sample and tested using one Xpert MTB/RIF Ultra cartridge. The diagram demonstrates how 16 individual sputum samples can be grouped into four pooled tests, thus increasing screening throughput while conserving testing resources. This strategy enhances case-finding efficiency, particularly in high-risk populations, and optimizes utilization of available molecular testing devices.*

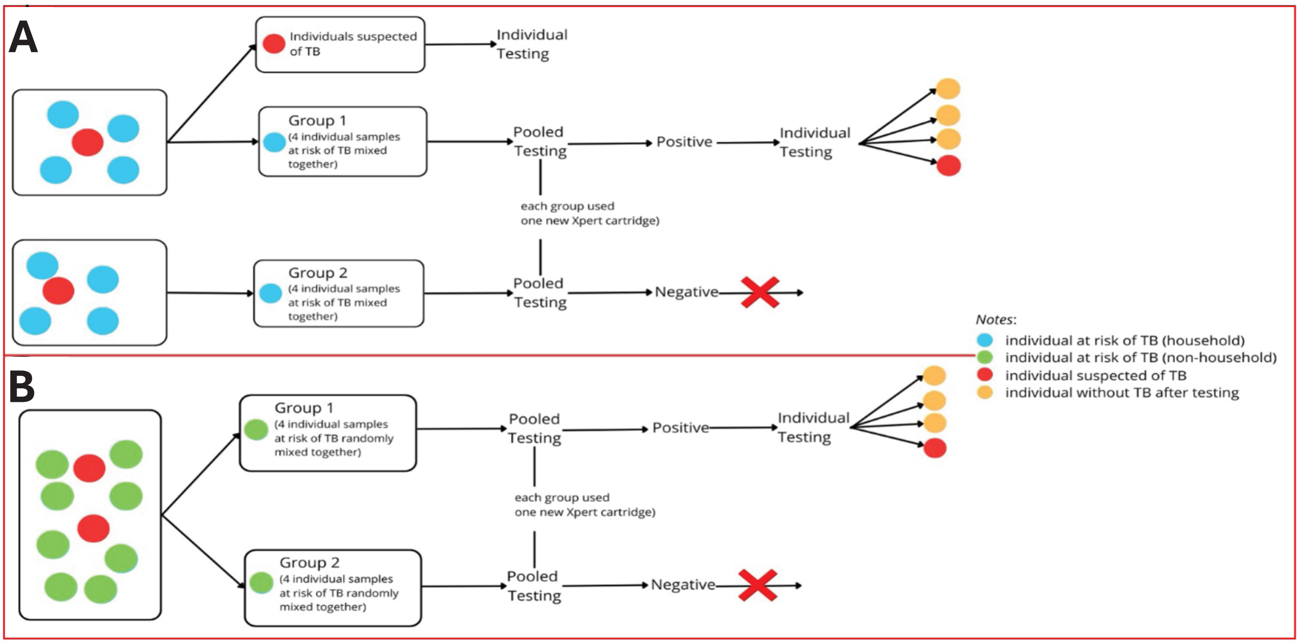

Figure 2. TB elimination strategy using screening of population groups at risk of TB. *The figure depicts the stratification of at-risk populations for tuberculosis screening using a pooling approach. A: household-based screening involves collecting sputum samples from individuals residing in households with a known TB-positive case, B: non-household-based screening targets community members or individuals with frequent contact outside the home, organized into risk groups. In both scenarios, sputum samples from four individuals are pooled for a single Xpert MTB/RIF Ultra test. If a pooled test yields a positive result, follow-up individual testing is conducted to identify the specific TB-positive case, thereby enabling efficient and targeted case detection.*

The workflow typically follows a two-step process (Figure 2). In Part A, two groups of households with TB-positive family members (Red Round) are grouped into two TB-risk population groups (Blue Round). If one of the groups tested TB-negative, it was not continued to individual testing. However, if the group is positive, then proceed to test each individual in the TB-positive group until finding an individual with TB. In Part B, the population at risk of TB (non-household) was randomly grouped into two groups. This approach ensures that resources for individual testing are only used on high-probability groups, which were defined according to WHO requirements. Next, the screening strategy was carried out in the same way as Part A to obtain suspected TB individuals.

