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Clinical outcomes and recurrence after treatment of asymptomatic pulmonary tuberculosis: A nationwide cohort study

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ABSTRACT

Objectives: Asymptomatic tuberculosis (TB) has gained programmatic recognition in WHO's 2025 framework, but large-scale real-world evidence on its prognosis remains limited. We compared clinical characteristics, treatment outcomes, and post-treatment recurrence between asymptomatic and symptomatic pulmonary TB in South Korea.

Methods: We conducted a nationwide retrospective cohort study linking the Korean National Tuberculosis Surveillance System, National Health Information Database, and cause-of-death registry. From Jan 1, 2016, to Dec 31, 2019, 88,929 patients with pulmonary TB were included. End-of-treatment outcomes were assessed using multivariable logistic regression. Recurrence among those with treatment success was evaluated through Dec 31, 2022 using competing-risks regression.

Results: At diagnosis, 37.9% (33,753/88,929) were asymptomatic, of whom 69.3% were bacteriologically confirmed. Compared with symptomatic patients, asymptomatic patients had higher treatment success and lower TB-related mortality during treatment (adjusted odds ratio 0.70; 95% CI, 0.64-0.75). Asymptomatic status was also associated with a reduced risk of post-treatment recurrence (adjusted subdistribution hazard ratio 0.84; 95% CI, 0.76-0.94).

Conclusions: Over one-third of pulmonary TB cases were asymptomatic at diagnosis, most with bacteriological confirmation. Asymptomatic TB showed more favorable short- and long-term outcomes, yet a non-trivial proportion remained potentially infectious. These findings support expanding active case finding beyond symptom-based approaches and highlight the need for risk-stratified treatment strategies.

Introduction

Tuberculosis (TB) remains a major global public health concern. Per the Global Tuberculosis Report 2024 by the World Health Organization (WHO), an estimated 10.8 million individuals developed TB and 1.25 million died from it in 2023, establishing TB as the leading cause of mortality attributable to a single infectious agent worldwide [1].

Traditionally, TB diagnosis has predominantly relied on hallmark clinical manifestations, including persistent cough, fever, or weight loss. However, prevalence surveys reveal that a substantial proportion of bacteriologically confirmed TB cases occur without these classical symptoms [2]. These asymptomatic presentations of TB are increasingly identified through expanded screening programs, chest radiography, and improved microbiological diagnostic modalities.

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In response to this shift, WHO in 2025 adopted the term "asymptomatic TB," replacing the inconsistently defined "subclinical TB" [3]. Asymptomatic TB is operationally defined as a person with TB who did not report classical TB-related symptoms, irrespective of the diagnostic modality employed [3]. Despite the absence of symptoms, such individuals may harbor active disease and, in some cases, remain capable of transmitting the pathogen—thus posing a challenge for TB control strategies that rely primarily on symptom-based screening protocols [4].

WHO further categorized asymptomatic TB into two operational subtypes based on microbiological confirmation status: (i) asymptomatic, bacteriologically confirmed TB, defined as individuals without classical TB-related symptoms but exhibiting microbiological evidence of disease; and (ii) asymptomatic unconfirmed TB, referring to individuals without symptoms and without bacteriological confirmation, yet presenting with radiographic or immunologic findings suggestive of active TB.

Although increasingly recognized, epidemiological and clinical implications of asymptomatic TB remain unclear. It is unknown whether absence of symptoms at diagnosis is associated with distinct clinical characteristics or differences in short- and long-term outcomes, such as treatment success, TB-related mortality, disease recurrence, or post-treatment mortality. Previous studies have suggested that individuals with asymptomatic TB tend to be younger, have fewer comorbidities, and exhibit less extensive radiologic and microbiologic abnormalities, potentially indicating better prognosis [5]. However, robust population-based evidence comparing outcomes between asymptomatic and symptomatic TB remains limited, especially with regard to long-term outcomes including recurrence and post-TB mortality.

To address this gap, we conducted a retrospective, population-based cohort study in South Korea by linking national TB surveillance and administrative health databases. Our objectives were to (i) compare the clinical and demographic characteristics of individuals with asymptomatic versus symptomatic pulmonary TB and (ii) assess differences in treatment outcomes and long-term prognosis—including recurrence and post-TB mortality—according to symptom status at the time of diagnosis.

