REVIEW ARTICLE

Impact of Drug-Resistant Tuberculosis on Time of Sputum Conversion and Recovery Criteria in indonesia: A Systematic Literature Review

Lyndia Effendy[1,2], Ni Made Mertaniasih[3,4], Soedarsono Soedarsono[5,6], Citrawati Dyah Kencono Wungu[4,7]

[1] Doctoral Program, Faculty of Medicine, Universitas Airlangga Surabaya, Indonesia
[2] School of Medicine, Universitas Ciputra Surabaya, Indonesia
[3] Department of Medical Microbiology Faculty of Medicine, Universitas Airlangga Surabaya, Indonesia
[4] Institute of Tropical Disease Universitas Airlangga Surabaya, Indonesia
[5] Sub-Pulmonology Department of Internal Medicine, Faculty of Medicine, Universitas Hang Tuah Surabaya, Indonesia
[6] Department of Pulmonology, Dr. Soetomo Academic General Hospital, Surabaya, Indonesia
[7] Department of Medical Biochemistry Faculty of Medicine, Universitas Airlangga Surabaya, Indonesia

ABSTRACT

Background: Multidrug-resistant tuberculosis remains a critical public health crisis in low- and middle-income countries. In Indonesia and similar settings, defining true recovery extends beyond treatment completion, necessitating robust, patient-centered benchmarks. Sputum culture conversion is a pivotal early indicator of treatment response. **Objective:** This systematic review synthesizes evidence on the time of sputum culture conversion and treatment success criteria for pulmonary MDR-TB in Indonesia and comparable LMICs. **Methods:** Adhering to PRISMA 2020 guidelines, we conducted a comprehensive search of PubMed, Scopus, and Web of Science (2015–2025). Observational studies and trials reporting TSC and recovery outcomes were included. Twenty six studies underwent qualitative and quantitative synthesis. **Results:** Our analysis uncovered dramatic regimen-dependent variability in time of sputum culture conversion. Conventional therapies across low- and middle-income countries showed a prolonged median time of sputum culture conversion of 59–91 days, with success rates frequently below 75%. Strikingly, Indonesia's novel BPaL regimen (Bedaquiline, Pretomanid, Linezolid) achieved a radically faster median TSC of just 32 days and a 97.6% success rate. Key barriers to recovery included cavitary disease, HIV co-infection, malnutrition, and extensive drug resistance. Critically, high loss to follow-up rates emerged as a dominant driver of treatment failure. **Conclusion:** The BPaL regimen represents a paradigm shift in MDR-TB management. However, this breakthrough alone is insufficient. Achieving durable recovery demands an integrated, patient-centric strategy that couples advanced therapy with aggressive comorbidity management, nutritional support, and reinforced patient support systems to combat loss to follow up incidence.

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Keywords: Multidrug-Resistant Tuberculosis; Time of Sputum Conversion; Treatment Outcome; Low- and Middle-Income Countries; Indonesia

Corresponding Author:
Prof., Dr. Ni Made Mertaniasih dr., M.S., Sp.MK(K)
Email: ni-made-m@fk.unair.ac.id
Tel : +62 813-3051-1063

INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB), an infectious pulmonary disease caused by Mycobacterium tuberculosis resistant to at least isoniazid and rifampicin, represents an escalating global public health crisis (1). This burden is disproportionately borne by low- and middle-income countries (LMICs), with Indonesia standing as a significant contributor to the global case load (2,3). The cumulative prevalence of MDR-TB in Indonesia is substantial, with national surveys estimating that 2.4% of new TB cases and 13% of previously treated cases are multidrug-resistant, affecting a wide range of the age demographic and posing a severe threat to all segments of the population (1,4).

The management of tuberculosis is complicated by the bacterium's unique pathophysiology. Despite the existence of standardized 6-9 month regimen therapeutic drugs for drug-susceptible TB, the characteristics of M. tuberculosis, including its slow growth, ability to enter a dormant state, and capacity to evade intracellular host mechanisms, create a high risk of disease recurrence (5). This, coupled with treatment non-adherence and other factors, can trigger the emergence of drug resistance, making subsequent cases more difficult and costly to treat (6).