Diagnostic accuracy

A primary concern for any screening strategy is its diagnostic accuracy. The pooling sputum method must be able to reliably detect TB without generating an unacceptable number of false negatives or false positives. Based on the literature review, the pooling method, when paired with the high-sensitivity Xpert MTB/RIF Ultra assay, maintains excellent diagnostic performance.

A summary of findings from key studies that met the inclusion criteria is presented in Table 1. Through these studies, which collectively analyzed hundreds of pooled samples, the method demonstrated a high probability of correctly identifying positive cases. The pooled sensitivity was calculated to be 97.35% (95% CI: 94.85-98.85%), with a specificity of 99.25% (95% CI: 95.91-99.98%). This means it correctly detected over 97% of TB-positive individuals within the pools. The specificity was even higher at 99.25% (95% CI: 95.91-99.98%), indicating a very low rate of false-positive results (Table 1).[10,12-15]

Evidence for cost-effectiveness

Beyond accuracy, the primary driver for adopting pooling sputum is its potential for significant cost savings. This is particularly relevant for countries like Indonesia facing funding gaps for their TB programs.[7],[8] Multiple studies conducted in diverse settings have quantified these economic benefits.

Table 2 summarizes cost-saving analyses from studies in Nigeria, Brazil, Lao, Cameroon, and Cambodia. The reported percentage of cost savings varied, ranging from a minimum of 12.4% in a Brazilian study to a maximum of 57%, also in Brazil.[10,12] On average, the implementation of a 4-sample pooling strategy resulted in a cost saving of 36.71% (±14.97%).[17,10,12,13,19,20]

The degree of cost savings is heavily influenced by the underlying prevalence of TB in the screened population, as illustrated in Table 3. In a low-prevalence community setting (11%), the strategy saved nearly 60% of testing costs.[18] However, in a higher-prevalence hospital setting (26%), where more pools test positive and require individual follow-up, the savings were much lower at 4.7%. This indicates that the strategy is most economically advantageous for mass screening in general or high-risk communities rather than in settings where a high positivity rate is already expected.

Projected impact on screening capacity and time in Indonesia

Pooled sputum testing at a suitable ratio using Xpert MTB/RIF Ultra provides a rapid, efficient, and cost-effective method for active TB case finding among high-risk groups in low-incidence and high-incidence areas.[21,10] Implementation of the innovation strategy will affect the total sample size of each province and automatically improve screening capability with a four times larger sample size. Data on the improvement of each province's screening capability is presented in Figure 3. With the previous strategy, Riau Province had a screening capability of 11,040 tests per month and increased to 44,160 tests per month after implementing the innovative strategy.[1,3] Thus, the province with the highest TB prevalence in Indonesia can prevent transmission by increasing the utility of one RMT instrument to the maximum every month.

