



Incidence, mortality, and case fatality due to tuberculosis in Paraná: temporal trend analysis between 2018 and 2023

Incidência, mortalidade e letalidade por tuberculose no Paraná: análise de tendência temporal entre 2018 e 2023
Incidencia, mortalidad y letalidad por tuberculosis en Paraná: análisis de tendencia temporal entre 2018 y 2023

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ABSTRACT

Background and Objectives: Tuberculosis is a public health problem, and Brazil aims to reduce the incidence rate of this disease to fewer than 10 cases per 100,000 inhabitants. This study aimed to analyze the trends in tuberculosis incidence, mortality and case fatality in the state of Paraná between 2018 and 2023. **Methods:** A time series study was conducted using secondary data from Paraná, Brazil, obtained through the Notifiable Diseases Information System. The incidence and mortality rates per 100,000 inhabitants and the case fatality rates—both overall and stratified by sex and age—were evaluated, as well as risk factors associated with death as an outcome. Trends were analyzed using linear regression and Prais–Winsten models, and risk factors were analyzed using the chi-square or Fisher's exact test and relative risk. **Results:** Incidence, mortality, and overall case fatality rates for tuberculosis in Paraná remained stagnant. Stratified mortality, however, showed an upward trend among females ($\beta=0.046$; 95%CI=0.01, 0.09; $p=0.042$) and in the age group between 20 and 39 years ($\beta=0.072$; 95%CI=0.01, 0.14; $p=0.043$). Individuals experiencing homelessness (RR=4.25; 95%CI=3.46, 5.22; $p<0.001$), those who consumed alcohol (RR=2.32; 95%CI=2.00, 2.68; $p<0.001$), and those with comorbidities such as mental disorders (RR=2.02; 95%CI=1.48, 2.76; $p<0.001$), diabetes mellitus (RR=1.88; 95%CI=1.52, 2.31; $p<0.001$), and other diseases (RR=2.30; 95%CI=1.93, 2.74; $p<0.001$) had a higher risk of death. **Conclusions:** The findings reveal a discrepancy between tuberculosis trends in Paraná and the goals set by Brazil's National Plan to End Tuberculosis by 2030. **Keywords:** Tuberculosis. Epidemiology. Incidence. Mortality. Risk Factors.

RESUMO

Justificativa e Objetivos: A tuberculose é um problema de saúde pública, e o Brasil tem como meta reduzir o coeficiente de incidência desta doença para menos de 10 casos/100.000 habitantes. Neste estudo, objetivou-se analisar a tendência da incidência, mortalidade e letalidade por tuberculose no estado do Paraná entre os anos de 2018 e 2023. **Métodos:** Estudo de análise de tendência temporal, realizado com dados secundários do Paraná, Brasil, obtidos através do Sistema de Informação de Agravos de Notificação. Avaliou-se a incidência e mortalidade dos casos a cada 100.000 habitantes e as taxas de letalidade gerais e estratificadas por sexo e faixa etária, além dos fatores de risco associados ao desfecho óbito. As tendências foram analisadas com modelos de regressão linear e Prais–Winsten, e os fatores de risco com o teste qui-quadrado ou exato de Fisher e risco relativo. **Resultados:** Obeve-se estagnação da incidência, mortalidade e letalidade geral por tuberculose no Paraná. A mortalidade estratificada, no entanto, apresentou uma tendência de crescimento entre o sexo feminino ($\beta=0.046$; IC95%=0,01; 0,09; $p=0.042$) e faixa etária entre 20 a 39 anos ($\beta=0.072$; IC95%=0,01; 0,14; $p=0.043$). Indivíduos em situação de rua (RR=4,25; IC95%=3,46; 5,22; $p<0.001$), que utilizavam álcool (RR=2,32; IC95%=2,00, 2,68; $p<0.001$) e apresentavam como multimorbidades transtornos mentais (RR=2,02; IC95%=1,48, 2,76; $p<0.001$), diabetes mellitus (RR=1,88; IC95%=1,52, 2,31; $p<0.001$), e outras doenças (RR=2,30; IC95%=1,93, 2,74; $p<0.001$) tiveram maior risco para óbito. **Conclusão:** Os achados apontam uma discrepância entre as tendências da tuberculose no Paraná e as metas estabelecidas pelo Plano Nacional pelo Fim da Tuberculose até 2030. **Descritores:** Tuberculose. Epidemiologia. Incidência. Mortalidade. Fatores de Risco.

RESUMEN

Justificación y Objetivos: La tuberculosis es un problema de salud pública, y Brasil tiene como meta reducir la tasa de incidencia de esta enfermedad a menos de 10 casos por cada 100.000 habitantes. En este estudio, se tuvo como objetivo analizar las tendencias de la incidencia, mortalidad y letalidad por tuberculosis en el estado de Paraná entre los años 2018 y 2023. **Métodos:** Estudio de análisis de tendencia temporal, realizado con datos secundarios de Paraná, Brasil, obtenidos a través del Sistema de Información de Enfermedades de Notificación Obligatoria. Se evaluaron las tasas de incidencia y mortalidad por 100.000 habitantes y las tasas de letalidad, tanto generales como estratificadas por sexo y edad, así como los factores de riesgo asociados al desenlace muerte. Las tendencias se analizaron mediante modelos de regresión lineal y Prais–Winsten, y los factores de riesgo mediante la prueba de chi-cuadrado o exacta de Fisher y el riesgo relativo. **Resultados:** La incidencia, mortalidad y letalidad general por tuberculosis en Paraná se mantuvieron estables. Sin embargo, la mortalidad estratificada mostró una tendencia creciente en mujeres ($\beta=0.046$; IC95%=0,01; 0,09; $p=0.042$) y en personas de 20 a 39 años ($\beta=0.072$; IC95%=0,01; 0,14; $p=0.043$). Las personas en situación de calle (RR=4,25; IC95%=3,46; 5,22; $p<0.001$), consumidoras de alcohol (RR=2,32; IC95%=2,00; 2,68; $p<0.001$) y con comorbilidades como trastornos mentales (RR=2,02; IC95%=1,48, 2,76; $p<0.001$), diabetes mellitus (RR=1,88; IC95%=1,52, 2,31; $p<0.001$), y otras enfermedades (RR=2,30; IC95%=1,93, 2,74; $p<0.001$) presentaron mayor riesgo de muerte. **Conclusión:** Los hallazgos muestran una discrepancia entre las tendencias de la tuberculosis en Paraná y las metas del Plan Nacional para Poner Fin a la Tuberculosis para 2030. **Palabras Clave:** Tuberculosis. Epidemiología. Incidencia. Mortalidad. Factores de Riesgo.

