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DEVELOPMENT AND VALIDATION OF A TU- BERCULOSIS CASE PRE- DICTION MODEL IN THE STATE OF GOIÁS (2025- 2026) WITH A FOCUS ON COMPUTATIONAL PATHOLOGY

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Abstract: Introduction: Globally, tuberculosis (TB) is a public health issue. In Goiás, in 2023, there was a 9.42% increase in TB cases compared to 2022. The approach of computational pathology is an essential tool for analyzing data that can contribute to controlling the TB epidemic. Objective: Develop and validate a model statistical capable of to predict the number of TB notifications for 2025 and 2026. Methods: A computational algorithm was developed to construct a time series model for predicting notifications. This model provided better estimates of AIC, BIC, MSE, and RMSE compared to an self-adjusting model from an R Studio software library. The model developed in this study was applied to TB notification data in Goiás from 2001 to 2023. Results: A gradual increase in TB notifications in Goiás was estimated for 2025 and 2026, with peaks observed in January, March, September, and October. Additionally, a decrease in TB notifications was noted in February, July, and December for 2025, and in February, June, and December for 2026. Conclusion: These findings can significantly contribute to public health planning and decision-making aimed at controlling TB in the region.

Keywords: Tuberculosis, Computational Pathology, Prediction, Goiás, Time Series, Public Health.

INTRODUCTION

Tuberculosis (TB) remains the leading cause of mortality from infectious diseases worldwide¹. According to the Pan American Health Organization (PAHO), in 2022, TB surpassed COVID-19 and regained the title of the leading cause of deaths from infectious diseases¹. It is estimated that about 25% of the world's population is infected with *Mycobacterium tuberculosis*, of which 5% to 10% develop TB over the course of their lives².

Prediction studies related to TB provide valuable insights for health systems, such as identifying epidemiological trends to anticipate outbreaks and prepare appropriate responses^{3,4}. Furthermore, they enable the planning and allocation of financial and human resources for the prevention, treatment, and control of the disease, contributing to continuous monitoring and the development of more effective health policies⁵⁻⁸. These studies also provide support for adjusting existing strategies, such as the TB screening program and BCG vaccination, helping to achieve global goals for the eradication of the disease^{9,10}.

The End TB Strategy, launched by the World Health Organization (WHO) and the United Nations Organization, set the goal of "Ending the global TB epidemic" by 2035, with ambitious targets such as a 95% reduction in TB mortality compared to 2015¹¹. However, in 2022, Brazil was ranked among the 30 countries with the highest burden of TB in the world, with an incidence of 36.3 cases and a mortality rate of 2.3 deaths per 100,000 inhabitants¹².

Brazil, with its vast territory representing 50% of South America, has five regions (North, Northeast, Southeast, South, and Central-West) with distinct climatic, socioeconomic, and political characteristics¹³. Although all regions are served by the Brazilian Unified Health System (SUS), there are organizational disparities in the services provided¹⁴. In this regard, understanding the TB trend in each region is essential for directing public health actions. As far as we know, there are no predictive models that analyze the epidemiological trend of TB for the state of Goiás, highlighting a significant gap.

Technological advances have driven innovation in the healthcare field, with a focus on computational pathology, which uses statistical modeling methods and deep learning to predict disease cases, develop diagnostic models, and identify new biomarkers¹⁵. Among the strate-

gies used, time series models stand out, such as the Seasonal Autoregressive Integrated Moving Average (SARIMA) model, which is widely applied for predicting infectious diseases, including dengue and COVID-19^{16, 17}. These models have the potential to be applied to public health data provided by the SUS, allowing for more precise and targeted analyses.

Thus, the objective of this study was to predict the number of TB notifications in Goiás for the period of 2025 to 2026, using SARI-MA. This analysis aims to provide support for the formulation of regional strategies and improve the planning of public health actions in the state.

METHODS

ETHICAL ASPECTS

The data used in this study were obtained from a publicly available and unrestricted database, as provided by the Information System for Notifiable Diseases (SINAN) through Tabnet / DataSUS¹⁸. According to Resolution 510/2016 of the National Health Council, studies that use exclusively publicly available and unrestricted data are exempt from approval by the Research Ethics Committee¹⁹. In addition, it was ensured that no individualized or sensitive information was disclosed.

