Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

COVID-19 Vaccination Coverage, Poverty, and Tuberculosis Treatment Outcomes in Indonesia: An Exploratory Multilevel Analysis

Putri Bungsu Machmud

putri.bungsu10@ui.ac.id

Universitas Indonesia

Husnul Khatimah

Poltekkes Kemenkes Jakarta I

Arie Wahyu Wijayanto

Politeknik Statistika STIS

I Wayan Gede Artawan Eka Putra

Universitas Udayana

Puhilan Puhilan

Kementerian Kesehatan Republik Indonesia

Andreas Wienke

Medical School of the Martin Luther University Halle- Wittenberg

Research Article

Keywords: COVID-19, tuberculosis, drug-sensitive tuberculosis, drug-resistant tuberculosis, vaccination, health system resilience

Posted Date: November 25th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11426197/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Introduction:

The COVID-19 pandemic disrupted tuberculosis services globally, but the association between pandemic response capacity and tuberculosis treatment outcomes in resources-limited setting remains underexplored. This study explored the ecological relationship between district-level COVID-19 vaccination coverage (as a marker of health system performance) and tuberculosis treatment success in Indonesia during 2020–2022.

Methods

We analysed 1,098,425 tuberculosis patients treated in Indonesia from 2020 to 2022 in a cross-sectional study, including 1,082,757 with drug-sensitive tuberculosis (DS-TB) and 15,668 with drug-resistant tuberculosis (DR-TB). Multilevel logistic regression models were used to assess associations between individual-level factors and district-level COVID-19 vaccination coverage (first-dose, second dose, and boosters) with successful tuberculosis treatment outcomes as an ecological analysis, causality cannot be inferred. Missing data for occupation (≈ 10%) were imputed using k-nearest neighbors (KNN) imputation. For HIV (≈ 50% missing) and diabetes (≈ 57% missing) in DS-TB, we conducted complete-case analysis and multiple imputation (20 imputations) with auxiliary variables (age, sex, occupation, treatment outcome, district vaccination coverage).

Results

Each 10-percentage point increase in district-level first-dose COVID-19 vaccination coverage was correlated with marginally higher odds of successful DR-TB treatment (aOR = 1.02; 95% CI = 1.00-1.04). Second-dose coverage showed a borderline opposite association (aOR = 0.97; 95% CI = 0.95-1.00). No association was found for DS-TB. Sensitivity analyses revealed a stark contrasting comorbidity pattern: diabetes's apparent protective effect (aOR = 1.27; 95% CI 1.25–1.30) reversed in complete-case (aOR = 0.86; 95%CI = 0.84–0.89) and multiple imputation (pooled aOR = 0.86; 95%CI = 0.84–0.89) analyses, indicating that the main estimate was sensitive to the handling of unascertained diabetes status. HIV remained consistently negative across models (main aOR = 0.26; 95%CI = 0.25–0.27 and sensitivity aOR = 0.24; 95%CI = 0.23–0.26), indicating a robust association.

Conclusions

In this ecological analysis, district with higher COVID-19 vaccination coverage had higher odds of successful DR-TB treatment outcomes; however, causal inference is not possible. Policy implications included: (1) prioritizing complete prospective comorbidity data and (2) further evaluating whether

vaccination coverage as a monitoring tool to identify district needing surge support during emergencies. No reliable conclusion about the direction of diabetes' effect on TB outcomes can be drawn; all comorbidity findings should be considered hypothesis-generating.

Clinical trial number

: Not applicable

1. Introduction

During the COVID-19 pandemic, patients with pulmonary tuberculosis faced a dual burden of two lethal respiratory diseases, with higher mortality risk than those with either condition alone [1–3]. The pandemic severely disrupted tuberculosis elimination programmes by overburdening healthcare systems, diverting resources, and causing delays in service access, drug supply, and delivery [1, 3]. The World Health Organization (WHO) reported many tuberculosis patients went undiagnosed or had delayed diagnosis due to overlapping symptoms with COVID-19 [4], and several Asian studies noted declines in tuberculosis notifications [5, 6]. Although the WHO declared the end of COVID-19 as a Public Health Emergency of International Concern in May 2023, the post-pandemic period continues to reshape the landscape of tuberculosis control. The recent and abrupt withdrawal of international funding for tuberculosis programs in 2025, including critical support from the United States Agency for International Development (USAID), has created a 'second crisis' just as health systems were beginning to recover [7]. Furthermore, recent studies demonstrate that the financial and health system disruption have aggravated the socioeconomic vulnerabilities of tuberculosis patients, potentially leading to a surge in catastrophic health costs and treatment default [7].

Indonesia, the country with the second-highest tuberculosis burden globally, reported 562,049 cases in 2019 (a 69% increase since 2015) [4]. Although Indonesia is now classified as an upper-middle income country by the World Bank [8], significant economic disparities persist, with approximately 9.4% of the population living below the national poverty line and many more vulnerable to falling into poverty due to health expenses [9, 10]. These poverty-related vulnerabilities were exacerbated during the COVID-19 pandemic [11, 12], particularly in districts with weaker health infrastructure [13].

The same report noted a 25–30% decline in diagnosed cases in Indonesia, India, and the Philippines from January to June 2020 compared to 2019 [4]. Jhaveri et al. described widening disparities in tuberculosis diagnosis and treatment during the pandemic, driven by patients' fear of COVID-19 infection in healthcare facilities. These disparities led to delayed or interrupted treatment and higher rates of loss to follow-up, treatment failure, and mortality [14].

Previous studies identified factors associated with successful drug-resistant tuberculosis (DR-TB) treatment, including ethnicity, smoking, comorbidities, and treatment regimens [15][16]. However, these studies were conducted before and at the onset of the pandemic and did not account for pandemic-

specific determinants such as COVID-19 vaccination status, although vaccination has been reported to enhance protection against active tuberculosis by > 90% [17].

This study examined the association between COVID-19 vaccination and tuberculosis treatment outcomes in Indonesia during 2020–2022, including individual-level factors. Using district-level vaccination coverage as an ecological proxy, we aimed to assess whether pandemic response capacity was associated with individual tuberculosis treatment outcomes, providing lessons for strengthening health systems against future crises.

2. Materials and Methods

2.1 Study design and Limitations

This is an ecological cross-sectional analysis using aggregated district-level vaccination data and individual-level TB treatment records. The unit of analysis for the exposure is the district, while the outcome is at the individual level. As an ecological study, findings are associated and cannot be interpreted as causal effects. Residual confounding by unmeasured district-level factors (e.g., health system quality, governance, poverty) is likely. These limitations are addressed further in the Discussion.

2.2 Study population

The study population was all adult patients (> 14 years old) with confirmed incident pulmonary tuberculosis from 2020 to 2022. This study classified tuberculosis patients into drug-sensitive tuberculosis (DS-TB), defined as infection with *Mycobacterium tuberculosis* susceptible to all first-line anti-TB drugs, and DR-TB, defined as resistance to at least one key anti-TB drug. Only patients treated according to standard national protocols were included.

2.3 Data sources

This study used data from two national databases. Tuberculosis treatment and patient characteristics were obtained from the Tuberculosis Information System (SITB), which records DS-TB and DR-TB cases from healthcare facilities nationwide. COVID-19 vaccination coverage data for first, second, and booster doses were obtained from the Directorate of Immunization, Ministry of Health, and aggregated at the district and city levels across 38 provinces in Indonesia. First-dose coverage was defined as the percentage of adults (≥ 18 years) in each district who had received at least one dose by December 31, 2021 (to allow for coverage to accumulate before outcome assessment). Only first-dose and second-dose vaccination coverage were considered in the main analysis. For descriptive mapping purposes only (Fig. 2), vaccination coverage was categorized as lowest coverage (< 50%), low coverage (50–79%), and high coverage (≥ 80%). In the main multilevel regression analyses, vaccination coverage was treated as a continuous variable representing the percentage of vaccinated adults per district.

Vaccination coverage was used an ecological indicator of district-level health system performance during the pandemic. While no formal validation against other health system indicators was possible due

to data constraints, COVID-19 vaccination coverage has been shown in previous studies to correlate with routine immunization coverage and overall health system strength. This supports its use as a modest proxy for pandemic response capacity, although it remains imperfect and may reflect vaccine acceptance, logistic, or political prioritization rather than overall health system resilience.

2.4 Outcome variables

Treatment outcomes were categorized as cured, complete treatment, failed, lost to follow-up, and death. For the multilevel logistic regression analysis, a binary outcome variable was created by combining “cured” and “complete treatment” as successful treatment, while “failed”, “lost to follow-up”, and “died” were combined as unsuccessful treatment. This binary classification follows standard WHO reporting guidelines for TB treatment outcomes.

2.5 Explanatory variables

This study included individual-level factors such as age (continuous), gender, occupation, and comorbidities (diabetes mellitus [DM] and HIV), as well as final treatment outcomes. At treatment initiation, DM and HIV were identified through patient history or diagnostic testing for patients with uncertain status, who were tested or referred to other health facilities when necessary. Patients who refused HIV testing or failed to report external test results were classified as having unknown HIV status.

Data were also collected on treatment regimens. Patients with DS-TB received either Category 1 or Category 2 treatment. Category 1 treatment is administered to newly diagnosed tuberculosis patients and begins with two months of daily Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol, followed by four months of Rifampicin and Isoniazid three times weekly. Category 2 treatment is administered to tuberculosis patients with prior treatment history, specifically those who have relapsed, failed Category 1 treatment, or discontinued treatment. It includes the same four oral drugs with Streptomycin injections for the first two months, followed by one month without Streptomycin and a four-month continuation phase with Rifampicin and Isoniazid three times weekly, for a minimum total duration of seven months.

Drug-resistant tuberculosis treatment in Indonesia is classified into Shorter Treatment Regimens (STR), Longer Treatment Regimens (LTR) (including injectable and oral options), Bedaquiline-Pretomanid-Linezolid (BPaL), and Isoniazid-monoresistant regimens (INH). The STR, 19–24 months, is primarily used for rifampicin-resistant/multidrug-resistant tuberculosis (RR/MDR-TB) without confirmed resistance to fluoroquinolone or second-line injectable drugs, following national guidelines. The LTR is used for patients with more extensive resistance. The BPal, a six-month oral regimen, is administered to patients with pre-XDR or XDR-TB. Isoniazid-monoresistant tuberculosis is treated with a regimen that excludes rifampicin but includes other first-line drugs.

2.6 Data analyses

Descriptive data were summarized as absolute and relative frequencies and medians with interquartile ranges (IQRs). Multilevel logistic regression assessed associations between individual-level factors and district-level COVID-19 vaccination coverage (first dose, second dose, and boosters), operationalized as

continuous variables representing the percentage of vaccinated adult per district. Given the ecological design, these analyses estimate associations rather than causal effects; no causal inference should be drawn. Missing data handling differed by variable based on missing proportions and assumed mechanisms: for occupational status (missing ≈ 10%), k-nearest neighbors (KNN) imputation was applied. The KNN imputes missing values by identifying the k most similar complete cases (neighbors) based on a distance metric (Euclidean distance) using auxiliary variables: age, sex, treatment outcome, and district-level vaccination coverage. The optimal k-value (k = 5) was selected via cross-validation minimizing root mean square error.