Material and methods

Study population and design

This study employed a retrospective cohort design utilizing linked national administrative databases in South Korea. We integrated data from three major sources: (i) the Korean National Tuberculosis Surveillance System (KTB-Surv), maintained by the Korea Disease Control and Prevention Agency (KDCA), which contains comprehensive records of all notified TB cases nationwide; (ii) the National Health Information Database (NHID), a complete claims repository managed by the National Health Insurance Service (NHIS); and (iii) the cause-of-death statistics compiled by Statistics Korea. These datasets were linked at the individual level using unique de-identified personal identifiers. The integration of nationwide databases enabled longitudinal follow-up and enables rigorous analysis of treatment outcomes and disease recurrence. Each data source structure and the list of included variables are described in previously published cohort and data source profiles [6–8].

We included individuals who were notified as having TB between January 1, 2016, and December 31, 2019 (n = 117,234). TB recurrence was assessed by following participants who achieved successful treatment outcomes for a fixed two-year period post-treatment completion, concluding on December 31, 2022. Exclusion criteria were as follows: (i) patients who did not undergo individual case investigation, resulting in missing key variables required for analysis (n = 1195); (ii) those that were diagnosed with extrapulmonary TB only (n = 24,583); (iii) those that had missing or implausible values for height or weight, such as 0, 1, or ≥300 (n = 2467); or (iv) those that had invalid microbiological test results (n = 60) (Supplementary Figure 1). After exclusions, a total of 88,929 individuals with pulmonary TB were included in the final analysis.

Measurements

Symptom information was systematically collected at the time of TB notification using the standardized case investigation form KTB-Surv administered by trained TB nurses through direct patient interview. The form captures symptom information in a hierarchical structure: (1) a global indicator for the presence or absence of TB-related symptoms; (2) a binary checklist of eight cardinal pulmonary TB symptoms—cough, sputum production, chest pain, dyspnea, weight loss, night sweats, hemoptysis, and fever—each recorded as present or absent; and (3) a free-text field for documentation of any additional symptoms. Asymptomatic TB was defined as cases in which the global "no symptoms" indicator was endorsed, all eight cardinal symptoms were recorded as absent, and no additional symptoms were entered in the free-text field at the time of diagnosis. Both categories of asymptomatic TB as defined by the WHO were analyzed: (1) asymptomatic, bacteriologically confirmed TB, and (2) asymptomatic unconfirmed TB. Additionally, we conducted a subgroup analysis restricted to bacteriologically confirmed TB to allow for a more homogeneous comparison and to align with clinical case definitions used in surveillance and treatment programs.

This study included two main outcome variables: End-of-treatment mortality (treatment success vs all-cause or TB-related mortality) and TB recurrence within 2 years following treatment success. Treatment outcomes were classified according to the WHO definitions: cured, treatment completed, treatment failed, lost to follow-up (LTFU), not evaluated (NE), and death [9]. We defined treatment success as either cured or treatment completed. Among individuals classified as deceased, we further distinguished TB-related death from non-TB-related death based on cause-of-death statistics from Statistics Korea. Deaths with ICD-10 codes A15-A19 were categorized as TB-related, and all other codes were classified as other causes. TB recurrence was defined as a new notification of TB in patients who had previously achieved treatment success, occurring within 2 years of treatment completion during the follow-up period.

The following covariates were included: age (≤40, 41-64, 65-79, ≥80 years), sex (men or women), and household income level (0 = lowest, 5 = highest). Case detection modality was ascertained from the KTB-Surv case investigation form item "reason for seeking care," which is recorded by trained TB nurses at the time of notification using nine pre-specified categories: (1) patient self-presentation; (2) national or workplace health screening; (3) private health check-up; (4) school screening; (5) household contact investigation; (6) contact epidemiologic investigation; (7) screening for health certificate issuance; (8) immigration/visa screening; and (9) other (free-text). Patients categorized as (1) were classified as passive case finding (PCF), while those categorized as (2) through (8) were classified as active case finding (ACF). Entries in category (9) were reviewed and classified as ACF when they contained screening-related descriptors. TB-related variables included the presence of cavitary lesions on chest X-ray, results of sputum smear, culture, nucleic acid amplification test (NAAT), and drug susceptibility testing (DST). Bacteriologically confirmed TB was defined as a positive result on any of the following diagnostic modalities: acid-fast bacilli (AFB) smear, culture, or NAAT.

Smoking status (never, former, or current smoker) and body mass index (BMI; ≤18.5, 18.5-24.9, 25.0-29.9, ≥30.0 kg/m²) were ascertained from the KTB-Surv case investigation form at the time of TB notification. The Charlson comorbidity index (CCI) was derived from ICD-10 diagnostic codes recorded in the linked NHID within 1 year prior to TB notification, and categorized into four groups: 0, 1, 2, and ≥3 points.