STUDY DESIGN AND CONTEXT

It is an observational study with a time series approach and followed the STROBE guidelines²⁰. The number of TB notifications in the state of Goiás was used, covering the period from 2001 to 2023. The data were extracted from SINAN through the Tabnet/DataSUS platform (<https://datasus.saude.gov.br/aceso-a-informacao/casos-de-tuberculose-desde-2001-sinan/>), which consolidates mandatory notifications made after clinical or laboratory confirmation, as established by the system itself¹.

Goiás was chosen as the study area due to the availability of data and the epidemiological relevance of TB in the region. In SINAN, the data were organized in annual spreadsheets, and after downloading, they were compiled into a single spreadsheet, where checks were applied to detect inconsistencies or missing values. The consolidated data were then divided into: Training group (data from 2001 to 2022), used for predictive modeling, and Test group (data from 2023), used for model validation. The methodology employed is summarized in the flowchart presented in Figure 1 below.

STATISTICAL ANALYSIS

The data were organized into monthly and annual time series for statistical analysis. Preliminary assessments were carried out to verify the characteristics of the time series, using the following hypothesis tests: Dickey-Fuller test (stationarity), Mann-Kendall test (trend), Kruskal-Wallis test (seasonality) and Box-Pierce test (autocorrelation of residuals).

Based on the results of these tests, the data were modeled using SARIMA. This model is represented by the computational equation SARIMA(p, d, q)(P, D, Q), where: i) p is the number of autoregressive parameters; ii) d is the number of differencings required for the series to become stationary; iii) q is the number of moving average parameters; iv) P is the order of the seasonal autoregressive term; v) D is the number of seasonal differencings; and vi) Q is the order of the seasonal moving average term.

The model was constructed and adjusted using data from the Treino group (2001–2022), using simulations to identify the optimal parameter configuration. These models were later validated with data from the Test group (2023). The methodology used is in accordance with the Anjos and Assunção protocol²¹.

