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Original research

Trends in tuberculosis incidence and mortality coefficients in Brazil, 2011–2019: analysis by inflection points

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ABSTRACT

Objective. To analyze the temporal trend of tuberculosis incidence and mortality rates in Brazil between 2011 and 2019.

Methods. This was an ecological time series study of tuberculosis incidence and mortality rates in Brazil between 2011 and 2019. Data were extracted from the Notifiable Disease Information System and the Mortality Information System, and population estimates were from the Brazilian Institute of Geography and Statistics. Trends were analyzed by Joinpoint regression, which recognizes inflection points for temporal analysis.

Results. The average incidence rate of tuberculosis in Brazil in the period was 35.8 cases per 100 000 population. From 2011 to 2015, this coefficient had an annual percentage change of –1.9% (95% CI [–3.4, –0.5]) followed by an increase of 2.4% (95% CI [0.9, 3.9]) until 2019. The average mortality rate between 2011 and 2019 was 2.2 deaths per 100 000 population, with an average annual percentage change of –0.4% (95% CI [–1.0, 0.2]). Amazonas was the only state with an increase in the annual average percentage variation for the incidence rate (3.2%; 95% CI [1.3, 5.1]) and mortality rate (2.7%; 95% CI [1.0, 4.4]) over the years, while Rio de Janeiro state had an increasing inflection for incidence from 2014 to 2019 (2.4%; 95% CI [1.4, 3.5]) and annual average of decreasing percentage variation (–3.5%; 95% CI [–5.0, –1.9]).

Conclusions. During the period analyzed, a decreasing trend in incidence was observed between 2011 and 2015, and an increasing trend for the period from 2015 to 2019. On the other hand, no change in the trend for mortality was found in Brazil.

Keywords Tuberculosis; epidemiology; time series studies; incidence; mortality; Brazil.

Tuberculosis (TB) continues to be one of the deadliest communicable diseases globally. It is estimated that about 9.9 million individuals became ill in 2020, equivalent to 127 cases per 100 000 population and, in the same year, approximately 1.3 million HIV-negative people died from TB (1).

According to the World Health Organization (WHO), Brazil is among the priority countries for the control of TB and TB–HIV coinfection in the world. The country accounts for 33% of total cases notified in 2020 in the Americas, being the country with the highest number of cases (2). In 2021, Brazil recorded 68 271 new TB cases, which corresponds to an incidence rate of 32.0 cases per 100 000 population. In the previous year, approximately 4 543 deaths from TB were reported, resulting in a mortality rate of 2.1 deaths per 100 000 population (3).

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This situation is worrying and points to the need to implement global policies directed at reaching the goals for TB control. The Ministry of Health of Brazil (MoH), in 2021, updated the National Plan to end TB as a public health problem, whose goals include reducing the incidence rate to less than 10 cases per 100 000 population and deaths to less than 230 by the year 2035 – a reduction of 90.0% and 95.0%, respectively, when compared to 2015 (4).

Despite the epidemiological relevance of monitoring the trend of these indicators (incidence and mortality) for TB, just a few studies describe them on a national scale. Studies on incidence (5) and mortality could be identified (6, 7), in isolation, with no joint interpretation and discussion of the temporal behavior for these indicators. In addition, MoH publishes an annual epidemiological bulletin with related analyses, but also without joint interpretation (3).

Time series analysis is an important statistical tool used to understand behavioral patterns of diseases over time, which can contribute to informing public health policies (8). In the context of TB, the population is not affected homogeneously, given the influences of biological and social determinants such as malnutrition, TB–HIV coinfection, inadequate housing and working conditions, and high population density, among others (9). Thus, this analysis is understood as a necessary and important tool because it has the potential to strengthen the evaluation and control of TB in Brazil, supporting strategic actions aimed at achieving the goals proposed by the End TB Strategy and the National Plan to end TB (4).

Therefore, this study aims to analyze the temporal trend of tuberculosis incidence and mortality rates in Brazil between 2011 and 2019.