Imputation was performed separately for DS-TB and DR-TB datasets. For HIV status (missing 50.4% in DS-TB, 29.4% in DR-TB) and diabetes status (missing 57.2% in DS-TB, 0% in DR-TB), we did not perform imputation in the main model. Missingness for these comorbidities was likely informative rather than missing at random: patients with unknown HIV status had substantially lower odds of successful treatment than those with documented HIV-negative status, indicating that unascertained status was associated with treatment outcome and probably reflected differential access to testing and healthcare engagement. Retaining an 'unknown' category therefore preserves this information instead of overwriting it with model-based values. In addition, because the proportion missing was very high for DS-TB, any Missing At Random-based (MAR-based) imputation would depend heavily on unverifiable model assumptions and could yield biased estimates if those assumptions were incorrect. We therefore retained a separate 'unknown' category in the main multilevel models and assessed the robustness of the comorbidity findings through complete-case analysis and multiple imputation as sensitivity analyses.

Sensitivity analysis 1, complete-case analysis

we restricted the DS-TB sample to patients with documented status for both HIV and diabetes (i.e., excluding the 'unknown' categories). The same multilevel model (model 3) was re-fitted on this complete-case subset.

Sensitivity analysis 2, multiple imputation: we performed multiple imputation using chained equations (MICE) with 20 imputed datasets. Missing values for HIV and diabetes were imputed using auxiliary variables: age, sex, occupation, treatment outcome, and district-level COVID-19 vaccination coverage (first dose, second dose). The imputation model included all variables from the main analysis. Pooled estimates were obtained using Rubin's rules. We chose 20 imputations because the proportion of missing data exceeded 50% [18].

Temporal sensitivity analysis

To address the potential temporal mismatch between tuberculosis treatment episodes and vaccination rollout (vaccination began in January 2021, but the study period included 2020), we conducted an additional sensitivity analysis restricted to patients who initiated tuberculosis treatment in 2021–2022 (i.e., after the start of Indonesia's national vaccination campaign). We re-ran Model 3 for DS-TB and DR-

TB using this restricted cohort and compared the results to the main analysis that included 2020 patients. This allowed us to assess whether inclusion of the 2020 cohort introduced bias.

Results from these sensitivity analyses were compared to the main model. If the direction or magnitude of the associations changed substantially, we considered the main findings non-robust and interpreted them with extreme caution. Statistical significance was not used as a criterion for robustness, because the sensitivity analyses used smaller samples.

To further explore whether district-level COVID-19 vaccination coverage reflected underlying socioeconomic gradients, we obtained district-level poverty data from the Indonesian National Statistics Agency (BPS, 2021 data). Poverty was defined as the proportion of the district population living below the national poverty line. We calculated Spearman's rank correlation coefficient between district-level first-dose COVID-19 vaccination coverage and district poverty rates, as the variables were not normally distributed (Shapiro-Wilk test,). Correlation analysis was performed using Stata version 17.0 (StataCorp, College Station, TX, USA).

To aid interpretation, odds ratios (ORs) for vaccination coverage represents the change in odds of successful treatment per 10-percentage point increase. Four models were built sequentially: null (Model 0) individual-level (Model 1), district-level (Model 2), and full (model 3). The intraclass correlation coefficient (ICC) and median odds ratio (MOR) were calculated to evaluate contextual effects. We used a two-level random-intercept logistic regression model with districts as the upper level. Models were fitted using adaptive Gauss-Hermite quadrature with 7 integration points. All analyses used Stata version 17.0 (StataCorp, College Station, TX, USA).

2.7 Use of generative AI and AI-assisted technologies

During the preparation of this work the author(s) used Grammarly and/or QuillBot for language editing, including grammar, syntax, and diction. These tools were not used to generate scientific content, analyse data, or interpret results. The authors reviewed and edited all output and take full responsibility for the content of the published article.

3. Results

3.1 Overview of tuberculosis case distribution and treatment outcomes

This study included 1,082,757 DS-TB and 15,668 DR-TB patients treated from 2020–2022 across all Indonesian provinces. The median age was 43 years (IQR 29–56) for DS-TB and 42 years (IQR 29–53) for DR-TB. Approximately, 60% of patients in both groups were male, and nearly half were unemployed (49.8% for DS-TB, 40.9% for DR-TB). HIV positivity was 2.2% among DS-TB and 2.7% among DR-TB patients. However, data on HIV status were missing for 50.4% of DS-TB patients (n = 546,388) and 29.4%

of DR-TB patients (n = 4,601). Similarly, diabetes status was missing for 57.2% of DS-TB patients (n = 619,035). Therefore, the reported frequencies for HIV and diabetes should be interpreted with caution.

The majority of DS-TB cases received Category 1 treatment (97.2%), while over 50% of DR-TB patients received LTR, either oral or injectable (Table 1, Table 2). Missing data frequencies are shown in Tables 1 and 2. For occupational status (≈ 10% missing), KNN imputation was performed (see Methods). For HIV and diabetes, missing values were retained as an ‘unknown’ category in subsequent regression models.

Table 1

Characteristics of drug-sensitive tuberculosis (DS-TB) patients in Indonesia, 2020–2022

Variable	Drug Sensitive Tuberculosis [n (%)]			Total
	2020 (n = 293,189)	2021 (n = 317,176)	2022 (n = 472,392)	(N = 1,082,757)
Age, median (IQR)	43 (29–56)	42 (28–55)	44 (30–57)	43 (29–56)
Men, n (%)	175 965 (60.0)	188 814 (59.5)	282 732 (59.8)	647 511(59.8)
Occupational status				
Employed	122 686 (41.8)	129 873 (41.0)	186 467 (39.5)	439 026 (40.5)
Unemployed	145 826 (49.7)	158 216 (49.9)	235 117 (49.8)	539 159 (49.8)
Missing†	24 677 (8.4)	29 087 (9.2)	50 808 (10.8)	104 572 (9.7)
HIV Status				
Negative	120 805 (41.2)	146 828 (46.3)	244 061(51.7)	511 694 (47.3)
Positive	6 506 (2.2)	6 900 (2.2)	11 003 (2.3)	24 409 (2.3)
Missing (treated ad 'unknown) ††	165 878 (56.6)	163 448 (51.5)	217 328 (46.0)	546 654 (50.5)
Diabetic status				
No	79 176 (27.0)	100 902 (31.8)	168 200 (35.6)	348 278 (32.2)
Yes	28 280 (9.6)	34 714 (10.9)	52 450 (11.1)	115 444 (10.7)
Missing (treated ad 'unknown) ††	185 733 (63.4)	181 560 (57.2)	251 742 (53.3)	619 035 (57.2)
Treatment category				
Category 1	280 213 (95.6)	308 784 (97.4)	469 256 (99.3)	1 058 253 (97.7)
Category 2	12 976 (4.4)	8 392 (2.6)	3 136 (0.7)	24 504 (2.3)
Outcome treatment				
Died	12 780 (4.4)	14 053 (4.4)	20 734 (4.4)	47 567 (4.4)
Failed	1 191 (0.4)	1 269 (0.4)	1 851 (0.4)	4 311 (0.4)

Variable	Drug Sensitive Tuberculosis [n (%)]			Total
	2020 (n = 293,189)	2021 (n = 317,176)	2022 (n = 472,392)	(N = 1,082,757)
Lost to follow up	20 483 (7.0)	22 633 (7.1)	38 224 (8.1)	81 340 (7.5)
Complete treatment	192 153 (65.5)	187 587 (59.2)	277 415 (58.7))	657 155 (60.7)
Cured	66 582 (22.7)	91 634 (28.9)	134 168 (28.4)	292 384 (27.0)

† Missing values for occupational status were imputed using k-nearest neighbors (KNN); the frequencies shown are pre-imputation values.

†† Missing values for HIV and diabetes were retained as an 'unknown' category in regression models.

Table 2

Tuberculosis drug-resistant tuberculosis patient characteristics in Indonesia, 2020–2022

Variable	Drug Resistance Tuberculosis [n (%)]			Total
	2020 (n = 4,201)	2021 (n = 4,999)	2022 (n = 6,468)	(N = 15,668)
Age, median (IQR)	42 (29–52)	41 (29–52)	43 (29–54)	42 (29–53)
Men, n (%)	2 539 (60.4)	2 957 (60.4)	3 842 (59.4)	9 338 (60.0)
Occupational status				
Employed	1 557 (37.1)	1 872 (38.2)	2 438 (37.7)	5 867 (37.7)
Unemployed	1 621 (38.6)	2 038 (41.6)	2 796 (43.2)	6 455 (41.5)
Missing†	1 023 (24.4)	1 089 (22.2)	1 234 (19.1)	3 346 (21.5)
HIV Status				
Negative	2 531 (60.3)	3 399 (69.4)	4 651 (71.9)	10 581 (68.0)
Positive	98 (2.3)	143 (2.9)	182 (2.8)	423 (2.7)
Missing (treated as ‘unknown) ††	1 572 (37.4)	1 457 (27.7)	1 635 (25.3)	4 664 (29.3)
Diabetic status				
No	3 375 (80.3)	3 899 (79.6)	5 035 (77.8)	12 309 (79.1)
Yes	826 (19.7)	1 100 (20.4)	1 433 (22.2)	3 359 (20.9)
Treatment regiment				
STR injection	1 148 (27.3)	78 (1.6)	13 (0.2)	1 239 (7.9)
STR Oral	598 (14.2)	2 015 (41.1)	2 722 (42.1)	5 335 (34.1)
LTR injection	490 (11.7)	53 (1.1)	7 (0.1)	550 (3.5)
LTR Oral	1 965 (46.8)	2 853 (58.2)	3 661 (56.6)	8 479 (54.1)
BPaL	0	0	61 (0.9)	61 (0.4)
Monoresistance INH	0	0	4 (0.1)	4 (0.0)
Outcome treatment				
Died	845 (20.1)	838 (17.1)	1 296 (20.0)	2 797 (19.1)
Failed	299 (7.1)	401 (8.2)	766 (11.8)	1 466 (9.4)
Lost to follow up	825 (19.6)	849 (17.3)	1 194 (18.5)	2 868 (18.4)

Variable	Drug Resistance Tuberculosis [n (%)]			Total
	2020 (n = 4,201)	2021 (n = 4,999)	2022 (n = 6,468)	(N = 15,668)
Complete treatment	400 (9.5)	446 (9.1)	642 (9.9)	1 488 (9.6)
Cured	1 832 (43.6)	2 365 (48.3)	2 570 (39.7)	6 767 (43.5)

STR= Short Treatment Regimen; LTR= Long Treatment Regimen; BPaL = Bedaquiline, Pretomanid, and Linezolid; INH= Isoniazid

† Missing values for occupational status were imputed using k-nearest neighbors (KNN); the frequencies shown are pre-imputation values.

†† Missing values for HIV and diabetes were retained as an 'unknown' category in regression models.

Table 1. **Tuberculosis drug-sensitive tuberculosis patient characteristics in Indonesia, 2020–2022**

Table 2. **Tuberculosis drug-resistant tuberculosis patient characteristics in Indonesia, 2020–2022**

Analysis of treatment outcomes trends from 2020 to 2022 revealed substantial improvements (Fig. 1). The number of cured DS-TB cases increased by 100%, rising from 66,582 cases in 2020 to 134,168 cases in 2022. The improvements in cure rates corresponded with increases in total case notifications, which rose 61.1% for DS-TB and 54% for DR-TB over the three-year study period.