INTRODUCTION

Classified as an infectious disease, tuberculosis (TB) is a preventable and curable condition, with efficient diagnostic and treatment methods available.¹ However, in 2022, TB was identified as the second leading cause of death attributed to a single infectious agent, surpassed only by Covid-19, causing an estimated 1.3 million deaths worldwide.² In Brazil, approximately 80,000 people fall ill with TB annually, and in 2022, more than 5,000 people died from the disease.¹

Tuberculosis is classified as a public health issue in Brazil, as the country ranks among the top 20 nations with the highest estimated incidence of the infection globally.³ In 2017, the National Plan to End Tuberculosis as a Public Health Problem (PNFTPSP) was published with the aim of reducing the TB incidence rate to fewer than 10 cases per 100,000 inhabitants and the mortality rate to 1 death per 100,000 inhabitants by 2035.⁴

In 2023, the Ministry of Health announced its intention to achieve these goals by 2030, reinforcing strategies for prevention, integrated care, and intensified research aimed at controlling the disease.⁵ However, the risk of developing TB increased, rising from 34.3 cases and 2.40 deaths per 100,000 inhabitants in 2021 to 38 cases and 2.72 deaths per 100,000 inhabitants in 2022.¹

In the state of Paraná, TB data have remained below national figures when analyzing the period from 2011 to 2019. However, there was an increase in the TB incidence rate from 18.3 cases per 100,000 inhabitants in 2017 to 20.4 cases per 100,000 inhabitants in 2022, possibly due to the Covid-19 pandemic, a pattern also observed in other Brazilian states.^{6,7} Although TB rates in Paraná remained relatively stable over the last ten years, mortality from the disease increased between 2017 and 2021, contrary to the national trend (stability).⁶

Furthermore, TB cases may be distributed differently across factors such as sex and age group. In 2023, the male sex showed a higher TB incidence rate compared to the female sex, excluding the 0–14 age group.¹ Regarding age groups, individuals aged 20 to 34 accounted for the highest rates of new cases between 2021 and 2023.¹ These variables can support the assessment of equity in access to health services, serving as a parameter for monitoring the effectiveness of public policies implemented in the country.⁷

Moreover, various factors may be associated with mortality in TB cases, such as lifestyle characteristics (alcohol and tobacco use); comorbidities or other diseases (HIV/Aids and diabetes mellitus); vulnerable populations (individuals deprived of liberty and healthcare workers) and clinical characteristics (drug resistance and treatment non-adherence).⁸ Recognizing these factors ensures adequate quality of TB treatment,

thereby reducing deaths caused by the infection.⁸

In the state of Paraná, characteristics such as male sex, the 40–59 age group, and alcohol consumption have been identified as common features among TB cases.⁶ Despite this, few studies have investigated temporal trends in the disease's incidence, mortality, and case fatality rates stratified by these features, particularly in analyses focused on regional contexts.⁷ This gap is significant given evidence indicating an increase in TB mortality in Paraná between 2011 and 2019, yet lacking stratified analyses capable of identifying potential inequalities among population groups.⁶

Thus, investigating the disease's profile over time and its epidemiological trends is a fundamental pillar for evaluating the performance of local TB control strategies.⁹ In light of this, the present article aims to analyze trends in TB incidence, mortality, and case fatality rates in the state of Paraná between 2018 and 2023.

METHODS

This study is a time-trend analysis in which publicly accessible secondary data on TB cases in the state of Paraná from 2018 to 2023, extracted from the Notifiable Diseases Information System (SINAN), were used.

Data were collected on November 4, 2024, via the TabNet platform, using data provided by the Brazilian Institute of Geography and Statistics (IBGE).^{10,11} Confirmed TB cases reported in Paraná from 2018 to 2023 were included to capture two-year periods before, during, and after the peak of the Covid-19 pandemic. Cases and variable categories recorded as “unknown” or left blank were excluded.

Data analysis was conducted in two stages: a time-trend analysis and an analysis of factors associated with TB clinical outcomes.

Time-Trend Analysis

During this stage, univariate analyses were performed using simple linear regression to examine TB incidence, case fatality, and mortality rates between 2018 and 2023 stratified by sex (female and male) and age group (0–19, 20–39, 40–59, and 60 years or older).

To calculate the overall TB incidence rate, the number of new cases reported in DATASUS was divided by the population estimated by the IBGE for the study years, and the result was multiplied by 100,000 inhabitants. The calculation was performed in accordance with guidelines from the Brazilian Ministry of Health. In addition to the category designated as “new case”, records classified as “unknown” and “post-mortem” were also considered new cases, due to the inclusion of individuals who had never used anti-tuberculosis medication or had used it for less than 30 days.¹²

To calculate overall TB mortality, the number of

deaths caused by TB was divided by the population estimated by the IBGE for the study years, and the result was multiplied by 100,000 inhabitants. Overall TB case fatality was calculated based on the number of deaths caused by TB and the number of confirmed TB cases, multiplied by 100.