Statistical analysis

Continuous variables were summarized using means and standard deviations. Categorical variables were presented as frequencies and proportions. Group differences were assessed using Pearson's chi-square test. To evaluate the association between asymptomatic TB and end-of-treatment mortality, we constructed multivariable logistic regression models, comparing treatment success (cured or completed) with death. Model 1 included age, sex, household income level, and CCI score. Model 2 incorporated additional covariates: bacteriological confirmation status, case detection strategy, presence of cavitary lesions, sputum smear results, rifampicin resistance, BMI, and smoking status. Separate models were fitted for two outcomes: all-cause mortality and TB-related mortality.

To assess TB recurrence risk within 2 years of treatment success, we used a competing risks regression model, treating death during the follow-up period as a competing event. Covariates included were identical to those in Models 1 and 2. To facilitate visual interpretation, Kaplan–Meier survival curves were generated for two outcomes: (1) all-cause and TB-related mortality within 1 year after treatment initiation, stratified by symptom status (symptomatic vs asymptomatic); and (2) TB recurrence within 2 years after treatment success, stratified into four groups based on bacteriological confirmation (confirmed vs unconfirmed) and symptom status (symptomatic vs asymptomatic). All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and Stata/MP version 18.0 (StataCorp LLC, College Station, TX, USA).

Ethics statement

This study protocol was approved by the Institutional Review Board of Severance Hospital (4-2022-0595) and the Korea National Health Insurance Service Medical Request Review Committee (NHIS-2024-1-186). The requirement for informed consent was waived, due to the retrospective nature of the study and the use of anonymized data. This study adheres to the tents of the Declaration of Helsinki and all relevant ethical and regulatory guidelines.

Results

Baseline characteristics according to symptom status at diagnosis

Among the 88,929 participants included, 33,753 (37.9%) were classified as asymptomatic and 55,176 (62.1%) as symptomatic at the time of diagnosis. Within the asymptomatic group, 23,402 (69.3%) had bacteriologically confirmed TB, whereas 10,351 (30.7%) were unconfirmed. In the symptomatic group, 45,728 (82.9%) were bacteriologically confirmed and 9448 (17.1%) were unconfirmed (Supplementary Figure 1).

Table 1 presents the baseline demographic and clinical characteristics stratified by symptom status. Patients with asymptomatic TB were younger compared to those with symptomatic TB (median age: 59.0 vs 64.0 years, respectively; $P < 0.001$), with a higher proportion of men (63.3% vs 60.4%, respectively; $P < 0.001$). The diagnostic pathway differed substantially between the two groups. Active case finding accounted for nearly one-third of asymptomatic cases compared to only 5.9% among symptomatic individuals ($P < 0.001$). Radiographic and microbiological findings suggested less extensive disease among asymptomatic patients. Cavitary lesions were identified in 19.4% of the asymptomatic group compared to 24.6% in the symptomatic group ($P < 0.001$). Similarly, the prevalence of sputum smear positivity (22.6% vs 43.6%, respectively) and culture positivity (60.6% vs 72.0%, respectively) was significantly lower in the asymptomatic group than in the symptomatic group ($P < 0.001$ for both).

Differences in nutritional status and comorbidity burden were also observed. The median BMI was higher among the asymptomatic group than among the symptomatic group (21.4 vs 20.9 kg/m², respectively; $P < 0.001$). The proportion of individuals with a high comorbidity burden (CCI≥3) was lower in the asymptomatic group compared to the symptomatic group (35.3% vs 41.8%, respectively; $P < 0.001$). These patterns were generally consistent when stratified by bacteriological confirmation status, as shown in Supplementary Table 1.

Tuberculosis treatment outcomes at the end of treatment by symptom status

Treatment outcomes at the end of TB treatment differed significantly by symptom status (Supplementary Table 2). Treatment success was achieved in 88.1% of patients in the asymptomatic group compared to 84.5% of patients in the symptomatic group ($P < 0.001$). All-cause mortality during treatment was lower among the asymptomatic group (8.9% vs 13.0%, respectively; $P < 0.001$) and TB-related mortality were less frequent (2.9% vs 6.0%, respectively; $P < 0.001$, Supplementary Table 2, Figure 1). These patterns remained consistent when stratified by bacteriological confirmation status. In multivariable logistic regression models adjusting for demographic and clinical covariates, asymptomatic TB was consistently associated with a lower risk of TB-related death. Crude odds ratio (OR) for TB-related death in the asymptomatic group was 0.46 (95% CI, 0.43-0.50) compared to that in the symptomatic group. This association remained significant after full adjustment (adjusted OR, 0.70; 95% CI, 0.64-0.76 in Model 2, Table 2).