MATERIALS AND METHODS

This is an ecological time series study of TB incidence and mortality coefficients. The analysis unit was Brazil and its regions and states. Data from TB cases reported in the Notifiable Diseases Information System (SINAN) and TB deaths reported in the Mortality Information System (SIM), between 2011 and 2019 were used. For population estimates, data from the Brazilian Institute of Geography and Statistics (IBGE) were used. Data from 2020 were excluded due to atypical behavior of the data and the functioning of health facilities during the COVID-19 pandemic (10).

All new TB cases were included, corresponding to SINAN entry categories: i) "new case" (never underwent TB treatment, or had it for less than 30 days); ii) "unknown" (unknown prior TB history); and iii) "post-death" (TB was discovered after death as a result of an epidemiological investigation). All non-fetal TB deaths recorded during the study period were included.

The TB incidence rate was calculated as the ratio of the number of new cases for all clinical forms of TB and the resident population, in a given year, expressed per 100 000 population. The TB mortality rate was calculated as the ratio of the number of TB deaths as the primary cause and the resident population in the corresponding year, also expressed per 100 000 population.

The trend of the coefficients was calculated through segmented regression (Joinpoint regression). For the coefficients with statistical significance, the annual percent change (APC) and the annual averages of percentage change (average annual percent change – AAPC) were calculated. In this way, it was possible to recognize the inflection points, which correspond to variations of the coefficients with greater significance in the elevation of the straight line.

$$APC = [-1 + 10b_1] * 100\%$$

The final modeling step comprised the calculation of 95% confidence intervals (95% CI), using the following equation:

$$_{95\%}CI = [-1 + 10(b_1 \pm t * EP)] * 100\%$$

Where: b_1 is the beta coefficient; t is the tabulated value of the Student's T distribution; EP is the standard error (8).

Joinpoint regression is used to find the best model, testing whether different line segments (with several Joinpoints) more adequately justify the trend in the defined time interval than a single line, using Monte Carlo permutation tests, aiming to compare the several models with 0, 1, 2, 3, 4, or 5 Joinpoints, according to the total number of time intervals of the time series, giving rise to the periods (11).

Thus, the trend was classified as "increasing trend" in case of positive APC and confidence interval that did not include zero, "decreasing trend" when negative APC and confidence interval that did not include zero, and "stationary" when there was no statistical difference between its value and zero (8).

For data storage, processing, and analysis, TabWin®, Microsoft Excel® 2019, and Joinpoint Regression Program version 4.9.0 software were used. This study was conducted using secondary, anonymous routine data available online on the official web page of the MoH, and did not require approval by research ethics committee.

RESULTS

The average incidence rate of TB in Brazil between 2011 and 2019 was 35.8 cases per 100 000 population. It was observed that most states (n = 14, 51.9%) had a higher incidence coefficient in 2019 compared to 2011: Acre, Amazonas, Roraima, Pará, Amapá, Tocantins, Rio Grande do Norte, Paraíba, Pernambuco, Sergipe, São Paulo, Rio Grande do Sul, Mato Grosso do Sul, and Distrito Federal (Figure 1).

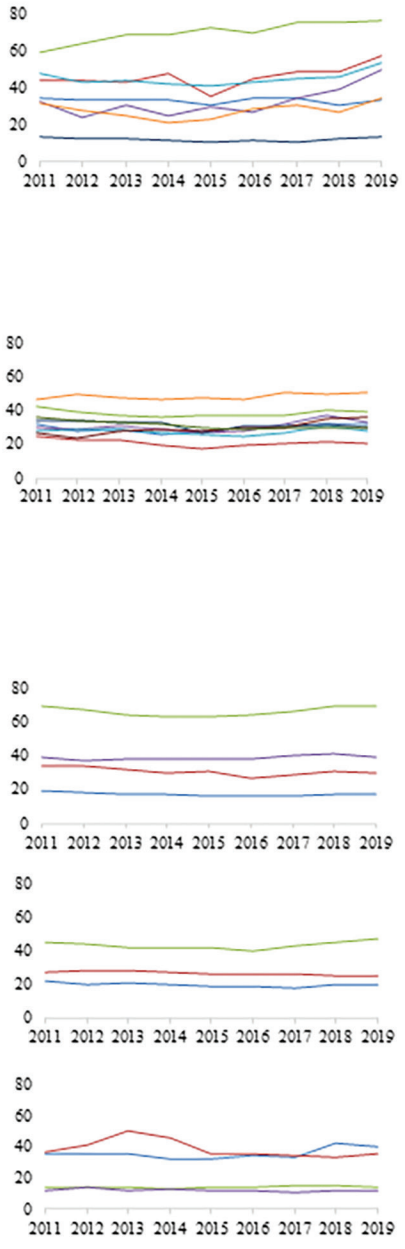
For the national data, there was a decreasing trend of TB incidence by –1.9% (95% CI [–3.4, –0.5]) from 2011 until 2015, followed by an increasing trend of 2.4% (95% CI [0.9, 3.9]) until 2019 (Table 1).