A critical challenge in clinical practice is that MDR-TB and drug-susceptible TB share nearly identical clinical and radiological presentations. This symptomatic overlap makes it impossible to distinguish between them based on signs, symptoms, or chest imaging alone (7). Consequently, accurate diagnosis is wholly dependent on advanced microbiological confirmation, specifically phenotypic culture-based drug susceptibility testing (DST) and genotypic molecular methods such as GeneXpert MTB/RIF or line probe assays (LPA) (8).

So far, the commonest form is pulmonary MDR-TB, which remains the primary driver of transmission. The treatment for pulmonary MDR-TB involves prolonged, toxic regimens lasting 9-18 months, making the monitoring of treatment efficacy paramount (7). However, a significant ambiguity exists in defining successful recovery. Is it solely defined by completing the regimen of antimycobacterial therapy, or are there more robust, patient-centered microbiological benchmarks (9)?

This systematic literature review, therefore, seeks to synthesize existing evidence to unify the criteria of recovery for pulmonary MDR-TB. It will specifically investigate two critical outcome measures: first, the time to sputum culture conversion (a key early indicator of treatment response), and second, the ultimate definition of treatment success itself. By analyzing and comparing data from Indonesia and other LMICs, this study aims to provide a clearer, evidence-based framework for defining recovery, which is essential for standardizing clinical care, improving patient outcomes, and strengthening public health interventions against MDR-TB.

METHODS

Search Strategy and Selection Criteria

A systematic literature review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The objective was to identify studies comparing the time to sputum culture conversion and recovery criteria between patients with drug-resistant tuberculosis (DR-TB) and drug-susceptible tuberculosis (DS-TB) in Indonesia and other low- and middle-income countries (LMICs).

A comprehensive electronic search was performed across three major bibliographic databases: PubMed, Scopus, and Web of Science. The search strategy was designed to capture all relevant studies published from the inception of each database from 2015 up to 2025.

The search strategy utilized a combination of Medical Subject Headings (MeSH) terms and keywords related to the core concepts of the review: Population: Patients with multidrug-resistant tuberculosis (MDR-TB) or drug-resistant tuberculosis, Intervention/Exposure: Diagnosis of drug resistance, Outcome: Sputum culture conversion time and treatment outcomes.

The following search string was developed for PubMed and adapted for the syntax of the other databases: Search Strategy using keyword " Time of sputum conversion in MDR Tuberculosis"

Study Selection and Eligibility Criteria

All identified records were imported into a reference management software, Mendeley where 242 duplicate records were automatically and manually identified and removed.

The remaining 350 unique records were screened by two independent reviewers based on their titles and abstracts. Studies were included if they met the following criteria: Population: Human subjects with confirmed pulmonary MDR-TB or DR-TB, Comparator: Patients with drug-susceptible TB (DS-TB), Outcome: Reported the primary outcome of time to sputum culture conversion and/or secondary outcomes related to recovery or treatment success criteria, Setting: Conducted in Indonesia or other LMICs (as defined by the World Bank classification), Study Design: Observational cohort studies (prospective or retrospective) or clinical trials.

A total of 274 records that did not meet these criteria were excluded. The full text of the remaining 76 articles was retrieved and assessed in detail for eligibility by the two independent reviewers. Any disagreements were resolved through discussion or by a third reviewer.

At the full-text screening stage, 50 articles were excluded for the following specific reasons:18 did not include a direct comparison between DR-TB and DS-TB groups,15 did not report the outcome of interest (time to sputum conversion), 10 were not conducted in low-and middle-income countries, 5 focused on extrapulmonary TB populations, 2 were not primary research articles (e.g., were reviews, editorials, or commentaries).

Finally, 26 studies were found to satisfy all eligibility criteria and were included in the qualitative synthesis and quantitative meta-analysis. The study selection process is summarized in the PRISMA flow diagram (Figure 1).