Post-treatment outcomes: recurrence and TB-related death

Patients with treatment success were followed up until December 31, 2022, allowing for a minimum of 2 years of post-treatment observation. The cumulative incidence of TB recurrence was significantly lower among the asymptomatic group than among the symptomatic group (1.9% vs 2.7%, respectively, $P < 0.001$; Supplementary Table 4, Figure 2A). Among individuals with bacteriologically confirmed TB, recurrence occurred in 2.3% of asymptomatic patients versus 2.9% of symptomatic patients. This association persisted after adjustment for demographic and clinical covariates (Table 2). In multivariable competing risk regression models, asymptomatic TB was associated with a reduced risk of TB recurrence (Table 3). The adjusted subdistribution hazard ratio (aSHR) for TB recurrence among the asymptomatic group was 0.84 (95% CI, 0.76-0.94) after controlling for age, sex, BMI, income level, comorbidities, bacteriological status, and initial disease severity (Table 3, Model 2). Subgroup analyses stratified by bacteriological confirmation status yielded consistent findings, with reduced recurrence risk observed in the asymptomatic group (Table 3, Figure 2B, C).

Post-treatment TB-related mortality was rare but lower among the asymptomatic group than among the symptomatic group (0.1% vs 0.2%, respectively, Supplementary Table 4). Owing to the limited number of events, multivariable adjustment for post-treatment TB-related mortality was not feasible.

Table 1
Baseline characteristics of the patients stratified by symptom status at diagnosis.

	Asymptomatic TB (n = 33,753)	Symptomatic TB (n = 55,176)	*P*
Age, years, median (IQR)	59.0 (44.0-74.0)	64.0 (48.0-78.0)	<0.001
Age, years			<0.001
≤40	7138 (21.1%)	9194 (16.7%)	
41-64	13,593 (40.3%)	18,905 (34.3%)	
65-79	8168 (24.2%)	15,319 (27.8%)	
≥80	4854 (14.4%)	11,758 (21.3%)	
Sex, Male	21,357 (63.3%)	33,307 (60.4%)	<0.001
Body mass index, kg/m^2, median	21.4 (19.5-23.5)	20.9 (18.8-23.2)	<0.001
Smoking history			<0.001
Never smoker	20,022 (59.3%)	33,207 (60.2%)	
Former smoker	6197 (18.4%)	11,115 (20.1%)	
Current smoker	7534 (22.3%)	10,854 (19.7%)	
CCI, score, n (%)			<0.001
0	8457 (25.1%)	8214 (14.9%)	
1	7603 (22.5%)	12,888 (23.4%)	
2	5767 (17.1%)	10,994 (19.9%)	
≥3	11,926 (35.3%)	23,080 (41.8%)	
Household income level			<0.001
0 (Lowest)	2652 (7.9%)	4756 (8.6%)	
1	5632 (16.7%)	9436 (17.1%)	
2	5200 (15.4%)	8312 (15.1%)	
3	5975 (17.7%)	9389 (17.0%)	
4	6338 (18.8%)	9908 (18.0%)	
5 (Highest)	7956 (23.6%)	13,375 (24.2%)	
Case detection strategy			<0.001
Active case finding	11,608 (34.4%)	3266 (5.9%)	
Passive case finding	22,145 (65.6%)	51,910 (94.1%)	
AFB smear, positive	7613 (22.6%)	24,065 (43.6%)	<0.001
Culture, positive	20,467 (60.6%)	39,748 (72.0%)	<0.001
NAAT, positive	14,037 (41.6%)	32,306 (58.6%)	<0.001
Presence of cavity	6532 (19.4%)	13,589 (24.6%)	<0.001
Drug susceptibility test			<0.001
DS-TB/HR-TB	32,796 (97.2%)	53,920 (97.7%)	
RR/MDR-TB	957 (2.8%)	1245 (2.3%)	

Note: Data are presented as numbers (%) or median (IQR, interquartile range).
Abbreviations: AFB, acid-fast bacillus; CCI, Charlson comorbidity index; DS-TB, drug-susceptible tuberculosis; HR-TB, isoniazid-resistant tuberculosis; NAAT, nucleic acid amplification test; RR/MDR-TB, rifampicin-resistant/multidrug-resistant tuberculosis; TB, tuberculosis.

