Impact of strategic public health interventions to reduce tuberculosis incidence in Brazil: a Bayesian structural time-series scenario analysis

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Summary

Background Despite government efforts, tuberculosis (TB) remains a major public health threat in Brazil. In 2023, TB incidence was 39.8 cases per 100,000 population, far above the WHO's target of 6.7 cases per 100,000. Using national-level datasets, we investigated and forecasted the potential impact of proposed public health interventions aimed at reducing TB incidence in Brazil.

Methods Monthly TB surveillance data (January 2018–December 2023) were collected from Brazilian national reporting systems: SINAN-TB (TB cases), SITE-TB (TB drug resistance), and IL-TB (preventive therapy). These data were used to create a multivariable Bayesian Structural Time-Series (BSTS) model, with 5000 Monte-Carlo simulations, which identified key predictors of TB incidence and forecasted these rates from 2024 to 2030 under various scenarios.

Findings Vulnerabilities including incarceration, TB-HIV coinfection and TB-diabetes mellitus, as well as coverages of directly observed therapy (DOT), contact investigation and preventive treatment (TPT) completion rates, were identified as key predictors of TB incidence. Under current trends, we forecasted TB incidence in Brazil to be 42.1 [34.1–49.8] per 100,000 person-years by 2030 (mean [95% prediction intervals]). A scenario considering decreases in TB cases among vulnerable populations resulted in an absolute reduction of –10.6 [–9.4 to –12.0] in projected TB incidence. Additional reductions were seen with increased coverage of DOT, TPT adherence, and contact investigation rates (–14.4 [–13 to –16.2]), and by combining these with efforts to reduce TB cases among vulnerable populations (–23.6 [–26.3 to –41.4]), potentially lowering incidence to 18.5 [7.8–28.4] per 100,000, though still above WHO targets.

Interpretation Our findings demonstrate that interventions focused on enhancing health policies focused on decreasing TB cases among vulnerable populations, such as individuals with TB-HIV coinfection, incarcerated populations, and those with TB-diabetes comorbidity, along with improvements in health management indicators

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such as DOT implementation, contact investigation coverage, and TPT completion rates, are effective in reducing TB incidence nationwide.

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Research in context

Evidence before this study

Global efforts to eliminate tuberculosis (TB) have been a significant public health challenge, particularly in high-burden countries, such as Brazil. On June 14, 2024, we conducted a comprehensive review of existing literature using PubMed to assess the impact of public health interventions and policies aimed at reducing TB incidence. Our search terms included: ("tuberculosis" AND "Incidence") AND ("intervention" OR "policy" OR "scenario") AND ("prediction" OR "forecast" OR "projection" OR "modelling") without language, geographical or temporal restrictions. The search resulted in 96 papers ranging from 1993 to 2024. Prior studies indicated a declining trend of TB incidence in Brazil before the COVID-19 pandemic, though still above the WHO targets. Nevertheless, these trends reversed after the pandemic ended, with increases in TB incidence being observed since 2022. Furthermore, isolated studies highlighted the beneficial effects of TB preventive treatment (TPT) and enhanced early case detection in reducing disease incidence. In addition, other studies have demonstrated how targeted interventions focused on reducing diabetes mellitus (DM) prevalence and poverty reduction policies, including the Family Allowance Program, can decrease TB incidence and mortality.

Added value of this study

Our study integrates data from multiple Brazilian national TB reporting systems, including the Tuberculosis Database System (SINAN-TB), Special Tuberculosis Treatment Information System (SITE-TB), and TPT information system (IL-TB), to comprehensively analyse TB incidence nationwide. To our knowledge, no previous report has employed Bayesian Inference and multivariable forecasting techniques to identify key predictors of TB incidence and evaluate the impact of targeted public health interventions nationwide. Using a multivariable Bayesian Structural Time-Series (BSTS) model, we forecasted future TB trends under various interventions. Our findings revealed that Brazil is unlikely to meet the WHO TB elimination goals of reducing incidence by 50% in 2025 and 80% in 2030, compared to 2015 rates, without significant changes in TB control measures. However, targeted improvements in key TB management indicators, including increasing coverage of directly observed therapy (DOT), contact investigation and adherence to TPT, as well as the enhancement of policies aimed at reducing TB cases among vulnerable populations, such as those under incarceration, with HIV co-infection or diabetes comorbidity, could substantially decrease incidence in the coming years. Our findings offer evidence-based recommendations for policymakers, emphasizing the need for combined and targeted public health policies to enhance TB control measures in Brazil. By addressing the critical predictors identified, our study provides the necessary steps for reducing disease incidence nationwide.

Implications of all the available evidence

The combined evidence from our study and the existing literature underscores the urgent need to enhance Brazil's TB control strategies to significantly reduce disease incidence. Our results suggest that targeted and combined interventions, particularly policies focusing on TB control in vulnerable populations and improving TB management strategies, are crucial to reduce Brazil's incidence rates in upcoming years. Creating and enhancing already existent health policies targeted to reduce TB among high-risk groups, including individuals with TB-HIV co-infection, incarcerated populations, and those with TB-diabetes comorbidity, is essential for disease control nationwide. Moreover, improving adherence to TB management practices, such as DOT and TPT completion rates, is also beneficial, given that current predictions show no significant increases in these parameters in upcoming years. These findings have significant public health implications that can be translated into practical applications for enhancing TB management in Brazil. By leveraging these insights, policymakers can design and implement comprehensive TB control programs addressing critical areas of disease burden and ultimately increasing the likelihood of achieving the WHO TB elimination targets in 2030.

Introduction

Tuberculosis (TB) remains a significant public health challenge in Brazil, one of the 30 countries with the highest TB burden globally.[1] The Brazilian Ministry of Health (BMoH) has committed to reducing TB incidence by 80% by 2030, compared to rates in 2015 (34.3

per 100,000 cases), aligning with the World Health Organization (WHO)'s End-TB Strategy.[2] However, recent data estimated an incidence rate of 39.8 per 100,000 inhabitants in 2023, indicating that Brazil is far from achieving global targets.[2]

To boost TB control efforts, in 2023, Brazil established an interministerial committee, fostering a multisectoral collaboration to accelerate actions to eliminate TB.[3] This initiative aims to address both biological and social vulnerabilities exacerbating TB incidence,[4] particularly among those affected by Brazil's economic recession, which has been associated with increases in TB cases since 2014.[5]

Brazil's comprehensive TB notification program is also a crucial support strategy for TB control. This includes the Brazilian Tuberculosis Database System (SINAN-TB),[6] which monitors epidemiological data from all TB cases nationwide. Additionally, other systems have been implemented to enhance TB monitoring, such as the IL-TB online system,[7] which tracks individuals with *Mycobacterium tuberculosis* (Mtb) infection who have initiated TB preventive treatment (TPT) since 2018, and the Special Tuberculosis Treatment Information System (SITE-TB), established in 2014 to monitor drug-resistant TB (DR-TB) treatment cases.[8]

Despite these initiatives, achieving TB elimination targets necessitates improvements in managing key drivers of the Brazilian TB epidemic, including HIV co-infection, TB in the incarcerated population, and diabetes mellitus (DM) comorbidity.[2,9] Therefore, this study collected monthly TB surveillance data from Brazil's national reporting systems and employed Bayesian Structural Time Series (BSTS)[10] modelling techniques to identify the critical predictors of disease incidence in Brazil and forecast future TB incidence rates by 2030, under distinct scenarios. Our central aim was to investigate whether implementing health policies targeting these key predictors, such as reducing TB cases among vulnerable populations and increasing participation in specific TB support strategies, classified as disease management indicators, could effectively reduce projected national incidence rates, while also comparing these projections to WHO targets for disease elimination.[1]

Methods

Ethics statement

Data were obtained from public government databases[6–8] and pre-processed by the BMoH for completeness, consistency, and removal of duplicates, following Resolution 466/12 guidelines by the National Health Council, Brazil.[11] Informed consent was not required since no personal identifiers were present in the databases.