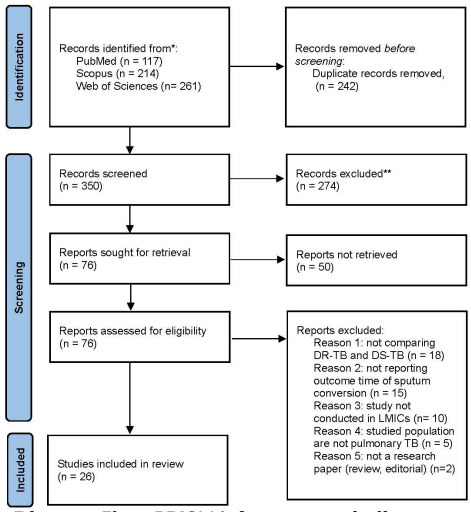

Figure 1: Diagram Flow PRISMA for systematic literature review of Impact of MDR Tuberculosis on Time of Sputum Conversion and Recovery Criteria in Low-and-Middle-Income Countries including Indonesia

RESULTS

Study Selection

The systematic search across PubMed, Scopus, and Web of Science yielded 592 records. After the removal of 242 duplicates, 350 unique records were screened by title and abstract. Following a detailed assessment of 76 full-text articles, 26 studies met the eligibility criteria and were included in the final analysis. The detailed selection process is illustrated in the PRISMA flow diagram (Figure 1). The results of analysis data of 26 studies included in systematic literature review can be seen in Table I.

Study Characteristics

The analyzed studies encompass a diverse range of study designs and geographical contexts focused on drug-resistant tuberculosis (DR-TB). The majority were retrospective cohort studies (n=14), supplemented by prospective cohorts (n=5), systematic reviews/meta-analyses (n=1), observational cohorts (n=5), and a cross-sectional study (n=1). Sample sizes varied widely, from 52 to 662 participants. The studies were conducted across multiple low- and middle-income countries (LMICs) with high TB burdens, including Ethiopia (n=6), Indonesia (n=4), Pakistan (n=4), India, Guinea, Vietnam, China, South Africa, and South Korea. For comparison, data from Germany and a multi-country systematic review were also included. The populations studied were primarily patients with rifampicin-resistant (RR-TB), multidrug-resistant (MDR-TB), pre-extensively drug-resistant (pre-XDR-TB), or extensively drug-resistant TB (XDR-TB).

Time to Sputum Culture Conversion

The time to sputum culture conversion (TSC), a critical early indicator of treatment efficacy, exhibited profound heterogeneity across low- and middle-income countries (LMICs), heavily dictated by the therapeutic regimens employed. This review uncovered a stark contrast between the performance of conventional therapies and that of novel, optimized regimens.

Analysis of data from Indonesia revealed a regimen-dependent evolution in treatment response. Older, protracted regimens (18-20 months) were associated with modest success rates of 50-56.6%, though they often failed to explicitly report median TSC, hinting at a historical focus on mere completion over rapid microbiological response. A shift to shorter regimens (9-11 months) provided further insight, yet still highlighted challenges, with one study reporting a median time to unsuccessful treatment outcome of 367 days. The most transformative data emerged from a recent prospective cohort study on the BPaL regimen (Bedaquiline, Pretomanid, and Linezolid), which demonstrated a paradigm-shifting median TSC of just 32 days (IQR: 30–56), achieving a 100% conversion rate by the third month. This represents a quantum leap in treatment kinetics.

In stark contrast, the median TSC across other LMICs utilizing conventional regimens was consistently and considerably longer. Studies from Ethiopia reported a range of 61 to 80 days, while Pakistan and China documented a mean of 2.34 months (~71 days) and a median of 85 days, respectively. Data from India showed a median TSC of 91.3 days, and Guinea reported 59 days. Vietnam's results, framed as conversion rates, showed 75% of patients converting by 2 months and 92.4% by 4 months. Even in South Africa, where shorter regimens were noted to be faster, the median TSC ranged from 29 to 59 days, with only 53% of MDR-TB patients converting before 60 days.

The introduction of the BPaL regimen in Indonesia thus signifies a dramatic and clinically monumental reduction in the time to sputum conversion. The median of 32 days stands in powerful contrast to the protracted timelines—ranging from approximately 59 to 91 days—observed with older regimens in Indonesia and with conventional therapies throughout other LMICs. This disparity underscores a new era in MDR-TB management, where therapeutic innovation can drastically accelerate the path to microbiological recovery.