Figure 1. Treatment outcome of drug-sensitive and drug-resistant tuberculosis in Indonesia, 2020–2022. The figure shows the distribution of treatment outcomes (cured, complete treatment, failed, lost to follow-up, and died) among patients with drug-sensitive tuberculosis (DS-TB) and drug-resistant tuberculosis (DR-TB).

3.2 Coverage of completed COVID-19 vaccination (first and second doses)

Figure 2 illustrates the geographic distribution of first dose and second-dose COVID-19 vaccination coverage across Indonesian districts. For first-dose coverage, most regions exhibited low coverage (> 50% to 79%), while several areas across the main islands (Java, Sumatra, and Sulawesi) achieved high coverage (≥ 80%). However, some regions, particularly in eastern Indonesia, recorded the lowest coverage (< 50%). In contrast, second-dose coverage revealed an increase in the number of regions with very low coverage, notable in parts of Sumatera, Java, and Kalimantan.

Figure 2. COVID-19 vaccination coverage in Indonesia: first and second doses. Maps show district-level first dose and second-dose COVID-19 vaccination coverage, categorized as lowest coverage (< 50%), low coverage (50–79%), and high coverage (≥80%).

3.3 Multilevel regression model of outcome treatment

The null model revealed intraclass correlation coefficient (ICC) values of 19.2% for DS-TB and 15.1% for DR-TB, indicating that 19% and 15% of the total residual variance in the odds of successful treatment were attributable to differences between districts, respectively, while the remaining variance was due to differences between individual patients within the same districts (Model 0, Tables 3 and 4). The median odds ratio (MOR) was 2.4 for DS-TB and 2.3 for DR-TB, confirming substantial between-district heterogeneity in treatment outcomes. The inclusion of individual-level factors reduced the variance for DS-TB and DR-TB, respectively (Model 1, Tables 3 and 4).

Table 3

Multilevel logistic regression model of drug sensitive tuberculosis (DS-TB)

Variables	Model 0	Model 1	Model 2	Model 3
	Odds Ratio (95% CI)			Adjusted Odds Ratio (95% CI)
Age	-	**0.98 (0.98–0.99)**	-	**0.99 (0.98–0.99)**
Sex (Ref: Men)				
Women	-	**1.02 (1.01–1.04)**	-	**1.02 (1.01–1.04)**
Occupational status (Ref: Unemployed)				
Employed	-	**1.03 (1.01–1.04)**	-	**1.03 (1.02–1.04)**
HIV Status (Ref: Negative)				
Positive	-	**0.26 (0.25–0.27)**	-	**0.26 (0.25–0.27)**
Unknown	-	**0.66 (0.50–0.87)**	-	**0.66 (0.50–0.87)**
Diabetic status (Ref: No)				
Yes	-	**1.27 (1.25–1.30)**	-	**1.27 (1.25–1.30)**
Unknown	-	**0.74 (0.73–0.75)**	-	**0.74 (0.73–0.75)**
Treatment category for drug sensitive tuberculosis Ref: Category 1)				
Category 2	-	**0.59 (0.57–0.62)**	-	**0.74 (0.72–0.77)**
District level[a]				
First-dose vaccine rate[b]	-	-	1 00 (0.98–1.01)	1.00 (0.98–1.01)
Second-dose vaccine rate[b]	-	-	1.01 (0.99–1.03)	1.01 (0.99–1.03)
Booster 1 vaccine rate[b]	-	-	1.00 (0.99–1.01)	1.00 (0.99–1.00)

Variables	Model 0	Model 1	Model 2	Model 3
	Odds Ratio (95% CI)			**Adjusted Odds Ratio (95% CI)**
Booster 2 vaccine rate[b]	-	-	1.00 (0.95–1.05)	1.00 (0.95–1.05)
Constant	**0.46 (0.42–0.50)**	**0.87 (0.80–0.95)**	**0.40 (0.28–0.57)**	**0.78 (0.55–1.11)**
Random Effects				
District variance (SE)	0.89 (0.03)	0.88 (0.03)	0.89 (0.03)	0.88 (0.03)
VPC	0.1953	0.1904	0.1952	0.1901
PCV (%)	-	1.57	0	1.57
Interclass Correlation (ICC %)	19.52	19.04	19.52	19.01
Median Odds Ratio (MOR)	2.39	2.39	2.40	2.30
Model fit statistics				
Log likelihood	-336104.54	-329646.33	-336103.88	-329645.44
AIC	672213.1	659312.7	672219.8	659318.9
$\chi 2$	39219.24	38751.15	38582.35	38245.56

Model 0. Model Null

Model 1. Multilevel binary logistic regression model with explanatory variables at individual-level

Model 2. Multilevel binary logistic regression model with explanatory variables at district-level

Model 3. Multilevel binary logistic regression model with explanatory variables at individual-level and district-level

a= Vaccine coverage variables are continuous, representing the percentage of the adult population vaccinated in each district

b= Odds ratios represent the chang in odds of successful treatment associated with a 10-percentage point increase in vaccination coverage

Table 4
Multilevel logistic regression model of drug resistance tuberculosis

Variables	Model 0	Model 1	Model 2	Model 3
	Odds Ratio (95% CI)		Adjusted Odds Ratio (95% CI)	
Age	-	**0.98 (0.97–0.98)**	-	**0.97 (0.97–0.98)**
Sex (Ref: Men)				
Women	-	**1.15 (1.07–1.24)**	-	**1.15 (1.07–1.24)**
Occupational status (Ref: Unemployed)				
Employed	-	**1.56 (1.44–1.68)**	-	**1.56 (1.44–1.68)**
HIV Status (Ref: Negative)				
Positive	-	**0.45 (0.36–0.57)**	-	**0.45 (0.36–0.57)**
Unknown	-	0.98 (0.57–1.06)	-	0.98 (0.58–1.67)
Diabetic status (Ref: No)				
Yes	-	**1.28 (1.17–1.40)**	-	**1.28 (1.17–1.40)**
Treatment category for drug resistance tuberculosis (Ref: STR)				
LTR	-	**1.24 (1.16–1.34)**	-	**1.25 (1.16–1.34)**
BPaL or Monoresistance INH	-	**2.66 (1.56–4.52)**	-	**2.70 (1.57–4.60)**
District level[a]				
First-dose vaccine rate[b]	-	-	**1.02 (1.00–1.04)**	**1.02 (1.00–1.04)**
Second-dose vaccine rate[b]	-	-	0.97 (0.95–1.00)	0.97 (0.95–1.01)
Booster 1 vaccine rate[b]	-	-	1.01 (1.00–1.02)	1.01 (1.00–1.02)

*Auxiliary variables for multiple imputation: age, sex, occupation, treatment outcome, and district-level COVID-19 vaccination coverage (first and second doses). All models were adjusted for the same covariates (age, sex, occupation, treatment regimen, and district-level vaccination coverage). aOR=adjusted odds ratio; CI=Confidence interval.

Variables	Model 0	Model 1	Model 2	Model 3
	Odds Ratio (95% CI)		Adjusted Odds Ratio (95% CI)	
Booster 2 vaccine rate[b]	-	-	0.94 (0.88–1.01)	0.95 (0.88–1.02)
Constant	**0.52 (0.47–0.59)**	1.00 (0.84–1.19)	**0.41 (0.25–0.69)**	0.80 (0.47–1.38)
Random Effects				
District variance (SE)	0.78 (0.06)	0.79 (0.06)	0.77 (0.06)	0.78 (0.06)
VPC	0.1572	0.1604	0.1527	0.1557
PCV (%)	-	-1.15	1.66	0.51
Interclass Correlation (ICC %)	15.1	16.0	15.3	15.6
Median Odds Ratio (MOR)	2.29	2.30	2.28	2.29
Model fit statistics				
Log Pseudolikelihood	-10373.53	-10083.21	-10370.26	-10079.82
AIC	20194.63	20186.42	20752.52	20187.64
$\chi 2$	646.35	645.41	657.87	629.67

Model 0. Model Null

Model 1. Multilevel binary logistic regression model with explanatory variables at individual-level

Model 2. Multilevel binary logistic regression model with explanatory variables at district-level

Model 3. Multilevel binary logistic regression model with explanatory variables at individual-level and district-level

a= Vaccine coverage variables are continuous, representing the percentage of the adult population vaccinated in each district

b= Odds ratios represent the chang in odds of successful treatment associated with a 10-percentage point increase in vaccination coverage

Table 5. Comparison of main model and sensitivity analyses for HIV and diabetes among drug-sensitive tuberculosis (DS-TB) patients, Indonesia, 2020–2022

*Auxiliary variables for multiple imputation: age, sex, occupation, treatment outcome, and district-level COVID-19 vaccination coverage (first and second doses). All models were adjusted for the same covariates (age, sex, occupation, treatment regimen, and district-level vaccination coverage). aOR=adjusted odds ratio; CI=Confidence interval.

Variables	Model 0	Model 1	Model 2	Model 3
	Odds Ratio (95% CI)			Adjusted Odds Ratio (95% CI)

Variables	Main model	Complete-case analysis	Multiple imputation	Interpretation
Sample size (N)	1,082,757	462,113 (42.7% of original)	1,082,757 (all)	
Diabetes mellitus (Ref: No diabetes)				
Yes	1.27 (1.25–1.30)	0.86 (0.84–0.89)	0.86 (0.84–0.89)	**NOT ROBUST – REVERSED**: The apparent protective association in the main model (aOR = 1.27) reversed direction in both sensitivity analyses (aOR = 0.86), indicating that the estimate was sensitive to the handling of unascertained diabetes status.
Unknown	0.74 (0.73–0.75)	(excluded)	(not imputed)	Informative missingness (worse outcomes among those with unknown status).
HIV Status (Ref: HIV-negative)				
Positive	0.26 (0.25–0.27)	0.24 (0.23–0.26)	0.24 (0.23–0.26)	ROBUST: The negative association remained highly stable across all models (aOR range 0.24–0.26), confirming HIV as a strong negative predictor.
Unknown	0.66 (0.50–0.87)	(excluded)	(not imputed)	Informative missingness (worse outcomes among those with unknown status).
Notes				
Missing data handling	'Unknown' as separate category	Listwise deletion	Multiple imputation with auxiliary variables*	

*Auxiliary variables for multiple imputation: age, sex, occupation, treatment outcome, and district-level COVID-19 vaccination coverage (first and second doses). All models were adjusted for the same covariates (age, sex, occupation, treatment regimen, and district-level vaccination coverage). aOR=adjusted odds ratio; CI=Confidence interval.

Variables	Model 0	Model 1	Model 2	Model 3
	Odds Ratio (95% CI)		Adjusted Odds Ratio (95% CI)	

Variables	Main model	Complete-case analysis	Multiple imputation	Interpretation
Population	All DS-TB	Only patients with documented HIV and diabetes status	All DS-TB patients	

*Auxiliary variables for multiple imputation: age, sex, occupation, treatment outcome, and district-level COVID-19 vaccination coverage (first and second doses). All models were adjusted for the same covariates (age, sex, occupation, treatment regimen, and district-level vaccination coverage). aOR=adjusted odds ratio; CI=Confidence interval.