In the early years analyzed, there was a stationary trend in the TB incidence in some regions (North, 2011–2015; Southeast, 2011–2014) or a decreasing trend (Northeast, 2011–2014; South, 2011–2016). The Central-West, in turn, maintained a stationary aspect throughout the period considered. All regions but the Central-West showed a tendency of increase in the incidence coefficient in the last years of the analyzed period: Southeast, since 2014; North and Northeast, since 2015; and South, from 2016 to 2019.

Since 2013, inflection points with positive variation have been identified for the incidence curves of 15 states, indicating a growing change in the course of this indicator. Of these states, five had a statistically significant trend for the segment after 2013: Amazonas (1.8%; 95% CI [0.2; 3.4]), Pará (5.9%; 95% CI [0.9, 11.2]), Ceará (2.3%; 95% CI [0.6, 4.0]), Rio de Janeiro (2.4%;

FIGURE 1. Tuberculosis incidence rate by region and state of residence (per 100 000 population), Brazil, 2011–2019

Region	2011	2012	2013	2014	2015	2016	2017	2018	2019	Line graph
North										
Rondônia	34.7	34.2	34.0	33.6	30.7	35.2	34.4	30.9	33.5	
Acre	44.4	44.2	43.6	48.0	35.8	44.9	49.2	49.1	58.3	
Amazonas	60.1	64.8	69.9	69.8	73.6	70.7	75.8	76.1	77.3	
Roraima	32.4	24.4	31.2	25.5	29.6	27.0	34.6	39.5	49.9	
Pará	48.0	43.7	44.6	42.6	41.8	43.5	45.4	46.5	54.0	
Amapá	31.9	27.7	24.7	21.6	23.2	29.1	31.1	27.0	34.4	
Tocantins	13.3	13.0	12.9	11.2	10.5	11.5	10.4	12.8	13.4	
North East										
Maranhão	32.3	28.3	28.8	26.3	28.0	29.9	30.4	32.1	31.6	
Piauí	24.8	22.2	22.3	19.8	17.7	19.6	20.3	21.8	20.7	
Ceará	42.1	39.3	37.7	36.2	36.9	37.0	37.8	40.4	39.8	
Rio Grande do Norte	30.3	29.0	30.7	28.5	26.5	28.2	32.1	37.6	32.6	
Paraíba	28.0	29.3	28.8	26.4	25.4	24.8	26.9	30.9	28.4	
Pernambuco	47.1	49.6	47.8	47.0	47.8	47.0	50.6	49.3	50.4	
Alagoas	34.2	34.0	33.2	32.7	27.1	31.3	30.7	32.4	29.5	
Sergipe	26.8	23.8	28.3	29.3	28.0	29.5	30.3	35.2	36.2	
Bahia	36.4	34.3	32.9	32.2	29.6	29.1	29.8	30.4	30.4	
Southeast										
Minas Gerais	19.3	17.8	17.6	17.5	16.4	16.3	16.5	17.0	17.4	
Espírito Santo	34.4	33.9	31.7	29.7	30.7	27.1	28.4	31.1	30.1	
Rio de Janeiro	69.7	67.7	64.1	62.6	63.4	64.3	66.7	69.4	69.5	
São Paulo	38.7	37.5	37.8	37.9	38.2	38.2	40.6	41.1	39.4	
South										
Paraná	21.7	20.1	20.9	20.0	19.3	19.1	18.1	20.3	20.1	
Santa Catarina	27.6	27.9	27.9	27.4	26.0	25.9	25.7	25.5	25.1	
Rio Grande do Sul	44.9	43.6	42.4	41.8	42.0	39.4	43.1	44.8	47.2	
Central-West										
Mato Grosso do Sul	36.0	36.0	35.2	31.7	31.6	34.6	33.2	42.2	40.2	
Mato Grosso	36.6	41.2	50.3	45.5	36.0	35.3	34.8	33.5	35.7	
Goiás	14.4	14.5	14.5	13.2	14.6	13.6	14.8	14.8	14.0	
Distrito Federal	11.9	13.7	11.6	13.3	12.4	11.9	10.6	12.3	12.2	
Brazil	37.0	35.9	35.6	34.7	34.3	34.4	35.9	37.1	37.1	



