phrp
OSONG PUBLIC HEALTH AND RESEARCH PERSPECTIVES

pISSN 2210-9099 eISSN 2233-6052
https://doi.org/10.24171/j.phrp.2025.0325
Osong Public Health Res Perspect 2026;17(2):145-154

Original Article

Barriers to treatment completion among drug-sensitive tuberculosis patients: evidence from Indonesia's tuberculosis surveillance system

Mahalul Azam[1], Latifa Hanan[1], Muhammad Azinar[1], Amelia Fitra Khasanah[1], Arulita Ika Fibriana[1], Moch Yunus[2], Dewi Susanna[3], Martha Irene Kartasurya[4], Shabbir Syed-Abdul[5]

[1]Department of Public Health, Faculty of Medicine, Universitas Negeri Semarang, Semarang, Indonesia
[2]Faculty of Medicine, Universitas Negeri Malang, Malang, Indonesia
[3]Department of Environmental Health, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia
[4]Department of Public Health Nutrition, Faculty of Public Health, Diponegoro University, Semarang, Indonesia
[5]Graduate Institute of Biomedical Informatics, College of Medical Science and Technology, Taipei Medical University, New Taipei City, Taiwan

ABSTRACT

Objectives: This study aimed to estimate the prevalence of loss to follow-up (LTFU) among tuberculosis (TB) patients in Indonesia and to identify associated factors.

Methods: This study analyzed data from the 2022 Tuberculosis Information System in Indonesia. A total of 71,665 drug-sensitive TB patients were included in the analysis. Age, sex, employment status, diagnosis type, human immunodeficiency virus (HIV) status, diabetes mellitus, TB type, mode of treatment, treatment standard, referral status, and type of residence. Categorical variables were analyzed using chi-square tests, followed by multivariable logistic regression to identify confounder-adjusted independent predictors of LTFU.

Results: The prevalence of LTFU was 18.4%. A higher likelihood of LTFU was observed among older adults aged ≥65 years (adjusted-prevalence-odds-ratio [aPOR], 1.862), men (aPOR, 1.187), unemployed individuals (aPOR, 1.136), non-referred patients (aPOR, 1.547), patients with HIV (aPOR, 3.712), and those obtaining TB drugs out of pocket (aPOR, 4.998). The strongest predictor was receipt of non-standard treatment, which was associated with a markedly increased likelihood of LTFU (aPOR, 26.912). In contrast, rural residence demonstrated a protective association (aPOR, 0.610). All associations were statistically significant ($p < 0.001$).

Conclusion: This study highlights a substantial burden of LTFU among TB patients in Indonesia, with nearly one in five patients discontinuing treatment. Multiple sociodemographic and clinical factors—particularly non-standard treatment, non-referral status, and HIV co-infection—were strongly associated with LTFU, underscoring gaps in the TB care continuum. These findings emphasize the need for targeted, patient-centered interventions, strengthened referral pathways, improved communication, and enhanced care coordination to reduce LTFU in high-risk groups.

Keywords: Health services accessibility; Lost to follow-up; Treatment outcome

Received: August 18, 2025
Revised: January 15, 2026
Accepted: February 18, 2026

Corresponding author:
Mahalul Azam
Department of Public Health, Faculty of Medicine, Universitas Negeri Semarang, Kelud Utara III No. 15, Semarang 50223, Indonesia
E-mail: mahalul.azam@mail.unnes.ac.id

Mahalul Azam and Latifa Hanan contributed equally to the work as the co-first authors.

The opinions expressed by authors contributing to this journal do not necessarily reflect the opinions of the Korea Disease Control and Prevention Agency and Korea National Institute of Health.

© 2026 Korea Disease Control and Prevention Agency.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Tuberculosis (TB) remains a major global infectious disease, with an estimated 10.6 million cases and 1.25 million deaths reported in 2023. It continues to pose a substantial public health burden, particularly in high-incidence countries such as Indonesia [1]. Indonesia ranks second globally in TB incidence, with 820,789 reported cases out of an estimated 1,060,000 in 2023. The disease remains a leading cause of mortality in the country, contributing to approximately 150,000 deaths annually [2]. Despite national and global efforts to control TB, Indonesia's treatment success rate in 2022 was 82%, well below the national target of 90% [2]. Successful TB treatment requires strict adherence to a minimum 6-month regimen; however, many patients face challenges in completing therapy, resulting in loss to follow-up (LTFU). LTFU is defined as discontinuation of treatment for 2 or more consecutive months and is a key contributor to Indonesia's suboptimal treatment success rate [1].

According to the Indonesian Ministry of Health, the LTFU rate has increased in recent years, rising from 4% in 2021 to 7.4% in 2022 and further to 7.7% in 2023 [2]. The consequences of LTFU in TB treatment are substantial, contributing to higher rates of treatment failure, drug resistance, and ongoing community transmission, thereby exacerbating the public health burden [3]. Patients who discontinue treatment are at increased risk of developing multidrug-resistant TB, which requires longer, more complex, and more costly therapy [1]. Furthermore, untreated TB patients may continue to transmit the disease within their communities, perpetuating the cycle of infection. Several studies have demonstrated the adverse impact of LTFU on treatment outcomes and mortality. A cohort study involving 24,265 TB patients reported an LTFU prevalence of 12.51%, which was associated with reduced treatment adherence and increased mortality [4]. Similarly, a study conducted in Kenya found that 6.3% of TB patients who were lost to follow-up experienced heightened risks of relapse and death [5].