3.4 COVID-19 vaccination coverage and successful treatment of tuberculosis

Model 3, which encompasses both individual-level and district-level factors, revealed contrasting patterns for first dose and second-dose COVID-19 vaccination coverage when modelled as continuous variables (Model 3, Tables 3 and 4).

For DR-TB patients, each 10-percentage point increase in district-level first-dose vaccination coverage was associated with 2% higher odds of successful treatment (OR = 1.02; 95%CI = 1.00-1.04). In contrast, each 10-percentage point increase in second-dose coverage showed a trend toward 3% lower odds of successful treatment (OR = 0.97; 95%CI = 0.95-1.00).

For DS-TB patients, no significant associations were found between either first-dose or second-dose coverage and treatment outcomes in DS-TB patients. First booster and second booster coverage showed no consistent associations with treatment success for either DS-TB or DR-TB patients.

3.5 Variables associated with successful treatment of tuberculosis

Several individual-level factors were significantly associated with successful treatment in both DS-TB and DR-TB patients (Model 3, Tables 3 and 4).

Age and gender: Older age was associated with lower odds of successful treatment for both DS-TB (OR = 0.99 per year; 95%CI = 0.98–0.99) and DR-TB (OR = 0.97 per year; 95%CI = 0.97–0.98). Female patients had higher odds of successful treatment compared to males for both DS-TB (OR = 1.02; 95%CI = 1.01–1.04) and DR-TB (OR = 1.15; 95%CI = 1.07–1.24).

Employment status: Employed patients had higher odds of successful treatment compared to unemployed patients for both DS-TB (OR = 1.03; 95%CI = 1.02–1.04) and DR-TB (OR = 1.56; 95%CI = 1.44–1.68). HIV status: HIV-positive status was strongly associated with lower odds of successful treatment for both DS-TB (OR = 0.26; 95%CI = 0.25–0.27) and DR-TB (OR = 0.45; 95%CI = 0.36–0.57) compared to HIV-negative patients. For DS-TB patients with unknown HIV status, the odds of successful treatment were also lower (OR = 0.66; 95%CI 0.50–0.87), though this finding should be interpreted with caution given the high proportion of missing data (see Limitations). No significant association was observed for unknown HIV status in DR-TB patients (OR = 0.98; 95%CI = 0.58–1.67).

Diabetes status: In contrast to expectations, patients with diabetes had higher odds of successful treatment compared to those without diabetes for both DS-TB (OR = 1.27; 95%CI = 1.25–1.30) and DR-TB (OR = 1.28; 95%CI = 1.17–1.40). However, DS-TB patients with unknown diabetes status had lower odds of successful treatment (OR = 0.74; 95%CI = 0.73–0.75). This counterintuitive finding for diabetes requires cautious interpretation and is addressed further in the discussion.

Treatment regimen: Among DS-TB patients, those receiving Category 2 treatment had 26% lower odds of successful treatment compared to those receiving Category 1 treatment (OR = 0.74; 95%CI = 0.72–0.77). Among DR-TB patients, those receiving LTR had higher odds of successful treatment compared to those receiving STR (OR = 1.25; 95% CI = 1.16–1.34). Patients receiving BPaL or monoresistance INH regimens had nearly three times higher odds of successful treatment compared to those on STR (OR = 2.70; 95% CI = 1.57–4.60) (Model 3, Tables 3 and 4).

Table 3. **Multilevel logistic regression model of drug sensitive tuberculosis**

Table 4. **Multilevel logistic regression model of drug resistance tuberculosis**

3.6 Sensitivity analyses for missing data in DS-TB

Given the high proportion of missing data for HIV (50.4%) and diabetes (57.2%) in the DS-TB cohort, we conducted two sensitivity analyses to assess the robustness of our main findings for these comorbidities.

Complete-case analysis

The complete-case subset included 462,113 DS-TB patients (42.7% of the original DS-TB cohort) with documented status for both HIV and diabetes. Compared to the full cohort, this subset had slightly lower median age (41 vs. 43 years) and higher proportion of employed patients (45.2% vs. 40.5%), indicating that missingness was not completely at random.

In the complete-case analyses (Table 5), the association for documented diabetes reversed compared with the main model (aOR = 0.86; 95%CI = 0.84–0.89), indicating that the main estimate was sensitive to the handling of unascertained diabetes status. For HIV-positive patients, the association remained

consistently negative and similar in magnitude (complete-case aOR = 0.24; 95%CI = 0.23–0.26; main model aOR = 0.26; 95%CI = 0.25–0.27).

Multiple imputation

Results from the multiply imputed datasets (20 imputations) were consistent with the complete-case analysis. The pooled aOR for diabetes was 0.86 (95%CI = 0.84–0.89), and for HIV-positive was 0.24 (95%CI = 0.23–0.26).

Table 5. Comparison of main model and sensitivity analyses for HIV and diabetes among drug-sensitive tuberculosis (DS-TB) patients, Indonesia, 2020–2022

3.7 Temporal sensitivity analysis (2021–2022 cohort)

When restricting the analysis to patients who initiated treatment in 2021–2022 (DS-TB: n = 789,568; DR-TB: n = 11,894), the association between district-level first-dose COVID-19 vaccination coverage and DR-TB treatment success remained largely consistent with the main analysis (Table 6). For DR-TB patients, the association between first-dose coverage and treatment success was slightly attenuated in the restricted cohort (aOR = 1.01; 95% CI = 0.99–1.03) compared to the main model (aOR = 1.02; 95% CI = 1.00–1.04). Second-dose coverage showed similar estimates (main: aOR = 0.97; 95% CI = 0.95–1.00; sensitivity: aOR = 0.99; 95% CI = 0.97–1.02),

Table 6
Temporal sensitivity analysis: Comparison of main analysis (2020–2022) and restricted analysis (2021–2022 cohort)

Variables	Main analysis (2020–2022)	Sensitivity analysis (2021–2022 only)	Interpretation
DS-TB (n)	1,082,757	789,568	
DR-TB (n)	15,668	11,894	
DS-TB: First-dose coverage	1.00 (0.98–1.01)	0.99 (0.98–1.02)	**Stable.** No association in either analysis
DS-TB: Second-dose coverage	1.01 (0.99–1.03)	1.00 (0.99–1.02)	**Stable.** No association in either analysis
DR-TB: First-dose coverage	1.02 (1.00–1.04)	1.01 (0.99–1.03)	**Stable.** Slightly attenuated but directionally consistent
DR-TB: Second-dose coverage	0.97 (0.95–1.00)	0.99 (0.97–1.02)	**Stable.** Remained non-significant in both analysis

Note: All models were adjusted for the same individual-level covariates (age, sex, occupation, HIV status, diabetes status, and treatment regimen). Values are adjusted odds ratio (aOR) with 95% confidence intervals. Vaccination coverage variables are continuous, representing the percentage of the adult population vaccination in each district.

For DS-TB patients, no association emerged for either dose in the sensitivity analysis (first dose: aOR = 0.99; 95% CI = 0.98–1.02; second dose: aOR = 1.00; 95% CI = 0.99–1.02), consistent with the main analysis. These estimates were similar in direction and magnitude to the main model, indicating that inclusion of 2020 patients did not substantially change the findings. However, residual temporal mismatch cannot be completely ruled out, as patients treated in early 2021 may have completed treatment before being fully vaccinated.

Table 6. **Temporal sensitivity analysis: Comparison of main analysis (2020–2022) and restricted analysis (2021–2022 cohort)**

3.8 Ecological correlation between vaccination coverage and district poverty

To assess whether district-level COVID-19 vaccination coverage reflected underlying socioeconomic gradients, we correlated first-dose coverage with district poverty rates obtained from BPS (2021) [19]. Spearman's rank correlation coefficients revealed no significant association between any vaccination indicator and poverty rates: first-dose coverage

(ρ=-0.063; p = 0.158), second-dose coverage (ρ=-0.064; p = 0.146), first booster (ρ=-0.027; p = 0.549), and second booster (ρ=-0.070; p = 0.117) (Supplementary table S1). These findings suggest that district-level vaccination coverage was not systematically associated with district poverty levels, indicating that vaccination coverage may reflect health system performance or other factors beyond economic deprivation rather than serving as a direct proxy for poverty.

4. Discussion

This study used an ecological cross-sectional design to explore the relationship between district-level COVID-19 vaccination coverage and tuberculosis treatment outcomes in Indonesia. Because the exposure was measured at the district level and the outcome at the individual level, and because both were assessed during the same period, the findings represent associations rather than causal effects. Unmeasured confounding by district-level factors, such as health system quality, poverty, governance, and health expenditure, is likely. The interpretation of these findings should therefore be cautions and hypothesis-generating.

4.1 Outcome treatment of tuberculosis

During 2020–2022, the cure rate for DR-TB was higher than for DS-TB (43.2% vs. 27%), with both showing annual improvements. However, DR-TB patients experienced four-times higher mortality (19% vs. 4.4%), more treatment failure (9.9% vs. 0.4%), and more loss to follow-up (18.3% vs. 7.5%) than DS-TB patients. These outcomes are inferior to pre-pandemic studies from Brazil and elsewhere, which reported higher cure and lower mortality [16, 20], suggesting that pandemic-related disruptions likely worsened tuberculosis treatment outcomes. Delayed diagnosis and reduced access to care during the

pandemic [5, 21, 22], as well as co-infection with COVID-19 which has been associated with more severe tuberculosis outcomes [3, 23], may have contributed to these poorer results. Conversely, an Indonesian study found tuberculosis co-infection to be protective against COVID-19 mortality, possibly due to better resources in tertiary care settings [24].

4.2 COVID-19 vaccination coverage and successful treatment of tuberculosis

In this ecological analysis, we observed a positive correlation between first-dose COVID-19 vaccination coverage at district level and DR-TB cure rates (aOR = 1.02; 95% CI 1.00–1.04 per 10-percentage point increase). Conversely, second-dose coverage showed a non-significant trend toward lower odds of success (aOR = 0.97; 95% CI 0.95–1.01 per 10-percentage point increase). No association was observed for DS-TB. Given the ecological design, these findings should not be interpreted as a direct biological effect of COVID-19 vaccines on M. Tuberculosis clearance. Instead, district-level vaccination coverage may serves as a marker of health system performance; districts with higher first-dose coverage also tended to have better TB outcomes, which may reflect underlying health system capacity (diagnosis, treatment adherence, drug supply) during the pandemic [5, 13, 14, 15]. This interpretation is supported by the fact that the association was weak and restricted to DR-TB patients, who require more complex and better-supported care [8, 9]. The contrasting finding for second-dose coverage may reflect heterogeneous timing of vaccine rollout, residual confounding, or chance (the confidence interval included 1.00).

The inconsistent direction of these associations for first dose versus second-dose coverage, and the absence of association for DS-TB, suggest that the relationship between district-level vaccination coverage and TB treatment outcomes is complex and unlikely to reflect a simple biological mechanism. These findings should be interpreted cautiously, as they may be influenced by contextual factors, temporal dynamics of the pandemic, or residual confounding.