Stratification of TB incidence, mortality, and case fatality by sex and age group was performed by calculating these measures separately for each population stratum. To calculate incidence stratified by sex and age group, the number of new cases in each group was divided by the corresponding estimated population for that stratum (from IBGE data) and multiplied by 100,000 inhabitants.

Similarly, mortality stratified by sex and age group was calculated using the number of TB deaths in each stratum divided by the corresponding population estimated from IBGE data. Case fatality was calculated as the ratio of TB deaths to the total number of confirmed cases within each group, multiplied by 100. Other variables were not included in the univariate models because annual population estimates required to calculate the respective measures were unavailable.

Initially, the data were tabulated in a Microsoft Office Excel 2021[®] spreadsheet and subsequently analyzed using R software (version 4.4.1) with the *Epitools*, *dplyr*, *car*, *lmtest*, and *ggplot2* packages.¹³ Linear regression models were constructed for the overall measures and for each stratification; the independent variable was the period from 2018 to 2023, and the dependent variables were the measures of TB incidence, mortality, and case fatality (both overall and stratified), using a 5% significance level.

For each model, the assumptions of residual normality (Shapiro–Wilk test), residual homoscedasticity (Breusch–Pagan test), and independence of error terms (Durbin–Watson test) were evaluated at a 5% significance level. No violation of the homoscedasticity assumption was observed for any of the models. Prais–Winsten regression models were constructed for models that violated the assumptions of residual normality and independence of error terms.

Temporal trends were classified as increasing when models showed a positive β coefficient and a p -value <0.05 ; decreasing when they showed a negative β coefficient and a p -value <0.05 ; and stationary when the p -value was >0.05 . The explanatory power of the models was evaluated using the coefficient of determination (R^2), which represents the proportion of the dependent variable's variability explained by the model.

Analysis of factors associated with TB outcomes

During this stage, all confirmed TB cases reported in

the state of Paraná between 2018 and 2023 were included, while cases and variable categories classified as “unknown” or reported as blank were excluded.

The independent variables assigned were: sociodemographic factors (sex and age group), vulnerable populations (incarcerated individuals, the homeless population, and healthcare professionals), lifestyle habits (tobacco, alcohol, and illicit drug use), multimorbidities and diseases (diabetes mellitus, mental disorders, HIV/Aids), directly observed treatment, and diagnostic or monitoring tests (smear microscopy, rapid testing, drug susceptibility testing, and culture). The outcome variable, categorized as cure or death due to TB, was used as the dependent variable.

These data were tabulated in a Microsoft Office Excel 2021[®] spreadsheet and analyzed using R software (version 4.4.1) with the *Epitools* package.¹⁴ To evaluate factors associated with TB patient outcomes, the Chi-square test or Fisher's exact test was applied, as appropriate, using a 5% significance level. Relative Risk (RR) was estimated from 2×2 contingency tables, calculated as the ratio of the outcome risk in the exposed group to the risk in the unexposed group, with death due to TB considered the event of interest.

In accordance with Resolution No. 510 of 2016 from the National Health Council, this study did not require submission to a research ethics committee, as it utilized public data accessed via TabNet and the IBGE.^{10,11}

RESULTS

Paraná recorded a total of 13,455 new TB cases between 2018 and 2023. There were 9,437 (70.14%) new TB cases reported among males. Regarding age groups, the highest incidence of the disease was observed in the 20–39 age group, with 5,623 cases (41.79%), followed by the 40–59 age group, with 4,644 cases (34.52%).

The highest incidence rates were observed in 2018 (20.44 cases/100,000 inhabitants) and 2023 (20.36 cases/100,000 inhabitants). Overall TB incidence showed a decrease over the years analyzed, although this was not statistically significant ($\beta = -0.112$; 95% CI = 1.02; 0.79; p -value = 0.748; $r^2 = 0.0287$) (Table 1) (Figure 1).

A total of 749 individuals died from TB during the analyzed period. Of these, 581 (77.57%) were male and 168 (22.43%) were female. Regarding age groups, 312 TB deaths (41.66%) occurred among individuals aged 40–59, 265 deaths (35.38%) in the group aged 60 or older, and 154 deaths (20.56%) in those aged 20–39 years.

Table 1. Temporal trend of overall incidence, mortality, and case fatality rates by sex and age group for tuberculosis cases in Paraná between 2018 and 2023, Brazil.

Variables	β coefficient*	95% CI*	p-value*	R ² *
Overall incidence	-0.112	(-1.02; 0.79)	0.748	0.0287†
Incidence by sex				
Male	-0.168	(-1.41; 1.08)	0.727	0.0338†
Female	-0.082	(-0.71; 0.54)	0.734	0.0322†
Incidence by age group				
0 to 19 years	-0.052	(-0.69; 0.58)	0.832	0.0127†
20 to 39 years	-0.287	(-1.40; 0.83)	0.515	0.1127†
40 to 59 years	-0.175	(-1.43; 1.08)	0.720	0.1838‡
60 years or older	-0.091	(-1.25; 1.07)	0.839	0.8353‡
Overall mortality	0.042	(-0.02; 0.11)	0.149	0.4426†
Mortality by Sex				
Male	0.069	(-0.06; 0.20)	0.214	0.3522†
Female	0.046	(0.01; 0.09)	0.042	0.6861†
Mortality by age group				
0 to 19 years	0.015	(-0.01; 0.04)	0.189	0.3846†
20 to 39 years	0.072	(0.01; 0.14)	0.043	0.6809†
40 to 59 years	-0.004	(-0.20; 0.19)	0.962	0.0006†
60 years or older	0.131	(-0.01; 0.27)	0.059	0.6325†
Overall case fatality rate	0.114	(-0.11; 0.33)	0.226	0.3383†
Case fatality rate by sex				
Male	0.094	(-0.11; 0.30)	0.278	0.2818†
Female	0.084	(-0.02; 0.19)	0.097	0.5385†
Case fatality rate by age group				
0 to 19 years	0.014	(-0.01; 0.04)	0.252	0.3094†
20 to 39 years	0.072	(-0.03; 0.17)	0.118	0.4967†
40 to 59 years	-0.019	(-0.22; 0.18)	0.811	0.0160†
60 years or older	0.116	(0.06; 0.17)	0.004	0.8986†

Abbreviation: * β coefficient: linear regression coefficient; 95% CI: 95% confidence interval; p-value: significance level; R²: model coefficient of determination. †Simple Linear Regression Model. ‡Prais-Winsten Regression Model.