LTFU is influenced by a complex interplay of individual, health system, and environmental factors. Individuals aged 15–64 years may face work-related barriers to adherence, whereas older adults may be more vulnerable because of age-related frailty and adverse drug effects [6,7]. Sex-based differences have also been reported; men are more likely to discontinue treatment because of work demands and stigma, whereas women generally demonstrate better adherence [8]. Comorbidities such as human immunodeficiency virus (HIV) and diabetes mellitus further increase the likelihood of LTFU because of complex treatment regimens and medication-related adverse effects [5,9]. Diagnostic certainty also plays an important role. Patients with bacteriological confirmation (e.g., sputum microscopy or GeneXpert) tend to adhere more consistently than those who are clinically diagnosed based solely on symptoms [5,9].

Health system factors also shape treatment continuity. Patients who obtain anti-TB drugs through out-of-pocket payment may face financial barriers and variable drug quality, which can increase the likelihood of treatment discontinuation [10,11]. In contrast, the national Directly Observed Treatment, Short-course (DOTS) program provides free, standardized anti-TB drugs, supporting improved adherence. Patients entering care through formal referral pathways typically access services earlier and receive clearer guidance, whereas non-referred individuals may be more prone to delayed treatment initiation and LTFU [12]. Moreover, patients receiving non-standard TB regimens have a substantially higher risk of discontinuation—26% versus 8% among those receiving standard protocols [4].

HIGHLIGHTS

- Standard treatment emerged as the most influential factor; patients receiving non-standard treatment had a significantly higher likelihood of loss to follow-up (LTFU).
- Older age (≥65 years), male sex, unemployment, receipt of out-of-pocket tuberculosis (TB) drugs, non-referral status, clinical diagnosis, TB–human immunodeficiency virus co-infection, and extrapulmonary TB were all significantly associated with an increased risk of LTFU.
- In contrast, rural residence was significantly associated with a lower likelihood of LTFU, suggesting a potential protective effect that may support continued engagement in TB care.
- Given the strong association between non-standard treatment and LTFU, greater emphasis should be placed on strengthening drug distribution monitoring and expanding access to standardized TB treatment programs. Although Indonesia's national TB program provides free treatment through public health facilities, limited integration of private providers into the national surveillance and supply system remains a challenge. Strengthening public–private mix strategies, improving reporting through the Tuberculosis Information System, and enforcing stricter regulation of anti-TB drug sales are essential to reduce treatment fragmentation.

https://doi.org/10.24171/j.phrp.2025.0325

Environmental and socioeconomic factors, including unstable employment, rural residence, and geographic barriers to care, may further contribute to LTFU. Individuals in informal employment may prioritize immediate income over health needs, whereas rural residents may face long travel distances, limited transportation, and fewer healthcare facilities [13,14].

The Tuberculosis Information System in Indonesia (*Sistem Informasi Tuberculosis*, *SITB*) is the national TB surveillance platform that captures data on TB cases, treatment adherence, and outcomes. Although SITB plays an important role in monitoring and evaluating TB control efforts, few studies have used these data to examine nationwide determinants of LTFU. Most existing research is hospital- or region-based, leaving a critical gap in understanding the national epidemiology of LTFU. Given projections that reducing LTFU could decrease TB re-treatment needs by 10%–20% [15], a comprehensive national analysis is needed. Identifying and addressing factors associated with LTFU is essential to improving treatment outcomes and advancing Indonesia's TB control goals. This study aimed to examine the recent rate of LTFU among TB patients in Indonesia and associated determinants.

Materials and Methods

Study Design and Setting

This study was conducted as a secondary data analysis using surveillance data from the Tuberculosis Information System (SITB), managed by the Directorate of Disease Prevention and Control, Ministry of Health, Republic of Indonesia. The dataset included all patients registered in SITB between January 1, 2022, and December 31, 2022. Patient data were derived from TB-03, a standardized registry used by healthcare facilities, including community health centers, hospitals, clinics, and laboratories. TB-03 records include demographic information; TB type; diagnostic methods; laboratory results (sputum, GeneXpert/Xpert MTB/RIF, culture); treatment category and regimen; HIV testing and linkage; and treatment outcomes [16].

Participants

The study sample consisted of all drug-sensitive TB patients (n = 637,554) recorded in SITB. Records meeting the eligibility criteria were included in the analysis. Inclusion criteria for the final analytical sample were: (1) a final treatment outcome recorded as either "recovery/cured" or "LTFU," and (2) complete data for all variables under investigation. Patients were excluded if the recorded treatment outcome was death or treatment failure. Additional exclusions were applied for duplicate records and entries with missing data for key variables. Figure 1 presents the participant selection process.