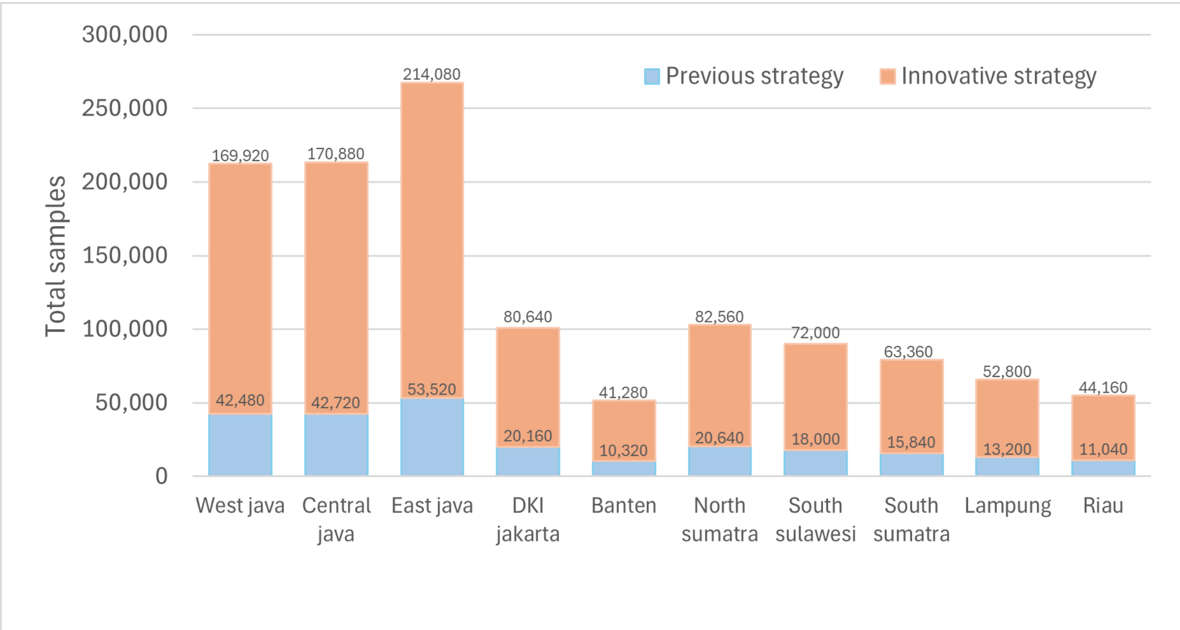

Figure 3. Comparison of the Number of samples potentially screened per one MRT per month between the previous strategy and the innovative strategy. *This figure compares the estimated number of individuals that can be screened per month using one Rapid Molecular Test (RMT) device under two strategies: the previous individual testing strategy versus the innovative pooling sputum method. The pooling approach demonstrates a fourfold increase in screening capacity per RMT unit, highlighting its potential to significantly expand diagnostic coverage in resource-constrained settings with high TB burdens.*

According to the Indonesian Ministry of Health (2022), an RMT instrument can only be used for 120 tests per month, using the previous strategy of screening individuals with suspected TB. With the implementation of the innovative strategy, the screening capacity will increase 4 times to 480 individuals per month.[1,2] Thus, 1 RMT device in good condition can screen 100,000 individuals within 8 months. When broken down further, each province can accelerate testing by 4 times to reach a total number of 100,000 individuals. In Riau Province, the implementation of the previous strategy took 9.1 months, then the innovative strategy can shorten the examination time to 2.3 months for 100,000 samples with 46 RMT devices. [1,3] In fact, the province with the highest TB prevalence in Indonesia was able to complete 100,000 tests in 0.6 months with the implementation of the innovative strategy (Figure 4).

