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Global tuberculosis incidence and its macrostructural determinants: A hybrid Explainable Boosting Machine–Bayesian Structural Equation Modeling analysis of socioeconomic, health system, and population-risk pathways

Leonov Rianto[1*], Gilang Al Qarana[1], Charles Charles[1] and Yanthy Susanti[1]

[1]Sekolah Tinggi Ilmu Kesehatan IKIFA, Jakarta, Indonesia

*Corresponding author: leonovrianto@ikifa.ac.id

Abstract

Tuberculosis (TB) remains a leading infectious cause of mortality worldwide, with marked cross-country disparities shaped by socioeconomic conditions, health system capacity, and population-level risk factors. The aim of this study was to investigate the macrostructural determinants of global TB incidence and to clarify the pathways through which socioeconomic, health system, and population-risk domains are associated with TB incidence. Country-level secondary data were obtained from WHO, World Bank Open Data, and UNDP. A hybrid analytical framework was applied in two stages. First, EBM was used to identify non-linear predictor signals and rank the relative importance of macrostructural determinants of TB incidence. Second, the empirically derived predictors were translated into BSEM to estimate latent measurement structures and structural pathways toward TB burden. A total of 172 countries were included in the final analytical dataset. In the EBM phase, the strongest predictor signal was observed for Education Index, followed by diabetes prevalence, HIV incidence, TB case detection rate, BCG coverage, and physician density. These signals were subsequently mapped into three latent constructs: socioeconomic conditions, health system capacity, and population-level health risk. In the final BSEM model, socioeconomic showed the strongest association with health system capacity (β=0.62), indicating that stronger socioeconomic conditions were associated with greater TB-relevant service capacity. Health system was subsequently associated with lower TB incidence (β=-0.26). Direct associations with TB incidence were also observed for socioeconomic (β=-0.46) and health risk (β=-0.33), although the health risk pathway required cautious interpretation because of limited latent coherence at the country level. The final model explained a substantial proportion of cross-country variation in TB incidence (posterior R^2=0.53). These findings indicate that the global TB burden is shaped by interconnected structural pathways rather than by a single macroeconomic gradient. Socioeconomic conditions appeared to influence TB burden primarily through health system capacity, particularly diagnostic reach, workforce availability, case detection, and immunization coverage. The hybrid EBM–BSEM framework provides an interpretable approach for identifying upstream determinants of TB burden and may support evidence-based prioritization of global TB prevention strategies.

Keywords: Tuberculosis, EBM, BSEM, cross-country variation, health risk

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Introduction

Although the global tuberculosis (TB) burden has declined over the past two decades, progress has stagnated in recent years, with evidence of resurgence in some regions following the COVID-19 pandemic [1-4]. WHO estimates indicated that approximately 10.8 million people developed TB in 2023, corresponding to an incidence of about 134 cases per 100,000 population, with more than 1.25 million TB-related deaths [5-7]. However, the decline in TB incidence from the 2015 baseline remains only approximately 8%, which is substantially below the End TB Strategy 2025 milestones of a 50% reduction in incidence and a 75% reduction in mortality [8-10]. In addition, an estimated diagnostic gap of approximately 2.7 million cases per year remains outside national surveillance systems [11,12], while post-TB sequelae continue to contribute to the long-term burden of disability-adjusted life years (DALYs) [13,14]. This burden is disproportionately concentrated in low-income countries, particularly in South Asia, Sub-Saharan Africa, and Southeast Asia, suggesting that cross-country TB trajectories are shaped by structural determinants rather than by isolated clinical factors alone [15-17].

Recurrent determinants identified in cross-country comparisons include low health literacy, limited primary care capacity, fragmented public financing, tobacco and alcohol use, metabolic comorbidities, particularly diabetes and hyperglycemia, and particulate matter ≤2.5 µm (PM2.5) exposure, all of which have been associated with an increased risk of pulmonary TB in previous analyses [18-21]. Undernutrition is also highly prevalent in many low- and middle-income countries and remains an important contributor to TB susceptibility and adverse outcomes [18,22-24]. These epidemiological vulnerabilities are further compounded by persistent fiscal constraints. Global TB financing needs are estimated at approximately US$17 billion per year, while the Global Fund provides approximately 70% of international TB financing, making TB programs vulnerable to aid instability and external funding shocks [25,26]. Scenario analyses suggest that reductions in financing could result in more than 10 million additional TB cases and 2 million additional deaths during 2025–2030 [27]. As progress continues to fall short of the End TB milestones, analytical approaches capable of capturing non-linear and interdependent relationships among structural determinants are increasingly needed [28,29].

Gross domestic product (GDP) per capita based on purchasing power parity (PPP) has been consistently associated with lower TB incidence across countries [29-32]. Educational indicators, including expected years of schooling, mean years of schooling, and the Education Index, are also closely related to care-seeking behavior, medical literacy, and treatment adherence [18-20]. From the environmental perspective, PM2.5 exposure has been associated with increased pulmonary TB risk in multi-country analyses [21]. Metabolic comorbidities, particularly diabetes, are associated with higher TB incidence and poorer clinical outcomes, as supported by evidence from systematic reviews and Mendelian randomization studies [33-35]. HIV incidence among people aged 15–49 years remains a major determinant of TB burden in many low- and middle-income countries [36], while variation in Bacillus Calmette-Guérin (BCG) vaccination coverage contributes to differences in protection, particularly in younger populations [37,38]. Collectively, these findings indicate that social, educational, environmental, infectious, and metabolic determinants interact in complex and potentially non-linear ways to shape global heterogeneity in TB burden.