Source: Prepared by the authors based on the results of the study. Source data from the Notifiable Diseases Information System (SINAN) and Brazilian Institute of Geography and Statistics (IBGE).

95% CI [1.4, 3.5]), and Rio Grande do Sul (5.6%; 95% CI [3.2, 8.1]). For the 12 states without Joinpoint identified, three had statistically significant trends, with one decreasing trend: Santa Catarina (–1.4%; 95% CI [–1.9, –1.0]); and two increasing trends: Sergipe (4.3%; 95% CI [2.3, 6.3]) and São Paulo (0.8%; 95% CI [0.1, 1.6]).

In the period from 2011 to 2019, the average mortality rate was 2.2 deaths per 100 000 population. An increase was observed in one-third of the states (n = 9; 33.3%): Acre, Amazonas, Roraima, Pará, Piauí, Espírito Santo, Paraná, Santa Catarina, and Distrito Federal (Figure 2).

Regarding the trend in the TB mortality rate for Brazil, an APC of –0.4% (95% CI [–1.0, 0.2]) was observed. The Southeast Region was classified with a significant downward trend, while the South Region presented an increasing trend. The other regions (North, Northeast, and Central-West) showed a stationary trend in the mortality rate between 2011 and 2019. However, there were two states in the North Region with an increasing

TABLE 1. Distribution of annual percentage change in tuberculosis incidence rate (per 100 000 population), Brazil, 2011–2019