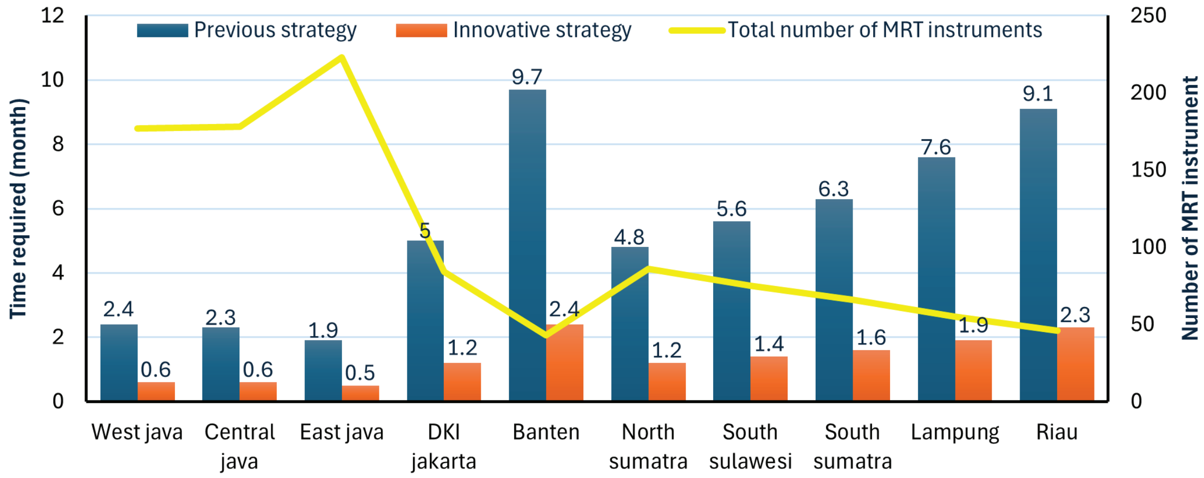

Figure 4. Comparison of the time required for each province based on the number of MRT instruments between the previous strategy and the innovative strategy. *This figure presents a comparative analysis of the time needed to screen 100,000 individuals across various provinces, based on existing RMT device availability. The innovative pooling sputum strategy dramatically reduces the time required for large-scale screening, particularly in high-burden provinces, thus enabling more rapid identification and treatment of active TB cases.*

Projected cost-effectiveness analysis for Indonesia

Based on the Technical Manual for Tuberculosis Testing Using GeneXpert Molecular Rapid Tests, the cost components of RMT testing are calculated based on the number of patients, including the cost of sending test samples to the laboratory and the cost of testing, with a total cost of IDR 50,000.[1,3] With the current screening strategy, the cost of conducting 100,000 tests is assumed to be IDR 5 billion. However, with the implementation of the proposed screening innovation strategy, the cost is IDR 1.25 billion per 100,000 screening tests. In addition, based on the theoretical study (Table 2), Indonesia can save costs with an average estimate of 36.71% by implementing the innovation strategy. If assumed based on the cost-saving average, the cost incurred is 1.84 billion per 100,000 tests.

Discussion

These performance metrics meet the minimum requirements set by the WHO for TB diagnostic tests, which call for at least 80% sensitivity and 97% specificity.[16] Even RT-PCR, the minimum proposed criteria have a sensitivity of 98.5% (95% CI: 97.5-99.5%) and specificity of 70% (95% CI: 65.8-74.2%). In fact, Sorsa and Kaso reported the sensitivity and specificity of GeneXpert to be 72-77% and 99% in smear-negative adults and 98-99% and 99-100% in smear-positive adults, respectively.[22] When compared to the previous 3 references, the pooling sputum method using Xpert MTB/RIF Ultra meets the specificity and sensitivity requirements to be implemented in the community. In fact, the specificity and sensitivity of the pooling sputum method are classified as very strong compared to Ag-RDT and RT-PCR in the COVID-19 case detection strategy.

Potential impact on TB case detection

The findings of this strategic review and analysis strongly suggest that pooling sputum is a transformative strategy for Indonesia's TB control program. By increasing screening capacity fourfold, this approach directly addresses the critical issue of RMT underutilization. This acceleration in case finding is crucial for breaking chains of transmission, as each active TB case can infect 10-15 others annually.

Under-reporting of TB is a major problem, as only 5.8 million individuals of the estimated 10 million individuals who developed TB were reported in 2020, and over 40% were missed by health services.[23] In Indonesia, the number of people suspected of having TB who did not undergo laboratory testing was 23% or 832,351 individuals.[1,2]

As explained in the feasibility and practicality section, the implementation of the innovative strategy can complete 100,000 tests with an average assumed time of 1.4 months per province, with the number of RMT instruments available. Compared to the previous strategy, which took 5.5 months per 100,000 tests per province. Thus, the implementation of the screening strategy using the pooling sputum method can save time by about 74.5%.