Study design

We conducted a nationwide ecological study using data from Brazilian national TB reporting systems. These data were used to develop a multivariable BSTS model to identify the key predictors of TB incidence and forecast incidence rates from 2024 to 2030 under different scenarios. We also assessed the likelihood of Brazil achieving the WHO goals for TB elimination, including both a reduction in TB incidence by 80% (compared to 2015 rates), and 90% coverage of essential TB support strategies, classified as TB management indicators, by 2030.

Data sources

Our study utilized data from SINAN-TB,[6] SITE-TB,[8] and IL-TB,[7] covering January 2018 to December 2023. We extracted national-level monthly clinical and sociodemographic data on all notified TB cases, including new and retreatment cases from SINAN-TB. SITE-TB provided monthly aggregate data on new cases of any type of DR-TB. The IL-TB system was used to extract data from persons with Mtb infection, undergoing preventive therapy (TPT). Due to incomplete data on TPT coverage, we used treatment completion rates (80% or more self-reported doses taken), to assess the effectiveness of TB prevention in Brazil.[7] Monthly data on BCG vaccination (BCGv) rates (2018–2022) and primary healthcare (PHC) access (2018–2023) for the Brazilian population were collected from the SUS Information Technology Department (DATASUS)[6] and the Information System for Primary Healthcare (SISAB).[12]

We selected this time period for our study because the BSTS model used in our analysis requires all predictor variables to have the same length and be free of missing values.[13] Since the IL-TB system was only implemented in 2018 and TPT is a crucial strategy to control TB incidence, we limited our analysis to the period starting from 2018, aiming to maintain consistency and ensure the inclusion of this essential variable. Further details on each notification system and data curation are described in the Supplementary Methods and Fig. S1.

Study outcome definition

The main outcome was TB incidence, calculated as the ratio of new TB cases to the resident Brazilian population per 100,000 inhabitants, with population estimates from the Brazilian Institute of Geography and Statistics (IBGE) spanning from 2018 to 2023.[14] This approach followed a methodology detailed by the BMoH in Brazil's Manual of Recommendations for TB Control and was chosen due to SINAN-TB possessing case notification data with monthly granularity up to 2023, allowing for a more detailed temporal analysis of our data.[14]

Variable definition

We extracted monthly aggregated data regarding candidate explanatory variables of TB incidence, including the number of TB cases in sociodemographic groups and specific clinical characteristics of TB cases from the

abovementioned databases. Vulnerable populations were defined in this study as individuals with higher risk of TB disease, lower socioeconomic status and poorer access to healthcare services.[15] The vulnerabilities in our model included: non-white ethnicity (self-identified, including "Yellow", "Black" or "Pardo"), lower educational attainment, substance usage (alcohol, tobacco or illicit drugs), TB-HIV, TB-DM, incarceration, homelessness, and retreatment cases. Detailed definitions and origins of these variables are presented in Supplementary Table S1.

TB management indicators

Data on adherence and coverage of specific TB support strategies were collected and classified as TB Management Indicators. These included HIV testing, Xpert MTB/RIF testing and receipt of directly observed therapy (DOT) among new TB cases, as well as rates of contact investigation. DOT was defined as medication intake observed by a healthcare or supervised professional for at least 24 doses during intensive phase and 48 doses in the maintenance phase of treatment.[14] Rates of TPT completion among Mtb infected cases, coverages of BCGv and access to PHC among the resident Brazilian population were also classified. Supplementary Table S1 presents definitions of all included TB Management Indicators.

Data preparation

Datasets were pre-processed by removing variables with >50% missing values. To address multicollinearity, a stepwise variation inflation factor (VIF) function was used to remove variables with high VIF values, recalculating all VIF values until all were below 10.[16] Twelve external regressors were selected: TB-HIV, TB-DM, incarceration, homelessness, DR-TB cases, retreatment cases, contact investigation, DOT coverage, Xpert MTB/RIF testing, TPT completion rate, BCGv and PHC access.

A new variable called "non-vulnerability" was created to control for cases without the characteristic vulnerabilities included in our model and listed above. Notification of COVID-19 cases could not be linked to the databases used in this study. Thus, to capture COVID-19's impact on TB notification rates, we created a binary variable to assess if the notification occurred between April 2020 and December 2021, when TB notification in Brazil was mostly affected by the pandemic.[2]

Statistical analysis

The statistical analysis used BSTS modelling and Bayesian linear regression (BLR) with spike-and-slab priors. All analyses were performed using R (version 4.3.1). Package descriptions are in Supplementary Table S2.

Model creation

A multivariable BSTS model of TB incidence was developed by combining the structural components of time-series data (trend, monthly seasonality) with regression components capturing the effects of multiple predictors of TB incidence. This model was trained using monthly data from January 2018 through December 2022, while predictions considered data up to December 2023, incorporating the most recent information for forecasting future trends. Model accuracy was evaluated using one-step-ahead prediction errors, including in-sample and out-sample validation, using Mean Absolute Percentage Error (MAPE), Symmetric Mean Absolute Percentage Error (sMAPE), Mean Absolute Error (MAE) and Root-Mean-Square Deviation (RMSE). Details on model specification and model fit are available in Supplementary Fig. S2 and Supplementary Methods.[10]

BLR analysis selected the most relevant predictors by calculating the probability of a predictor being excluded, due to having minimal impact on TB incidence, across 5000 Markov-Chain Monte-Carlo (MCMC) simulations.[10,17] Bayesian inference determined the importance of each variable using posterior inclusion probability (PIP). Variables with high PIPs were more likely associated with TB incidence.[10,17] Finally, Bayesian model averaging integrated the trend, seasonal, and regression components, generating samples from the posterior distribution using the MCMC simulations.[10]

Scenario analysis

Scenario analysis was performed using our multivariable BSTS model to evaluate the impact of different public health interventions aimed at reducing TB incidence. This involved forecasting TB incidence under various scenarios to understand how changes in key predictors could affect the future TB burden. In BLR analysis, key predictors of TB incidence were defined as variables with a PIP > 0.50. The non-vulnerability variable was not altered, as it was included to control for non-vulnerable cases.