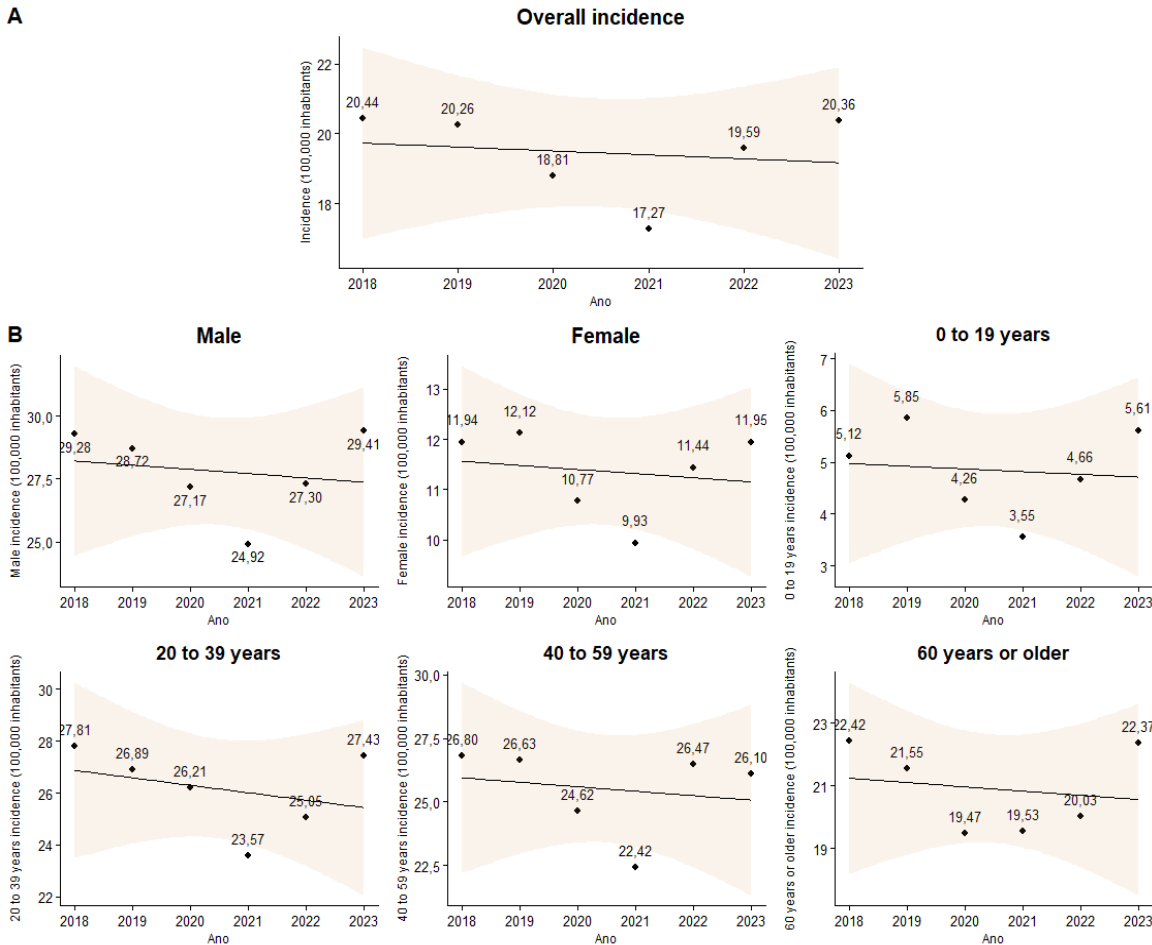


Figure 1. Temporal trend of overall, sex-specific and age-specific tuberculosis incidence per 100,000 inhabitants in Paraná, Brazil, from 2018 to 2023.

Abbreviation: (A) Overall TB incidence per 100,000 inhabitants. (B) TB incidence - by sex (male and female) and age group (0–19 years, 20–39 years, 40–59 years, and 60 years or older) - per 100,000 inhabitants. Overall incidence / Male / Female / 0–19 years / 20–39 years / 40–59 years / 60 years or older.

The highest rates of mortality from TB were in years 2022 (1.25 deaths/100,000 inhabitants) and 2023 (1.12 deaths/100,000 inhabitants). This pattern was also observed in 2023 among males (1.88 deaths/100,000 inhabitants) and females (0.63 deaths/100,000 inhabitants). That same year, the highest mortality rates were reported in the 20–39 age group (0.93 deaths/100,000 inhabitants) and the 60 years or older age group (3.00 deaths/100,000 inhabitants).

Overall TB mortality during the analyzed period showed a non-significant upward trend, rising from 0.93 deaths/100,000 inhabitants in 2018 to 1.12 deaths/100,000 inhabitants in 2023, according to the

univariate model performed ($\beta = 0.042$; CI = -0.02; 0.11; p-value = 0.149; $r^2 = 0.4426$). This upward trend in TB mortality was significant among females, showing an increase of 0.046 deaths per 100,000 inhabitants per year ($\beta = 0.046$; 95% CI = 0.01; 0.09; p-value = 0.042; $r^2 = 0.6861$).