Recovery and Treatment Success Criteria

Treatment success, as defined by World Health Organization (WHO) criteria, integrates both cure, sustained culture-negative status in the latter stages of therapy and treatment completion, finishing the prescribed regimen in the absence of confirmed cure or failure. However, this systematic review uncovered profound disparities in success rates, delineating a clear hierarchy dictated by therapeutic efficacy and

Table I: Analysis data of Systematic Literature Review

First Author (Year)	Country/ Region	Study Design	Age (yrs)	Sample Size	Population Characteristics	TB Resistance (MDR/XDR/DS)	Outcome: Time to Sputum Conversion (and other recovery criteria)	Determinants of Prolonged Conversion / Recovery
Wenlu et al., (2024)	Multi-country	Systematic Review/Meta-analysis	Varies (Mean/ Median 18-45)	Varies	DR-TB, MDR/RR, XDR, pre-XDR, all ages	DR-TB, MDR-TB, XDR-TB, pre-XDR-TB, RR-TB, DS-TB	Median range: 53–125 days (IQR varies by country). Conversion rate up to 91%	High smear grade, cavitary lesions, HIV, low BMI, alcohol
Tekalegn Y (2020)	Ethiopia	Retrospective cohort	Median 28	228	All DR-TB	DR-TB	Median 61 days (IQR 34–92)	Not specified in summary
Velayutham B (2016)	India	Retrospective cohort	Not reported	787	MDR-/RR-TB	MDR/RR-TB	Median 91.3 days (IQR 91.3–121.7); 83% conversion	Not specified
Diallo A (2020)	Guinea	Retrospective cohort	Median 34	118	RR-TB	RR-TB	Median 59 days (IQR 31–61); 89% conversion	Not specified
Reimann M (2019)	Germany	Retrospective cohort	Non-smoker: 36.5/ Smoker: 37.4	65	MDR-TB/XDR-TB	MDR-TB, XDR-TB	Non-smoker: 53d (19–89), Smoker: 60.7d (33.3–76)	Smoking associated with longer conversion
Shibabaw A (2018)	Ethiopia	Retrospective cohort	Mean 30	235	MDR/RR-TB	MDR/RR-TB	Median 72 days (IQR 44–123); 85.5% conversion	HIV, low BMI (underweight), high smear grade, Rx regimen
Muluye Abebe (2024)	Ethiopia	Retrospective cohort	Median 30	120	MDR-TB, males 57.5%	MDR-TB	Median 80 days (IQR 60–90); 89.2% converted	HIV comorbidity, weight loss, history PTB, smear positivity
Akalu T.Y. (2018)	Ethiopia (Amhara)	Retrospective cohort	Median Age 29,5 year (IQR (20± 40 years)	392	MDR-TB	MDR-TB	Median 65 days (IQR 60–70); 86.7% converted	Alcohol, high sputum grade, cavitations, consolidation
Putri F.A. (2014)	Indonesia	Observational cohort	Mean age 37 year	212	MDR-TB	MDR-TB	Not clearly stated; focus on probability of conversion within 4 mo	Underweight (BMI <16), female, resistance to injectables
Soeroto (2021)	West Jawa, Indonesia	Retrospective Cohort	Age ≤45 year	492	MDR-TB patients on longer regimens (18-20 months)	MDR-TB	- Median TSC: Not explicitly stated for this cohort. - Success Rate: 50% (combined cure/ treatment completion).	Factors for Success: Culture conversion ≤2 months (RR 2.79), Age ≤45, Male, Normal BMI, No previous TB treatment, AFB smear ≤+1. Risk for Failure: HIV (RR 0.14), Chronic Kidney Disease, Cavitary lesions.
Indarti (2022)	East Jawa, Indonesia	Retrospective Cohort	Age≥18 year	99	MDR-TB patients on Shorter (STR) vs. Bedaquiline (BDQ) regimens	MDR-TB	- Success Rate: 41.4% overall; 52.9% (BDQ) vs. 35.4% (STR). - Smear conversion at 1-3 months: 58.3% (BDQ) vs. 52.2% (STR).	Factors for Success: Negative smear status (RR 0.503), Negative culture status (RR 0.434). Main Outcome Driver: High loss to follow-up (LTFU) rate (42.4%), especially in the STR group (49.2%), was the primary barrier to success.
Burhan (2025)	Indonesia (Multisite)	Prospective cohort (OR)	Age ≥18 year	84 (evaluation)	Pre-XDR or MDR-TB patients intolerant/ to previous treatment failure on BPaL regimen	Pre-XDR (52.4%) & MDR	- Median TSC: 32 days (IQR: 30–56). - 100% conversion by 3 months. - Success Rate: 97.6% (BPaL regimen).	No significant determinants of conversion time were found for sex, age, resistance type, comorbidity, BMI, or cavitary lesions. The BPaL regimen was highly effective across all patient groups. Unfavorable outcomes were attributed to poorly managed comorbidities (sepsis, poorly managed HIV).
Hadayna (2025)	Jakarta, Indonesia	Retrospective Cohort	Aged ≥15 year	166	MDR-TB patients on a short-term regimen (9-11 months)	MDR-TB	- Median time to Unfavourable Treatment Outcome: 367 days. - Success Rate: 56.6%. - Unfavoruable Treatment Outcome Rate: 43.4% (Failure 22.9%, LTFU 12%, Death 8.4%).	Significant Predictors of Unfavourable Treatment Outcome: HIV-positive status (aHR = 2.98), Diabetes Mellitus comorbidity (aHR = 1.92). Age, gender, treatment history, and treatment delay were not significant in the multivariate model.