Health system capacity is commonly reflected by physician density, expressed as the number of physicians per 1,000 population, which influences the timeliness of TB screening, diagnosis, and clinical management. Countries with lower health worker density are more likely to experience delayed detection and poorer clinical outcomes [39,40]. Program performance indicators, particularly the TB case detection rate (CDR), are directly related to the diagnostic gap and treatment coverage [41]. Financing structures further determine service responsiveness, as high out-of-pocket (OOP) expenditure can restrict access to care and undermine treatment continuity, while reliance on external funding, including the Global Fund, may expose national TB programs to systemic vulnerability during aid shocks [42-44]. Overall, cross-country variation in TB burden reflects the combined influence of service capacity, program performance, and financing arrangements, operating alongside broader social determinants and population-level risk factors.

These relationships are unlikely to be purely additive. Across countries, socioeconomic conditions, service access, environmental exposures, and metabolic comorbidities may overlap through non-linear and interdependent pathways [45,46]. Conventional linear regression models summarize these relationships using average coefficients and therefore provide limited information on functional form, threshold effects, or changes in association across levels of income and health system capacity [47-49]. Conversely, many high-performing machine learning approaches, such as extreme gradient boosting, random forest, and neural network models, often function as black-box prediction tools and are difficult to translate into policy-relevant causal or structural narratives, particularly when cross-institutional interventions require transparent and traceable evidence [50].

The Explainable Boosting Machine (EBM) provides a suitable starting point because it is a generalized additive model with pairwise interactions (GA^2M). It can estimate predictor-specific shape functions and identify data-driven interaction patterns while preserving model interpretability [51-53]. In this study, EBM served as an exploratory layer to identify non-linear patterns among macrostructural determinants before specifying a formal structural model. This approach allowed empirical pattern recognition without imposing linearity assumptions at the outset. Following this exploratory phase, Bayesian Structural Equation Modeling (BSEM) was then applied as a structural modeling step to estimate the direction and strength of pathways between latent constructs, quantify posterior uncertainty, and accommodate cross-loading and small-variance priors that are appropriate for cross-country data [54,55].

The aim of this study was to examine how socioeconomic conditions, environmental exposures, and metabolic factors are associated with TB burden, and to determine the extent to which these relationships operate through health system capacity. Conceptually, it was hypothesized that countries with weaker socioeconomic conditions would have lower health system capacity, that environmental and metabolic risks would be associated with higher TB incidence, and that the effect of socioeconomic conditions on TB burden would be mediated primarily through health system capacity rather than occurring only through direct pathways. In this study, EBM was applied to explore non-linear signals and rank the relative contribution of macrostructural determinants of TB incidence. These empirical signals were then incorporated into BSEM to estimate the direction and magnitude of pathways between latent constructs, quantify posterior uncertainty, and allow cross-loading with small-variance priors suitable for cross-country data.

Methods

Data sources

This study integrated cross-country indicators from the World Bank, WHO, and UNDP [56-66]. The primary outcome was TB incidence per 100,000 population, obtained from the WHO Global TB Report 2022 [59]. Predictors were extracted using the latest available value for each indicator, mainly from 2022, except for PM2.5 exposure, which was based on 2020 data, and education-related indicators, which were based on 2023 data [62,66]. Core predictors included GDP per capita based on PPP, expected years of schooling, mean years of schooling, Education Index, physicians per 1,000 population, PM2.5 exposure, HIV incidence among populations aged 15–49 years, diabetes prevalence, BCG coverage, TB case detection rate, and out-of-pocket health expenditure. After applying the inclusion criterion, defined as the exclusion of countries with ≥2 missing core predictors, 172 countries remained in the analytical dataset.

A broad set of health system, socioeconomic, metabolic, and environmental indicators was collected at the data acquisition stage, although not all indicators were retained in the final latent measurement model. This approach was used to reduce post hoc selection bias and to allow EBM to empirically evaluate the full candidate predictor space before structural restrictions were imposed. For example, the Education Index is derived from expected years of schooling and mean years of schooling; therefore, both subcomponents were initially collected to preserve transparency and auditability of the HDI-related computational pathway.

Similarly, PM2.5 exposure and out-of-pocket health expenditure were included in the initial candidate set because environmental particulate exposure and household financial protection are theoretically plausible determinants of population-level TB susceptibility and access to care. Their inclusion therefore reflected an a priori decision to maintain construct breadth during the initial modeling phase, rather than data-driven predictor selection after observing model results.