Regarding age groups, the 20–39 age range showed a significant positive linear trend over the years, with an increase of 0.072 deaths per 100,000 inhabitants per year ($\beta = 0.072$; 95% CI = 0.01; 0.14; p-value = 0.043; $r^2 = 0.6809$) (Figure 2).

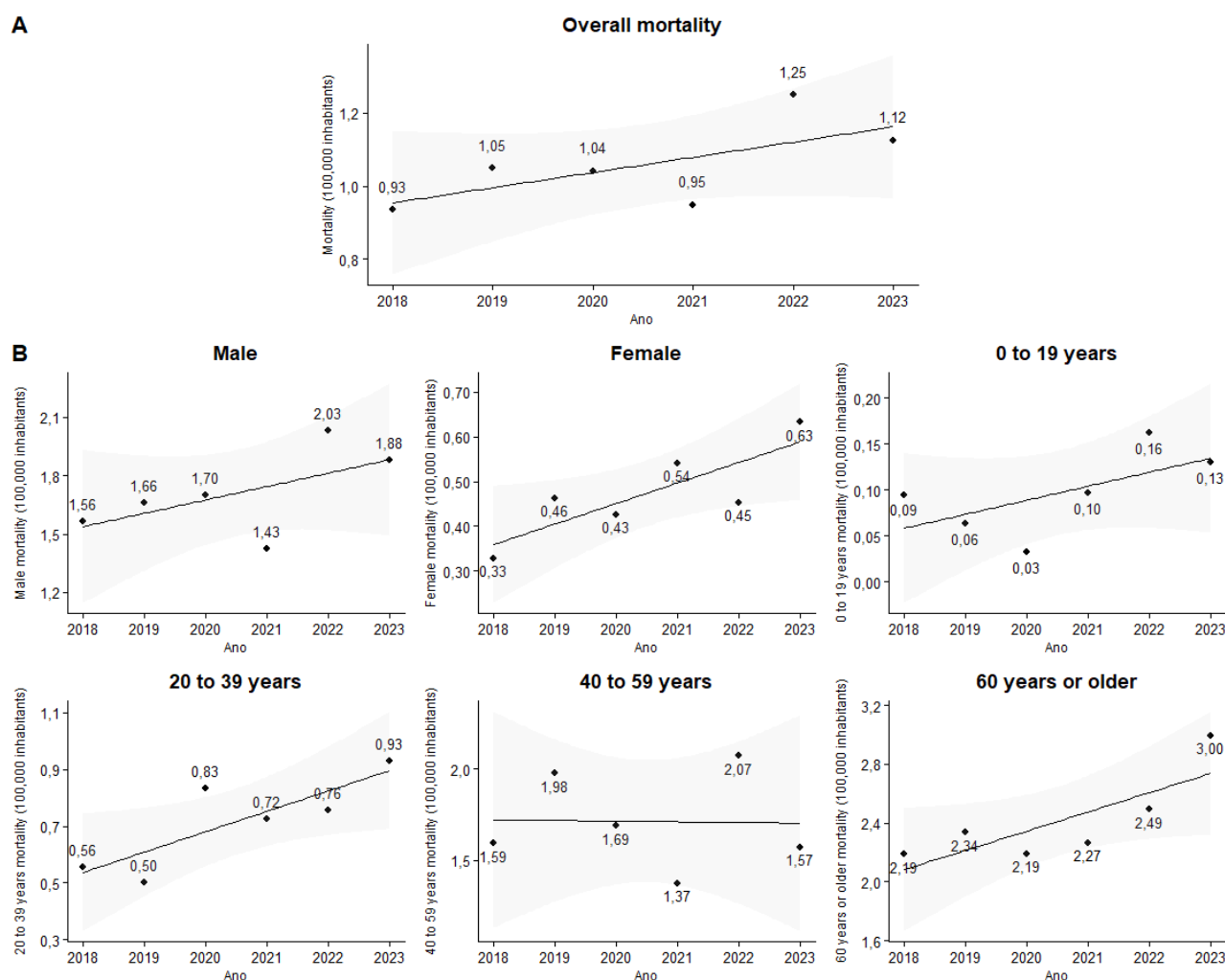


Figure 2. Temporal trend of overall, sex-specific, and age-specific tuberculosis mortality per 100,000 inhabitants in Paraná, Brazil, from 2018 to 2023.

Abbreviation: (A) Overall TB mortality per 100,000 inhabitants. (B) TB mortality - by sex (female and male) and age group (0–19 years, 20–39 years, 40–59 years, and 60 years or older) - per 100,000 inhabitants. Overall mortality / Male / Female / 0–19 years / 20–39 years / 40–59 years / 60 years or older.

The highest proportions of overall TB case fatality were observed in 2022 (5.02%), followed by 2020 (4.53%) and 2019 (4.49%). Among males, the highest ratios were observed in 2022 (4.07%), while among females they were observed in 2022 and 2023 (1.26%). Regarding age groups, the highest percentages were reported in 2022 for the 40–59 age group (2.25%); in 2023 for those aged 60 or older (1.99%); in 2020 for the 20–39 age group (1.13%); and in 2022 for the 0–19 age group (0.17%).

Among the variables analyzed regarding TB case fatality, only the age group of 60 years or older showed a significant upward trend (0.12%) between 2018 and 2023 ($\beta = 0.116$; 95% CI = 0.06–0.17; p-value = 0.004; $r^2 = 0.8986$) (Figure 3).