Each scenario was designed to reflect how potential public health policies aimed at TB control can impact projections of TB incidence from 2024 to 2030. They included: **(I) Baseline Scenario:** Assumed that current trends in TB predictors will continue without significant changes in control efforts in upcoming years. **(II) Reducing TB Cases Among Vulnerable Populations:** Assumed a 10% linear annual reduction rate from 2024 to 2030 in the number of TB cases among the vulnerable populations identified as key predictors (PIP $\geq$ 0.50) positively affecting TB incidence by the BLR analysis. **(III) Improvement in Key TB Management Indicators:** Assumed a 10% linear annual growth rate (capped at 100%), from 2024 to 2030, in the group of TB management indicators identified as key predictors (PIP $\geq$ 0.50) negatively affecting incidence rates. **(IV) Combined Intervention Scenario:** Combined reduction of TB in vulnerable populations with improvements in key TB

management indicators. A summary of these scenarios is presented in Fig. 1.

We selected a 10% annual improvement rate to represent a realistic yet ambitious scenario for sustained improvements in TB management. This figure aligns with global health guidelines, particularly the WHO's estimate that globally, a net reduction in TB incidence of 8.7% was achieved from 2015 to 2022.[1] However, to reach global milestones a 10% annual decline in TB incidence is required by 2025, accelerating to 17% per year afterwards.[1] Thus, our assumption of 10% improvements in critical TB management indicators represents an ambitious goal for Brazil, but also reflects recent efforts to enhance TB control programs and commitments to elimination targets.[18]

For each scenario, mean and 95% prediction intervals (PI) forecasts of TB incidence were generated and compared to TB elimination goals set by the WHO. Those goals included a reduction in TB incidence of 20% by 2020, 50% by 2025 and 80% by 2030, all compared to incidence rates in 2015 (34.3 per 100,000 cases).[2,18]

Further scenarios were modelled to evaluate the effects of more intensive, albeit less practical, TB control interventions. These included increased improvements in TB management indicators with 20% and 30% annual growth rates from 2024 to 2030 and the impact of more aggressive policies to reduce TB cases among vulnerable groups, with 20–30% annual reduction rates. Additionally, a more conservative scenario of 5% improvements in TB management indicators was also simulated to assess the impacts of less aggressive interventions. All these scenarios served as a sensitivity analysis to explore how varying levels of improvements in these critical predictors of TB incidence could influence overall disease management and Brazil's likelihood of achieving TB elimination targets.

Forecasting coverage and adherence to TB management indicators

A sub-analysis was performed to assess the likelihood of achieving the WHO's 90% coverage and adherence targets for TB support strategies by 2025 and 2030.[2,14,18] Separate binary BSTS models were created for each indicator, including DOT, HIV testing, Xpert MTB/RIF diagnosis, contact investigation rates and TPT completion. Additional models were created for BCGv coverage and PHC access in the Brazilian population. These models used logit-transformed values and included historical data from each TB management strategy, while also controlling for the impacts of COVID-19.

The mean and 95% PI forecasted by each model were compared to the target of 90% coverage or completion rates, according to each management strategy. Bayesian modelling estimated probabilities of achieving WHO goals by calculating the proportion of the 5000 MCMC simulations' posterior distribution forecasts that exceeded thresholds.[19]

Role of the funding source

The funding source had no role in study design, data collection, analysis, interpretation or decision to submit for publication.

Results

Key predictors of TB incidence

From January 2018 to December 2023 there were 465,276 new TB cases and 100,646 retreatment TB cases

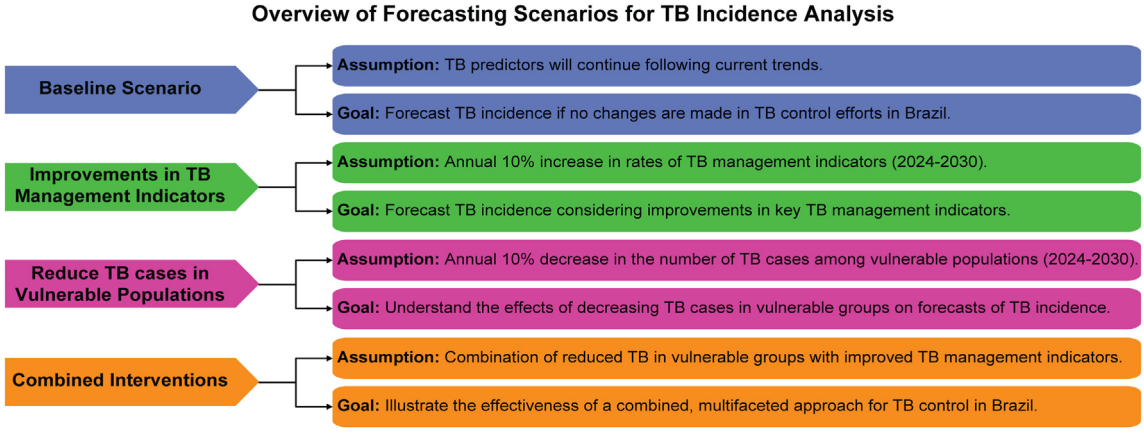

Fig. 1: **Overview of scenarios for TB incidence forecast analysis.** Summary of the assumptions and goals of four different scenarios used in the TB incidence forecast analysis using our multivariable Bayesian Structural Time-Series Model. The scenarios included: **(I)** Baseline Scenario; **(II)** Improvements in Key TB Management Indicators with PIP > 0.5 (rates of TPT completion, coverage of DOT participation, contact investigation and access to PHC); **(III)** Reduce TB in Vulnerable Populations with PIP > 0.5 (TB-HIV coinfected cases, Incarcerated TB cases, TB-DM comorbidity and retreatment cases); **(IV)** Combined Intervention. **Abbreviations:** TB: Tuberculosis; TPT: TB Preventive treatment; DOT: Directly Observed Therapy.

reported to SINAN-TB. There were also 6144 new DR-TB cases reported to SITE-TB, and 105,773/158,014 (66.9%) persons with *Mtb* infection who completed TPT reported in the IL-TB system.

The BLR analysis identified 9 key predictors of TB incidence (i.e., PIP $\geq$ 0.50) from the 14 pre-candidate regressors: PHC coverage, retreatment cases, TB-DM, contact investigation, DOT coverage, incarcerated TB cases, TPT completion rate, TB-HIV infection, and non-vulnerable TB cases (Fig. 2).

Among predictors of increased TB incidence, non-vulnerable TB cases and TB-HIV coinfection were the most important, each with a PIP of 1.00. For TB-HIV coinfection, we estimated that an increase in co-infected cases would result in 4.11×10^{-04} additional TB cases per 100,000 population [95% credible interval (CrI): 2.75×10^{-04}–5.21×10^{-04}] if other factors remained constant. Similarly, non-vulnerable TB cases were associated with an estimated mean increase of 4.11×10^{-04} TB cases per 100,000 population [95% CrI: [2.75×10^{-04}–5.21×10^{-04}]. Persons with TB who were incarcerated, with TB-DM, and retreated also exhibited high inclusion probabilities, with their impacts in incidence rates and regressor coefficients [rC] being detailed in Table 1.

Conversely, several TB management indicators emerged as key predictors of decreased TB incidence. The most critical included TPT completion rates and DOT coverage. For TPT completion, a percent increase in adherence among *Mtb* infection cases was associated with a decrease in TB incidence by approximately 8.02×10^{-03} per 100,000 population [95% CrI: -1.26×10^{-02} to -3.58×10^{-03}]. Similarly, a percent increase in DOT coverage among TB disease cases resulted in a reduction of approximately -1.34×10^{-02} TB cases per 100,000 population [95% CrI: -2.17×10^{-02} to -5.25×10^{-03}]. Contact investigation showed a PIP of 0.95, while the coverage of PHC access was also notable (PIP: 0.60) (Table 1, Fig. 2).