Importantly, the temporal sensitivity analysis does not provide evidence for a direct biological effect of COVID-19 vaccination on TB treatment outcomes. If vaccination itself were biologically protective, we would expect a consistent dose-response relationship and an association in both DS-TB and DR-TB. Instead, the association was weak, restricted to DR-TB, and not consistent across first and second doses. The attenuation of the first dose estimate for DR-TB in the 2021–2022 cohort (from aOR 1.02 to 1.01) is negligible in magnitude and may reflect reduced statistical power rather than a genuine change in the association. This pattern argues against a direct biological mechanism and is more consistent with vaccination coverage acting as a distal marker of district health-system performance, although this interpretation remains speculative given the ecological design.

4.3 Why COVID-19 still matters: long-term interplay with tuberculosis

The relevance of pandemic response capacity for tuberculosis outcomes extends beyond the acute crisis. Emerging evidence suggests that SARS-CoV-2 infection may induce sustained T cell dysregulation and systemic inflammation, and an uncoordinated adaptive immune response that could increase the risk of latent tuberculosis reactivation [25]. Infection-associated inflammation has also been shown to durably imprint CD4 T cell memory, affecting the long-term function of these cells and potentially influencing susceptibility to other pathogens [26].

Importantly, viruses can remodel the mammalian immune system, modulating the risk of reactivating latent microbes such as Mycobacterium tuberculosis. While evidence regarding the specific impact of SARS-CoV-2 on tuberculosis risk remains mixed, this represents a plausible biological mechanism by which the pandemic could influence tuberculosis epidemiology for years to come [27]. Modelling studies have estimated that pandemic-related disruptions to tuberculosis services, including delays in diagnosis and interruptions in treatment, could increase transmission and progression from latent to active tuberculosis, leading to higher true tuberculosis incidence and mortality in high-burden countries over subsequent years, even though notified cases initially declined. Tuberculosis death over five years could increase by up to 20% compared to a scenario without COVID-19 [28].

4.4 Health system resilience, poverty, and tuberculosis outcomes

Our findings must be understood within the broader context of socioeconomic vulnerability in Indonesia. Although Indonesia has been classified as an upper-middle income country by the World Bank since 2020, significant economic disparities persist, and poverty-related barriers to tuberculosis care remain substantial. A systematic review of tuberculosis-related costs in Indonesia found that catastrophic health expenditure income (define as out-of-pocket costs exceeding 20% of annual household income) occurred in 83% of DR-TB-affected households and 36% of DS-TB household [29]. Moreover, the total cost of DR-TB treatment episode was estimated at USD 2,342 in Indonesia, representing approximately 9–24 months of pre-treatment household income [30]. Although Indonesia had implemented universal health coverage since 2014, Fuady et al. found that 36% of TB-affected households still faced catastrophic total costs, increasing to 43% in poor households and 83% in MDR-TB-affected households, mainly due to uncovered direct non-medical costs [31].

The financial vulnerability associated with tuberculosis is particularly acute for DR-TB patients, who face longer treatment duration (often exceeding 18 months), more frequent clinic visits, higher transportation costs, and greater risk of income loss due to prolonged inability to work. A study across Ethiopia, Indonesia, and Kazakhstan found that 38–92% of DR-TB patients reported income loss, and 26–76% lost their jobs due to their illness [30]. In Indonesia specifically, 82.3% of tuberculosis patients lost their jobs during treatment, with indirect costs from lost revenue reaching Rp 481.5 million (approximately USD 31,000) for MDR-TB cases [29]. The COVID-19 pandemic dramatically worsened these financial hardships. A mixed-methods study conducted in Bandung and Yogyakarta during the pandemic found that 5.13% of tuberculosis and HIV affected households faced catastrophic health spending, with non-

medical costs, particularly transportation and food supplements for clinic visits, forming the largest share of expenditure [11]. Patients coped through borrowing, family support, and asset sales, strategies that further entrench poverty [11]. These pandemic-exacerbated financial barriers may help explain why DR-TB patients, who require more intensive, longer-term care, appeared more sensitive to district-level health system disruptions. This context is consistent with the observed correlation between higher COVID-19 vaccination coverage (as a marker of system resilience) and better DR-TB outcomes, although causality cannot be established.

Importantly, the financial and health system vulnerabilities described above are not uniformly distributed across Indonesia. Significant economic disparities exist between districts, with poverty rates ranging substantially between provinces. According to Indonesia National Statistic (BPS) data, while the national poverty rate stood at 8.6% (approximately 24.1 million people) in September 2024 [32], the poverty rate in eastern Indonesia (Maluku and Papua) reached 19.4% more than double the national average [33]. Income inequality, as measured by the Gini coefficient, was 0.402 in urban areas and 0.308 in rural areas of September 2024, indicating that economic resources are distributed unevenly across regions [34] .

Our ecological correlation analysis further explored whether district-level COVID-19 vaccination coverage reflected socioeconomic gradients. Contrary to our expectation, we found no significant correlation between vaccination coverage and district poverty rates (Spearman's ρ ranged from − 0.027 to -0.070; see Supplementary Table S1). This suggests that vaccination coverage may not simply be a marker of economic capacity but could instead reflect other dimensions of health system performance, such as logistical capacity, community engagement, or prior immunization infrastructure. Importantly, the lack of correlation with poverty does not diminish the interpretation of vaccination coverage as a proxy for health system resilience during the pandemic; rather, it indicates that districts with higher vaccination coverage achieved this through effective service delivery mechanisms that may be independent of baseline poverty levels. This finding underscores that health system strengthening, including vaccine rollout, can succeed even in poorer districts when political will and operational capacity are mobilized. However, the substantial between-district heterogeneity observed in our multilevel models (ICC = 19.2% for DS-TB, MOR = 2.4) suggests that unmeasured district-level factors, which may include health system resources, governance, and infrastructure, strongly influence TB treatment outcomes beyond poverty alone.

These subnational disparities mean that patients in poorer districts face a double burden: higher baseline poverty rates that exacerbate the financial toxicity of tuberculosis treatment, and weaker local health system capacity to absorb pandemic-related disruption. Our multilevel analysis supports this interpretation, showing that district-level factors accounted for 19.2% of the total variance in DS-TB treatment success (ICC = 19.2%) and 15.1% for DR-TB, with median odds ratio (MOR) of 2.4 and 2.3, respectively, meaning that the odds of successful treatment differed by more than twofold between two randomly selected district, even before accounting for individual-level factors. This substantial between-district heterogeneity may reflect, in part, the unequal distribution of poverty and health system resources across Indonesian districts. However, our ecological correlation analysis did not find a

statistically significant association between vaccination coverage and poverty rates, so this interpretation remains speculative.

4.5 Variables associated with successful treatment of tuberculosis

Treatment regimens were categorized according to case type. Among DS-TB patients, the majority (97.4%) received Category 1 treatment. A systematic review indicated no difference in outcomes for tuberculosis patients co-infected with COVID-19, with first-line anti-tuberculosis drugs (rifampicin, isoniazid, ethambutol, and pyrazinamide) remaining the standard therapy [23]. The review also noted that Paxlovid is contraindicated and Hydroxychloroquine ineffective for COVID-19 co-infection [23].

Among DR-TB patients, nearly 60% underwent LTR, predominantly oral. Contrary to the findings of Mleoh et al. in Tanzania, where STR were more common (87.5% vs. 72.0%) [16], STR use in Indonesia is restricted to specific resistance profile. In Indonesia, STRs are administered solely to DR-TB patients exhibiting fluoroquinolone resistance (pre-XDR) or dual resistance to fluoroquinolones and Bdq/Lzd [35]. Treatment with LTR exhibited a higher frequency of grade 3 or higher side effects in other studies [16], though patients experiencing side effects from SLR still achieved favourable outcomes in Guinea [36].

The treatment for DR-TB has improved with the new oral regimen Bedaquiline, Pretomanid, and Linezolid (BPaL), which is more effective, efficient, and increasingly adopted worldwide [37–41]. Evans et al. reported that BPaL costs less than STR and LTR [39], while studies in Kyrgyzstan and Nigeria showed better compliance and reduced health system burden [16, 23, 37, 41]. In this study, DR-TB patients treated with BPaL had nearly three times higher odds of cure than those treated with STR.

Comorbidities such as HIV and diabetes mellitus significantly affected tuberculosis treatment success. Patients with HIV had 74% and 55% lower odds of cure for DS-TB and DR-TB, respectively, consistent with prior studies [15, 20, 42]. This is associated with immune disorders that reduce treatment efficacy [15].

However, these findings must be interpreted in the context of substantial missing data for HIV status. Approximately half of DS-TB patients had missing HIV information, and these patients had significantly lower odds of cure (OR = 0.66; 95% CI = 0.50–0.87) compared to those with known HIV-negative status. This suggests that patients with unknown HIV status may represent a distinct group with different risk profiles or healthcare access patterns. It is possible that some patients with unknown status were HIV-positive but not tested, which would bias our estimate for HIV-positive patients toward the null if these untreated HIV-positive patients had poorer outcomes. Alternatively, patients with unknown status may have been tested elsewhere and not recorded or may have refused testing due to lower health literacy, both of which could be associated with treatment outcomes through different pathways.

To assess the robustness of the HIV and diabetes findings for DS-TB (where missingness was highest), we conducted two sensitivity analyses. In the complete-case analysis restricted to patients with

documented status (n = 462,113; 42.7% of DS-TB cohort), the association for HIV remained consistently negative, with aOR = 0.24 (95%CI = 0.23–0.26), nearly identical to the main model estimate of 0.26 (95%CI = 0.25–0.27). Multiple imputation yielded a pooled aOR of 0.24 (95%CI 0.23–0.26). These results confirm that HIV is a strong and robust negative predictor of TB treatment success, and the effect size is stable despite the missing data. For DR-TB, where missingness was lower (29.4%), the main model estimate (aOR = 0.45; 95%CI = 0.36–0.57) is likely reliable, but replication in datasets with complete HIV ascertainment is still warranted.

Contrary to expectations, the main model showed that DS-TB patients with documented diabetes had higher odds of successful treatment (aOR = 1.27; 95%CI = 1.25–1.30). However, this estimate was not robust: in both complete-case analysis (aOR = 0.86; 95%CI 0.84–0.89) and the multiple imputation analysis (pooled aOR = 0.86; 95%CI = 0.84–0.89), the association reversed direction. This reversal indicates that the main-model estimate was highly sensitive to the handling of unascertained diabetes status and is consistent with informative missingness or selection related to healthcare engagement. Patients with documented diabetes may represent a subgroup with better healthcare access, more frequent monitoring, and more complete medical records, factors associated with better TB outcomes. However, because complete-case analysis is restricted to a non-random subgroup and multiple imputation relies on the missing-at-random assumption, neither estimate can be assumed to be closer to the true effect. For HIV, the negative association was consistent in direction and magnitude across all models (aOR range: 0.24–0.26). All HIV and diabetes findings in DS-TB should be interpreted cautiously because of the high proportion of missing data; the diabetes finding was not robust, and no reliable conclusion about its direction can be drawn. Future research must prioritize prospective, complete data collection on comorbidities, ideally through routine testing protocols rather than relying on medical records.