Region	Segment 1		Segment 2		2011–2019
	Time course	APC% (95% CI)	Time course	APC% (95% CI)	AAPC% (95% CI)
North	2011–2015	–0.8 (–3.8 to 2.3)	2015–2019	**4.4*** (1.2 to 7.7)	**1.8*** (0.2 to 3.4)
Rondônia	2011–2019	–0.6 (–2.1 to 0.9)	NA	NA	–0.6 (–2.1 to 0.9)
Acre	2011–2019	2.7 (–0.9 to 6.4)	NA	NA	2.7 (–0.9 to 6.4)
Amazonas	2011–2013	7.4 (–1.9 to 17.7)	2013–2019	**1.8*** (0.2 to 3.4)	**3.2*** (1.3 to 5.1)
Roraima	2011–2016	–1.3 (–11.6 to 10.1)	2016–2019	21.9 (–4.6 to 55.8)	6.8 (–1.5 to 15.8)
Pará	2011–2015	–3.3 (–7.9 to 1.5)	2015–2019	**5.9*** (0.9 to 11.2)	1.2 (–1.2 to 3.7)
Amapá	2011–2014	–11.0 (–26.5 to 7.7)	2014–2019	8.7 (8.7 to –0.2)	0.8 (–5.3 to 7.4)
Tocantins	2011–2017	–3.8 (–7.6 to 0.0)	2017–2019	14.6 (–9.2 to 44.7)	0.5 (–4.1 to 5.2)
North East	2011–2015	**–3.0*** (–5.1 to –0.8)	2015–2019	**2.6*** (0.4 to 4.9)	–0.2 (–1.3 to 0.9)
Maranhão	2011–2014	–5.1 (–11.7 to 2.1)	2014–2019	4.0 (0.7 to 7.4)	0.5 (–1.9 to 2.9)
Piauí	2011–2015	**–7.0*** (–11.4 to –2.4)	2015–2019	4.1 (–0.8 to 9.2)	–1.6 (–3.9 to 0.8)
Ceará	2011–2014	**–5.0*** (–8.5 to –1.3)	2014–2019	**2.3*** (0.6 to 4.0)	–0.5 (–1.7 to 0.7)
Rio Grande do Norte	2011–2019	1.9 (–0.9 to 4.9)	NA	NA	1.9 (–0.9 to 4.9)
Paraíba	2011–2019	0.0 (–2.3 to 2.4)	NA	NA	0.0 (–2.3 to 2.4)
Pernambuco	2011–2019	0.6 (–0.2 to 1.4)	NA	NA	0.6 (–0.2 to 1.4)
Alagoas	2011–2019	–1.5 (–3.5 to 0.5)	NA	NA	–1.5 (–3.5 to 0.5)
Sergipe	2011–2019	**4.3*** (2.3 to 6.3)	NA	NA	**4.3*** (2.3 to 6.3)
Bahia	2011–2016	**–4.3*** (–5.5 to –3.0)	2016–2019	1.9 (–1.0 to 4.9)	**–2.0*** (–3.0 to –1.1)
Southeast	2011–2014	–2.3 (–5.7 to 1.3)	2014–2019	**1.6*** (0.0 to 3.2)	0.1 (–1.0 to 1.3)
Minas Gerais	2011–2016	**–3.1*** (–4.9 to –1.3)	2016–2019	2.6 (–1.6 to 6.9)	–1.0 (–2.4 to 0.3)
Espírito Santo	2011–2016	**–4.3*** (–7.4 to –1.1)	2016–2019	3.3 (–3.9 to 11.1)	–1.5 (–3.9 to 0.9)
Rio de Janeiro	2011–2014	**–3.9*** (–6.0 to –1.7)	2014–2019	**2.4*** (1.4 to 3.5)	0.0 (–0.7 to 0.8)
São Paulo	2011–2019	**0.8*** (0.1 to 1.6)	NA	NA	**0.8*** (0.1 to 1.6)
South	2011–2016	**–2.2*** (–2.9 to –1.5)	2016–2019	**3.4*** (1.6 to 5.1)	–0.1 (–0.7 to 0.4)
Paraná	2011–2017	**–2.3*** (–3.9 to –0.8)	2017–2019	5.2 (–4.4 to 15.7)	–0.5 (–2.4 to 1.4)
Santa Catarina	2011–2019	**–1.4*** (–1.9 to –1.0)	NA	NA	**–1.4*** (–1.9 to –1.0)
Rio Grande do Sul	2011–2016	**–2.1*** (–3.1 to –1.1)	2016–2019	**5.6*** (3.2 to 8.1)	0.7 (–0.0 to 1.5)
Central-West	2011–2019	**–0.8** (–2.4 to 0.8)	NA	NA	**–0.8** (–2.4 to 0.8)
Mato Grosso do Sul	2011–2015	–3.8 (–11.7 to 4.8)	2015–2019	7.1 (–1.7 to 16.7)	1.5 (–2.8 to 5.9)
Mato Grosso	2011–2019	–2.8 (–6.4 to 0.9)	NA	NA	–2.8 (–6.4 to 0.9)
Goiás	2011–2019	0.0 (–1.3 to 1.3)	NA	NA	0.0 (–1.3 to 1.3)
Distrito Federal	2011–2019	–0.9 (–3.1 to 1.5)	NA	NA	–0.9 (–3.1 to 1.5)
Brazil	2011–2015	**–1.9*** (–3.4 to –0.5)	2015–2019	**2.4*** (0.9 to 3.9)	0.2 (–0.5 to 0.9)

Notes: APC: annual percent change (percentage of annual variation); 95% CI: 95% confidence interval; AAPC: average annual percent change (annual average of percentage change); NA: not applicable; *p-value <0.05
Source: Prepared by the authors based on the results of the study. Source data from the Notifiable Disease Information System (SINAN) and Brazilian Institute of Geography and Statistics (IBGE).

trend in the period 2011–2019 (Amazonas) and 2014–2019 (Roraima) (Table 2).

Inflection points of this indicator were identified for four states, and only in Roraima did the increasing trend between the years 2014 and 2019 remain statistically significant, with an APC of 35.1% (95% CI [7.3, 70.2]). In addition, for the entire period, the states of Alagoas (–4.8%; 95% CI [–8.4, –1.1]) and Rio de Janeiro (–3.5%; 95% CI [–5.0, –1.9]) had a decreasing trend, and Amazonas (2.7%; 95% CI [1.0, 4.4]) had an increasing one.