Variables

Patients classified as LTFU were defined as having discontinued TB treatment for 2 or more consecutive months (8 weeks) for any reason without medical consent. The independent variables extracted from SITB were age, sex, employment status, diagnosis type (clinical or bacteriological), HIV status, diabetes mellitus, TB type (extrapulmonary or pulmonary), mode of treatment (government program vs. out of pocket, including private health insurance), treatment standard (standardized vs. non-standard according to the National Clinical Practice Guidelines for Tuberculosis Management), referral status (non-referral vs. referral), and type of residence (urban vs. rural, based on administrative

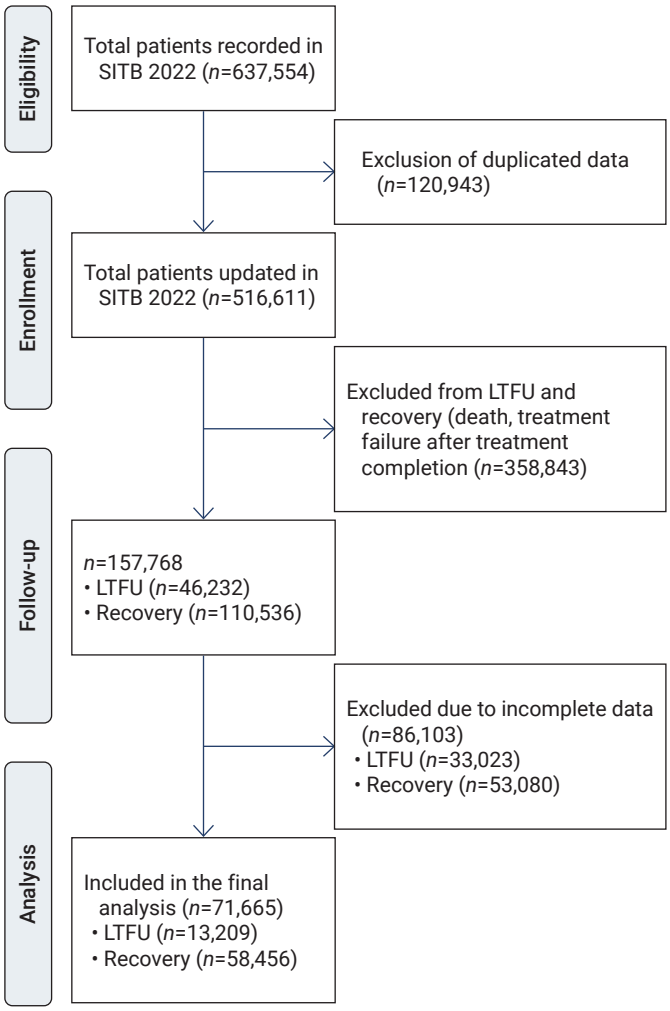


Figure 1. Recruitment flow.
SITB, Tuberculosis Information System; LTFU, loss to follow-up.

area codes). Non-standard treatment included prescriptions issued by private practitioners or facilities not integrated into the DOTS program; regimens that did not comply with the fixed-dose combination supplied by the program; incomplete treatment monitoring; or the absence of standardized follow-up sputum examinations.

Bias

To minimize selection bias, this study used data from the national SITB. Although underreporting may still occur—particularly among private providers—SITB remains the most comprehensive national source of notified TB case data and provides broad geographic coverage of drug-sensitive TB patients across Indonesia.

Inclusion and exclusion criteria were applied systematically to reduce the risk of arbitrary sample selection. Information bias was addressed through data cleaning, including the removal of duplicate records and the exclusion of incomplete entries to improve data reliability. Confounding was addressed using multivariable logistic regression, enabling estimation of the independent association between each variable and LTFU while adjusting for other covariates.

Statistical Methods

Analyses began with univariate summaries to describe the frequency and percentage of each variable. Bivariate associations between independent variables and LTFU were assessed using chi-square tests, with statistical significance set at $p<0.05$. Associations were quantified using prevalence odds ratios (PORs) with 95% confidence intervals (CIs); a POR >1 indicated higher odds of LTFU, whereas a POR <1 indicated lower odds (protective association). Variables associated with LTFU in bivariate analyses were entered into a multivariable logistic regression model to identify the most relevant determinants while adjusting for other covariates.

Ethics Statement

This study received ethical approval from the Ethics Committee of the Faculty of Medicine, Universitas Negeri Semarang (No. 933/KEPK/FK/KLE/2025).

Results

(1) The prevalence of LTFU in the analytical sample was 18.4%. (2) Standard treatment emerged as the most influential factor; patients receiving non-standard treatment showed a substantially higher likelihood of LTFU. (3) Older age (≥65 years), male sex, unemployment, receipt of out-of-pocket TB drugs, non-referral status, clinical diagnosis, TB–HIV co-infection, extrapulmonary TB, and receipt of non-standard treatment were all significantly associated with an increased likelihood of LTFU. (4) In contrast, rural residence was significantly associated with a lower likelihood of LTFU, suggesting a potential protective association that may support continued engagement in TB care.

A total of 71,665 patients were included in the final analysis. As shown in Table 1, the prevalence of LTFU in the

Table 1. Characteristics of the final analytical sample from the Indonesian Tuberculosis Information System, 2022 ($n=71,665$)

Characteristic	Value
Age (y)	
≥65	8,569 (12.0)
15–64	63,069 (88.0)
Sex	
Male	43,311 (60.4)
Female	28,354 (39.6)
Employment status	
Unemployed	28,331 (39.5)
Employed	43,334 (60.5)
Mode of treatment	
Out of pocket	1,059 (1.5)
Government program	70,606 (98.5)
Referral status	
Non-referral	57,554 (80.3)
Referral	14,111 19.7
Type of residence	
Rural	48,605 (67.8)
Urban	23,060 (32.2)
Diagnosis type	
Clinical	6,393 (8.9)
Bacteriological	65,272 (91.1)
HIV infection	
Yes	1,815 (2.5)
No	69,850 (97.5)
Diabetes mellitus	
Yes	14,599 (20.4)
No	57,066 (79.6)
Type of tuberculosis	
Extrapulmonary	1,152 (1.6)
Pulmonary	70,513 (98.4)
Treatment standard	
Non-standard	345 (0.5)
Standard	71,320 (99.5)
Treatment outcome	
Loss to follow-up	13,209 (18.4)
Recovery	58,456 (81.6)