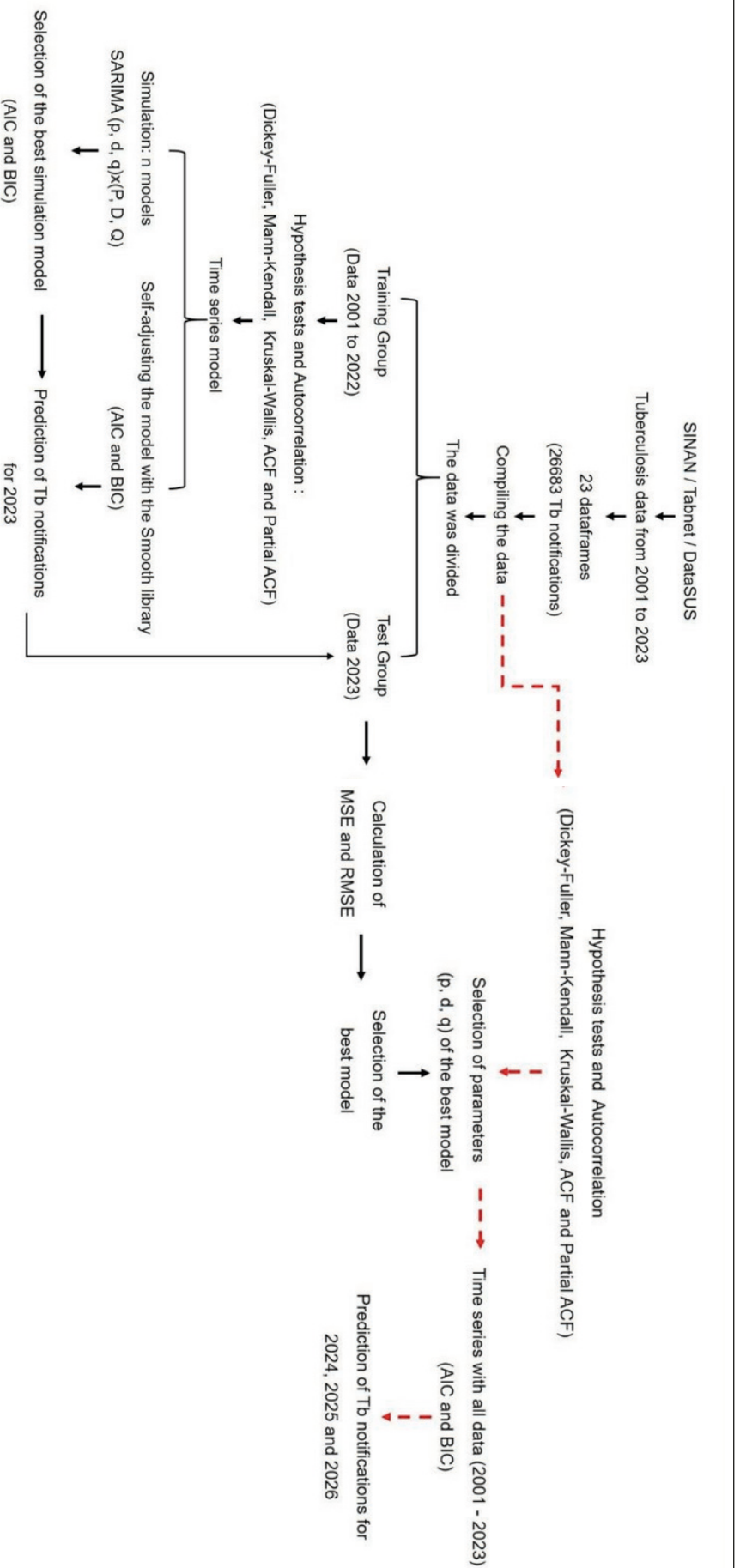


Figure 1. Flowchart representing the methodology used in this study. SARIMA: Seasonal Auto-Regressive Integrated Moving Average Model; p: number of autoregressive parameters; d: number of differences for the series to become stationary; q: number of moving average parameters; P: order of the seasonal autoregressive term; D: number of seasonal differences; Q: order of the seasonal moving average term. ACF: Autocorrelation Function; AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion; MSE: Mean Squared Error; RMSE: Root Mean Squared Error.

DEFINITION AND DIAGNOSIS OF THE BEST MODEL

The SARIMA model parameters were estimated using the maximum likelihood method. The selection of the best models was based on the analysis of the autocorrelation (FAC) and partial autocorrelation (FACP) functions of the residues, in addition to the application of Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC). These criteria penalize model complexity by considering the number of fitted parameters and sample size, providing a balanced approach to identifying the most appropriate model.

Subsequently, the model's self-adjustment was used through the *Smooth* library of the R Studio software. The models with the best parameters AIC, BIC, Mean Square Error (MSE) and Root Mean Square Error (RMSE) were identified by simulation and by library self-adjustment, being used in predicting TB notifications for the year 2023.

The results of the predictions were compared with the real data of the Test group (2023) to calculate the MSE and the RMSE. The model generated by simulation was selected as the best model based on these error indicators.

With the final model selected, hypothesis tests were applied to the complete data set (2001 - 2023) to confirm the observed patterns of stationarity, seasonality and trend previously identified.

TB NOTIFICATION PREDICTIONS FOR 2024 - 2026

The prediction of future values was performed using the forecasting library, which is the most frequently used in this type of study. This library implicitly applies methods based on differential equations, random shocks and reversal of differentiation, which contributes to the reliability of projections. To construct

the time series model, the complete data set (2001-2023) was considered, using the parameters defined in the previous step (p,d,q).

Although 2024 is the current year, the prediction for this period was necessary due to the unavailability of real data until the analysis. This initial prediction allowed the extension of the model for the following years, 2025 and 2026.

The prediction estimates were generated based on statistical inference at a point and interval, using a 95% confidence interval, which ensures greater robustness to the projections. All analyses were performed in Microsoft Excel 2020 spreadsheets, with support of R software, version 4.3.2, for statistical processing and modeling²².