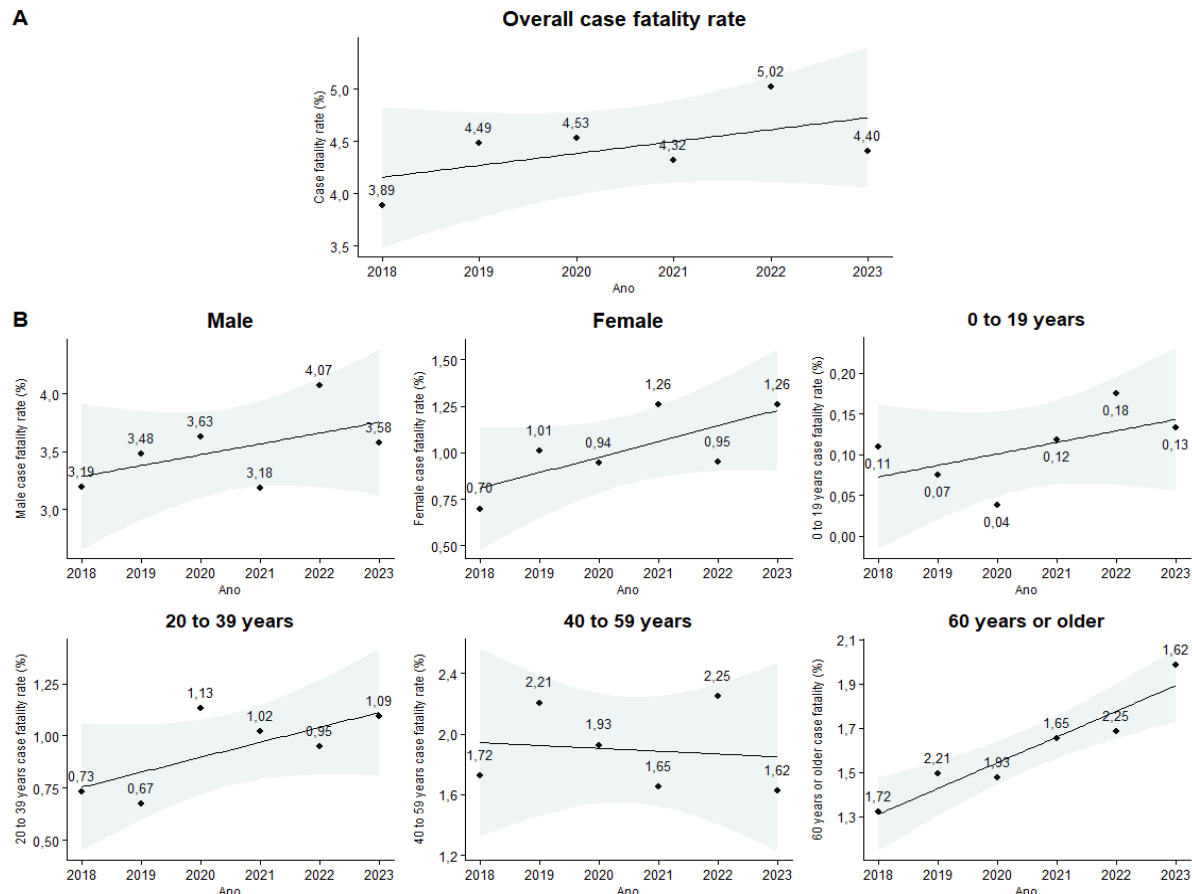


Figure 3. Temporal trend of overall, sex-specific, and age-specific TB case fatality in Paraná, Brazil (2018–2023). Abbreviation: (A) Overall TB case fatality. (B) TB case fatality by sex (female and male) and age group (0–19 years, 20–39 years, 40–59 years, and 60 years or older). Overall case fatality / Male / Female / 0–19 years / 20–39 years / 40–59 years / 60 years or older.

Among the outcomes observed in incident TB cases, 514 males (8.59%) died; 239 (15.92%) were aged 60 years or older, and 76 (28.79%) were experiencing homelessness. Regarding the form of TB, 61 cases (21.03%) were reported as pulmonary TB combined with an extrapulmonary form (Table 2).

Among incident TB cases resulting in death, 262 (12.38%) were individuals with alcohol use disorder, 43 (7.72%) were HIV-positive, 93 (12.47%) had diabetes,

36 (14.12%) had a mental disorder, and 156 (14.03%) had other diseases (Table 2).

Among sociodemographic factors, mortality was significantly associated with male sex (RR = 1.57; 95% CI = 1.32–1.88; $p < 0.001$) and all analyzed age groups ($p < 0.05$). Individuals aged 60 years or older had a 7.38-fold higher risk of death than those aged 0–19 years, whereas the 40–59 age group had a 5.02-fold higher risk ($p < 0.001$).

Table 2. Outcomes of incident tuberculosis cases according to sociodemographic variables, vulnerable populations, lifestyle habits, and multimorbidities/diseases in Paraná between 2018 and 2023, Brazil.

Variables	Death N (%)	Cure N (%)	RR* (95% CI)*	p-value*
Sex				
Female	150 (5.45)	2602 (94.55)	-	
Male	514 (8.59)	5472 (91.41)	1.57 (1.32; 1.88)	$p<0.001^\dagger$
Age				
0 to 19 years	13 (2.16)	590 (97.84)	-	
20 to 39 years	137 (3.79)	3476 (96.21)	1.76 (1.00; 3.08)	0.045 [†]
40 to 59 years	274 (10.83)	2256 (89.17)	5.02 (2.90; 8.70)	$p<0.001^\dagger$
60 years or older	239 (15.92)	1262 (84.08)	7.38 (4.26; 12.80)	$p<0.001^\dagger$
Persons Deprived of Liberty				
No	618 (6.78)	7182 (92.10)	-	
Yes	26 (3.10)	803 (96.90)	0.40 (0.27; 0.58)	$p<0.001^\dagger$
Experiencing Homelessness				
No	566 (6.78)	7785 (93.22)	-	
Yes	76 (28.79)	188 (71.21)	4.25 (3.46; 5.22)	$p<0.001^\dagger$
Healthcare Professional				
No	166 (2.08)	7810 (97.92)	-	
Yes	1 (0.16)	643 (99.84)	0.07 (0.01; 0.53)	$p<0.001^\dagger$
Form				
Pulmonary	540 (7.45)	6713 (92.55)	-	
Extrapulmonary	63 (5.27)	1132 (94.73)	0.71 (0.55; 0.91)	0.006 [†]
Pulmonary and Extrapulmonary	61 (21.03)	290 (78.97)	2.33 (1.83; 2.97)	$p<0.001^\dagger$