Data preprocessing and variable transformation

Zero-value entries in numeric indicators were not treated as true structural zeros. For epidemiological and service-capacity variables, including physicians per 1,000 population, BCG coverage, TB case detection, HIV incidence, and PM2.5 exposure, a literal value of "0" was considered more likely to reflect incomplete national reporting than an actual population-level state [18-21]. Therefore, all numeric zero values were recoded as missing, and missingness was quantified at the country level. Countries with ≥2 missing core predictors were excluded. Missing values for physicians per 1,000 population were imputed using the median within income-group strata to preserve comparability across countries with similar economic profiles.

All retained numeric indicators were standardized using z-score transformation, and TB incidence was log-transformed to stabilize variance and reduce skewness [67]. The Education Index was used as an eligibility gate variable; countries without this HDI component were not retained for modeling [68]. Expected years of schooling and mean years of schooling, both based on 2023 data, were initially included as candidate predictors. However, because both indicators are incorporated into the UNDP Education Index, they were subsequently represented through the composite Education Index to reduce redundancy and multicollinearity. Accordingly, the final modeling pipeline used the Education Index as the sole education measure.

Explainable Boosting Machine and Bayesian Structural Equation Modeling

EBM was trained to quantify global predictor importance and generate an empirical ranking of macrostructural predictors associated with TB incidence [69]. This ranking was used to guide the allocation of observed indicators into three conceptual latent domains: (1) Socioeconomic, represented by Education Index, GDP per capita based on PPP, and out-of-pocket health expenditure; (2) Health System, represented by physicians per 1,000 population, TB case detection rate, and BCG coverage; and (3) Health Risk, represented by HIV incidence among populations aged 15–49 years, diabetes prevalence, and PM2.5 exposure. These empirically informed domains were then formalized in the BSEM phase to estimate directional pathways toward TB burden [70,71].

Weakly informative priors were applied to reduce over-shrinkage while maintaining regularization appropriate for cross-country data. Markov Chain Monte Carlo (MCMC) sampling was performed using multiple chains, and model convergence was assessed using posterior diagnostics, including R-hat, effective sample size, and divergent transitions.

Results

Predictive performance

To provide empirical context before predictive and structural modeling, the descriptive characteristics of the global indicators used in the cross-country analysis were first presented. The final analytical dataset included 172 countries after countries with ≥2 missing core predictors had been excluded. Summary statistics, including the mean, distribution, and range for each key variable analyzed in this study, are presented in **Table 1**. Substantial variation across countries was observed. For example, GDP per capita, PM2.5 exposure, and the number of physicians per 1,000 population varied by orders of magnitude, indicating that global structural inequalities represent a relevant domain for evaluating cross-country differences in TB burden (**Table 1**).

Table 1. Descriptive characteristics of country-level indicators included in the analysis

Variable/predictor	Mean	Standard deviation	Minimum	Maximum
TB incidence per 100,000 (2022)	110.033	141.551	0.49	665
GDP per capita, PPP (USD, 2022)	23111.338	25062.503	829.387	133572
Expected years of schooling (2023)	13.382	3.085	5.635	20.846
Mean years of schooling (2023)	8.897	3.161	1.412	14.296

Variable/predictor	Mean	Standard deviation	Minimum	Maximum
Education Index (0–1)	0.666	0.176	0.249	0.964
Physicians per 1,000 population	1.884	1.663	0.021	9.429
PM2.5 exposure (μg/m³)	25.343	15.169	5.106	85.122
HIV incidence per 1,000 (15–49y)	0.591	1.123	0.01	7.9
Diabetes prevalence (%)	9.935	5.465	1.5	31.4
BCG coverage (%)	90.76	13.46	39.6	134.45
TB case detection rate (%)	74.271	15.742	18	110
Out-of-pocket health expenditure (%)	31.043	18.461	0.369	79.221

BCG: Bacillus Calmette–Guérin; GDP: gross domestic product; HIV: human immunodeficiency virus; PM2.5: particulate matter ≤2.5μm; PPP: purchasing power parity; TB: tuberculosis

Substantial cross-country heterogeneity was observed across nearly all structural indicators (**Table 1**). TB incidence ranged from <1 to >600 cases per 100,000 population, indicating marked epidemiological disparities across countries. Wide variation was also observed in health system indicators, with physician density ranging from nearly 0 to >9 per 1,000 population, and BCG coverage ranging from <40% to >130%, the latter likely reflecting over-reporting or coverage estimates exceeding 100% in some low-population countries. GDP based on PPP also varied by several orders of magnitude. These findings indicate that global variation in TB burden is unlikely to be explained by a single determinant domain and support the use of a hybrid predictive and structural modeling approach to characterize the underlying latent pathways.

Before the graphical patterns were interpreted, it was important to recognize that relationships among indicators in global epidemiological data are rarely purely linear. Therefore, non-parametric smoothing using Locally Weighted Scatterplot Smoothing (LOWESS) was applied to visualize local relationship patterns without imposing a predefined functional form. This approach provided an initial empirical assessment of curve shapes before formal predictive and structural models were estimated.