RESULTS

In the SINAN/ Tabnet/ DataSUS database, 23 dataframes were identified containing a total of 26683 TB notifications in the state of Goiás, from 2001 to 2023 (Figure 1). All these notifications were included in the study and the distribution of the monthly and annual frequency are shown in the Supplementary Figure 1.

The hypothesis tests applied to the Training group (2001 - 2022) indicated that the series was not stationary (Dickey-Fuller test: p-value = 0.167), demonstrating the presence of trend in the time series (Mann-Kendall test: p-value = 0.011), and confirming the presence of seasonality (Kruskal-Wallis test: p-value = 0.003). These results are represented in Supplementary Figure 2.

Figure 2 shows the distribution of reported of TB notifications in the state of Goiás, from 2001 to 2023. The analysis revealed a monthly fluctuation in notifications over the years, with peaks concentrated between different months and reductions in February, July, November and December in some years, showing a seasonal pattern.

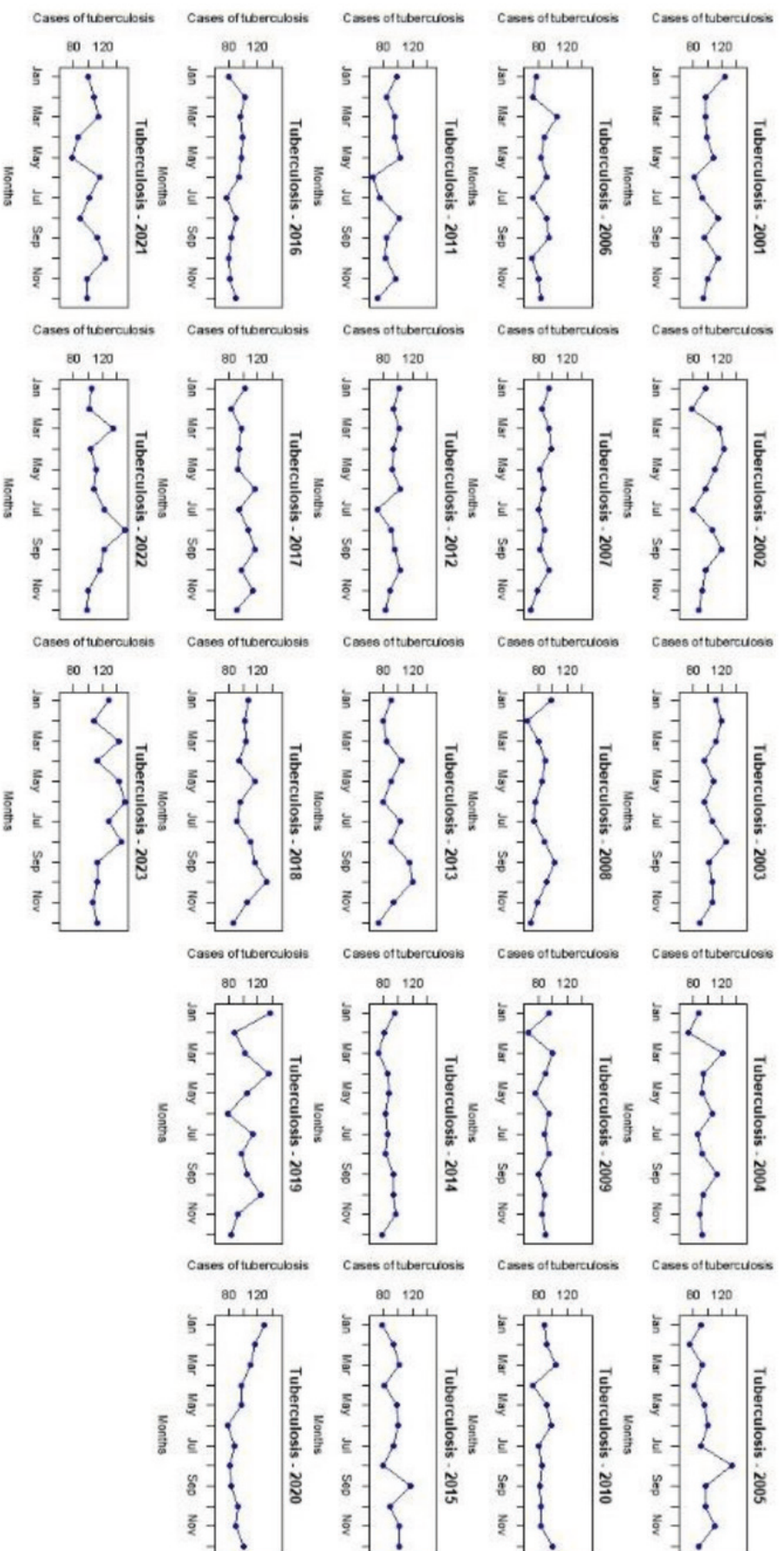


Figure 2. Graphic representing the profile of TB notifications in Goiás in the period 2001 - 2023

There was no clear trend of increase or decrease in the number of TB notifications over the years, with the exception of 2020, when there was a general reduction in TB notifications. In 2023, there was a greater variation in the number of TB notifications compared to previous years, accompanied by an overall increase in reported cases. Additionally, the years of 2013, 2015, 2018, early 2019, 2021 and 2022 showed more accentuated peaks in specific months, suggesting the existence of contextual factors that may have contributed to these increases.

The simulation of SARIMA models generated 44 different models, of which the best model was identified with the parameters $(p, d, q) = (3, 1, 1)$; $(P, D, Q) = (3, 1, 1)$. The values of $AIC = 1997.80$ and $BIC = 2029.53$ indicate a better fit compared to other models detailed in the Supplementary Table 1.