DISCUSSION

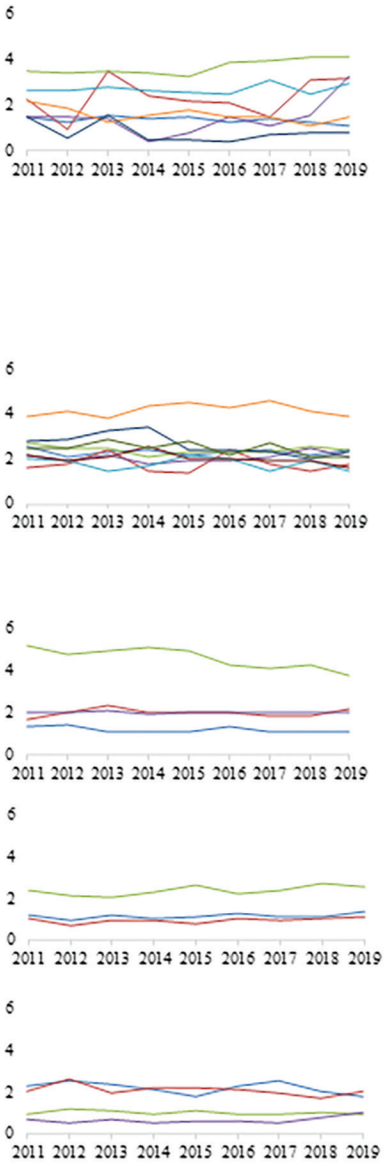
Through the analysis by inflection points, the percentage variations of the TB incidence and mortality rates for the 27 states in Brazil and their respective regions was estimated for the period 2011 to 2019. The results of this study showed a decreasing trend in the TB incidence coefficient between 2011 and 2015, followed by an increase until 2019, both statistically significant.

The drop in incidence observed in this study may be linked to the global historical context of TB control. Between 2006 and 2015, in order to reach the Millennium Development Goals, the Stop TB strategy was implemented, which, through increased investments by countries and international donors, may have contributed to the drop in incidence observed in the period. In the meantime, a 42% reduction in the prevalence of the disease was observed. Such effects were facilitated by the progress in financial investments in TB control actions, in addition to the expansion of access to treatment (4, 12).

In addition, Brazil experienced important changes in living conditions when it advanced in social protection between 2011 and 2015. Social policies were implemented to mitigate poverty and inequality, such as the distribution of transportation vouchers and the expansion of the Bolsa Família cash transfer

FIGURE 2. Distribution of the tuberculosis mortality rate (per 100 000 population), by region and state of residence, Brazil, 2011–2019