The non-linear associations between log-transformed TB incidence and selected country-level structural indicators are presented in **Figure 1**. The relationship between log-transformed TB incidence and GDP per capita based on PPP is shown in **Figure 1A**. The LOWESS curve indicated that the steepest reduction in TB burden occurred within the lower GDP range, suggesting that the transition from extreme poverty to middle-income status was associated with a marked decline in TB incidence. However, after GDP reached approximately 50–60 thousand USD, the curve became relatively flat, with a slight upward pattern observed at the upper tail of the distribution.

The relationship between log-transformed TB incidence and the Education Index is shown in **Figure 1B**. A non-linear but monotonic decreasing pattern was observed, in which TB incidence remained relatively high and stable at lower to middle levels of education, approximately 0.3–0.65, before declining more sharply once the Education Index exceeded approximately 0.70. This pattern supports the interpretation that educational attainment may not operate only as a linear exposure, but may have a threshold-like protective association with TB burden.

The relationship between log-transformed TB incidence and physician density is shown in **Figure 1C**. A non-linear decay pattern was observed, but with a different curvature profile from that of GDP and education. Very low physician availability, particularly <1 physician per 1,000 population, was associated with a higher TB burden. However, the slope became flatter once physician density reached approximately 3–4 physicians per 1,000 population, suggesting diminishing marginal returns after a minimum threshold of clinical service availability had been reached.

Across the analytical sample of 172 countries, robust generalization performance was achieved by the EBM model, with an in-sample R^2 of 0.836 and an out-of-sample R^2 of 0.518. This level of explanatory performance indicated that global structural covariates, despite substantial heterogeneity across countries, contained a consistently recoverable signal for explaining cross-country variation in TB burden. However, the remaining unexplained variance suggested that residual uncertainty was still present, likely reflecting unmeasured institutional, programmatic, and context-specific mechanisms.