Data are presented as *n* (%).
HIV, human immunodeficiency virus.

https://doi.org/10.24171/j.phrp.2025.0325

analytical sample was 18.4%, and 81.6% were reported as recovered. Participants aged 15–64 years accounted for 88.0% of the sample, and men comprised 60.4%. Employed individuals accounted for 60.5% of the sample, and 98.5% received medication through the government program. Non-referral cases were the most prevalent (80.3%), and 67.8% of participants resided in rural areas. Bacteriological diagnosis was most common (91.1%); most participants were HIV-negative (97.5%) and without diabetes mellitus (79.6%). Pulmonary TB accounted for 98.4% of cases, and nearly all patients (99.5%) received standardized treatment.

Table 2 summarizes bivariate associations between participant characteristics and LTFU. Age was strongly associated with LTFU: participants aged ≥65 years had higher LTFU prevalence (27.0%) than those aged 15–64 years (17.3%), corresponding to a POR of 1.566 (95% CI, 1.506–1.627; $p < 0.001$). Men had a slightly higher LTFU prevalence (19.3%) than women (17.1%) (POR, 1.124; 95% CI, 1.088–1.160; $p < 0.001$). Unemployed participants also had higher LTFU prevalence (19.2%) than employed participants (18.0%) (POR, 1.067; 95% CI, 1.035–1.101; $p < 0.001$). Mode of treatment showed one of the strongest associations: participants

Table 2. Treatment outcome based on subjects' characteristics from the Indonesian Tuberculosis Information System, 2022

Variable	Treatment outcome (*n*, %)		POR (95% CI)	*P**
	LTFU	Recovery		
Age (y)			1.566 (1.506–1.627)	<0.001
≥65	2,323 (27.0)	6,273 (73.0)		
15–64	10,886 (17.3)	52,183 (82.7)		
Sex			1.124 (1.088–1.160)	<0.001
Male	8,347 (19.3)	34,964 (80.7)		
Female	4,862 (17.1)	23,492 (82.9)		
Employment status			1.067 (1.035–1.102)	<0.001
Unemployed	5,429 (19.2)	22,902 (80.8)		
Employed	7,780 (18.0)	35,554 (82.0)		
Mode of treatment			3.001 (2.832–2.181)	<0.001
Out of pocket	569 (53.7)	490 (46.3)		
Government program	12,640 (17.9)	57,966 (82.1)		
Referral status			1.446 (1.383–1.512)	<0.001
Non-referral	11,294 (19.6)	42,620 (80.4)		
Referral	1,915 (13.6)	12,196 (86.4)		
Type of residence			0.673 (0.653–0.694)	<0.001
Rural	7,749 (15.9)	40,856 (84.1)		
Urban	5,460 (23.7)	17,600 (76.3)		
Diagnosis type			9.576 (9.364–9.794)	<0.001
Clinical	6,393 (100.0)	0 (0)		
Bacteriological	6,816 (10.4)	58,456 (89.6)		
HIV infection			2.501 (2.370–2.639)	<0.001
Yes	806 (44.4)	1,009 (55.6)		
No	12,403 (17.6)	57,447 (82.2)		
Diabetes mellitus			0.822 (0.789–0.857)	<0.001
Yes	2,296 (15.7)	12,303 (84.3)		
No	10,913 (19.1)	46,153 (80.9)		
Type of tuberculosis			5.848 (5.754–5.944)	<0.001
Extrapulmonary	1,152 (100.0)	0 (0)		
Pulmonary	12,057 (17.1)	58,456 (82.9)		
Treatment standard			4.821 (4.616–5.034)	<0.001
Non-standard	301 (87.2)	44 (12.8)		
Standard	12,908 (18.1)	58,412 (81.9)		

LTFU, loss to follow-up; POR, prevalence odds ratio; CI, confidence interval; HIV, human immunodeficiency virus.
*$p < 0.05$ (statistically significant).

obtaining drugs through out-of-pocket payment had substantially higher LTFU prevalence (53.7%) than those receiving drugs through the government program (17.9%) (POR, 3.001; 95% CI, 2.832–3.181; $p < 0.001$). Non-referral participants had higher LTFU prevalence (19.6%) than referral participants (13.6%) (POR, 1.446; 95% CI, 1.383–1.512; $p < 0.001$). Urban residents were more likely to be LTFU (23.7%) than rural residents (15.9%), with rural residence demonstrating a protective association (POR, 0.673; 95% CI, 0.653–0.694; $p < 0.001$). Diagnosis type was strongly associated with LTFU: clinically diagnosed participants had 100.0% LTFU versus 10.4% among bacteriologically confirmed participants (POR, 9.576; 95% CI, 9.364–9.794; $p < 0.001$). HIV-positive participants had higher LTFU prevalence (44.4%) than HIV-negative participants (17.6%) (POR, 2.501; 95% CI, 2.370–2.639; $p < 0.001$). Participants with diabetes mellitus had lower LTFU prevalence (15.7%) than those without diabetes (19.1%), indicating a protective association (POR, 0.822; 95% CI, 0.789–0.857; $p < 0.001$). Finally, extrapulmonary TB cases had 100.0% LTFU compared with 17.1% among pulmonary TB cases (POR, 5.848; 95% CI, 5.754–5.944; $p < 0.001$).