Scenario analysis of TB incidence

Next, using the above set of predictors, we created a multivariable BSTS model of TB incidence. The out-sample accuracy of this model (MAPE: 4.46%; sMAPE: 4.20%; MAE: 0.11; RMSE: 0.16) was better than those from a univariate model (MAPE: 7.90%; sMAPE: 7.90%; MAE: 0.23; RMSE: 0.30) composed solely of historical data of disease incidence, indicating the usefulness of these predictors in forecasting TB incidence (Supplementary Table S3).

Under current trends, the model forecasted TB incidence to be 38.8 [95%CrI: 35.9–41.7] per 100,000 inhabitants in 2025. While this value is excessively higher than the WHO target of 16.7, annual increases in key TB management indicators, including adherence rates to TPT, DOT coverage, contact investigation, and

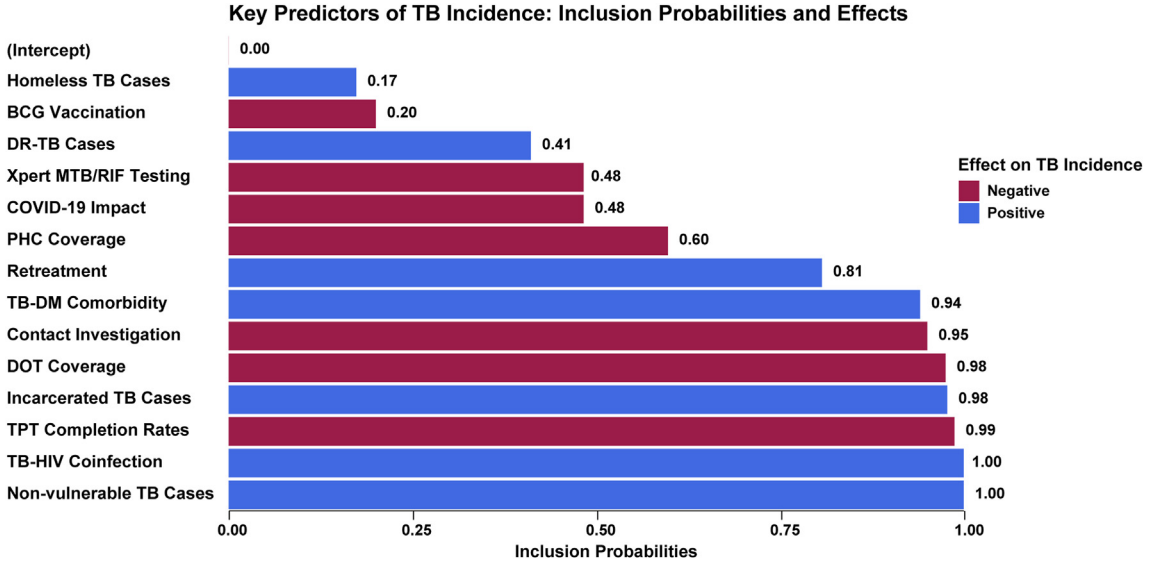

Fig. 2: **Inclusion probabilities and effects of key predictors on TB incidence.** This figure illustrates the inclusion probabilities and effects of key predictors of TB incidence, as determined by a multivariable Bayesian Structural Time-Series model. Each bar represents the inclusion probability of a predictor being part of the model, with the numbers indicating the exact probabilities. Predictors are colour-coded based on their effect on TB incidence: red bars represent predictors with a negative effect (reducing TB incidence), while blue bars represent predictors with a positive effect (increasing TB incidence). Predictors with over 50% inclusion probability were considered significant and included in scenario analysis. **Abbreviations:** TB: Tuberculosis, BCG: Bacillus Calmette-Guérin; DR: Drug-resistant; PHC: Access to Primary Healthcare; DM: Diabetes Mellitus; DOT: Directly Observed Therapy; TPT: Tuberculosis Preventive Treatment; HIV: Human Immunodeficiency Virus.

Regressor	Regressor coefficient mean [95% CrI]	Posterior inclusion probability	Effect on TB incidence
Non-vulnerable TB cases	4.11×10^{-04} [2.75×10^{-04} to 5.21×10^{-04}]	1.00	Positive
TB-HIV coinfection	7.21×10^{-04} [3.44×10^{-04} to 1.12×10^{-03}]	1.00	Positive
TPT completion rates	-8.02×10^{-3} [-1.26×10^{-02} to -3.58×10^{-03}]	0.99	Negative
Incarcerated TB cases	5.62×10^{-04} [2.31×10^{-04} to 8.87×10^{-04}]	0.98	Positive
DOT coverage	-1.34×10^{-02} [$-2.17 \times 10^{-02}$to -5.25×10^{-03}]	0.98	Negative
Contact investigation	-6.69×10^{-03} [-1.13×10^{-02} to -2.20×10^{-03}]	0.95	Negative
TB-DM comorbidity	5.41×10^{-04} [1.80×10^{-04} to 8.93×10^{-04}]	0.94	Positive
Retreatment cases	2.33×10^{-04} [4.05×10^{-05} to 4.42×10^{-04}]	0.81	Positive
Coverage of PHC access	-3.39×10^{-03} [-6.90×10^{-03} to 1.20×10^{-04}]	0.60	Negative
COVID-19 impact	-1.03×10^{-01} [-2.18×10^{-01} to -9.43×10^{-03}]	0.48	Negative
Xpert MTB/RIF coverage	-5.53×10^{-03} [-1.30×10^{-02} to 1.92×10^{-03}]	0.48	Negative
DR-TB cases	1.18×10^{-03} [-2.31×10^{-05} to 2.62×10^{-03}]	0.41	Positive
BCG vaccination	-1.33×10^{-04} [-3.17×10^{-03} to 2.59×10^{-03}]	0.20	Negative
Homeless TB cases	3.41×10^{-04} [-3.74×10^{-04} to 1.27×10^{-03}]	0.17	Positive
Intercept	0.00×10^{0} [0.00×10^{0} to 0.00×10^{0}]	0	Negative

TB: Tuberculosis; BCG: Bacillus Calmette-Guérin; DR: Drug-resistant; PHC: Access to Primary Healthcare; DM: Diabetes Mellitus; DOT: Directly Observed Therapy; TPT: Tuberculosis Preventive Treatment; HIV: Human Immunodeficiency Virus. This table presents a consolidated view of the effects and posterior inclusion probability of all TB predictors calculated by Bayesian linear regression with spike-and-slab priors and included in the multivariable Bayesian Structural Time-Series model of TB incidence. Regressor coefficients were reported though mean and 95% credible interval (CrI), using scientific notation (10^{x}), with each coefficient representing the absolute change in TB incidence per 100,000 population associated with a one-unit change in the predictor variable. The posterior inclusion probability represents the ratio of models in which the predictor was included in 5000 Markov-Chain Monte-Carlo simulations. Positive regressor coefficients were considered to possess an increasing influence in TB incidence, while negative regressor coefficients are variables with decreasing effects in TB incidence.