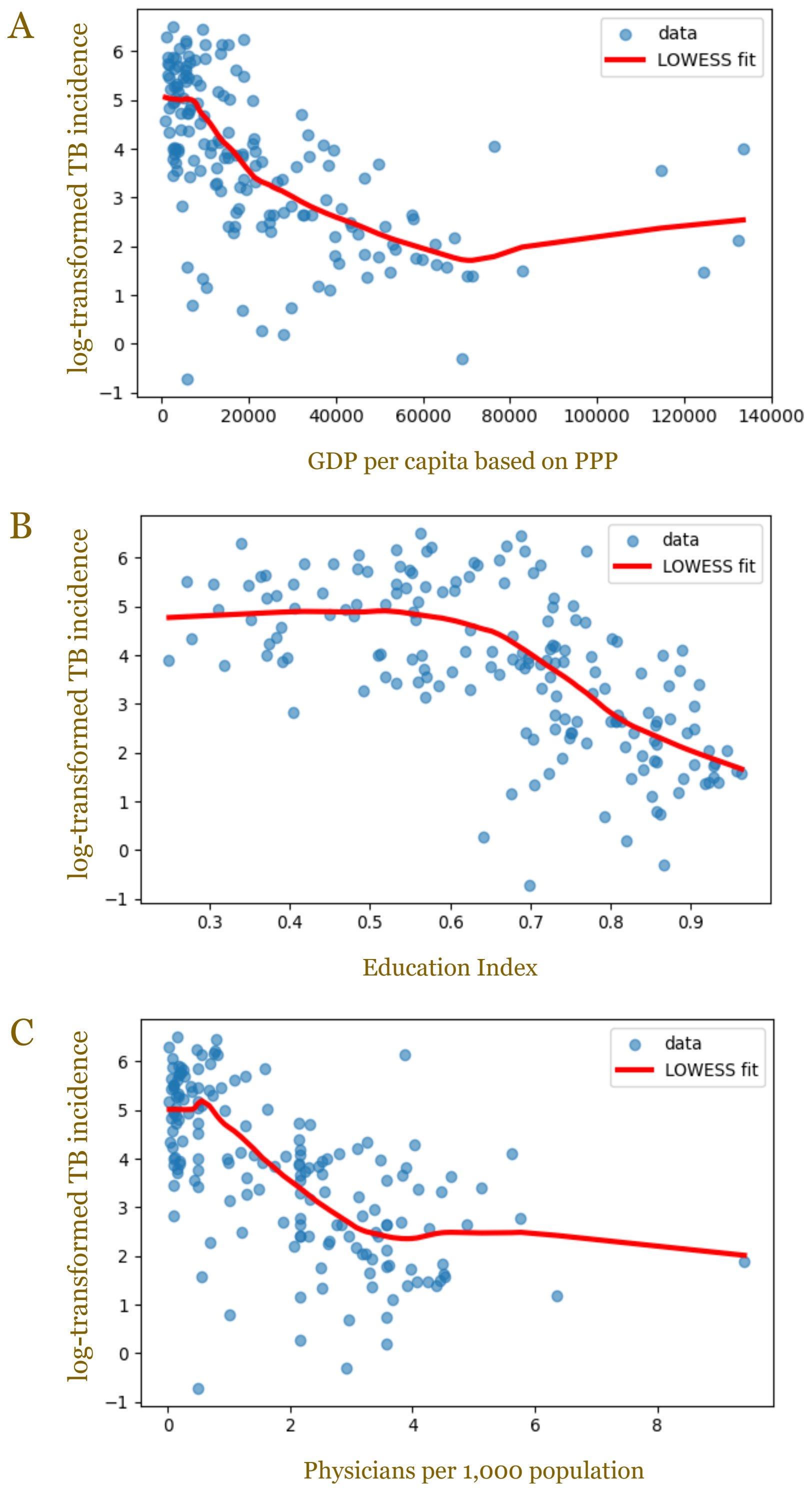

Figure 1. Non-linear associations between log-transformed TB incidence and selected country-level structural indicators. (A) Association between log-transformed TB incidence and GDP per capita based on PPP; (B) association between log-transformed TB incidence and Education Index; and (C) association between log-transformed TB incidence and physicians per 1,000 population. LOWESS curves were used to visualize non-linear relationship patterns without imposing a predefined functional form.

Predictor importance and latent domain mapping

The EBM model was applied not only as a predictive approach, but also as an empirical ranking framework to identify which predictors carried the strongest independent signals for TB incidence. Unlike conventional linear models, EBM decomposes predictor contributions additively and non-parametrically, allowing non-linear patterns and constrained monotonic relationships to be estimated directly from the data without imposing parametric assumptions.

This step was methodologically important because the latent constructs used in the BSEM framework were not specified solely on theoretical grounds but were empirically anchored to predictors with the strongest contribution to cross-country variation in TB burden. Accordingly, the predictor importance rankings generated by EBM provided a quantitative basis for structuring the latent domains and for distinguishing indicators that represented socioeconomic conditions, health system capacity, and population-level health risk.

The complete predictor importance ranking is presented in **Table 2**. Predictor importance reflects the relative contribution of each predictor to the target function, including second-order interaction terms, as evaluated across the boosting ensemble. A higher importance score indicates a larger marginal predictive contribution after adjustment for the other predictors included in the model. The highest-ranking predictors, including Education Index, diabetes prevalence, and HIV incidence, indicated that structural human capital and metabolic–immunologic vulnerability pathways provided more consistent explanatory signals for cross-country variation in TB burden than income level alone (**Table 2**). This finding supported the conceptual separation of socioeconomic and health-risk latent domains before BSEM estimation.

Table 2. EBM-derived importance ranking of country-level predictors of TB incidence

Rank	Predictors	Importance score
1	Education Index	0.4429
2	Diabetes prevalence (%)	0.2604
3	HIV incidence (per 1,000, age 15–49)	0.2348
4	TB case detection rate (%)	0.2179
5	BCG immunization coverage (%)	0.1868
6	Physicians per 1,000 population	0.1867
7	Out-of-pocket health expenditure (%)	0.1074
8	GDP per capita (PPP)	0.0896
9	PM2.5 exposure (μg/m³)	0.0532
10	(Top interaction term) PM2.5 × BCG coverage	0.0084

BCG: Bacillus Calmette–Guérin; GDP: gross domestic product; HIV: human immunodeficiency virus; PM2.5: particulate matter ≤2.5μm; PPP: purchasing power parity; TB: tuberculosis

The translation of EBM-derived predictive signals into structural measurement domains before BSEM estimation is presented in **Table 3**. This mapping was based on the principle that predictors with higher EBM importance scores represented more stable empirical expressions of population-level heterogeneity. Three interpretable latent domains were therefore specified: socioeconomic conditions, health system capacity, and population-level health risk. At this stage, all candidate indicators were retained for posterior evaluation rather than being excluded solely on the basis of the initial ranking. PM2.5 exposure was initially assigned to the health-risk domain during the conceptual mapping stage. However, subsequent BSEM diagnostics indicated insufficient latent coherence between PM2.5 exposure and the retained metabolic–immunologic indicators. Therefore, in the final BSEM specification, PM2.5 exposure was re-specified as an exogenous direct predictor of TB incidence rather than as a manifest indicator of the health-risk latent construct. TB burden was modeled as an endogenous outcome predictor and was represented by log-transformed TB incidence.

Table 3. EBM-derived mapping of observed predictors into BSEM latent domains

Latent construct	Observed manifest predictor
Socioeconomic	Education Index
	GDP per capita (PPP)
	Out-of-pocket health expenditure
Health system	Physicians per 1,000 population
	TB case detection rate
	BCG immunization coverage
Health risk	HIV incidence (per 1,000, age 15–49)
	Diabetes prevalence (%)
	PM2.5 exposure (μg/m³)
TB outcome (endogenous)	Log (TB incidence per 100,000)

BCG: Bacillus Calmette–Guérin; GDP: gross domestic product; HIV: human immunodeficiency virus; PM2.5: particulate matter ≤2.5μm; PPP: purchasing power parity; TB: tuberculosis

Latent structural effects

A reproducible empirical ordering of predictors was established during the EBM phase (**Table 2**). These empirical signals were subsequently translated into the BSEM framework to evaluate latent structural relationships underlying global TB burden. The final BSEM structural model is presented in **Figure 2**. Three latent constructs were included, namely socioeconomic conditions (Socioeconomic), health system capacity (Health System), and population-level health risk (Health Risk), together with their observed indicators and standardized structural pathways associated with national TB incidence. PM2.5 exposure was specified as a direct environmental predictor outside the latent construct structure because insufficient latent coherence was observed with the retained metabolic–immunologic indicators.