This study found that older age and male gender were associated with lower odds of successful treatment for both DS-TB and DR-TB, consistent with previous findings [15, 20, 24]. Zou et al. reported that patients over 60 had nearly twice the likelihood of treatment failure due to decreased immunity [15]. Studies in South Korea [43] and Brazil [20] indicated poorer treatment outcomes among men, possibly due to higher smoking prevalence, a behavioural factor strongly associated with reduced tuberculosis treatment success [15, 20, 43, 44].

4.6 Strength and Limitation

This study has several strengths: (1) a very large sample size (over 1 million patients) covering all Indonesian provinces; (2) the use of national routine surveillance data, reducing selection bias; (3) a multilevel analytic approach that accounts for clustering at the district level; (4) comprehensive sensitivity analyses for missing data and temporal effects; and (5) an exploratory ecological correlation analysis with poverty, which while not statistically significant, provides context for interpretation.

the use of national data combining aggregate vaccination coverage with individual tuberculosis treatment records across Indonesia, a large sample size, and a multilevel analytic approach allowed us

to examine both individual- and district-level factors simultaneously.

However, several limitations must be acknowledged. First, the cross-sectional ecological design precludes causal inference. We cannot determine whether vaccination coverage preceded or followed treatment outcomes, nor can we rule out reverse causality or confounding by unmeasured district-level factors. The observed associations should therefore be interpreted as exploratory and hypothesis-generating. Second, district-level vaccination coverage is an imperfect proxy for “pandemic response capacity” or health system resilience. It may reflect vaccine acceptance, logistical capacity, political prioritization, or other factors unrelated to TB services. No formal validation against other health system indicators was possible due to data constraints. Future studies should use more direct measures of health system performance (e.g., TB service coverage, diagnostic capacity, treatment adherence support).

Third, the use of district-level aggregated vaccination data (rather than individual-level vaccination status) introduces the potential for ecological fallacy. We cannot determine whether patients who successfully completed tuberculosis treatment were the same individuals who received COVID-19 vaccinations, which limits causal inferences about direct biological effects. Our temporal sensitivity analysis (restricted to the 2021–2022 cohort) helped mitigate concerns about temporal mismatch, but the ecological fallacy remains inherent to the study design.

Fourth, there is a temporal mismatch between tuberculosis treatment episodes and vaccination coverage measurement. Vaccination rollout began in January 2021, but the study period includes 2020, meaning many patients completed treatment before vaccines were available. Their outcomes are thus attributed to district-level coverage that did not exist during their treatment, potentially introducing bias. To address this, we conducted a sensitivity analysis restricted to patients who initiated treatment in 2021–2022. The results were largely similar to the main analysis, with the association between first-dose coverage and DR-TB success slightly attenuated (aOR = 1.01; 95% CI = 0.99–1.03) compared to the main model (aOR = 1.02; 95% CI = 1.00–1.04). For DS-TB, no association emerged for either dose in the sensitivity analysis, consistent with the main analysis (Table 6). These findings suggest that the inclusion of 2020 patients did not substantially bias our main conclusions. Nevertheless, we cannot completely rule out residual temporal mismatch, as patients treated in early 2021 may have completed treatment before being fully vaccinated. Moreover, measuring coverage at a single time point (December 2021) ignores within-district temporal variation in rollout speed.

Fifth, the inconsistent findings between first- and second-dose coverage highlight the limitations of ecological analyses and may reflect unmeasured confounding, temporal mismatches, or heterogeneous pandemic experiences across districts. This lack of a dose-response pattern supports our interpretation that vaccination coverage is a proxy for health system resilience rather than a direct biological effect.

Sixth, missing data for HIV (≈50% missing in DS-TB, ≈29% missing in DR-TB) and diabetes (≈57% missing in DS-TB, 0% missing in DR-TB) represent a major limitation. We deliberately chose not to impute these variables in the main model because missingness was likely informative (not missing at random), as

evidenced by the worse outcomes among patients with unknown HIV status, and because the very high proportion missing meant that any MAR-based imputation would depend heavily on unverifiable assumptions. However, we conducted two sensitivity analyses, complete-case analysis and multiple imputation, to assess the robustness of our findings. Both sensitivity analyses revealed that the apparent protective effect of diabetes was entirely reversed (aOR = 0.86; 95% CI = 0.84–0.89) compared to the main model (aOR = 1.27; 95% CI 1.25–1.30), confirming that the original finding was a product of selection bias and no reliable conclusion can be drawn. In contrast, the negative association for HIV was highly stable (aOR 0.24–0.26), providing reassurance that the direction and magnitude of this effect are robust despite the missing data. Future studies must prioritize complete, prospective data collection on comorbidities, including routine HIV and diabetes testing for all TB patients at treatment initiation.

Seventh, key determinants such as smoking [15, 20, 43, 44], drug adherence [45], and concurrent medications (including antidiabetic or antiretroviral drugs) were excluded due to data constraints and may confound the observed association.

Eighth, we lacked individual-level socioeconomic data to directly adjust for poverty in our regression models. Nonetheless, our ecological correlation analysis (see Supplementary table S1) explored the relationship between district-level vaccination coverage and poverty rates. Contrary to expectations, we found no significant association (Spearman's ρ ranged from − 0.027 to -0.070), suggesting that vaccination coverage may reflect health system operational capacity, such as logistics, human resources, and community engagement, rather than solely district economic status. Additionally, the substantial between-district heterogeneity observed in our multilevel models (ICC = 19.2% for DS-TB, MOR = 2.4) suggests that unmeasured district-level factors strongly influence TB treatment outcomes. These factors may include poverty, healthcare infrastructure, quality of care, and governance, among others. However, ecological correlations are subject to ecological fallacy and cannot replace individual-level data. Future studies should incorporate individual-level socioeconomic measures to better isolate the pathways linking health system resilience, poverty, and tuberculosis treatment outcomes.

4.7 Implications for Health System Resilience and Future Pandemics

Notwithstanding these limitations, the relevance of this research extends beyond the immediate pandemic context. The post-pandemic period present unique challenges that require sustained attention to COVID-related factors, and our findings offer several implications for strengthening health system resilience.

First, the immune modulation induced by SARS-CoV-2 infection may have created a large population of individuals with altered susceptibility to tuberculosis, as discussed above. Health systems must therefore maintain capacity for tuberculosis screening among individuals with a history of COVID-19, particularly those with prolonged respiratory symptoms or known risk factors for LTBI reactivation. More broadly, the pandemic exposed critical vulnerabilities in diagnostic capacity, treatment adherence support, and supply chain resilience that are essential for tuberculosis control. Our finding that district-

level vaccination coverage (a marker of health system performance) was correlated with better DR-TB outcomes provides preliminary, hypothesis-generating evidence that strengthening health systems may help protect TB services against future shocks. However, longitudinal studies with individual-level vaccination data and validated health system indicators are needed to confirm this. Although district-level vaccination coverage was not correlated with district poverty rates in our data, TB-affected households, particularly those with DR-TB-face substantial financial hardship, and social protection schemes addressing indirect costs remain important for protecting TB treatment outcomes during future health system shocks. Evidence from Indonesia shows that financial support for income loss (transportation, and food supplements, currently provided as 'enabler payments' by the Global Fund) can reduce catastrophic cost incidence from 36% to 11% for DS-TB and from 83% to 23% for DR-TB, but high remaining costs persist, underscoring the need for more comprehensive social protection [46].

Second, the long-term respiratory consequences of COVID-19, including pulmonary fibrosis and reduced lung function, could complicate tuberculosis diagnosis (e.g., radiological interpretation) and worsen treatment outcomes for patients who develop post-tuberculosis lung disease. Additionally, the pandemic has created a multi-year setback in global tuberculosis eliminations efforts; lessons from this period is essential for designing effective catch-up strategies. Specifically, catch-up efforts should include expanded social protection schemes that address indirect costs (income loss, transportation, nutrition) rather than focusing solely on indirect medical costs, as the former represents the largest share of catastrophic expenditure for TB-affected households [11].

Third, the funding landscape for tuberculosis has become more precarious following the post-pandemic withdrawal of international support, making it essential to identify high-yield, low-cost intervention, such as leveraging existing vaccination infrastructure for integrated service delivery, that our findings suggest may be effective. Our methodological approach, using vaccination coverage as a proxy for health system resilience, offers a framework applicable to other contexts and future public health emergencies to identify districts with weaker performance that require targeted support for vulnerable populations requiring long-term care.

5. Conclusion

This ecological analysis suggests that districts with higher COVID-19 vaccination coverage also had better DR-TB treatment outcome in Indonesia, but not with DS-TB patients. However, causal inference is not possible due to the cross-sectional design and the ecological nature of the exposure. This association should be interpreted as reflecting health system performance rather than a direct biological effect of vaccination, especially given the inconsistent findings for second-dose coverage. Individual-level factors (treatment regimen, HIV, diabetes, age, gender, and occupation) were also significantly associated with treatment success. However, due to very high missing data for HIV and diabetes in DS-TB, findings for these comorbidities require careful interpretation. Sensitivity analyses revealed that the association between diabetes and treatment success was not robust; it reversed from aOR = 1.27 in the main model to aOR = 0.86 in both complete-case and multiple imputation analyses, suggesting selection

bias. For HIV, the negative association was stable across models, consistent with its role a s a predictor of unsuccessful treatment. Nevertheless, no reliable conclusion about the direction of diabetes' effect on TB treatment outcomes can be drawn from this study, and all comorbidity findings should be considered hypothesis-generating.

These findings are hypothesis-generating. They suggest that strengthening health system capacity, including vaccination infrastructure, may help maintain essential TB services during future crises, but longitudinal studies are needed to confirm this. Policy efforts should prioritize district with weaker health system performance, as indicated by lower vaccination coverage, and should include social protection schemes that address indirect costs (transportation, nutrition income loss). Further research should use longitudinal designs with individual-level vaccination data, time-varying exposure, and validated health system indicators to establish temporality and causality. Complete prospective comorbidity data collection is also essential to clarify the role of HIV and diabetes in TB treatment outcomes.

Abbreviations

aOR
Adjusted odds ratio
BPaL
Bedaquiline-Pretomanid-Linezolid
CI
Confidence interval
DM
Diabetes mellitus
DR-TB
Drug-resistant tuberculosis
DS-TB
Drug-sensitive tuberculosis
ICC
Intraclass correlation coefficient
INH
Isoniazid
IQR
Interquartile range
KNN
k-nearest neighbors
LTR
Longer treatment regimen
MAR
Missing at random
MICE

Multiple imputation by chained equations

MOR

Median odds ratio

MDR-TB

Multidrug-resistant tuberculosis

RR-TB

Rifampicin-resistant tuberculosis

SITB

Sistem Informasi Tuberkulosis

STR

Shorter treatment regimen

TB

Tuberculosis

WHO

World Health Organization

XDR-TB

Extensively drug-resistant tuberculosis

Declarations

Ethics approval and Consent to Participate

The study was approved by the Research Ethics Committee of the Faculty of Public Health, University of Indonesia (No. ND-304/UN2.F10.D2/PPM.00/2024) and conducted in accordance with the Declaration of Helsinki. The committee authorized access to anonymized data collected since May 27, 2024, for analysis of the association between COVID-19 vaccination and tuberculosis treatment outcomes. Data were completely anonymized before access, and no personally identifiable information was present. The requirement for informed consent was waived because the study anonymized secondary data.