The comparison between the models selected by simulation and the model generated by self-adjustment of the *Smooth* library showed that the first presented better parameters. In detail, the simulation-generated model presented $MSE = 409.25$; $RMSE = 20.23$; $AIC: 1997.80$; $BIC: 2029.53$ (Table 1); The model generated by self-adjustment of the *Smooth* library presented $MSE: 1292,50$; $RMSE: 35,95$; $AIC: 2301,49$ and $BIC: 2330,10$ (Table 1); In addition, the p-value of the Box-Pierce test for both models indicated absence of residual correlation (simulation: 0.85; auto-adjustment: 0.20), confirming the adequacy of the model generated by simulation (Table 1 and Figure Supplementary 2).

The selected model was applied to the complete data set (2001 - 2023), confirming the previously observed patterns: stationarity (p-value = 0.18); trend (p-value = 0.00); seasonality (p-value = 0.01); and autocorrelation of residuals (p-value = 0.83); The values of $AIC = 2019.02$ and $BIC = 2141.17$, for the total period, maintain the good fit pattern.

The predictions made by the SARIMA model (Figure 3) point to a gradual increase in TB notifications in Goiás in the years 2025 and 2026 (Supplementary Table 2), with moderate annual variations and slight stability trend (blue line) in the number of notifications compared to previous years. The confidence interval is represented by the line in red (Figure 3A) is narrow, suggesting the certainty inherent to the prediction.

Figure 3B highlights the gradual and seasonal increase in TB notifications from 2024 to 2026 in the state of Goiás. The patterns include seasonal peaks in 2025 (red line), in January, March, September and October as well as seasonal reductions in February, July and December. In addition, it was possible to predict, in 2026 (blue line), a marked increase in TB notifications in the state of Goiás in January, March, September and October, and a sharp reduction in February, June and December for the year 2026.

DISCUSSION

Tuberculosis remains a global public health problem, requiring robust predictive studies to support disease control strategies^{3, 23}. This study used data from the SINAN/ Tabnet / DataSUS database to predict TB notifications in the state of Goiás for the years 2025 and 2026. The DataSUS platform, managed by the Ministry of Health, contains comprehensive information for epidemiological analyses and sanitary action planning²⁴. The Tabnet application, a data tabulation tool for epidemiological data, integrates indicators such as SINAN, which covers all notifiable diseases²⁵.