Operational Health System indicators also showed non-trivial predictive signals. TB case detection rate and physicians per 1,000 population had importance scores of 0.22 and 0.19, respectively, exceeding the contribution of PM2.5 exposure at 0.05 (**Table 2**). This supported the interpretation that programmatic performance and diagnostic coverage were more proximal to TB case ascertainment than exogenous environmental exposure. Accordingly, the transition from EBM to BSEM was used to formalize data-driven regularities into structural latent domains, rather than to interpret each observed predictor independently.

Predictor allocation into latent domains is shown in **Table 3**. Indicators representing Socioeconomic included Education Index, GDP, and out-of-pocket health expenditure. Indicators representing Health System included physicians per 1,000 population, TB case detection rate, and BCG coverage. HIV incidence and diabetes prevalence were retained as indicators of Health Risk, while PM2.5 exposure was modeled as a direct environmental predictor. Thus, the conceptual assignment was converted into a statistically testable measurement structure.

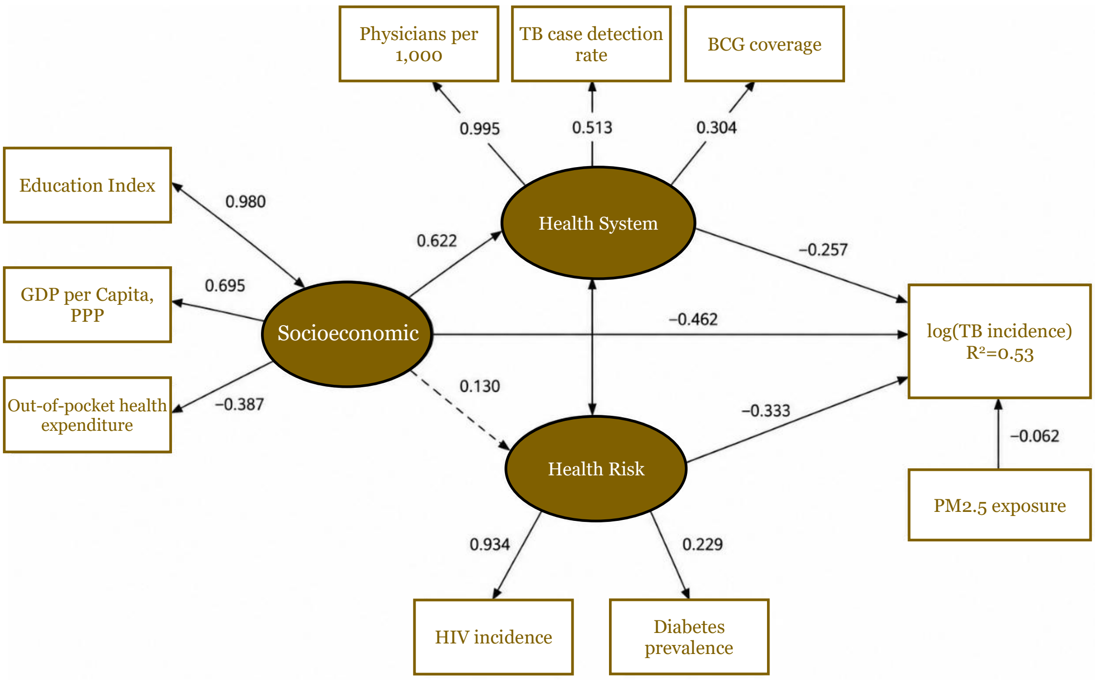

Figure 2. Final Bayesian Structural Equation Modeling (BSEM) model of country-level pathways associated with TB incidence. The model included three latent constructs, namely socioeconomic conditions (Socioeconomic), health system capacity (Health System), and population-level health risk (Health Risk). PM2.5 exposure was specified as a direct environmental predictor of log-transformed TB incidence. Standardized path coefficients are presented for the structural pathways.

Posterior standardized factor loadings from the final BSEM measurement model are presented in **Table 4**. Within Socioeconomic, the Education Index showed the strongest loading (0.980), followed by GDP (0.695), indicating that cross-country socioeconomic heterogeneity was expressed primarily through human capital accumulation. Out-of-pocket health expenditure showed a negative loading (-0.387), indicating that higher household financial burden was associated with weaker Socioeconomic conditions.

The Health System construct was strongly anchored by physicians per 1,000 population (0.995), while TB case detection rate (0.513) and BCG coverage (0.304) showed secondary institutional signals (**Table 4**). Health Risk was primarily driven by HIV incidence (0.934), whereas diabetes prevalence showed a weaker metabolic vulnerability signal (0.229). Overall, the factor loadings supported the separation between Health System and Health Risk as distinct latent domains.