Table 1: **Regressors coefficients and inclusion probabilities of all predictors of TB incidence from Bayesian Linear Regression.**

access to PHC, from 2024 to 2025, decreased the forecasted incidence to 35.3 [31.5–39.0]. This represents a modest reduction of –3.5 [–2.7 to –4.4] incident cases per 100,000 population compared to the baseline, likely due to the scenario representing a gradual 10% annual increase in these indicators.

Further decreases were observed in the scenario focusing on reducing TB among vulnerable populations with the highest impact on TB incidence (TB-HIV, incarcerated, TB-DM, and retreatment cases). This scenario had a forecasted incidence of 33.0 [29.0–36.8], translating to a –5.8 [–4.9 to –6.9] reduction in incidence projections from baseline. Finally, the combined intervention scenario provided the most significant impact, forecasting a decrease of –8.0 [–6.9 to –9.3] incident cases from the baseline (Table 2, Fig. 3).

In 2030, the baseline scenario forecasted a TB incidence of 42.1 [34.1–49.8] per 100,000 population, well above the WHO target of 6.7. Increasing rates of key TB management indicators from 2024 to 2030 projected a decrease to 31.5 [22.1–40.4]. Reductions in TB cases among high-impact vulnerable populations forecasted an incidence of 27.7 [17.9–36.8]. The combined intervention scenario showed the greatest impact, with a forecasted incidence of 18.5 [7.8–28.4], achieving a reduction of –23.6 [–26.3 to –41.4] in incidence from the baseline (Table 2, Fig. 3). Observed and forecasted values of TB incidence under each scenario are detailed in Table 3. Notably, when considering a more conservative approach with 5% annual improvements, the combination of reducing TB cases among vulnerable groups and improving disease management indicators still led to a significant reduction in projected TB incidence, with a forecasted rate of 25.2 [15.3–34.5] per 100,000 population by 2030 (Supplementary Table S7).

Finally, when assessing the impacts of more ambitious scenarios to reduce TB incidence, our findings demonstrated that only combined interventions have a high chance of reaching WHO goals. As seen in Supplementary Tables S5 and S6, while a 20% annual improvement in key TB predictors forecasted an incidence rate of 8.2 [0.0–20.2] by 2030, only when considering the implementation of more intense TB control policie translating into an annual 30% reduction in TB cases among vulnerable populations and a 30% increase in critical TB management indicators, Brazil could effectively reach WHO TB elimination targets, with a forecasted incidence of 6.0 [0.0–18.4] by 2030 (Supplementary Fig. S3).

National coverage of TB management indicators

Next, we forecasted projections of coverage and adherence rates for the TB management indicators for 2025 and 2030. By 2025, all management indicators, except for BCGv coverage, had extremely low probabilities of achieving WHO/BMoH targets. By 2030, in addition to BCGv coverage, PHC and HIV testing among new TB cases were also forecasted to achieve the 90% coverage target, as detailed in Table 4 and Fig. 4. All observed and

Year	WHO targets	Observed data	Baseline scenario		Increases in management indicators		Reducing TB in vulnerable populations		Combined interventions	
			Forecasts mean [95% PI]	Probability to reach targets (%)	Forecasts mean [95% PI]	Probability to reach targets (%)	Forecasts mean [95% PI]	Probability to reach targets (%)	Forecasts mean [95% PI]	Probability to reach targets (%)
2020	26.8	32.7	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
2025	16.7	N/A	38.8 [35.9–41.7]	0.00%	35.3 [31.5–39]	0.00%	33.0 [29.0–36.8]	0	30.8 [26.6–34.8]	0
2030	6.7	N/A	42.1 [34.1–49.8]	0.00%	31.5 [22.1–40.4]	0.00%	27.7 [17.9–36.6]	0.02%	18.5 [7.8–28.4]	1.71%

TB: Tuberculosis; WHO: World Health Organization. Table presents the mean forecasts of TB incidence for the years 2025 and 2030 under different intervention scenarios compared to WHO/Ministry of Health targets. Targets were calculated as reduction in TB incidence of 20% by 2020, a 50% in 2025 and 80% in 2030, all compared to incidence rates in 2015 (34.3 per 100,000 cases).[2] The scenarios evaluated include baseline projections, increases in TB management indicators, reductions in TB among vulnerable populations, and combined interventions. The forecasts are provided with 95% prediction intervals. Probabilities of reaching WHO/Ministry of Heath targets are also presented based the proportion of the 5000 MCMC samples from the posterior distribution of forecasts that exceeded thresholds.

Table 2: **Predictions of TB incidence by 2025 and 2030 under different scenarios.**

forecasted values for TB Management Indicators are presented in Table 5.

Discussion

Despite efforts to improve prevention, diagnosis, and treatment, TB incidence in Brazil remains significantly higher than the targets set by the WHO for reducing disease incidence by 2030.[1,2] This demonstrates that while current policies are valuable, they are insufficient to reduce TB burden according to the WHO's elimination plan.[1,18] Our study represents a nationwide epidemiological analysis in Brazil, integrating data from three national databases, to identify the primary predictors of TB incidence in Brazil. Using these predictors, we forecasted the potential impact of health policies aimed at reducing TB cases among vulnerable groups and increasing participation in critical support strategies, evaluating how these interventions could reduce national TB incidence rates by 2025 and 2030.