With the implementation of innovative strategies, individuals suspected of TB can be quickly identified in diverse and at-risk populations. Individuals found to be positive for TB in this screening method will be quickly treated, so that TB transmission can be suppressed in groups at risk of TB, such as family members, HIV sufferers, and others. By identifying suspected TB individuals, preventive measures can be taken for both suspected TB individuals and their populations.[24] The speed of screening in innovative strategies will increase the percentage of new case finding in Indonesia, which is targeted by 2030. Improvements in RMT screening capabilities and new case finding will negatively correlate with the increase in TB cases in Indonesia.

Implications for health inclusivity and equity

In most low-income countries, direct sputum smear microscopy is the mainstay of TB diagnostics, as this test is inexpensive and highly specific, but it has low to moderate sensitivity. Conversely, sputum culture, in particular, automated liquid culture, is the most sensitive and specific diagnostic tool available for TB and facilitates drug susceptibility testing. However, culture requires a laboratory infrastructure, including biosafety equipment, not widely available in low-resource settings, and results typically take 2 to 6 weeks and, therefore, are rarely helpful for initial treatment decisions.[9] If sputum smear microscopy and culture are maintained to achieve 90% case finding in low-income countries, the speed of TB transmission will defeat this ambition. Therefore, the proposed innovation strategy that is fast and cheap can be a solution for low-income countries.

As this innovation strategy emphasizes screening using a pooling sputum method more quickly and economically, all levels of society have equal opportunity and a greater chance of detection. The innovation strategy can still be applied to both high and low prevalence population groups. There was no significant difference in the results of the two groups (Table 3).

In populations with the least number of devices, for example, North Kalimantan Province, which only has 14 devices, and Bengkulu, which has the lowest RMT utility, this innovation strategy can improve device performance 4 times faster and the number of tests 4 times more. A simulation of the improvement in time and number of tests in implementing the innovative strategy can be seen in Figures 3 and 4. Thus, equitable health services at every level of society can be achieved.

Limitations

The authors acknowledge several limitations. First, as this analysis relies on projections from secondary data, the actual operational performance may vary. Second, the cost-saving and diagnostic accuracy data were derived from studies conducted in other countries and require validation through a pilot study within the Indonesian healthcare system. Third, the analysis does not quantify the potential for reduced sensitivity due to sample dilution (the "dilution effect")[9], especially in cases with low bacterial loads. Finally, the logistical complexity of implementation, including staff training and sample tracking, presents an operational hurdle that requires careful planning.

Conclusion

This strategic review and cost-effectiveness analysis demonstrates that the implementation of a pooling sputum strategy holds substantial potential to overcome critical barriers in Indonesia's TB control program. Based on strong evidence from international literature, the method is highly accurate and cost-effective, particularly in lower-prevalence settings. The projected fourfold increase in screening capacity, significant time reduction for mass screening, and considerable cost savings present a compelling case for its adoption. For Indonesia, a country struggling with RMT underutilization and a significant TB burden, these findings are highly relevant. While logistical challenges must be addressed, the evidence strongly supports the consideration and piloting of pooling sputum as a core component of Indonesia's national TB control strategy. To translate these promising projections into practice, we strongly recommend conducting a pilot study in diverse Indonesian settings to validate the findings and assess operational feasibility for a national scale-up. Adoption of this innovative approach could be a pivotal step in accelerating Indonesia's progress toward its 2030 TB elimination goals.

Ethical approval

This article is an analysis based on publicly available data and did not involve the collection of primary data from human participants or animals. Therefore, ethical approval was not required.

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Conflict of interest

The authors declare no conflicts of interest related to the content of this manuscript.

CRediT authorship contribution statement

Febri Sembiring: conceptualization, methodology, formal analysis, writing: original draft; **Hafizah Ilmi Sufa**: data curation, visualization; **Yuli Yantika Syahputri** and **Wardati Humaira**: validation, writing: original draft.

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