CONTINUE

Table I: Analysis data of Systematic Literature Review (CONT.)

First Author (Year)	Country/ Region	Study Design	Age (yrs)	Sample Size	Population Characteristics	TB Resistance (MDR/XDR/ DS)	Outcome: Time to Sputum Conversion (and other recovery criteria)	Determinants of Prolonged Conversion / Recovery
Wrohan et al. (2022)	Vietnam (Hanoi & Thanh Hoa)	Retrospective cohort study	43 (32-55)	662 (612 included in outcome analysis)	- 76.4% Male - 82.7% with previous TB treatment - 7.0% HIV+ - 72.7% with Social Health Insurance - Most common comorbidity: Respiratory disorders (11.8%) & Diabetes (11.4%) - 96.4% Pulmonary TB	- RR/MDR-TB: 88.0% (n=388) - pre-XDR-TB: 8.2% (n=36) - XDR-TB: 3.8% (n=17) Based on available DST for 441 pts	- Smear conversion: 2-mo: 85.8% (503/586) 4-mo: 96.6% (519/537) - Culture conversion: 2-mo: 75.0% (415/553) 4-mo: 92.4% (488/528) - Treatment Success: 65.5% (401/612)	Factors associated with LOWER odds of treatment success (aOR): Male gender (aOR 0.56, 95% CI 0.34–0.90) HIV co-infection (aOR 0.44, 95% CI 0.20–1.00) pre-XDR or XDR-TB (vs RR/MDR-TB) (aOR 0.53, 95% CI 0.29–0.97) Factors associated with HIGHER odds of treatment success (aOR): Culture conversion by 4 months (aOR 2.93, 95% CI 1.33–6.45) *Social Health Insurance was associated with lower odds of loss to follow-up (aOR 0.55, 95% CI 0.32–0.95).*
Khan (2022)	Pakistan	Retrospective cohort	Mean ± SD) age was 36.75 ± 15.69 years.	277	DR-TB patients at a national referral center (2014-2019)	MDR/RR (95.67%), XDR (1.44%), Mono/ Poly (4.33%)	- Success Rate: 63.9% (Cured 55.2%, Completed 8.7%). - Unsuccessful Rate: 36.1% (Death 21.7%, LTFU 11.5%, Failure 2.9%). - TSC: Not reported.	Significant Predictors of Unsuccessful Outcome: Male gender (AOR: 1.92), Age >60 years (AOR: 3.34), Presence of any comorbidity (AOR: 2.69), History of second-line drug use/resistance prior to MDR-TB diagnosis (AOR: 3.51). High baseline fluoroquinolone resistance (22%) was noted.
Sajjad Ali (2025)	Pakistan	Cohort comparative	Age > 36 year	138	DR-TB, smokers vs non-smokers	MDR-TB/DR-TB	Not explicit, but >66% conversion for non-/light smokers	Urban living, high cigarette #, cavities, high smear grade
Zafar Iqbal (2022)	Pakistan	Cross-sectional	Age > 45 year	252	MDR-TB	MDR-TB	76.6% converted by 6 months	Not specified
Li Q (2020)	China (Hangzhou)	Observational	Mean 41.7	384	MDR-TB	MDR-TB	Median 85 days (IQR 40-112); 93.5% conversion	Age, gender, previous TB, HIV, baseline positivity
Ncha R (2019)	South Africa	Observational cohort	Median 38 year	230 MDR, 32 XDR	MDR/XDR-TB	MDR/XDR-TB	53% MDR converted <60 days, 41% XDR in 61–180 days	Underweight, AFB+ admission, XDR-TB, older age prolong
Meshesha MD (2022)	Ethiopia	Cohort	Mean 29,6 year	146	MDR/RR-TB	MDR/RR-TB	Oromia: median 61 days, Amhara: 65 days	Cavitary disease predicts longer time
Diktanas S (2021)	Lithuania	Cohort	Mean Age 47,9 year	115	RR-TB	RR-TB	Median 1.1 months (0.9–1.8)	Age ≥60, smoking, positive smear, cavities, FQ resistance
Park HO (2016)	South Korea	Observational	Median 41 year	176	MDR-TB	MDR-TB	Median 3 months (IQR 2–3.5)	Poor nutritional status, low BMI
Wahid A (2025)	Pakistan	Retrospective cohort	Mean 32.4	462	MDR-TB	MDR-TB	Mean 2.34 ± 1.58 months; 91.8% conversion	Cure linked to conversion speed
Hosu MC (2025)	South Africa	Retrospective cohort	mean age 37.8 (±14.8) years	Not stated	DR-TB, high HIV-burden	DR-TB	Median 29–59 days; 88% converted	Short-regimen faster, HIV, baseline BMI, comorbidities
Chiang CY (2024)	Multi-country	Cohort (STREAM trial cohort)	Age≥18 year	689	RR/MDR-TB on short/ standard regimens	RR/MDR-TB/ DS-TB	Cavitation increases time; variable per regimen	Cavitary radiography, high smear
Kim J (2016)	South Korea	Observational	Median 41 (MDR/XDR)	52 OD-R, 35 MDR/XDR	All TB, MDR/XDR, OD-R, DS-TB	DS-TB, OD-R, MDR/XDR-TB	Mean time longer in MDR/XDR; catchup by 8–12 wks	Drug-resistance, previous TB history, AFB+