In the multivariable analysis presented in Table 3, several factors were significantly associated with LTFU. Higher likelihood of LTFU was observed among participants aged ≥65 years (adjusted POR [aPOR], 1.862; 95% CI, 1.765–1.965), men (aPOR, 1.187; 95% CI, 1.133–1.244), and unemployed participants (aPOR, 1.136; 95% CI, 1.084–1.189). LTFU was also more likely among those obtaining drugs through out-of-pocket treatment (aPOR, 4.998; 95% CI, 4.404–5.672), non-referral participants (aPOR, 1.547; 95% CI, 1.466–1.632), and HIV-positive participants (aPOR, 3.712; 95% CI, 3.367–4.092). In contrast, rural residence was associated with a lower likelihood of LTFU (aPOR, 0.610; 95% CI, 0.586–0.635). The strongest association was observed for receipt of non-standard treatment (aPOR, 26.912; 95% CI, 19.500–37.141). All associations were statistically significant ($p < 0.001$).

Discussion

The national TB program, including DOTS, provides free, standardized, quality-assured medications along with structured follow-up, education, and adherence support. A primary objective of this model is to reduce LTFU among TB patients. Indonesia supports TB surveillance and case reporting through SITB. Despite these systemic efforts, this study identified several factors significantly associated with LTFU in Indonesia, including receipt of non-standard treatment, obtaining TB drugs out of pocket, TB–HIV co-infection, older age (≥65 years), non-referral status, male sex, unemployment, and rural residence. Among these factors, receipt of non-standard treatment showed the strongest association, with patients being 26.9 times more likely to experience LTFU. Adherence to standard TB treatment, typically a 6-month DOTS-based course, is essential for treatment success and prevention of drug resistance [17]. Standard protocols include counseling, follow-up, and support that can promote adherence, particularly when tailored to patient needs [18]. In contrast, patients receiving non-standard TB regimens may have longer treatment durations, less familiar or less tolerated medications, and non-standard dosing or monitoring, which may increase uncertainty and hinder continuation. This finding is consistent with a previous study reporting higher LTFU rates among patients receiving non-standard regimens [4]. The World Health Organization also emphasizes that non-standard or second-line regimens require additional support, including enhanced counseling and monitoring, to reduce patient burden [19].

Another important determinant was mode of treatment: participants obtaining anti-TB drugs through out-of-pocket payment had a 4.9-times higher likelihood of LTFU than those receiving drugs through the TB program, consistent with studies in Indonesia and China [12,20].

Table 3. Multivariate analysis with binary logistic regression of the sample from the Indonesian Tuberculosis Information System, 2022

Variable	B	Wald	*p*	aPOR (95% CI)
Aged ≥65 y	0.622	511.970	<0.001	1.862 (1.765–1.965)
Male	0.172	51.813	<0.001	1.187 (1.133–1.244)
Unemployed	0.127	28.979	<0.001	1.136 (1.084–1.189)
Out-of-pocket treatment	1.609	621.387	<0.001	4.998 (4.404–5.672)
Non-referral	0.436	253.254	<0.001	1.547 (1.466–1.632)
Rural residence	−0.494	584.016	<0.001	0.610 (0.586–0.635)
Non-standard treatment	3.293	401.269	<0.001	26.912 (19.500–37.141)
HIV	1.311	694.757	<0.001	3.712 (3.367–4.092)
Constant	−5.203	788.320	<0.001	

aPOR, adjusted prevalence odds ratio; CI, confidence interval; HIV, human immunodeficiency virus.

https://doi.org/10.24171/j.phrp.2025.0325

The national TB program, including DOTS, provides free, standardized, quality-assured drugs along with structured follow-up, education, and adherence support, and has been associated with improved adherence rates (from 79% to 94%) [21]. Prior evidence also suggests that access through national programs can reduce socioeconomic barriers and support adherence [18]. In contrast, patients using private pharmacies or non-government providers may lack adherence support and face high drug costs, variable drug quality, and limited supervision, all of which may contribute to LTFU [10,22]. Uncoordinated care, adverse effects, and patient confusion may further hinder treatment continuation [11]. Some individuals may choose non-program sources because of stigma, distrust, or a desire for privacy—particularly in urban areas—although this may be associated with poorer outcomes. This pattern is consistent with findings from Vietnam, where default rates were higher among patients treated outside formal programs [23].

HIV status was also strongly associated with LTFU, with TB–HIV co-infected patients being 3.7 times more likely to be LTFU. The immune system plays a central role in TB pathogenesis, with macrophages, dendritic cells, and neutrophils contributing to control of *Mycobacterium tuberculosis*. TB can disrupt these immune responses, and in HIV co-infection, CD4+ T-cell depletion further impairs both innate and adaptive immunity. This can increase disease severity, complicate diagnosis and treatment, and contribute to immune reconstitution inflammatory syndrome after initiation of antiretroviral therapy [24,25]. This finding is consistent with global evidence; a study in Kenya reported lower treatment completion and a higher risk of LTFU among HIV-positive TB patients [5]. Contributing factors may include medication adverse effects and pill burden from antiretroviral (and anti-TB drug combinations, complex regimens, frequent clinic visits, and psychological distress [26]. Social stigma may also contribute, as fear of discrimination and unintended disclosure can discourage sustained engagement in care. A previous study reported that stigma, depression, and limited social support were major drivers of LTFU among co-infected individuals [27].