Table 4. Posterior standardized factor loadings in the final BSEM measurement model

Latent construct	Manifest indicator	Standardized loading
Socioeconomic	Education Index	0.98
	GDP per capita based on PPP	0.695
	Out-of-pocket health expenditure	−0.387
Health System	Physicians per 1,000 population	0.995
	TB case detection rate	0.513
	BCG coverage	0.304
Health Risk	HIV incidence (per 1,000, age 15–49)	0.934
	Diabetes prevalence	0.229

The standardized structural path coefficients are presented in **Table 5**. The strongest structural association was observed between Socioeconomic and Health System (β=0.622), indicating that stronger educational, economic, and financial protection profiles were associated with greater TB-relevant service capacity. A weaker association was observed between Socioeconomic and Health Risk (β=0.130), suggesting that population vulnerability was only partly aligned with socioeconomic structure. For the TB outcome model, Socioeconomic showed the strongest direct association with lower log-transformed TB incidence (β=-0.462), followed by Health Risk (β=-0.333) and Health System (β=-0.257) (**Table 5**). The negative coefficient for Health Risk should be interpreted cautiously and should not be taken to indicate that HIV incidence or diabetes prevalence reduced TB burden. Rather, this estimate reflected the empirical scaling and latent composition of the Health Risk construct, which showed limited coherence at the country level.

The direct pathway from PM2.5 exposure to TB incidence was weak (β=-0.062) (**Table 5**). Its retention was supported by the EBM signal and by its theoretical relevance as an environmental exposure. Therefore, PM2.5 exposure was treated as a direct predictor rather than as a manifest indicator within Health Risk.

Table 5. Posterior standardized structural path coefficients in the final BSEM model

Outcome	Predictor	Standardized path coefficient
Health System	Socioeconomic	0.622
Health Risk	Socioeconomic	0.13
Log-transformed TB incidence	Socioeconomic	−0.462
	Health System	−0.257
	Health Risk	−0.333
	PM2.5 exposure	−0.062

Posterior predictive adequacy was evaluated using Bayesian R^2. The posterior R^2 estimates for endogenous nodes are presented in **Table 6**. Health System had a posterior R^2 of approximately 0.39, indicating that nearly 40% of between-country variation in Health System was explained by Socioeconomic. In contrast, Health Risk had a posterior R^2 of approximately 0.02, indicating limited coherence as a single latent block at the country level. The final TB outcome model had a posterior R^2 of approximately 0.53, indicating that the latent constructs, together with the direct PM2.5 pathway, explained more than half of the cross-country variation in TB incidence (**Table 6**). Collectively, these findings indicated that capacity alignment, rather than risk clustering alone, was the dominant systemic pathway underlying global TB burden variation.

Table 6. Posterior R^2 estimates for endogenous nodes in the final BSEM model

Endogenous node	Posterior R^2
Health System	0.387
Health Risk	0.017
Log-transformed TB incidence	0.530

Discussion

In this study, cross-country variation in TB burden was shown to be strongly structured by upstream socioeconomic conditions and their relationship with health system capacity. The final BSEM model indicated that Socioeconomic had the strongest structural association with Health System, suggesting that countries with stronger educational attainment, greater economic capacity, and lower household financial burden were more likely to have stronger TB-relevant service capacity. This finding supports the interpretation that socioeconomic development does not reduce TB burden only through direct improvement in living conditions, but also through consolidation of diagnostic capacity, workforce availability, immunization coverage, and case detection performance. This pattern is consistent with previous evidence showing that development-related gains are often mediated through institutional and service delivery pathways rather than through income growth alone [73,74].

The direct association between Socioeconomic and lower TB incidence further indicated that structural socioeconomic conditions remain central to global TB control. In the present model, the Education Index was the strongest manifest indicator of Socioeconomic, exceeding GDP in both EBM importance and BSEM loading. This finding suggests that human capital may represent a more stable marker of cross-country TB vulnerability than macroeconomic income alone. Education is likely to influence TB burden through multiple downstream mechanisms, including health literacy, care-seeking behavior, treatment adherence, household risk perception, and the capacity of communities to engage with prevention and treatment systems. This interpretation is aligned with previous studies indicating that social and educational determinants play a central role in TB susceptibility, access to care, and treatment outcomes [18-20,81].

The Health System also showed a direct association with lower TB incidence, although the magnitude was smaller than that observed for Socioeconomic. This finding suggests that health system capacity is an important intermediate mechanism, but not the only pathway through which TB burden is shaped. Physician density, TB case detection rate, and BCG coverage collectively represented the operational capacity of national TB-relevant service systems. These indicators are closely related to timely screening, diagnostic access, treatment initiation, and continuity of care. The observed pathway therefore supports the view that TB reduction requires not only general socioeconomic progress, but also functional health system capacity capable of translating structural resources into programmatic performance [39-44].

Health Risk construct showed a more complex pattern. HIV incidence and diabetes prevalence were retained as indicators of metabolic–immunologic vulnerability, consistent with previous evidence that these conditions increase TB susceptibility and worsen clinical outcomes [33-36]. However, the low posterior R^2 for Health Risk indicated that these indicators did not form a highly coherent latent domain at the country level. This finding should not be interpreted as evidence that HIV or diabetes are unimportant for TB epidemiology. Rather, it suggests that population-level vulnerability may be distributed heterogeneously across countries and may not follow a single shared structural pattern when the country is used as the unit of analysis. This is plausible because HIV burden, diabetes prevalence, environmental exposure, urbanization, and demographic transition may vary through different historical, epidemiological, and health system pathways [45,75-77].