programmatic strength.

The pinnacle of success was demonstrated by novel, highly effective regimens. Most notably, the BPaL regimen achieved an exceptional success rate of 97.6% in an Indonesian cohort, setting a new benchmark for MDR-TB management and affirming the potential for outcomes that rival those of drug-susceptible TB. In contrast, studies employing standard or shorter conventional regimens reported moderate success rates clustered between 60% and 75%, as evidenced by outcomes in Vietnam (65.5%) and Pakistan (63.9%). A similar Indonesian study on a short-term regimen reported a success rate of 56.6%, underscoring the limitations of these therapies.

Most alarmingly, this synthesis identified cohorts experiencing profoundly low success rates of approximately 50% or less. These outcomes were prevalent in settings utilizing older, longer regimens and, most critically, in contexts plagued by catastrophic system-level failures. In one stark example, an extremely high loss to follow-up (LTFU) rate of 42.4% catastrophically eroded the overall success rate to 41.4%, demonstrating that even adequate chemotherapy is futile if patients are not retained in care. Consequently, this review identifies high LTFU not merely as a contributing factor but as the predominant barrier to recovery in LMIC settings, effectively undermining both microbiological advances and clinical efforts to achieve WHO-defined treatment success.

Determinants of Prolonged Sputum Conversion and Recovery

The determinants of prolonged conversion and unsuccessful treatment outcomes were consistent across many studies and can be categorized as in table 2 as follows.

The Indonesian context exemplifies the evolving narrative of DR-TB management; while the recent Burhan (2025) study on the highly effective BPaL regimen found no significant determinants for prolonged conversion, underscoring its efficacy across diverse patient profiles, studies on older regimens confirmed that patients faced a significantly prolonged time to sputum culture conversion shaped by traditional risk factors consistent across LMICs. These multifactorial determinants, encompassing high bacterial load (cavities, high smear grade), poor host status (low BMI, HIV, as highlighted by Putri et al.), and behavioral factors, prolong infectiousness and increase the risk of adverse outcomes, a challenge that aligns Indonesia's experience with the broader LMIC profile.