continue

Variables	Death N (%)	Cure N (%)	RR* (95% CI)*	p-value*
Alcohol use				
No	407 (5.35)	7206 (94.65)	-	
Yes	262 (12.38)	1854 (87.62)	2.32 (2.00; 2.68)	p<0.001†
Tobacco use				
No	373 (5.66)	6214 (94.34)		
Yes	291 (9.18)	2879 (90.82)	1.62 (1.40; 1.88)	p<0.001†
Illicit drug use				
No	519 (6.37)	7624 (93.63)	-	
Yes	138 (8.73)	1443 (91.27)	1.37 (1.14; 1.64)	p<0.001†
HIV				
Negative	514 (6.97)	6863 (93.03)	-	
Positive	43 (7.72)	514 (92.28)	1.10 (0.82; 1.49)	0.503‡
Antiretroviral				
No	80 (7.72)	956 (92.28)	-	
Yes	14 (3.26)	415 (96.74)	0.42 (0.24; 0.74)	0.001†
Aids				
No	41 (6.90)	490 (93.10)	-	
Yes	570 (6.99)	7333 (93.01)	0.93 (0.69; 1.27)	0.661†
Diabetes mellitus				
No	514 (6.64)	7225 (93.36)		
Yes	93 (12.47)	653 (87.53)	1.88 (1.52; 2.31)	p<0.001†
Mental Disorder				
No	573 (6.99)	7627 (93.01)	-	
Yes	36 (14.12)	219 (85.88)	2.02 (1.48; 2.76)	p<0.001†
Other Diseases				
No	403 (6.09)	6209 (93.91)	-	
Yes	156 (14.03)	956 (85.97)	2.30 (1.93; 2.74)	p<0.001†

Abbreviation: *RR: Relative Risk; 95% CI: 95% confidence interval; p-value: significance level. †Chi-square test ‡Fisher’s exact test.

Regarding vulnerable populations, individuals experiencing homelessness had a 4.25-fold higher risk of death compared to those not in such a situation (RR = 4.25; 95% CI = 3.46–5.22; p < 0.001). Concerning the form of the disease, individuals with both pulmonary and extrapulmonary TB had a 2.33-fold higher risk of death compared to those with pulmonary TB alone (RR = 2.33; 95% CI = 1.83–2.97; p < 0.001).

Regarding lifestyle habits, individuals who used alcohol had a 2.32-fold higher risk of death compared to non-users (RR = 2.32; 95% CI = 2.00–2.68; p < 0.001). Associations with illicit drug use and tobacco use were also statistically significant among individuals who died (p < 0.001).

Regarding multimorbidities and diseases, no statistically significant associations were found between death and HIV coinfection (p = 0.503) or Aids (p = 0.661). Treatment of these coinfections with antiretrovirals acted as a protective factor against death. Individuals undergoing treatment showed a 58% lower risk of death compared to those who did not adhere to treatment (RR = 0.42, 95% CI = 0.24–0.74, p < 0.001).

Other variables related to multimorbidities and diseases also showed statistically significant associations with death, specifically regarding diabetes mellitus (RR = 1.88, 95% CI = 1.52–2.31; p < 0.001), mental disorders (RR = 2.02, 95% CI = 1.48–2.76; p < 0.001), and other diseases (RR = 2.30, 95% CI = 1.93–2.74; p < 0.001) (Table 2).

DISCUSSION

The results obtained demonstrated a trend of stagnation in the incidence, mortality, and overall case

fatality rate for TB in the state of Paraná between 2018 and 2023, contrasting with the targets for reducing TB incidence and mortality rates advocated by the PNFTPSP.⁴

These findings corroborate those in the national literature.^{6,15} Over the last decade, between 2011 and 2022, the average TB incidence rate remained stable at 20 cases per 100,000 inhabitants.⁶ According to a study conducted across Brazil’s five regions, the annual percentage change (APC) in the TB incidence rate was 5.2%, though not statistically significant, reinforcing the stagnation of incident TB cases during the period evaluated (APC% = 5.2; 95% CI = –4.4, 15.7; p > 0.05).¹⁵

This stagnation may stem from a smaller reduction in TB-related epidemiological indicators in the country’s Southern region and a higher frequency of treatment abandonment and retreatment, suggesting weaknesses in case control and monitoring.¹⁶ Furthermore, the Covid-19 pandemic led to reduced investment in Tuberculosis Control Program activities, reversing years of progress in controlling the pathogen.¹⁷ Although an increase in cases was expected given this scenario, the maintenance of these indicators may also represent stagnation, as it fails to reflect the reduction anticipated by the Program or progress toward the targets set for 2035.⁴

Regarding mortality, and contrary to the targets advocated by the PNFTPSP, females and the 20–39 age group showed a statistically significant upward trend in mortality rates over the years.⁴ Although the rate remains below the target of 1 death per 100,000 inhabitants recommended by the PNFTPSP, the rise in this indicator may highlight disparities in access to healthcare among different groups analyzed.^{4,7}

Globally, men exhibit higher TB incidence and mortality rates than women, with a ratio ranging from 1.1 to 2.5 depending on the geographic region.¹⁸ These differences may stem from contrasting lifestyles between men and women, as men are more exposed to risk factors such as alcohol and tobacco use.¹⁹ Nevertheless, time-trend studies show a significant reduction in mortality for both sexes in various countries up to 2019.²⁰