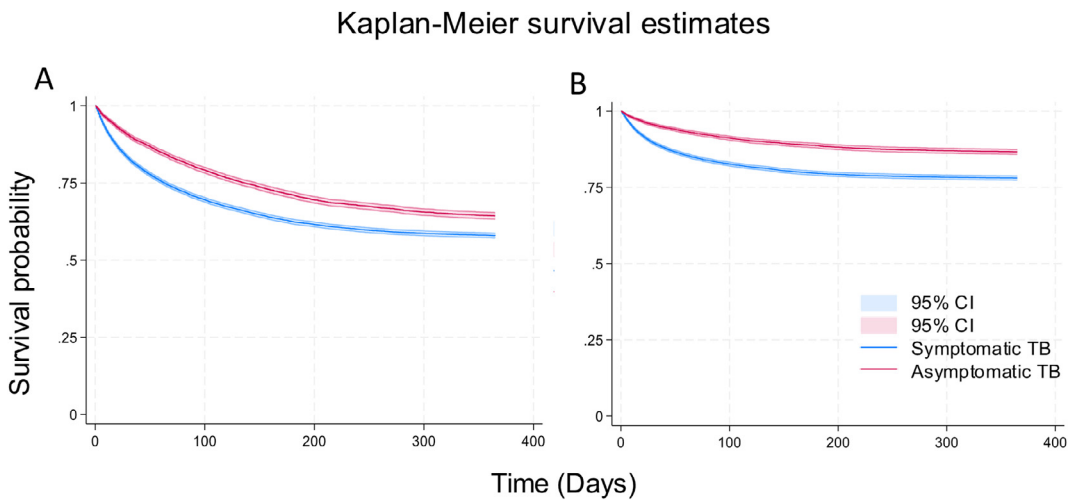

Figure 1. Kaplan–Meier curves of mortality within one year after tuberculosis (TB) treatment initiation, stratified by symptom status. (A) All-cause mortality; (B) TB-related mortality.

Discussion

This study is the first to generate population-based evidence on treatment outcomes and long-term prognosis—including disease recurrence and mortality following treatment completion—among individuals with asymptomatic pulmonary TB, utilizing a large-scale, nationwide cohort derived from integrated administrative and surveillance datasets. In this nationwide cohort comprising over 88,000 patients with TB in South Korea, 38% were asymptomatic at the time of diagnosis, and nearly 70% of these cases were bacteriologically confirmed. Compared to patients with symptomatic TB, those with asymptomatic TB experienced significantly lower TB-related mortality during treatment and a reduced risk of disease recurrence after treatment completion. These results highlight prognostic differences between asymptomatic and symptomatic TB, which may reflect differences in disease severity, host

Table 2
Association between symptom status and end-of-treatment mortality, as analyzed by multivariable logistic regression.

		Symptoms	Event, n	Crude			Model 1			Model 2		
				OR	95% CI	*P*	aOR	95% CI	*P*	aOR	95% CI	*P*
Total	TB-related mortality	No	977	0.46	0.43-0.50	<0.001	0.58	0.53-0.62	<0.001	0.70	0.64-0.75	<0.001
		Yes (ref)	3312									
	All-cause mortality	No	2997	0.65	0.63-0.68	<0.001	0.81	0.77-0.85	<0.001	0.97	0.92-1.02	0.272
		Yes (ref)	7179									
Bacteriologically confirmed TB	TB-related mortality	No	863	0.54	0.50-0.58	<0.001	0.61	0.56-0.66	<0.001	0.71	0.65-0.77	<0.001
		Yes (ref)	3032									
	All-cause mortality	No	2577	0.77	0.73-0.80	<0.001	0.87	0.82-0.91	<0.001	1.01	0.95-1.06	0.853
		Yes (ref)	6390									
Bacteriologically unconfirmed TB	TB-related mortality	No	114	0.35	0.28-0.44	<0.001	0.53	0.42-0.67	<0.001	0.61	0.48-0.78	<0.001
		Yes (ref)	280									
	All-cause mortality	No	420	0.46	0.41-0.52	<0.001	0.65	0.57-0.74	<0.001	0.81	0.70-0.93	0.003
		Yes (ref)	789									

Model 1 was adjusted for age, sex, household income level, and Charlson comorbidity index. Model 2 was additionally adjusted for smoking history, body mass index, presence of cavitation, bacteriological confirmation (in the total population only), case detection strategy, and rifampin resistance.
Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; TB, tuberculosis.