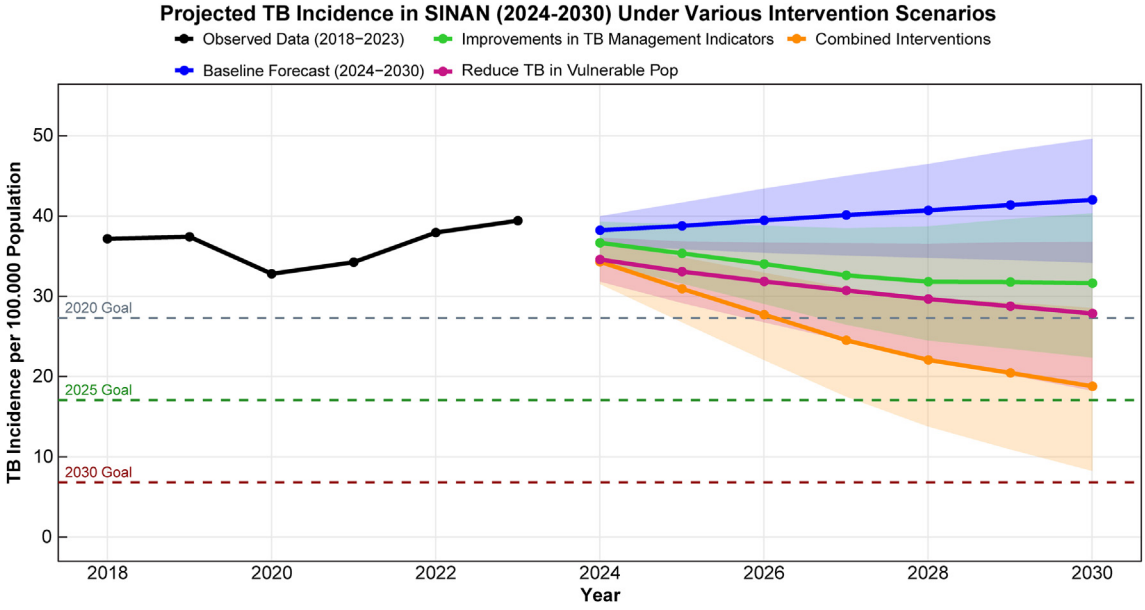

Fig. 3: **Scenario forecasting of TB incidence in Brazil from 2024 to 2030.** This figure presents projections of TB incidence in Brazil from 2024 to 2030 under various intervention scenarios, using a multivariable Bayesian Structural Time-Series model. Predictions are presented as the mean forecast accompanied by a 95% prediction interval. Scenario analysis was performed solely on key predictors with over 50% inclusion probability, as identified in Fig. 1. The black line shows observed TB incidence data from 2018 to 2023. The blue line represents the baseline forecast for 2024 to 2030, assuming current trends continue without new interventions. The green line illustrates a scenario where TB support indicators' coverage increases by 10% annually from 2024 to 2030, while other factors remain constant. The purple line shows the impact of a 10% annual reduction in the number of TB patients in key vulnerable groups, with other factors unchanged. The orange line represents the combined effect of both increasing TB management indicators' coverage by 10% annually and reducing TB cases in vulnerable groups by 10% annually. Dashed lines indicate TB incidence goals for 2020, 2025, and 2030. **Abbreviations:** TB: Tuberculosis.

Year	Baseline scenario	Improvement in TB management indicators	Reduce TB in vulnerable populations	Combined interventions
2018	37.2	37.2	37.2	37.2
2019	37.4	37.4	37.4	37.4
2020*	32.7	32.7	32.7	32.7
2021*	34.2	34.2	34.2	34.2
2022	38.0	38.0	38.0	38.0
2023	39.5	39.5	39.5	39.5
2024	**38.2 [36.4–40.0]**	**36.7 [34–39.3]**	**34.5 [31.7–37.3]**	**34.3 [31.4–37]**
2025	**38.8 [35.9–41.7]**	**35.3 [31.5–39.1]**	**33 [29.0–36.8]**	**30.8 [26.6–34.8]**
2026	**39.5 [35.4–43.5]**	**34 [28.9–38.8]**	**31.8 [26.6–36.7]**	**27.5 [21.8–32.9]**
2027	**40.2 [35.1–45.1]**	**32.5 [26.3–38.5]**	**30.6 [24.2–36.6]**	**24.3 [17.2–31]**
2028	**40.8 [34.8–46.6]**	**31.7 [24.3–38.8]**	**29.5 [22.0–36.5]**	**21.8 [13.4–29.6]**
2029	**41.4 [34.5–48.4]**	**31.7 [23.2–39.7]**	**28.6 [19.9–36.7]**	**20.2 [10.5–29.1]**
2030	**42.1 [34.1–49.8]**	**31.5 [22.1–40.4]**	**27.7 [17.9–36.8]**	**18.5 [7.8–28.4]**

TB: Tuberculosis; BSTS: Bayesian Structural Time-Series. The table presents observed and forecasted values predicted with the multivariable BSTS model under different scenarios. The values in bold font type represent the forecasted values, while the non-bold values correspond the observed data. All models were trained using monthly data from January 2018 through December 2022, while predictions were made by considering incidence data up to December 2023. The forecasted values were generated on samples from the posterior predictive distribution, based on 5000 MCMC simulations, and are accompanied by the 95% prediction intervals with lower and upper bounds. Data from 2020 to 2021 were labelled with an asterisk (*) to denote the years mostly impacted by the COVID-19 pandemic.

Table 3: **Observed and forecasted values for TB incidence in Brazil from 2024 to 2030 across various scenarios.**

Since 2003, the BMoH has classified TB as a public health priority and implemented strategies to control the high burden.[3,18] However, fundamental challenges such as limited healthcare access, treatment non-adherence, and the COVID-19 pandemic impact have hampered the ability to meet global targets.[2] Furthermore, stable TB control resources over the last decade have limited innovative actions for disease elimination in Brazil.[1]

Our findings demonstrate that most TB management indicators evaluated in this study will not meet WHO goals of 90% coverage by 2030, with only HIV testing among TB patients, BCGv, and access to PHC among the Brazilian population being predicted to achieve targets. Nonetheless, this is insufficient to eliminate the disease in Brazil, as the indicators with the highest impact in reducing TB incidence, including TPT completion rates, DOT coverage and contact investigation are predicted to remain far from these set targets. To re-establish control and achieve the outlined objectives, identifying key predictors of TB incidence and improving disease management are essential.

We identified HIV, incarceration, and DM as the key predictors that mostly elevate TB incidence rates nationwide. Numerous studies highlighted the impact of these vulnerable populations on Brazil's TB burden, underscoring the complexity of TB management.[20–22] To

Indicators	Observed rates	Predicted coverage [95% PI]		Probability of reaching target (90%)		Mann–Kendall test for trend (2018–2030)	
	Year 2020	Year 2025	Year 2030	Year 2025	Year 2030	Tau values	p-value
BCG vaccination coverage	81.8	96.8 [78.8–100]	96.5 [52.0–100]	75.8%	60.5%	0.308	0.16
PHC coverage	75.6	82.5 [74.1–90.1]	91.4 [68.4–100]	4.70%	53.70%	0.821	**0.0001**
HIV testing coverage	84.1	88.7 [86.2–90.7]	91.6 [86.7–95.1]	11.3%	75.9%	1.000	**<0.0001**
Xpert MTB/RIF testing coverage	40.1	55.9 [40.2–71.1]	78.1 [40–94.9]	0.1%	15.6%	1.000	**<0.0001**
TPT completion rates	74.9	74.1 [65.1–83.7]	72.4 [48.4–97.3]	0.4%	11%	−0.256	0.24
Contact investigation	69.1	68.1 [57.8–77.0]	69.3 [44.4–86.3]	0%	1.62%	0.000	1.00
DOT coverage	30.9	32.5 [26.8–38.8]	33.1 [20–49.7]	0%	0%	0.179	0.42

TB: Tuberculosis; PI: Prediction Interval; BCG: Bacillus Calmette-Guérin; PHC: Primary Healthcare; HIV: Human Immunodeficiency Virus; TPT: Tuberculosis Preventive Treatment; DOT: Directly Observed Therapy; MCMCs: Markov-Chain Monte-Carlo. Forecasts of coverage and adherence rates for TB management indicators by 2025 and 2030. Predictions were assessed regarding their likelihood of achieving WHO's targets of at least 90% rates, among samples from 5000 MCMC simulations. Trend exploration was performed using the Mann–Kendall test spanning data from 2018 to 2030. BCG vaccination coverage and PHC coverage were calculate among the entire Brazilian population. Coverages of HIV testing, Xpert MTB/RIF testing, contact investigation and DOT were calculated in reference to the total number of new TB cases. TPT completion rates represented the number of Mtb infection patients which began TPT and completed treatment scheme. Predictions of DOT coverage, BCG Vaccination, Contact Investigation and TPT completion used data up to December-2022, as these measures only had complete data available until that year.