Consent for publication

Not applicable. This study used anonymized secondary data from national databases; no individual patient data are presented.

Funding

This study was supported by the Directorate of Research and Development, Universitas Indonesia (Hibah PUTI 2024, Grant No. NKB-358/UN2.RST/HKP.05.00/2024). The funder had no role in study design, data collection, analysis, interpretation, or manuscript writing.

Author Contribution

PBM: conceptualization, methodology, formal analysis, writing-original draft, supervision. HK: data curation, writing-review and editing. AWW: formal analysis, validation, writing-review and editing. IWGAEP: writing-review and editing. AW: supervision, validation, writing-review and editing. All authors read and approved the final manuscript.

Acknowledgement

The Directorate of Research Ecosystem and Funding, Universitas Indonesia, supported this study (Hibah PUTI 2024, Grant No. NKB-358/UN2.RST/HKP.05.00/2024). Data access was provided by the Ministry of Health of Indonesia. The authors thank Innas Khoirun Chisan for data management support.

Data Availability

The data supporting this study are not publicity available due to restrictions from the Indonesian Ministry of Health. However, de-identified data may be requested from the corresponding author with permission from the Ministry of Health. COVID-19 vaccination coverage data are available from the directorate of Immunization, Ministry of Health of Indonesia upon reasonable request.

References

1. Migliori GB, Casco N, Jorge AL, Palmero DJ, Alffenaar JW, Denholm J, et al. Tuberculosis and COVID-19 co-infection: description of the global cohort. Eur Respir J. 2022;59. https://doi.org/10.1183/13993003.02538-2021.
2. Jassat W, Cohen C, Tempia S, Masha M, Goldstein S, Kufa T, et al. Risk factors for COVID-19-related in-hospital mortality in a high HIV and tuberculosis prevalence setting in South Africa: a cohort study. Lancet HIV. 2021;8:e554–67. https://doi.org/10.1016/S2352-3018(21)00151-X.
3. Shariq M, Sheikh JA, Quadir N, Sharma N, Hasnain SE, Ehtesham NZ. COVID-19 and tuberculosis: the double whammy of respiratory pathogens. Eur Respiratory Rev. 2022;31. https://doi.org/10.1183/16000617.0264-2021.
4. WHO, Global Tuberculosis R. 2021. https://www.who.int/publications/i/item/9789240037021
5. Hasan T, Nguyen VN, Nguyen HB, Nguyen TA, Le HTT, Pham CD, et al. Retrospective Cohort Study of Effects of the COVID-19 Pandemic on Tuberculosis Notifications, Vietnam, 2020. Emerg Infect Dis. 2022;28:684–92. https://doi.org/10.3201/eid2803.211919.
6. Zhang Y, Zhang L, Gao W, Li M, Luo Q, Xiang Y, et al. The impact of COVID-19 pandemic on reported tuberculosis incidence and mortality in China: An interrupted time series analysis. J Glob Health. 2023;13. https://doi.org/10.7189/JOGH.13.06043.

7. Heitkamp P, Chijioke-Akaniro O, Pai M. From dependence to self-reliance: The future of the global tuberculosis response. PLoS Med. 2025;22. https://doi.org/10.1371/journal.pmed.1004824.
8. gsphub.eu. Indonesia Country Profile. https://gsphub.eu/country-info/Indonesia#comments. 2024.
9. World Bank. Gini index - Indonesia: World Bank Data. https://data.worldbank.org.2024
10. World Bank. Poverty headcount ratio at national poverty lines (% of population) - Indonesia. https://data.worldbank.org.2024
11. Fardousi N, Negara SNS, Subronto YW, Mashuri YA, Cheng Q, Wulandari LPL, et al. Understanding the financial hardships faced by TB and HIV patients during the COVID-19 pandemic: A mixed-method study in Bandung and Yogyakarta, Indonesia. Health Policy Plan. 2025;40:1102–15. https://doi.org/10.1093/heapol/czaf058.
12. Asyary A, Behera DK, Hafidz F. Out-of-pocket expenditure and catastrophic costs due to COVID-19 in Indonesia: A rapid online survey. 2019.
13. Soko RN, Burke RM, Feasey HRA, Sibande W, Nliwasa M, Henrion MYR, et al. Effects of coronavirus disease pandemic on tuberculosis notifications, malawi. Emerg Infect Dis. 2021;27:1831–9. https://doi.org/10.3201/eid2707.210557.
14. Jhaveri TA, Fung C, LaHood AN, Lindeborg A, Zeng C, Rahman R, et al. Clinical Outcomes of Individuals with COVID-19 and Tuberculosis during the Pre-Vaccination Period of the Pandemic: A Systematic Review. J Clin Med. 2022;11. https://doi.org/10.3390/jcm11195656.
15. Zou L, Kang W, Guo C, Du J, Chen Q, Shi Z, et al. Treatment Outcomes and Associated Influencing Factors Among Patients with Rifampicin-Resistant Tuberculosis: A Multicenter, Retrospective, Cohort Study in China. Infect Drug Resist. 2024;17:3737–49. https://doi.org/10.2147/IDR.S467971.
16. Mleoh L, Mziray SR, Tsere D, Koppelaar I, Mulder C, Lyakurwa D. Shorter regimens improved treatment outcomes of multidrug-resistant tuberculosis patients in Tanzania in 2018 cohort. Trop Med Int Health. 2023;28:357–66. https://doi.org/10.1111/tmi.13867.
17. Palupi S, Pambudi I, Surya A, Bramanthi R, Arfi M, Suyanto S, et al. Sequence of COVID-19 Vaccination and COVID-19 Infection and Their Association With the Development of Active Tuberculosis: A Case-Control Study. Cureus. 2023. https://doi.org/10.7759/cureus.46353.
18. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. Stat Med. 2011;30:377–99. https://doi.org/10.1002/sim.4067.
19. Indonesian Statistic (BPS). Data Informasi Kemiskinan Kabupaten/Kota Tahun 2021. 2021. https://www.bps.go.id/id/publication/2021/11/30/9e3602ea496ecc2f4751836f/data-dan-informasi-kemiskinan-kabupaten-kota-tahun-2021.html. Accessed 8 Jun 2026.
20. Ryuk DK, Pelissari DM, Alves K, Oliveira PB, Castro MC, Cohen T, et al. Predictors of unsuccessful tuberculosis treatment outcomes in Brazil: an analysis of 259,484 patient records. BMC Infect Dis. 2024;24. https://doi.org/10.1186/s12879-024-09417-7.
21. Han E, Nabity SA, Dasgupta-Tsinikas S, Guevara RE, Moore M, Kadakia A, et al. Tuberculosis Diagnostic Delays and Treatment Outcomes among Patients with COVID-19, California, USA, 2020. Emerg Infect Dis. 2024;30:136–40. https://doi.org/10.3201/eid3001.230924.

22. Geric C, Saroufim M, Landsman D, Richard J, Benedetti A, Batt J, et al. Impact of COVID-19 on Tuberculosis Prevention and Treatment in Canada: A Multicenter Analysis of 10 833 Patients. Journal of Infectious Diseases. Oxford University Press; 2022. pp. 1317–20. https://doi.org/10.1093/infdis/jiab608.
23. Wang Q, Guo S, Wei X, Dong Q, Xu N, Li H, et al. Global prevalence, treatment and outcome of tuberculosis and COVID-19 coinfection: A systematic review and meta-analysis (from November 2019 to March 2021). BMJ Open. 2022;12. https://doi.org/10.1136/bmjopen-2021-059396.
24. Muflihah H, Yulianto FA, Rina, Sampurno E, Ferdiana A, Rahimah SB. Tuberculosis Coinfection among COVID-19 Patients: Clinical Presentation and Mortality in a Tertiary Lung Hospital in Indonesia. Int J Mycobacteriol. 2024;13:58–64. https://doi.org/10.4103/ijmy.ijmy_19_24.
25. Yin K, Peluso MJ, Luo X, Thomas R, Shin MG, Neidleman J, et al. Long COVID manifests with T cell dysregulation, inflammation and an uncoordinated adaptive immune response to SARS-CoV-2. Nat Immunol. 2024;25:218–25. https://doi.org/10.1038/s41590-023-01724-6.
26. Gray-Gaillard SL, Solis SM, Chen HM, Monteiro C, Ciabattoni G, Samanovic MI et al. SARS-CoV-2 inflammation durably imprints memory CD4 T cells. 2025. https://doi.org/10.5281/zenodo.10814886
27. Darboe F, Reijneveld JF, Maison DP, Martinez L, Suliman S. Unmasking the hidden impact of viruses on tuberculosis risk. Trends Immunol. 2024;45:649–61. https://doi.org/10.1016/j.it.2024.07.008.
28. Hogan AB, Jewell BL, Sherrard-Smith E, Vesga JF, Watson OJ, Whittaker C, et al. Potential impact of the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income countries: a modelling study. Lancet Glob Health. 2020;8:e1132–41. https://doi.org/10.1016/S2214-109X(20)30288-6.
29. Nova H, Nita Y, Priyandani Y. Evaluation and Study of the Cost of Illness of Tuberculosis in Indonesia: A Systematic Review. J Public Health Pharm. 2025;6:49–65. https://doi.org/10.56338/jphp.v6i1.6854.
30. van den Hof S, Collins D, Hafidz F, Beyene D, Tursynbayeva A, Tiemersma E. The socioeconomic impact of multidrug resistant tuberculosis on patients: Results from Ethiopia, Indonesia and Kazakhstan. BMC Infect Dis. 2016;16. https://doi.org/10.1186/s12879-016-1802-x.
31. Fuady A, Houweling TAJ, Mansyur M, Richardus JH. Catastrophic total costs in tuberculosis-affected households and their determinants since Indonesia's implementation of universal health coverage. Infect Dis Poverty. 2018;7. https://doi.org/10.1186/s40249-017-0382-3.
32. Indonesian Statistic (BPS). In. September 2024, the percentage of the poor population decreased into 8.57 percent. 2025. https://www.bps.go.id/en/pressrelease/2025/01/15/2401/in-september-2024–the-percentage-of-the-poor-population-decreased-into-8-57-percent-.html. Accessed 24 Sep 2025.
33. Indonesian Statistic (BPS). Profil Kemiskinan. 2024.
34. Indonesian Statistic (BPS). Indonesian Expenditure Inequality Rate in. 2024.