Table 3
Association between symptom status and post-treatment TB recurrence, as analyzed by competing-risks regression.

	Symptoms	Event, n	Crude			Model 1			Model 2		
			HR	95% CI	*P*	aSHR	95% CI	*P*	aSHR	95% CI	*P*
Total	No	577	0.71	0.64-0.78	<0.001	0.71	0.64-0.78	<0.001	0.84	0.76-0.94	0.002
	Yes (ref)	1275									
Bacteriologically confirmed TB	No	460	0.78	0.70-0.87	<0.001	0.76	0.68-0.85	<0.001	0.87	0.77-0.98	0.018
	Yes (ref)	1111									
Bacteriologically unconfirmed TB	No	117	0.62	0.49-0.78	<0.001	0.64	0.50-0.82	<0.001	0.71	0.55-0.92	0.008
	Yes (ref)	164									

Note: Subdistribution hazard ratios (aSHR) with death as a competing event; follow-up to 2 years after treatment completion.
Model 1 was adjusted for age, sex, household income level, and Charlson comorbidity index. Model 2 was additionally adjusted for smoking history, body mass index, presence of cavitation, bacteriological confirmation (in the total population only), case detection strategy, and rifampin resistance.
Abbreviations: aSHR; adjusted subdistribution hazard ratio; CI, confidence interval; HR, hazard ratio; TB, tuberculosis.

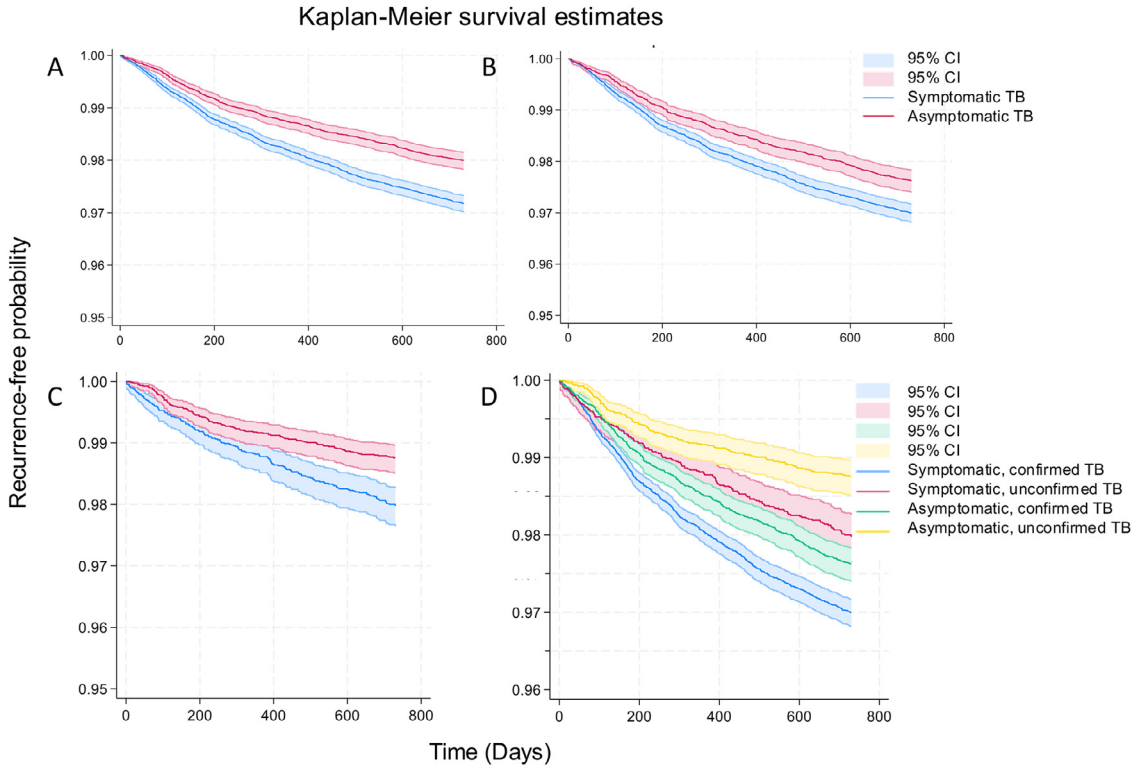

Figure 2. Kaplan–Meier curves of tuberculosis (TB) recurrence after treatment completion, stratified by symptom status and bacteriological confirmation. (A) Total cohort: symptomatic vs asymptomatic; (B) Bacteriologically confirmed TB: symptomatic vs asymptomatic; (C) Bacteriologically unconfirmed TB: symptomatic vs asymptomatic; (D) Four-group comparison: symptomatic confirmed, symptomatic unconfirmed, asymptomatic confirmed, asymptomatic unconfirmed.