In addition, age was significantly associated with LTFU in TB treatment. This study observed higher odds of LTFU among non-working-age groups, including teenagers and older adults, which may reflect biological, behavioral, and socioeconomic factors. Older adults may misattribute TB symptoms to normal aging, reducing perceived need for treatment [28]. Frailty, comorbidities, and mobility limitations may further contribute to treatment interruption [6,29]. In contrast, working-age individuals may be more likely to complete treatment because of greater health literacy, autonomy, and perceived responsibility [30]. In children, adherence often depends on caregivers; when caregivers face financial or logistical barriers, treatment interruption may be more likely. Prior studies have noted that pediatric TB is frequently underdiagnosed and may be suboptimally managed because children rely on adult supervision for diagnosis, follow-up, and medication administration [31].

Referral status was significantly associated with LTFU, with non-referral patients demonstrating a higher likelihood of LTFU than referral patients. This finding is consistent with prior work identifying referral status as a determinant of LTFU in the context of public–private mix implementation [20]. Formal referrals may facilitate earlier diagnosis, integration into national systems, and access to monitoring and support services [12]. In contrast, self-presenting (non-referred) patients may experience delays, have less understanding of the treatment process, and receive weaker adherence support [13]. Referral status may also reflect clinical oversight and perceived urgency, which can promote treatment continuation. The World Health Organization highlights referral systems as important for timely diagnosis, treatment initiation, and continuity across levels of care [19]. Prior evidence also suggests that patients lost between facilities may miss key steps in care, such as drug initiation and sputum monitoring, underscoring the need for robust referral networks in TB programs [32].

Sex was also significantly associated with LTFU, with men showing a higher likelihood of LTFU than women (aPOR, approximately 1.1). This disparity is consistent with prior literature describing sex-based differences in TB care. For example, evidence from South Africa suggests that men may delay care-seeking and are more likely to discontinue therapy because of work-related responsibilities, traditional gender norms, and stigma [33]. This finding is also consistent with studies in Indonesia reporting higher non-adherence among men and with findings from Selangor, Malaysia, where missed follow-up was more common among men and was attributed to financial constraints, work priorities, and limited family support [6,34]. In contrast, women may be more likely to seek initial care at private facilities and may report higher trust in healthcare providers, which can support treatment adherence [8].

These sex-based differences in LTFU may intersect with socioeconomic factors, including employment status. In this study, unemployment was associated with a higher likelihood of LTFU compared with employment, consistent with prior studies [35,36]. Unemployment may contribute to financial hardship, transportation barriers,

lower health literacy, and reduced social support, which can hinder completion of TB treatment. In contrast, formal employment may support adherence by providing structure, routine, and access to resources, including stable income and workplace support [37]. Similarly, individuals working in informal sectors may prioritize daily income over health needs, increasing vulnerability to treatment interruption [36]. Consistent with this explanation, 1 study reported that civil construction workers—who often experience precarious employment—were more likely to be LTFU [14].

Finally, the type of residence was significantly associated with LTFU, with rural residents showing a lower likelihood of LTFU than urban residents. This finding is consistent with evidence from India highlighting strengths of community-based TB programs in rural settings, including social cohesion, family involvement, and structured primary care [38]. These factors may support supervision and accountability, thereby promoting adherence. However, this result contrasts with several studies reporting poorer TB outcomes among rural populations. Research from Ethiopia, India, and Indonesia has documented access barriers in rural areas, including long travel distances, limited transportation, and constrained health infrastructure. For example, rural TB patients in Ethiopia were nearly twice as likely to be lost to follow-up [29]. Another study reported similar challenges in rural Indonesian districts, potentially related to delayed diagnosis and socioeconomic hardship [39]. These differences may reflect context-specific factors, including variation in local health system capacity, primary care investment, and urban barriers to continuity of care. Despite geographic proximity to health services, urban patients—particularly those living in informal settlements—may experience high mobility, work constraints, stigma, limited social support, and fragmented care, which can increase the likelihood of LTFU [40,41].

These findings have important implications for achieving Sustainable Development Goal 3 (Good Health and Well-Being), particularly by reducing LTFU in support of the End TB Strategy. Strengthening adherence support through standardized regimens, coordinated referral systems, and integrated care for TB–HIV and TB–diabetes mellitus comorbidities may improve treatment completion and reduce transmission. Expanding outreach and adherence support in urban settings for high-risk patients may also be important. Overall, addressing LTFU likely requires integrated, multi-level approaches that combine patient-centered support with health system strengthening.

Generalizability

This study has high generalizability to drug-sensitive TB patients in Indonesia because it used a large, nationwide dataset from SITB and reflects routine programmatic data. However, caution is warranted when applying these findings to other countries because determinants of LTFU are context-specific. The findings are limited to drug-sensitive TB and may not apply to drug-resistant TB populations. In addition, restricting the analysis to a single year (2022) and excluding records with missing data may affect representativeness and introduce selection bias.

We did not perform subgroup analyses; therefore, potential interactions between variables may remain unexamined. However, we conducted a multivariable analysis in which all relevant variables were entered simultaneously, yielding aPORs. Potential effect modification by biologically plausible factors (e.g., HIV status) could not be evaluated because of the small number of HIV-positive cases (n=806), which represented 6.10% of the 13,209 participants classified as LTFU.

Limitations

This study has several limitations. First, reliance on secondary data from the 2022 SITB restricted the analysis to variables available in the surveillance system and did not capture psychosocial, behavioral, or environmental factors that may influence adherence. Second, the use of routine surveillance data may introduce bias because of inaccuracies, misclassification, or inconsistencies in data entry. Third, the analysis may not fully address complex inter-variable relationships; although associations observed in bivariate analyses remained similar after multivariable adjustment, this does not preclude residual confounding or effect modification.