In 2023, 111467 TB notifications were recorded in Brazil, highlighting an alarming scenario of uncontrolled spread of this infectious disease²⁵. Specifically in Goiás, a state with approximately 7 million inhabitants spread across 246 municipalities, 1499 TB notifications were reported, representing an increase of

Models	AIC	BIC	MSE	RMSE	Box-pierce
SARIMA (0,0,3) x (0,0,3)	2301.49	2330.10	1292.50	35.95	<i>p-value</i> = 0.20
SARIMA (3,1,1) x (3,1,1)	1997.80	2029.53	409.25	20.23	<i>p-value</i> = 0.85

Table 1- Parameters generated by the SARIMA model and auto-adjustment

AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion; MSE: Mean Squared Error; RMSE: Root Mean Squared Error;

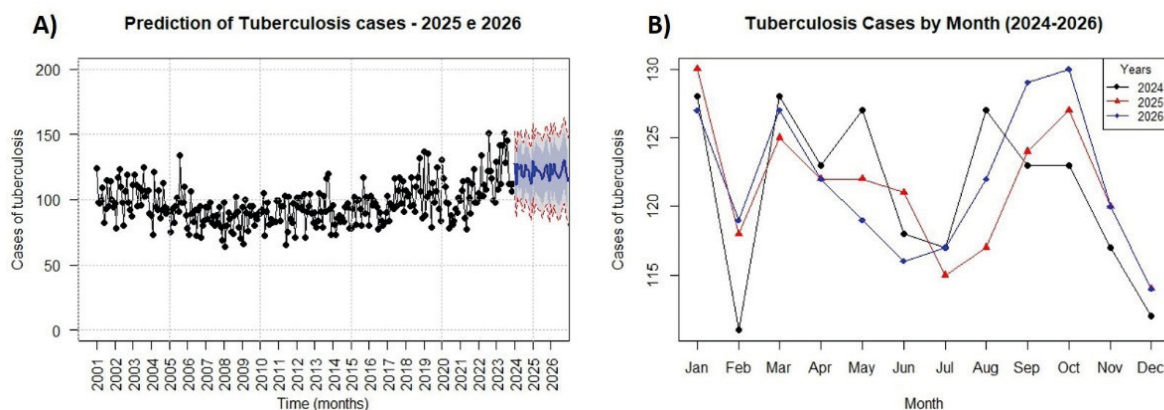


Figure 3. Prediction of TB notifications for the years 2025 and 2026

9.42% compared to the previous year^{25, 26}. This growth follows the national trend and reflects regional challenges such as demographic barriers, including hard-to-reach rural populations, large urban clusters, interstate migratory flow, the region's socioeconomic diversity, and limitations in access to healthcare services.

Predictive methods are indispensable tools for anticipating epidemiological trends, identifying vulnerable populations, diagnosing issues, and optimizing health policies. During the COVID-19 pandemic, for example, predictive models anticipated scenarios and forecasted epidemic peaks with highly specific details, such as the number of ventilation units that would be required in Italy²⁷. It is essential for health systems to utilize optimal prediction models to forecast the number of disease cases, thereby supporting preventive measures, interventions, and other control actions²⁸.

Our study revealed a gradual upward trend in TB notifications in Goiás in the coming years, with consistent seasonal variations. Peaks in notifications were observed in January,

March, and October, while reductions occurred in February, June, and December. It is important to consider that this pattern of TB in Goiás, as well as in other regions around the world, has been influenced by the long-term impact of COVID-19²⁹.

The pandemic overwhelmed healthcare systems and hindered TB management strategies, such as diagnosis and treatment. This scenario resulted in an atypical disease profile from 2020 to 2022, with a reduction in notifications, similar to what was observed in the study conducted in China²⁹. In the aforementioned study, an atypical pattern of decline in TB incidence was identified, which was temporary, followed by a gradual increase as healthcare services adapted and resumed activities. This phenomenon highlights the importance of considering external events, such as pandemics, when analyzing time series and forecasting the incidence of infectious diseases. Another study suggested that seasonal patterns can be explained by numerous environmental, behavioral, and operational factors³⁰.