35. Indonesia Ministry of Health. Temukan TB Obati Sampai Sembuh: Penatalaksanaan Tuberkulosis Resistan Obat di Indonesia. 2020.
36. Hassane-Harouna S, Cherif GF, Ortuno-Gutierrez N, Cisse D, Camara LM, Diallo BD, et al. Better programmatic outcome with the shorter regimen for the treatment of multidrug-resistant tuberculosis (MDR-TB) in Guinea: A retrospective cohort study. PLoS ONE. 2020;15:e0237355. https://doi.org/10.1371/journal.pone.0237355.
37. Wares DF, Mbenga M, Mirtskhulava V, Quelapio M, Slyzkyi A, Koppelaar I, et al. Introducing BPaL: Experiences from countries supported under the LIFT-TB project. PLoS ONE. 2024;19. https://doi.org/10.1371/journal.pone.0310773. 11 November.
38. Myrzaliev B, Ahmatov M, Duishekeeva A, Kulzhabaeva A, Kadyrov A, Toktogonova A, et al. Experiences in the introduction of bedaquiline pretomanid linezolid for drug-resistant tuberculosis in Kyrgyzstan. J Clin Tuberc Other Mycobact Dis. 2024;36. https://doi.org/10.1016/j.jctube.2024.100472.
39. Evans D, Hirasen K, Casalme DJ, Gler MT, Gupta A, Juneja S. Cost and cost-effectiveness of BPaL regimen used in drug-resistant TB treatment in the Philippines. IJTLD OPEN. 2024;1:242–9. https://doi.org/10.5588/ijtldopen.24.0094.
40. van de Berg SEJ, Pelzer PT, van der Land AJ, Abdrakhmanova E, Ozi AM, Arias M, et al. Acceptability, feasibility, and likelihood of stakeholders implementing the novel BPaL regimen to treat extensively drug-resistant tuberculosis patients. BMC Public Health. 2021;21. https://doi.org/10.1186/s12889-021-11427-y.
41. Gomez GB, Siapka M, Conradie F, Ndjeka N, Garfin AMC, Lomtadze N, et al. Cost-effectiveness of bedaquiline, pretomanid and linezolid for treatment of extensively drug-resistant tuberculosis in South Africa, Georgia and the Philippines. BMJ Open. 2021;11. https://doi.org/10.1136/bmjopen-2021-051521.
42. Ridolfi F, Peetluk L, Amorim G, Turner M, Figueiredo M, Cordeiro-Santos M, et al. Tuberculosis Treatment Outcomes in Brazil: Different Predictors for Each Type of Unsuccessful Outcome. Clin Infect Dis. 2023;76:E930–7. https://doi.org/10.1093/cid/ciac541.
43. Lee JH, Hwang JH, Jang EJ, Kim RK, Lee KH, Park SK, et al. Risk Factors Related to COVID-19 Reinfection and Fatality During the Omicron (BA.1/BA.2) Period in Korea. J Korean Med Sci. 2023;38. https://doi.org/10.3346/jkms.2023.38.e269.
44. Bay JG, Patsche CB, Svendsen NM, Gomes VF, Rudolf F, Wejse C. Tobacco smoking impact on tuberculosis treatment outcome: an observational study from West Africa. Int J Infect Dis. 2022;124:S50–5. https://doi.org/10.1016/j.ijid.2022.07.067.
45. Alipanah N, Jarlsberg L, Miller C, Linh NN, Falzon D, Jaramillo E, et al. Adherence interventions and outcomes of tuberculosis treatment: A systematic review and meta-analysis of trials and observational studies. PLoS Med. 2018;15. https://doi.org/10.1371/journal.pmed.1002595.
46. Fuady A, Houweling TAJ, Mansyur M, Burhan E, Richardus JH. Effect of financial support on reducing the incidence of catastrophic costs among tuberculosis-affected households in Indonesia:

Eight simulated scenarios. Infect Dis Poverty. 2019;8. https://doi.org/10.1186/s40249-019-0519-7.

Figures

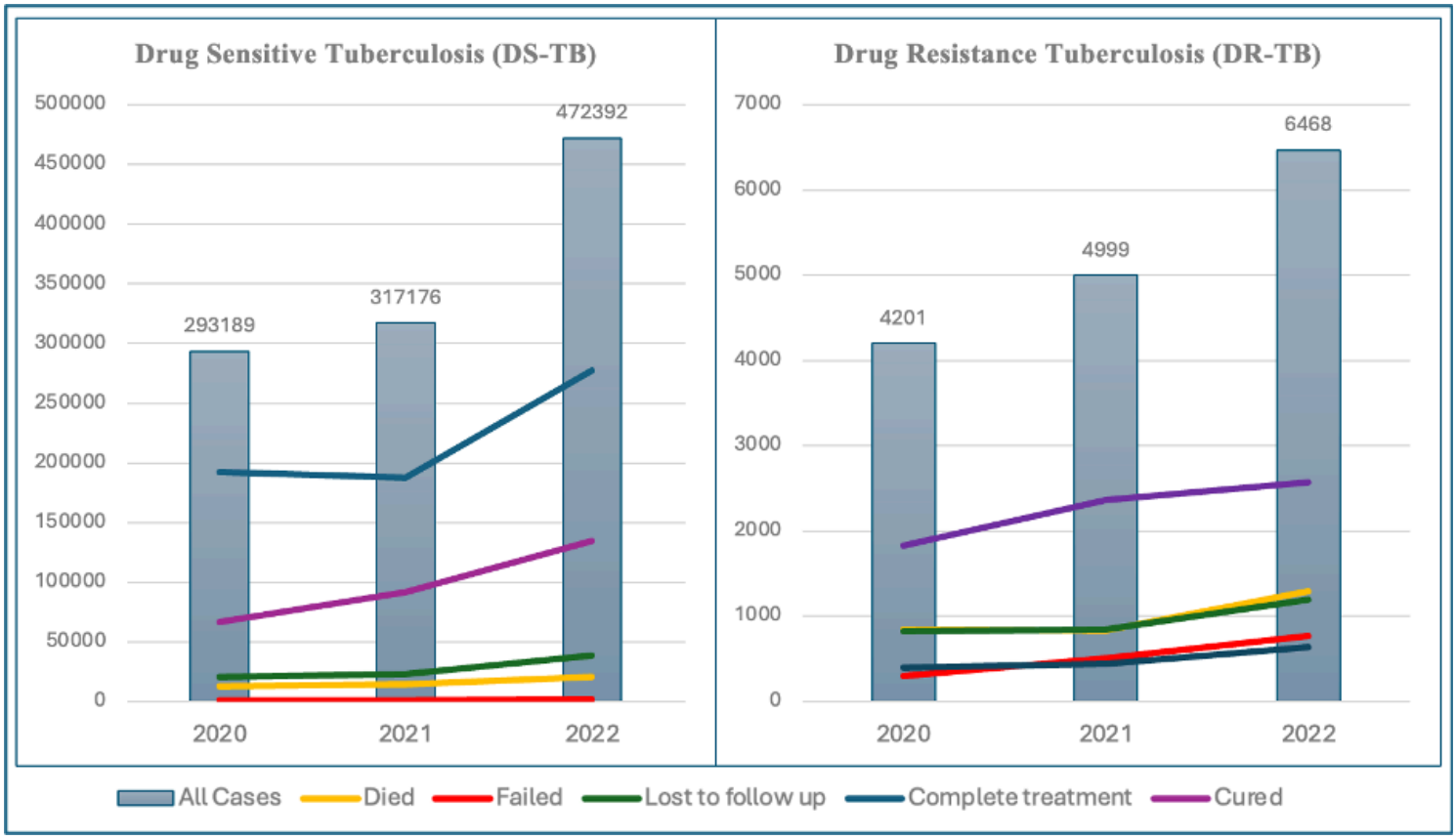

Figure 1

Treatment outcome of drug-sensitive and drug-resistant tuberculosis in Indonesia, 2020–2022. The figure shows the distribution of treatment outcomes (cured, complete treatment, failed, lost to follow-up, and died) among patients with drug-sensitive tuberculosis (DS-TB) and drug-resistant tuberculosis (DR-TB).

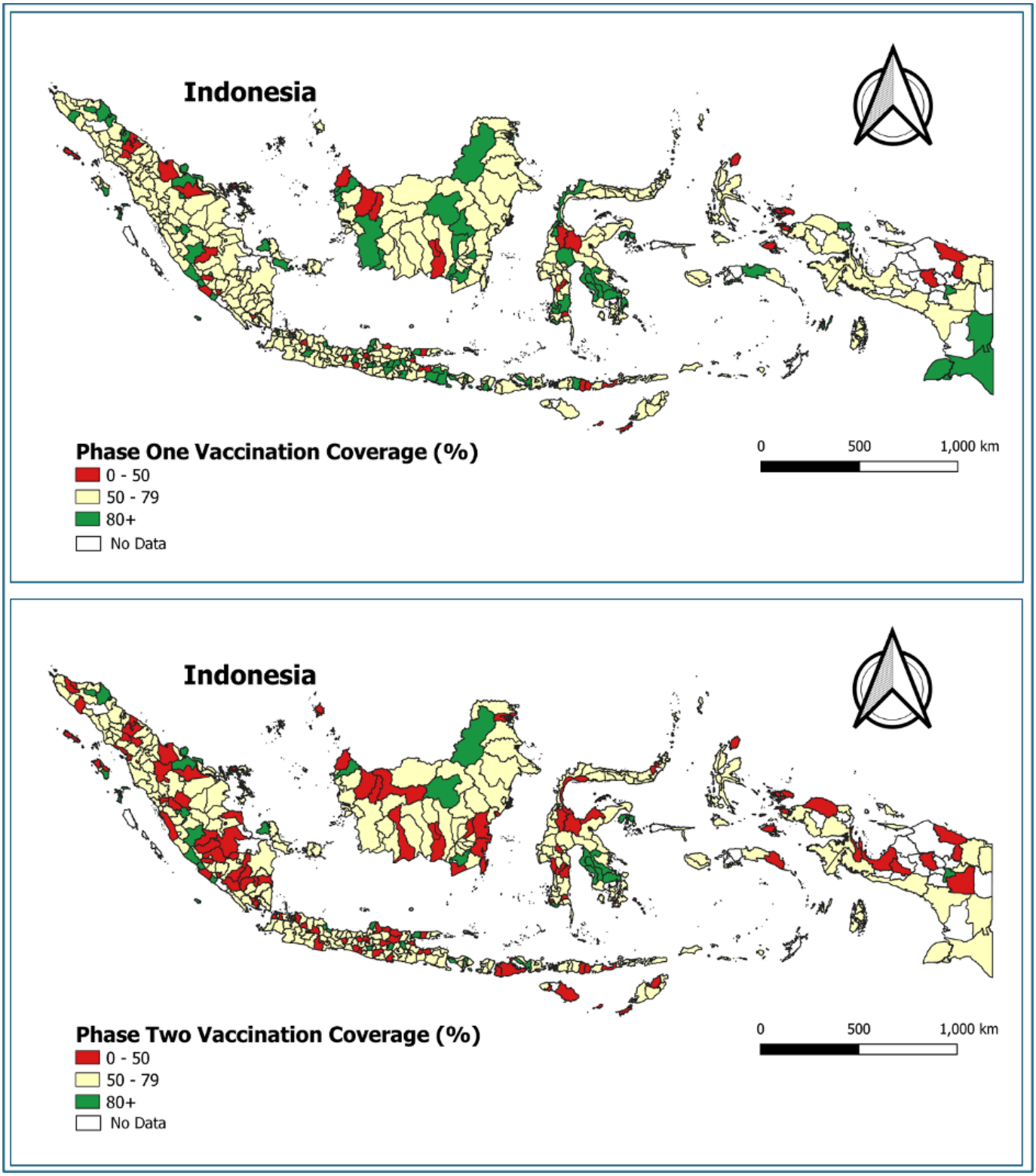

Figure 2

COVID-19 vaccination coverage in Indonesia: first and second doses. Maps show district-level first dose and second-dose COVID-19 vaccination coverage, categorized as lowest coverage (<50%), low coverage (50–79%), and high coverage (³80%).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryS1PUTITB.docx