Conclusion

This analysis identified several factors significantly associated with LTFU among drug-sensitive TB patients in Indonesia. Older age, male sex, unemployment, non-referral status, HIV co-infection, and obtaining drugs outside the national program were all associated with a higher likelihood of LTFU. Notably, receipt of non-standard treatment showed the strongest association, whereas rural residence was associated with a lower likelihood of LTFU. Overall, nearly 1 in 5 TB patients discontinued treatment, indicating a substantial burden of LTFU. Multiple sociodemographic and clinical factors—particularly non-standard treatment, non-referral status, and HIV co-infection—were strongly associated with LTFU, suggesting important gaps in the

https://doi.org/10.24171/j.phrp.2025.0325

care continuum. These findings underscore the need for targeted, patient-centered interventions, improved care coordination and communication, strengthened referral pathways, and strategies to reduce use of non-standard treatment to support adherence and reduce LTFU in high-risk groups.

Notes

Ethics Approval

This study was approved by the Ethics Committee of the Faculty of Medicine, Universitas Negeri Semarang (Approval number 933/KEPK/FK/KLE/2025).

Conflicts of Interest

The authors have no conflicts of interest to declare.

Funding

This work was supported by the UNNES-Taipei Medical University Research Collaboration with the contract number 291.14.3/UN37/PPK.11/2025.

Availability of Data

The datasets are not publicly available but are available from the corresponding author upon reasonable request.

Authors' Contributions

Conceptualization: MaA, LH; Data curation: LH, MuA; Formal analysis: all author; Funding acquisition: MaA, SSA, AIF; Investigation: AFK, MaA; Methodology: AIF, SSA, MaA; Project administration: LH, AIF; Resources: MaA, AIF; Software: LH; Supervision: MuA, AFK, MY; Validation: MY, MaA; Visualization: MIK, SSA, LH; Writing–original draft: LH; Writing–review & editing: all authors. All authors read and approved the final manuscript.

Additional Contributions

Directorate of Disease Prevention and Control, Ministry of Health, Republic of Indonesia, for providing the data in the Indonesian Tuberculosis Information System.

References

1. World Health Organization (WHO) (CH). Global tuberculosis report 2023. WHO; 2023.
2. Ministry of Health of the Republic of Indonesia (ID). Laporan program penanggulangan tuberkulosis tahun 2022. Ministry of Health of the Republic of Indonesia; 2022. Indonesian.
3. Bea S, Lee H, Kim JH, et al. Adherence and associated factors of treatment regimen in drug-susceptible tuberculosis patients. Front Pharmacol 2021;12:625078.
4. Chen RT, Liu CY, Lin SY, et al. The prevalence, clinical reasoning and impact of non-standard anti-tuberculosis regimens at the initial prescription. Sci Rep 2024;14:5631.
5. Ngari MM, Rashid MA, Sanga D, et al. Burden of HIV and treatment outcomes among TB patients in rural Kenya: a 9-year longitudinal study. BMC Infect Dis 2023;23:362.
6. Agus Z, Junadi P, Rusadi RA. Factors associated for anti tuberculosis treatment non-adherence among tuberculosis patients: scoping review. Media Publ Promosi Kesehat Indones 2024;7:2273–9.
7. Oh SJ, Lee JK, Shin OS. Aging and the immune system: the impact of immunosenescence on viral infection, immunity and vaccine immunogenicity. Immune Netw 2019;19:e37.
8. Chandru BA, Varma RP. Factors affecting ability of TB patients to follow treatment guidelines: applying a capability approach. Int J Equity Health 2023;22:176.
9. Komissarova OG, Abdullaev RY, Aleshina SV. Frequency and characteristics of adverse events caused by anti-tuberculosis drugs in pulmonary tuberculosis patients with diabetes myelitis. Tuberc Lung Dis 2020;98:10–4.
10. San Lin K. Loss to follow-up (LTFU) during tuberculosis treatment [Internet]. IntechOpen; 2019 [cited 2024 Dec 29]. Available from: https://doi.org/10.5772/intechopen.81900.
11. Mulaku MN, Nyagol B, Owino EJ, et al. Factors contributing to pre-treatment loss to follow-up in adults with pulmonary tuberculosis: a qualitative evidence synthesis of patient and healthcare worker perspectives. Glob Health Action 2023;16:2148355.
12. Martinez L, Xu L, Chen C, et al. Delays and pathways to final tuberculosis diagnosis in patients from a referral hospital in urban China. Am J Trop Med Hyg 2017;96:1060–5.
13. Asemahagn MA, Alene GD, Yimer SA. A qualitative insight into barriers to tuberculosis case detection in East Gojjam Zone, Ethiopia. Am J Trop Med Hyg 2020;103:1455–65.
14. Eufrasio R, Alcobia MC, Cordeiro CR, et al. Loss to follow-up: understand its determinants among tuberculosis patients, in Coimbra District (2005-2017). Indian J Tuberc 2025;72:226–32.
15. Ministry of Health of the Republic of Indonesia (ID). National strategy for tuberculosis control in Indonesia 2020-2024. Ministry of Health of the Republic of Indonesia; 2020. Indonesian.
16. Ministry of Health of the Republic of Indonesia (ID). Technical guidelines for contact investigation of tuberculosis [Internet]. Ministry of Health of the Republic of Indonesia; 2020 [cited 2025 Jul 16]. Available from: https://htbs.tbindonesia.or.id/wp-content/uploads/2020/03/Petunjuk-Teknis-Investigasi-Kontak.pdf?utm_source=chatgpt.com. Indonesian.
17. Adhani R, Musafaah M, Khan MA, et al. Global research trends on factors affecting tuberculosis (TB) adherence and dropout: a bibliometric study. Malahayati Nurs J 2024;6:4466–83. Indonesian.
18. Elmuttalut M. The key factors influencing tuberculosis treatment outcomes: a literature review. IJRIMCR 2024;6:76–9.
19. World Health Organization (WHO) (CH). Management of tuberculosis: training for health facility staff: second edition. G. Ensure continuation of TB treatment. WHO; 2018.
20. Rahayu SR, Susilastuti MS, Saefurrohim MZ, et al. Lost to follow-up among tuberculosis patients during the public-private mix era in rural area of Indonesia. Ethiop J Health Sci 2023;33:115–22.
21. Min S, Kwon SH, Lee EK, et al. Cost-effectiveness of improving patients' adherence to tuberculosis treatment in South Korea using