Table 4: **National forecasts of TB management indicators and likelihood of achieving WHO targets of coverage and completion rates.**

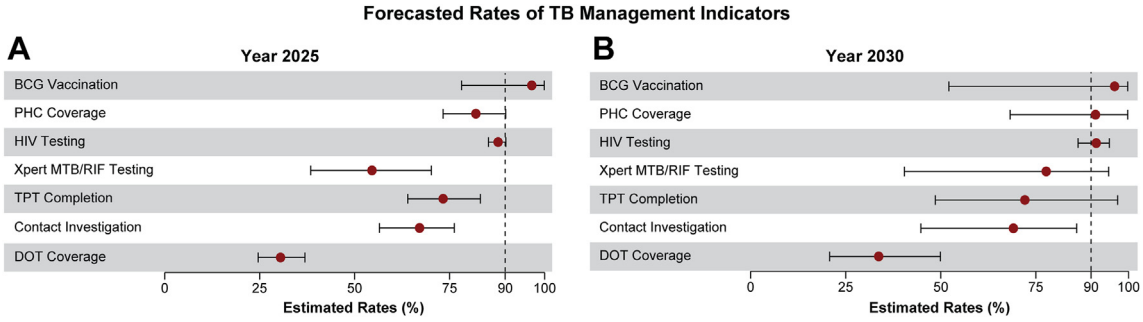

Fig. 4: **Projected coverage of TB management indicators in Brazil by 2025 and 2030.** This figure displays the forecasted rates of various TB management indicators in Brazil by 2025 and 2030, derived from bivariate Bayesian Structural Time-Series models, considering historical trends of each variable as well as the impact of the COVID-19 pandemic. Predictions of DOT coverage, BCG Vaccination, contact investigation and TPT completion used data up to December-2022, as these measures only had complete data available until that year. Red spheres represent the mean forecast for the coverage rate of a specific TB support strategy, while the horizontal lines indicate the 95% prediction intervals. The dashed vertical line at the 90% mark represents WHO and Ministry of Health targets for the coverage and adherence to TB management indicators.[18] **Abbreviations:** TB: Tuberculosis; BCG: Bacillus Calmette-Guérin; PHC: Primary Healthcare; HIV: Human Immunodeficiency Virus; TPT: Tuberculosis Preventive Treatment; DOT: Directly Observed Therapy.

effectively reduce TB incidence, our study underscores the need for policies tailored to these high-risk groups. Enhancing TB control programs in prison settings by improving screening, TPT access, and treatment completion, as well as better co-management of TB-HIV and DM through increased testing and treatment initiation, can significantly lower national TB incidence rates.[23,24] Our model also incorporated various control measures, among which DOT, TPT, and contact investigation emerged as the most critical in reducing TB incidence. These findings are consistent with evidence suggesting that robust engagement in these areas is vital for effective TB management. Notably, TPT and contact investigation have been demonstrated as effective interventions in reducing TB incidence,[25] given the high risk of disease transmission among contacts in Brazil.[26]

Additionally, our findings corroborate a previous nationwide study in China which also demonstrated that high DOT coverages are associated with decreases in incidence rates.[27] These results, combined with studies identifying DOT as a determinant of favourable anti-TB treatment outcomes, offer substantial evidence on the

Year	BCG Vaccination	PHC Coverage	HIV Testing Coverage	Xpert MTB/RIF Testing Coverage	TPT Completion Rates	Contact Investigation	DOT Coverage
2018	94.9	75.1	83.6	33.8	79	71.1	37.6
2019	88.3	74.3	84	36.2	74.9	68.9	35.5
2020*	81.8	75.6	84.1	40.1	72.2	69.1	30.9
2021*	79	64.8	84.7	41.8	71.3	68.6	30.5
2022	92.6	72.3	86.4	45.6	72	68.5	33.3
2023	**96.4 [86.2–100]**	77.6	87.4	49.0	**70.3 [65.8–73.4]**	**64.9 [62.4–73.12]**	**32.2 [28.3–35.2]**
2024	**97 [86.3–100]**	**80.2 [77–83.7]**	**88 [86.3–89.4]**	**50.8 [42.3–59.3]**	**74.5 [68.5–80.6]**	**68 [61.3–74.1]**	**32.4 [29–35.9]**
2025	**96.8 [78.8–100]**	**82.5 [74.1–90.1]**	**88.7 [86.2–90.7]**	**55.9 [40.2–71.1]**	**74.1 [65.1–83.7]**	**68.1 [57.8–77]**	**32.5 [26.8–38.8]**
2026	**96.7 [72.5–100]**	**83 [72.2–95.6]**	**89.4 [86.3–91.9]**	**61 [39.6–78.9]**	**73.7 [61.8–86.4]**	**68.3 [55–79.4]**	**32.6 [25.1–41.1]**
2027	**96.5 [67.4–100]**	**85.9 [70.9–99.8]**	**90 [86.2–92.9]**	**65.8 [39.7–84.9]**	**73.4 [58.3–89.3]**	**68.5 [52.2–81.4]**	**32.7 [23.6–43.3]**
2028	**96.5 [62.7–100]**	**87.8 [70.3–100]**	**90.6 [86.3–93.7]**	**70.2 [39.9–89.5]**	**73.1 [54.8–91.8]**	**68.7 [49.6–83]**	**32.8 [22.4–45.5]**
2029	**96.5 [57.1–100]**	**89.8 [69.2–100]**	**91.2 [86.5–94.4]**	**74.4 [39.6–92.6]**	**72.7 [51.9–94.6]**	**68.9 [46.9–84.7]**	**33 [21.2–47.6]**
2030	**96.5 [52–100]**	**91.4 [68.4–100]**	**91.6 [86.7–95.1]**	**78.1 [40–94.9]**	**72.4 [48.4–97.3]**	**69.3 [44.4–86.3]**	**33.1 [20–49.7]**

TB: Tuberculosis, BSTS: Bayesian Structural Time-Series; BCG: Bacillus Calmette-Guérin; PHC: Primary Healthcare; HIV: Human Immunodeficiency Virus; TPT: Tuberculosis Preventive Treatment; DOT: Directly Observed Therapy. The table presents observed and forecasted values of each TB management indicators included in this study, predicted with a bivariate BSTS model which considered historical trends of each variable as well as the impact of the COVID-19 pandemic. The values in bold font type represent the forecasted values, while the non-bold values correspond the observed data. All models were trained using monthly data from January 2018 through December 2022. Predictions for coverages of PHC access, HIV testing and Xpert MTB/RIF testing were made by considering incidence data up to December 2023. While, predictions of DOT coverage, BCG Vaccination, Contact Investigation and TPT completion used data up to December-2022, as these measures only had complete data available until that year. The forecasted values were generated on samples from the posterior predictive distribution, based on 5000 MCMC simulations, and are accompanied by the 95% prediction intervals with lower and upper bounds. Data from 2020 to 2021 were labelled with an asterisk (*) to denote the years mostly impacted by the COVID-19 pandemic.