DISCUSSIONS

This systematic review provides a critical comparative analysis of the time to sputum culture conversion (TSC) and recovery criteria for multidrug-resistant tuberculosis (MDR-TB) in Indonesia and other low- and middle-income countries (LMICs). The findings reveal both stark contrasts and shared challenges, painting a complex picture of MDR-TB management across these settings.

The results demonstrate that recovery criteria and TSC are not uniform across Indonesia and other LMICs; they are profoundly influenced by the treatment regimen available. In Indonesia, the landscape is dichotomous. Studies utilizing older, conventional regimens (18-20 months) reported prolonged TSC and alarmingly low success rates of 41.4% to 56.6%, driven predominantly by catastrophic loss to follow-up (LTFU) reaching 42.4%. This highlights a system struggling with retention and adherence. In stark contrast, a recent Indonesian study on the novel BPaL regimen reported a paradigm-shifting median TSC of just 32 days and a phenomenal success rate of 97.6%. This places Indonesia at the forefront of MDR-TB management, demonstrating that outcomes can surpass those of many other LMICs when cutting-edge therapy is deployed effectively. Conversely, other LMICs, such as Ethiopia, India, Pakistan, and China, consistently reported a prolonged median TSC ranging from 59 to 91 days with conventional therapies, with success rates often clustered between 60-75%. This indicates that the struggle with delayed conversion and modest success rates using older drugs is a shared burden across the LMIC landscape.

A pivotal aspect that dictates this timeline is the critical need for accurate molecular diagnostic tools. The prolonged TSC seen with conventional regimens is frequently a consequence of diagnostic delay and initiating therapy without a comprehensive resistance profile. Molecular tools like the Xpert MTB/XDR assay are indispensable for starting therapeutic regiment and achieving rapid conversion. By providing a extensive resistance profile within 90 minutes, this technology enables clinicians to bypass ineffective therapy and start patients on a potent, tailored regimen from day one. This precision is the catalyst for the dramatically accelerated microbiological response observed with the BPaL regimen. The accuracy of these tools is not diminished by host factors, providing reliable results for patients with comorbidities or malnutrition, which is crucial for effective stratification.

However, this review definitively concludes that a narrow focus on microbiological conversion is insufficient. The determinants of prolonged TSC and poor outcomes, such as HIV co-infection, diabetes mellitus, malnutrition, and a history of previous treatment failure, are consistent across LMICs. This underscores that the host environment is as important as the drug regimen. A patient who is malnourished or psychologically distressed is less likely to achieve timely conversion and sustained cure. Therefore, achieving a durable and

achievable recovery, defined by no relapse, minimal side effects, and a return to functional well-being, requires a holistic strategy. This entails integrating comorbidity management, nutritional support, and psychological counseling directly into the treatment framework. This integrated approach is the most effective strategy to mitigate the psychological distress and socio-economic barriers that lead to LTFU, a dominant driver of failure in Indonesia and a significant problem elsewhere.

Finally, time to sputum culture conversion remains an extremely relevant and critical measure because it is the strongest early predictor of ultimate treatment success, as evidenced by the Vietnamese study where this cohort study was being treated with a shorter-course regimen with overall recovery success rate was 65.5%, culture conversion by 4 months was a very strong predictor of ultimate treatment success (aOR 2.93), significant barriers to success included HIV co-infection, pre-XDR/XDR-TB, and male gender, furthermore, a very important programmatic finding was that having Social Health Insurance was associated with lower odds of loss to follow-up (LTFU) (aOR 0.55), highlighting the critical role of socioeconomic support. TSC is a powerful biomarker of treatment efficacy. However, for a recovery criteria to be truly patient-centered, it must expand beyond this microbiological milestone to include treatment completion, functional restoration, and for high-risk patients, comorbidity control and nutritional recovery.

CONCLUSIONS

In conclusion, the path to achieving the 2030 TB elimination goals is through a dual strategy. The first is the rapid and universal deployment of highly effective novel regimens and the molecular diagnostics that enable them, ensuring a potent time to sputum conversion. The second, equally vital pillar is the implementation of aggressive, integrated adjunctive care that addresses host vulnerability. By embracing this comprehensive framework, we can secure a durable recovery for individuals and build a healthier nation, making a sustainable TB elimination program an achievable reality.

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