characteristics, and other factors influencing disease progression. The results have implications for TB screening, risk stratification, and post-treatment monitoring strategies, particularly in settings where asymptomatic TB is increasingly identified through active case detection and enhanced diagnostic modalities.

Several pathophysiological mechanisms may account for the more favorable prognosis in patients with asymptomatic TB. First, this group exhibited less extensive radiological disease, lower rates of sputum smear and culture positivity, and fewer cavitary lesions, consistent with a lower bacillary burden [10–13]. This disease profile is associated with reduced risk of tissue destruction and subsequent pulmonary sequelae, thereby contributing to the favorable treatment outcomes. Second, earlier detection through active case finding likely facilitated diagnosis at a less advanced stage of disease, providing a lead-time advantage [14,15]. Third, patients with asymptomatic TB demonstrated fewer comorbidities and superior nutritional status, both of which are associated with enhanced treatment response [16]. Reduced competing mortality risk and improved pharmacologic tolerance and adherence among individuals with fewer comorbidities and adequate BMI represent plausible mechanistic pathways through which baseline health status influences clinical outcomes.

WHO recently reclassified “asymptomatic TB” as a programmatic category, replacing the previously used term “subclinical TB” [3]. This revision reflects growing recognition that symptom-based screening alone may fail to identify a substantial proportion of bacteriologically positive and potentially infectious cases. Experts advocate symptom-agnostic screening modalities, such as chest radiography, to expand treatment coverage and interrupt transmission chains [17]. Prevalence surveys conducted across multiple countries have revealed that 40-60% of bacteriologically confirmed TB cases were asymptomatic at the time of detection [10,18]. In our cohort, 38% of individuals were asymptomatic, and 70% of these were bacteriologically confirmed, indicating that a significant pool of undetected infectious disease may exist within the community. Although asymptomatic TB is generally associated with a lower bacillary burden, subsets of patients still demonstrate features of infectiousness, such as sputum smear positivity and cavitary lesion [10,11,13,19]. These findings underscore the importance of early detection and prompt initiation of therapy in improving individual outcomes and advancing public health goals in TB control.

Approximately one-third of asymptomatic cases in our study were diagnosed through active case finding, demonstrating the critical role of systematic screening, contact investigation, and health check-ups in uncovering otherwise undetected cases. Comparable findings from prevalence surveys reinforce the utility of such approaches in reducing diagnostic delays and curbing transmission [10,14]. From a policy perspective, these findings suggest that strengthening active case finding is essential, particularly among high-risk populations such as the elderly, people with diabetes mellitus, and those who are immunocompromised [20]. Cost-effectiveness analyses indicate that active case finding can be beneficial in high-burden settings, especially when targeted at high-risk groups [21,22]. However, patients with asymptomatic disease may perceive themselves as healthy, leading to delays in treatment initiation or poor adherence [22]. In our cohort, 2.1% of patients were LTFU among the asymptomatic and bacteriologic confirmed group versus 1.5% in the symptomatic group (Supplementary Table 2). This emphasizes the necessity for patient education, counseling, and adherence support, particularly in asymptomatic populations identified through screening rather than self-presentation.

Although asymptomatic TB was associated with more favorable clinical outcomes, the majority of cases were bacteriologically positive and thus potentially capable of transmitting infection. Data from 14 countries across Africa and Asia suggests that approximately two-thirds of global TB transmission may originate with asymptomatic TB [4]. Consequently, prompt initiation of treatment is essential, and delaying therapy in the expectation of spontaneous resolution is not advisable. Nevertheless, the relatively mild clinical phenotype observed in many asymptomatic patients raises the possibility of risk-stratified treatment approaches. For example, the SHINE trial demonstrated that a 4-month regimen was non-inferior to the conventional 6-month regimen in children with non-severe, drug-susceptible TB [23]. Although direct evidence in adults is lacking, similar shortened regimens could be evaluated in carefully selected low-risk adults with asymptomatic TB, ideally guided by biomarker profiles and clinical risk stratification. Recent WHO guidance and expert commentaries emphasize the urgent need for research to optimize treatment regimens for asymptomatic and low-burden TB as part of global elimination efforts [1].