Table 5: **Observed and forecasted values for TB management indicators from bivariate BSTS model.**

Main findings	Public health impact and policy implications
Challenges in achieving WHO targets	Current predictions indicate that Brazil TB incidence rates will continue to stay far above WHO targets in 2025 and 2030. This difficulty in meeting targets underscores the necessity for more robust, innovative, and sustained public health efforts and interventions to control TB nationwide.
Identifying key predictors of TB incidence	Identifying key predictors such as TB-HIV coinfection, incarcerated TB cases, and TB-DM comorbidity allows for the development of targeted interventions. Policies should focus on high-risk populations, enhancing screening, prevention, and treatment indicators tailored to these groups to effectively reduce TB incidence.
Scenario analysis of TB incidence	The highest effectiveness of combined intervention strategies, targeting both improvements management indicators and TB in vulnerable populations, underscores the need for integrated public health approaches that combine multiple strategies to achieve greater impacts on TB control.
Projections for TB management indicators	Strengthening and scaling up key TB management indicators like DOT coverage, contact investigation, and adherence to TPT are essential, as these rates are not only predicted to be farthest from reaching WHO targets but also lacking indicators of expected growth in upcoming years.
Improvements of multivariable models	The multivariable BSTS model demonstrated improved accuracy in forecasting TB incidence compared to a univariate model. This finding suggests that incorporating multiple predictors in TB incidence forecasting can lead to better-informed public health indicators and resource allocation.

Table 6: **Public Health Implications derived from the findings in this study.**

significance of this strategy for TB control. This is particularly important because the WHO does not currently include DOT coverage as a priority indicator in the END TB strategy.[1,18] However, our results indicate that maintaining DOT as mandatory for TB cases, particularly among highly vulnerable populations, can enhance TB control, most likely due to improved adhesion rates resulting in reduced disease transmission. These insights underscore the need to revise and improve public health strategies to ensure more effective TB management nationwide. Table 6 outlines how the significant public health implications from our study's findings can be translated into practical applications to reduce TB incidence in Brazil.

While most of the predictors utilized in our models have been previously established in the literature as significant contributors to TB incidence,[22,25] our study adds value by utilizing the BSTS model to perform a combined and granular evaluation of both current TB management strategies and key socio-epidemiological drivers of TB burden in Brazil. Our model provides a dynamic analysis that integrates these predictors over time, offering new insights into their collective impact on TB incidence. Thus, this study not only reaffirms the importance of targeting high-risk populations to improve TB management nationwide, but also identifies which current TB management strategies are most effective in reducing incidence rates.

Furthermore, our forecasts revealed that, under current circumstances, Brazil will not meet the WHO's targets for reductions in TB incidence. The baseline scenario projects TB incidence of 38.8/100,000 inhabitants by 2025, far above the WHO's target of 16.7.[2,28] While enhancing TB management indicators and improving policies targeted at disease control on vulnerable populations yield reductions in incidence, forecasted values remain substantially above set goals. Nevertheless, decreases of 25.1% in projected incidence by 2025 and 56.1% by 2030, were observed with combined interventions, highlighting the potential of integrated strategies.[2,28]

Importantly, the persistent gap between forecasted incidences and WHO targets, even in the most optimistic scenarios, underscores the need for more aggressive TB control measures in Brazil. Only the most intensive intervention, combining 30% annual improvements from 2024 to 2030 in all critical predictors, was projected to achieve global TB elimination goals. However, this scenario is unrealistic from a public health perspective, requiring extensive and rapid enhancements of existing TB control methods and health policies tailored to strongly reduce TB cases among vulnerable populations in a limited period. Alternatively, the introduction of novel TB vaccines, could also significantly accelerate progress towards End-TB targets.[29]

Of note, it is important to mention that our model aimed to account for potential confounders which may have impacted the increases in incidence rates from 2018 to 2023, as well as the future projections under the baseline scenario. To address the potential impact of the COVID-19 pandemic on TB notification rates, we included a binary variable covering the period from April 2020 to December 2021, when TB notifications were most affected due to disruptions in healthcare access and reporting practices. Additionally, we further controlled our model for the gradual improvements in TB diagnosis over time by including trends in Xpert MTB/RIF coverage throughout this time period.

This study has several limitations that should be taken into account when interpreting the results. First, our analysis was constrained by the reliance on secondary data, which included high levels of missing information. Efforts were made to mitigate this issue by excluding variables with particular missingness levels. Second, the BSTS model requires all predictor variables to have consistent lengths and no missing values.[13] To meet this requirement, we limited our analysis to data from 2018 onward, aligning with the implementation of the IL-TB system that provided crucial TPT data, necessary for our study. This approach ensured the inclusion of this essential variable, allowing us to maintain

data consistency and accurately assess the impact of TPT on TB incidence at the expense of not including older data that could help calibrate the forecast analysis. Third, although the model incorporated crucial predictors of TB, the lack of access to complete data meant that we did not have information on TPT coverage. Consequently, we used adherence rates as a *proxy* to assess the effectiveness of TB prevention in Brazil. This approach, while practical, may not fully capture the nuances of TPT coverage and its direct impact on reducing TB incidence. Finally, our study used TB incidence estimates calculated using SINAN-TB notification data, as recommended by the BMoH,[14] due to the monthly granularity it offers, up to December 2023, compared to WHO estimates, which are only available yearly up to 2022. However, while this estimation method allowed for the level of detailed temporal analysis required for our study, it also introduces limitations to our findings, as these calculations may not fully represent true TB incidence due to underdiagnosis and reporting biases.

In conclusion, our forecasting model provides robust insights into key predictors and the potential effectiveness of targeted interventions in improving TB control in Brazil. Our results demonstrated how enhancements in rates of specific high-impact TB management indicators, including increasing coverage and adherence to TPT, DOT, contact investigation, and PHC access, reduced future projections of TB incidence. While enhancements in policies aimed at decreasing TB cases among key vulnerable populations, encompassing those with HIV, incarceration, DM and retreatment cases, as well as a combination of both scenarios, demonstrated even greater decreases in projected TB incidence. This comprehensive methodological approach allowed us to demonstrate how through evidence-based decision-making Brazil can develop targeted public health strategies and control strategies to effectively reduce TB incidence rates by 2030, significantly assisting in reaching WHO elimination goals.

Contributors

Conceptualization, K.V-S., B.B-D., M.M.R, M.A-P. and B.B.A.; Data verification and curation, K.VS-., B.B-D., M.M.R, A.T.L.Q., M.A-P., and B.B.A.; Investigation, K.V-S., B.B-D, M.M.R., L.M., J.C., A.L.K., V.C.R., T.R.S., M.A-P., B.B.A., and B.B.A.; Formal analysis, KV-S., M.A-P., and B.B.A.; Funding acquisition, J.C., A.L.K., V.C.R., T.R.S., M.C.S., M.M.R., and B.B.A.; Methodology, KV-S, B.B-D., M.M.R., M.A-P., and B.B.A.; Project administration, T.R.S., M.A-P. and B.B.A.; Resources, K.V-S., B.B.-D., T.R.S., M.A-P. and B.B.A.; Software, KV-S, B.B-D., M.A-P., and B.B.A.; Supervision, M.A-P. and B.B.A.; Writing—original draft, K.V-S., B.B-D., M.A-P., and B.B.A.; Writing—review and editing, all authors.

Data sharing statement

The data that support the findings of this study will be available upon reasonable request to the corresponding author of the study.

Declaration of interests

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

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Disclaimer: This summary is available in Portuguese in the Supplementary Material.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2024.100963.

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