It is likely that the high humidity characteristic of late summer (February) may temporarily alleviate respiratory symptoms, similar to viral respiratory infections, reducing the demand for healthcare services in February³¹. During this period, the traditional Carnival celebration also takes place, marked by a long national holiday. This period is often dedicated to leisure and recreation, which may result in a decrease in the demand for healthcare services. However, we believe that the end of summer and the return to activities after Carnival, in March, contribute to the increase in TB notifications. This increase may be related to co-infection with seasonal respiratory viruses that spread in the crowds typical of Carnival, the worsening of respiratory symptoms characteristic of the end of summer, and consequently, the growing demand for healthcare services^{32, 33}.

It is important to highlight the atypical behavior in the number of TB notifications in February in the years 2003 and 2016. An increase in notifications is observed in February, when compared to January and/or March. Interestingly, in 2003, Carnival took place in March instead of February, which may have influenced this change in the pattern observed in other years³⁴.

In addition, in 2014, a slightly different behavior in the number of TB notifications is noticeable, especially in February, but also in the following months. It is believed that the approval of the new global strategy for tackling TB, with the vision of a TB-free world by 2035, has strengthened the fight against this disease, contributing to the overall reduction in the number of TB notifications in Goiás³⁵. In 2016, the implementation of the Global Plan to End Tuberculosis 2016-2020 further intensified these strategies, including the adoption of specific regional plans for the six strategic regions of the WHO. This context may explain the overall reduction in the number of TB notifications in 2016³⁶.

In Brazil, the month of July, traditionally marked by school holidays, is a period of greater movement and crowding of people, which increases exposure to new contact networks and the risk of transmission of *Mycobacterium tuberculosis*. However, due to the focus on leisure activities during this month, it is common for the demand for healthcare services to be reduced. After this period, the incubation time of tuberculosis coincides with the increase in notifications, with significant peaks observed in September and October³⁷.

Finally, in Brazil, the month of December is characterized by year-end festivities, such as Christmas and New Year's, which typically reduce the demand for and operation of healthcare services. During this period, many people prioritize family matters and recreational activities, postponing the search for medical diagnoses. Additionally, travel and outings may contribute to the postponement of medical attention, resulting in an increase in demand in January, a month when a peak in TB notifications often occurs in Goiás²⁵.

TB is a significant challenge for public health in Goiás and globally. Therefore, it is essential to forecast the epidemiological situation of this disease so that the healthcare system can operate more efficiently³⁸. Our study forecasts an epidemiological trend for Goiás, and these findings highlight the importance of considering seasonal and behavioral factors in the planning of public health actions. For example, educational campaigns and intensified screening strategies could be targeted at specific periods, such as the end of summer and the beginning of spring.

Although our model demonstrated good predictive capacity, some limitations should be highlighted. The underreporting of TB, due to barriers in access to healthcare services and diagnostic challenges, may have impacted the estimates. As this variable could not be controlled, the prediction may also have been underestimated. Additionally, the

seasonality of TB notifications may vary in different geographic and temporal contexts, limiting the generalization of the results. Still, this study provides valuable contributions to strategic health planning, offering data for the efficient allocation of resources and targeted interventions. Future studies could explore complementary data, such as socioeconomic and climatic variables, to enhance predictive models and deepen the understanding of the determining factors of TB in Goiás.

CONCLUSION

A gradual increase in TB notifications in Goiás is projected for 2025 and 2026, with peaks in January, March, September, and October, and decreases in February, July, and December (2025) and February, June, and December (2026). These insights support public health planning for TB control in the region.

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AVAILABILITY OF DATA AND MATERIALS

All raw data are available on SINAN / Tabnet / DataSUS. The SARIMA model developed in this study was made available in the protocol "Algorithm with time series simulation versus auto-adjustment in R for predicting tuberculosis cases in Goiás."

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

AUTHORS CONTRIBUTION

The authors LRBA and LPA contributed equally to the preparation of this article. LRBA and LPA contributed to the conceptualization, methodology, investigation, and creation of the figures. LRBA: drafting the original manuscript and editing the figures. LPA: statistical analysis and review and editing of the manuscript. All authors agreed on the final version of the manuscript prior to submission.

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