The major strengths of this study include its nationwide coverage, large sample size, and extended follow-up, which together enabled a robust evaluation of both treatment outcomes and disease recurrence. The use of linked national databases allowed for comprehensive case identification and accurate mortality verification.

However, several limitations warrant consideration. First, symptom status was ascertained at a single timepoint through TB nurse-administered case investigation forms, and recall bias or under-reporting of mild or transient symptoms cannot be entirely excluded. Such residual misclassification—patients with milder symptoms inadvertently classified as asymptomatic—would tend to attenuate the observed difference between groups. Second, although case detection modality was recorded using standardized categories on the KTB-Surv case investigation form, ACF and PCF may not have been clearly distinguished in some cases due to heterogeneity in reporting practices across the healthcare system. Third, end-of-treatment outcomes were analyzed using multivariable logistic regression by comparing treatment success with death, and patients with LTFU, failure, or not-evaluated outcomes were excluded as their mortality status at the end-of-treatment time point could not be reliably ascertained. Although LTFU was uncommon and the absolute difference between groups was small (2.3% vs 1.8%), this exclusion could introduce bias. Furthermore, although our cohort was linked to the national cause-of-death registry, post-LTFU mortality was not separately analyzed by symptom status; future studies addressing this aspect could provide a more complete picture of the long-term prognosis of TB patients with treatment interruption, particularly in relation to symptom status at diagnosis. Fourth, in the recurrence analysis, although death was treated as a competing event, additional administrative censoring (such as for emigration) was not separately applied; given the very low proportion of foreign nationals in the Korean TB cohort (<3%) and the short 2-year follow-up window, the impact on our estimates is expected to be minimal. Fifth, bacteriologically unconfirmed TB cases carry inherent diagnostic uncertainty, which could influence the outcome estimates. Finally, as with all observational studies, residual confounding cannot be excluded (e.g., unmeasured health-seeking behavior, time to treatment initiation, regimen/adherence details, or radiographic severity beyond cavitation), and generalizability may be constrained by the low-incidence setting with established screening infrastructure.

Conclusion

Asymptomatic pulmonary TB accounted for more than one-third of all TB cases in South Korea, with nearly 70% bacteriologically confirmed. Compared to symptomatic disease, asymptomatic TB was associated with lower TB-related mortality during treatment and a reduced risk of post-treatment recurrence. These findings highlight the need to complement symptom-based diagnostic strategies with systematic, symptom-agnostic screening ap-

proaches and to ensure rapid linkage-to-care after screening-based detection. Prompt treatment initiation is essential as it confers direct benefit with lower mortality and recurrence observed in our study. The milder clinical phenotype of asymptomatic TB also warrants further evaluation of risk-stratified treatment regimens, such as shorter regimens in selected low-risk adults.

Data sharing statement

The data used in this study were obtained from the database of the National Health Insurance Sharing Service (NHISS) (https://nhiss.nhis.or.kr/bd/ay/bdaya001iv.do). In accordance with NHISS policies and national data governance regulations, researchers are not permitted to redistribute or publicly release individual-level data. However, the NHISS allows access to anonymized datasets for approved research purposes. Researchers may apply for access through the NHISS portal and must agree to abide by ethical guidelines and data use agreements. A processing fee may apply. The dataset used in this article is available to qualified researchers upon request and approval from NHISS.

Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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Ethical approval

This study protocol was approved by the Institutional Review Board of Severance Hospital (4-2022-0595) and the Korea National Health Insurance Service Medical Request Review Committee (NHIS-2024-1-186). The requirement for informed consent was waived, due to the retrospective nature of the study and the use of anonymized data. This study adheres to the tents of the Declaration of Helsinki and all relevant ethical and regulatory guidelines.

Author contributions

Se Hyun Kwak, Hongjo Choi, and Young Ae Kang conceived and designed the study. Se Hyun Kwak, Hongjo Choi, Seung Won Lee, Dawoon Jeong, Hojoon Sohn and Young Ae Kang contributed to data collection and analysis. Se Hyun Kwak, Hongjo Choi, and Young Ae Kang interpreted the data and drafted the manuscript. All authors revised and approved the final version of the manuscript. All authors accept responsibility for the accuracy of the content of the final manuscript. Generative artificial intelligence was not used in writing any part of the manuscript.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2026.108805.

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