PM2.5 exposure was ultimately specified as a direct environmental predictor rather than as a manifest indicator within Health Risk. This decision was supported by the weak latent coherence between PM2.5 and the retained metabolic–immunologic indicators. Although PM2.5 exposure has been associated with pulmonary TB risk in previous studies, its contribution in this cross-country model appeared relatively small compared with socioeconomic and health system pathways [21,75-77]. This does not negate the relevance of environmental exposure, but indicates that ambient air pollution may operate through a distinct exposure pathway rather than as part of a unified population vulnerability construct.

The posterior R^2 estimates provided further support for the central role of health system capacity as a mediator of structural disadvantage. Nearly 40% of the between-country variation in Health System was explained by Socioeconomic, indicating that health system capacity was substantially patterned by upstream socioeconomic conditions. In contrast, Health Risk showed very limited explained variance, reinforcing the interpretation that risk clustering was less structurally coherent than capacity alignment at the country level. The final model explained more than half of the cross-country variation in TB incidence, indicating that the combination of Socioeconomic, Health System, Health Risk, and PM2.5 captured a substantial proportion of global TB heterogeneity.

These findings have direct implications for TB policy in resource-constrained settings. If TB burden is shaped primarily through the pathway from socioeconomic capacity to health system performance, then isolated investments in advanced diagnostic technologies or disease-specific programs may have limited impact unless the broader service delivery chain is strengthened. Priority should therefore be given to improving primary care capacity, case detection, treatment continuity, and financial protection for households. At the same time, long-term TB prevention should be integrated with education, poverty reduction, and community-based health literacy interventions. Such integrated strategies are consistent with the broader view that TB control requires both biomedical intervention and structural action on the social determinants of disease [78-81].

Several limitations should be acknowledged. First, the study used cross-sectional country-level data; therefore, causal direction cannot be confirmed despite the use of theoretically informed structural pathways. Second, the analysis relied on secondary data from international databases, and differences in reporting quality, surveillance capacity, and indicator completeness across countries may have influenced the estimates. Third, country-level indicators may not capture within-country inequalities, subnational TB hotspots, or population-level heterogeneity in access to care. Fourth, the use of latent constructs necessarily involved conceptual simplification, particularly for Health Risk, which showed limited coherence at the country level. Future studies should combine longitudinal country-level data with subnational indicators to evaluate whether the pathways identified in this study are stable over time and across different epidemiological contexts.

Overall, the findings suggest that global TB burden is shaped less by isolated biomedical risk factors than by the extent to which socioeconomic capacity is translated into effective health system performance. The hybrid EBM–BSEM framework allowed non-linear predictor importance to be integrated with latent structural modeling, providing an interpretable approach for identifying upstream determinants and system-level pathways of TB burden. This approach may support more targeted prioritization of TB prevention strategies, particularly in countries where socioeconomic disadvantage and health system constraints remain closely interconnected.

Conclusion

This study showed that cross-country variation in TB burden was shaped by interconnected socioeconomic, health system, and population-level risk pathways rather than by a single macroeconomic gradient. Through the hybrid EBM–BSEM framework, dominant country-level predictors were first identified empirically and then translated into interpretable latent structural pathways. The findings indicated that Socioeconomic was the dominant upstream construct, with its strongest pathway operating through Health System. This suggests that socioeconomic development may reduce TB burden primarily by strengthening service capacity, including workforce availability, diagnostic reach, case detection, and routine immunization coverage. The final model also indicated that Health Risk and PM2.5 exposure contributed to TB burden through more heterogeneous and less coherent pathways at the country level. Therefore, while metabolic, immunologic, and environmental risks remain epidemiologically relevant, their population-level effects appear to be strongly conditioned by broader structural and health system contexts. Overall, these findings support the prioritization of integrated TB prevention strategies that combine socioeconomic development, financial protection, primary care strengthening, and improved programmatic capacity. The hybrid EBM–BSEM approach may provide a useful analytical framework for identifying upstream determinants of TB burden and guiding evidence-based global TB policy.

Ethics approval

Not required.

Acknowledgments

Not applicable.

Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

This study used artificial intelligence (AI) tools and methodologies in the following capacities: (1) data analysis and modeling: machine learning algorithms, including Explainable Boosting Machine (EBM) and Bayesian Structural Equation Modeling (BSEM), were used to analyze cross-country data and predict TB incidence patterns. These were implemented using Python with libraries such as Scikit-learn and PyMC; (2) data preprocessing: AI-assisted techniques were applied for data cleaning, predictor transformation, and normalization prior to modeling; (3) visualization: data visualization libraries (Matplotlib and Seaborn) were used to generate graphs and visualization of model outputs; and (4) manuscript writing support: AI-based language model, ChatGPT (OpenAI, GPT-5), was employed to improve grammar, refine sentence structure, and enhance clarity of the manuscript without generating or altering the scientific results or interpretations. We confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were solely made by the authors.

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