discrete event simulation. J Infect Public Health 2024;17:478–85.
22. Monique O, Ilse DP. Factors contributing to pulmonary tb treatment lost to follow-up in developing countries: an overview. Afr J Infect Dis 2023;17:60–73.
23. Hoa NB, Cobelens FG, Sy DN, et al. Diagnosis and treatment of tuberculosis in the private sector, Vietnam. Emerg Infect Dis 2011;17:562–4.
24. Ahor HS, Vivekanandan M, Harelimana JD, et al. Immunopathology in human pulmonary tuberculosis: inflammatory changes in the plasma milieu and impaired host immune cell functions. Immunology 2024; 172:198–209.
25. Rahman F. Characterizing the immune response to Mycobacterium tuberculosis: a comprehensive narrative review and implications in disease relapse. Front Immunol 2024;15:1437901.
26. Navasardyan I, Miwalian R, Petrosyan A, et al. HIV-TB coinfection: current therapeutic approaches and drug interactions. Viruses 2024; 16:321.
27. Turi E, Simegnew D, Fekadu G, et al. High perceived stigma among people living with HIV/AIDS in a resource limited setting in Western Ethiopia: the effect of depression and low social support. HIV AIDS (Auckl) 2021;13:389–97.
28. Adane AA, Alene KA, Koye DN, et al. Non-adherence to anti-tuberculosis treatment and determinant factors among patients with tuberculosis in northwest Ethiopia. PLoS One 2013;8:e78791.
29. Watumo D, Mengesha MM, Gobena T, et al. Predictors of loss to follow-up among adult tuberculosis patients in Southern Ethiopia: a retrospective follow-up study. BMC Public Health 2022;22:976.
30. Adu G, Harris BN, Beke A. Patient and health system factors associated with first line tuberculosis treatment adherence, 2009-2014. J Tuberc Res 2022;10:220–9.
31. Basile FW, Nabeta P, Ruhwald M, et al. Pediatric tuberculosis diagnostics: present and future. J Pediatric Infect Dis Soc 2022;11: S85–93.
32. Mando TC, Sandy C, Chadambuka A, et al. Tuberculosis cohort analysis in Zimbabwe: the need to strengthen patient follow-up throughout the tuberculosis care cascade. PLoS One 2023;18:e0293867.
33. Medina-Marino A, Bezuidenhout D, Ngcelwane N, et al. qualitative identification of intervention preferences to support men's engagement and retention in TB care in South Africa. Am J Mens Health 2022;16:15579883221129349.
34. Zulkifli AZ, Salleh RAM, Omar NF. Demographic characteristics associated with missed follow-up appointments among tuberculosis patients at Hospital Shah Alam, Selangor: a retrospective study from January to June 2023. Int J Pub Health Res 2024;14:1858–64.
35. Tola HH, Tol A, Shojaeizadeh D, et al. Tuberculosis treatment non-adherence and lost to follow up among TB patients with or without HIV in developing countries: a systematic review. Iran J Public Health 2015;44:1–11.
36. Oh AL, Makmor-Bakry M, Islahudin F, et al. Tuberculosis treatment interruption: a qualitative exploration of barriers, challenges, coping strategies and facilitators in Malaysia. Health Promot Int 2024;39:daae176.
37. Verma M, Furin J, Langer R, et al. Making the case: developing innovative adherence solutions for the treatment of tuberculosis. BMJ Glob Health 2019;4:e001323.
38. Trivedi PR, Khakhkhar TM. Treatment outcome of tuberculosis patients under directly observed treatment short-course and factors affecting the outcome in tertiary care hospital. Int J Basic Clin Pharmacol 2019;8:981–6.
39. Mahendradhata Y, Syahrizal BM, Utarini A. Delayed treatment of tuberculosis patients in rural areas of Yogyakarta province, Indonesia. BMC Public Health 2008;8:393.
40. Sapkota S, Tiwary MR, Zare MK, et al. Access to healthcare facilities and social well-being in urban areas. J Appl Bioanal 2024;10:243–51.
41. Graham S, Muir NM, Formsma JW, et al. First nations, Inuit and Métis peoples living in urban areas of Canada and their access to healthcare: a systematic review. Int J Environ Res Public Health 2023; 20:5956.

https://doi.org/10.24171/j.phrp.2025.0325