However, our results demonstrated a significant upward trend of 0.046 deaths per 100,000 inhabitants annually among women. This finding may have been driven by the Covid-19 pandemic. A Taiwanese time-series study analyzed crude mortality rates between 1978 and 2022 and found a significant decrease during the pandemic (2020–2022) among males, but not among females.²¹

Furthermore, a US study based on over 18,000 TB death records showed that females experienced a relative increase in mortality compared to males during the pandemic (26.33% vs. 2.17% in 2020; 21.48% vs. 3.23% in 2021).²² This disproportionate rise may be explained by pandemic-related disruptions in health services. Although women typically seek healthcare more frequently than men, widespread service overburdening, restricted access, and delayed TB diagnosis during the pandemic severely hindered timely treatment, ultimately driving up female mortality.^{21,22}

Regarding age groups, contrary to our findings of an upward trend in mortality among those aged 20–39, other studies have reported a significant increase in mortality among individuals aged 60 or 75 and older.²³ However, the rise in mortality among the 20–39 age group may occur because young adults and adults are more socially active than other age groups, and thus more likely to be exposed to TB in the community, and to risk factors such as alcohol and tobacco use and HIV coinfection.²⁴

Several factors were associated with death in our study, as shown in Table 2. Among the vulnerable populations analyzed, individuals experiencing homelessness had a 4.25-fold higher risk of death compared to those not in this situation (RR = 4.25; 95% CI = 3.46–5.22; $p < 0.001$). These findings were also observed in a cohort study conducted in Minas Gerais (RR = 2.45; 95% CI = 1.49–4.49; $p < 0.001$).²⁵ Frequent loss to follow-up during TB treatment, drug use, lack of knowledge about the disease, and HIV coinfection pose challenges for TB prevention and management in this population and may be associated with death.²⁶

The use of tobacco, alcohol, and other illicit drugs showed a statistically significant association with death, as presented in Table 2. These findings corroborate data found in the literature.^{27,28} Alcohol consumption increases susceptibility to TB infection due to immune system suppression and increased oxidative stress, while

smoking induces a cytotoxic effect on the respiratory epithelium, impairing protective mechanisms against *M. tuberculosis*.^{27,28}

In our study, individuals with TB who used alcohol faced a higher risk of death than those who used tobacco (RR = 2.32 vs. RR = 1.62; $p < 0.001$). Although alcohol use is a known risk factor well-documented in the literature, this finding may stem from the fact that the State Plan for Ending Tuberculosis in Paraná identified only tobacco users.⁶

Regarding individuals with TB, in our study, death was associated with multimorbidities including diabetes mellitus, mental disorders, and other diseases. The presence of these multimorbidities has been described as a predictor of death in several studies.²⁹ Multimorbidities, including diabetes mellitus, cancer, chronic lung diseases, mental disorders, liver diseases, and chronic kidney diseases, significantly increase mortality risk among individuals with TB.²⁹

The association between TB and diabetes may arise because *M. tuberculosis* infection hinders glycemic control, reducing the efficacy of TB medications and increasing mortality risk.³⁰ Among people with mental disorders and TB, psychological distress and depressive symptoms can lead to poor treatment adherence and cause alterations in the immune system and neurotransmitter balance, potentially influencing the outcome.³⁰

Finally, our results indicated that incarcerated individuals had a lower risk of death compared to non-incarcerated individuals (RR = 0.40; 95% CI = 0.27–0.58; $p < 0.001$). These findings contrast with the literature, as incarcerated individuals in low- and middle-income countries face a higher risk of negative outcomes compared to non-incarcerated individuals (RR = 2.17; $p < 0.001$).³¹ This may result from the underreporting of cases among incarcerated individuals, who may die without correct diagnosis or treatment for the disease.^{31,32}

A study using data from 199 countries and territories estimated that the actual number of TB cases was substantially higher than that reported, with a global detection rate of only 53% of occurrences in 2019.³² This finding underscores the need to expand discussions regarding disease underreporting among regional and international authorities and to implement more appropriate strategies for this population, focusing on both timely diagnosis and the prevention of TB transmission.^{31,32}

This study has certain limitations, such as the use of secondary data from SINAN, which may contain errors in form completion and underreported data. Furthermore, such data may be updated retroactively, potentially altering the analyzed sample. The fact that the study period encompassed the Covid-19 pandemic was another limitation, as this may have affected TB

case underreporting and diagnosis, thereby influencing the representativeness of the information recorded in SINAN. Nevertheless, this study can support future research, particularly given the significant increase in TB mortality across sexes and age groups, trends that should inform new public policies.

The results indicated an increase in mortality among females and individuals aged 20–39, as well as an increase in the case fatality rate among those aged 60 and older—contrary to the targets for reducing TB incidence and mortality rates set by the PNFTSP. Therefore, to alter this pattern, authorities must strengthen the link between TB patients and Primary Health Care by expanding active case finding among symptomatic individuals in women’s health services, prenatal and postpartum care settings, and long-term care facilities for older adults, aiming to reduce diagnostic and therapeutic delays in these populations.

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AUTHORS' CONTRIBUTIONS

Adriele da Mota de França Pinto contributed to the literature review; the writing of the abstract, introduction, methodology, discussion, and interpretation and description of results; the preparation of tables; and the conclusions and statistical analysis. **Camila Marinelli Martins** contributed to project administration; the literature review; the writing of the abstract, introduction, methodology, discussion, and interpretation and description of results; the conclusions; the review; and statistical analysis. **Maria Dagmar da Rocha Gaspar** contributed to the writing of the abstract, introduction, methodology, and discussion, as well as the review. **Stellamaris Cordeiro Silvestre Rosa** contributed to the writing of the abstract, introduction, methodology, and discussion, as well as the review. **Bruna Pereira Madruga** contributed to the writing of the abstract, introduction, methodology, and discussion, as well as the review.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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