Region	2011	2012	2013	2014	2015	2016	2017	2018	2019	Line graph
North										
Rondônia	1.5	1.3	1.6	1.4	1.5	1.3	1.4	1.3	1.1	
Acre	2.3	1.0	3.5	2.4	2.2	2.1	1.5	3.1	3.2	
Amazonas	3.5	3.4	3.5	3.4	3.3	3.9	4.0	4.1	4.1	
Roraima	1.5	1.5	1.4	0.4	0.8	1.5	1.1	1.6	3.3	
Pará	2.7	2.7	2.8	2.7	2.6	2.5	3.1	2.5	3.0	
Amapá	2.2	1.9	1.3	1.6	1.8	1.5	1.5	1.1	1.5	
Tocantins	1.5	0.6	1.6	0.5	0.5	0.4	0.7	0.8	0.8	
North East										
Maranhão	2.6	2.1	2.3	2.4	2.2	2.3	2.4	2.2	2.4	
Piauí	1.6	1.8	2.4	1.5	1.4	2.4	1.8	1.5	1.8	
Ceará	2.7	2.5	2.5	2.1	2.3	2.3	2.3	2.6	2.4	
Rio Grande do Norte	2.2	1.9	2.2	1.8	1.9	1.9	2.1	2.5	2.1	
Paraíba	2.0	1.9	1.5	1.7	2.2	2.0	1.5	1.9	1.5	
Pernambuco	3.9	4.1	3.8	4.4	4.5	4.3	4.6	4.1	3.9	
Alagoas	2.8	2.9	3.3	3.4	2.4	2.4	2.3	2.0	2.3	
Sergipe	2.2	1.9	2.1	2.6	2.0	2.0	1.9	1.9	1.6	
Bahia	2.5	2.5	2.9	2.5	2.8	2.2	2.7	2.1	2.1	
Southeast										
Minas Gerais	1.3	1.4	1.1	1.1	1.1	1.3	1.1	1.1	1.1	
Espírito Santo	1.7	2.0	2.3	2.0	2.0	2.0	1.8	1.8	2.2	
Rio de Janeiro	5.2	4.8	4.9	5.1	4.9	4.3	4.1	4.3	3.8	
São Paulo	2.0	2.0	2.1	1.9	2.0	2.0	2.0	2.0	2.0	
South										
Paraná	1.2	0.9	1.2	1.0	1.1	1.3	1.1	1.1	1.4	
Santa Catarina	1.0	0.7	0.9	0.9	0.8	1.0	0.9	1.0	1.1	
Rio Grande do Sul	2.4	2.1	2.0	2.3	2.6	2.2	2.4	2.7	2.5	
Central-West										
Mato Grosso do Sul	2.3	2.5	2.4	2.1	1.8	2.3	2.5	2.0	1.8	
Mato Grosso	2.0	2.6	1.9	2.2	2.2	2.1	1.9	1.7	2.0	
Goiás	0.9	1.2	1.1	0.9	1.1	0.9	0.9	1.0	0.9	
Distrito Federal	0.7	0.5	0.7	0.5	0.6	0.6	0.5	0.8	1.0	
Brazil	2.3	2.2	2.3	2.2	2.3	2.2	2.2	2.2	2.2	



Source: Prepared by the authors based on the results of the study. Source data from the Notifiable Diseases Information System (SINAN) and Brazilian Institute of Geography and Statistics (IBGE).

program, which may have contributed to increased access to essential services. There is also the historic milestone of Brazil's exit from the United Nations hunger map in 2014, which positively impacted adherence to TB treatment (13).

However, despite the advances made regarding the reduction of TB incidence in the country until 2015, and even with the End TB Strategy after 2015 aiming to reduce the incidence of the disease to less than 10 cases per 100 000 population by 2035, compared to 2015 (4), this study identified an increase in the trend of this coefficient.

A population-based study of TB cases, carried out in a municipality in the Central-West of Brazil, pointed to the relationship between TB in incarcerated people and the urban population, in which 54% of *Mycobacterium tuberculosis* strains came from people in prisons (14). The incarcerated population had a 22 times higher risk of developing TB compared to the general population, strongly interfering in the incidence of TB in Brazilian municipalities with prisons, in which inequality in income distribution and exposure in prison are negative risk factors, for both incarcerated and non-incarcerated persons (15).

TABLE 2. Distribution of the annual percentage change in mortality coefficients (per 100 000 population), Brazil, 2011–2019

Region	Segment 1		Segment 2		2011–2019
	Time course	APC% (95% CI)	Time course	Region and federative unit	Time course
North	2011–2019	0.7 (–1.4 to 2.9)	NA	NA	0.7 (–1.4 to 2.9)
Rondônia	2011–2019	–2.9 (–5.2 to 0.1)	NA	NA	–2.9 (–5.2 to 0.1)
Acre	2011–2019	4.9 (–7.1 to 18.5)	NA	NA	4.9 (–7.1 to 18.5)
Amazonas	2011–2019	**2.7*** (1.0 to 4.4)	NA	NA	**2.7*** (1.0 to 4.4)
Roraima	2011–2014	–32.5 (–59.7 to 13.1)	2014–2019	**35.1*** (7.3 to 70.2)	4.2 (–12.1 to 23.5)
Pará	2011–2019	0.5 (–1.8 to 2.9)	NA	NA	0.5 (–1.8 to 2.9)
Amapá	2011–2019	–4.8 (–9.5 to 0.1)	NA	NA	–4.8 (–9.5 to 0.1)
Tocantins	2011–2019	–5.7 (–18.6 to 9.3)	NA	NA	–5.7 (–18.6 to 9.3)
North East	2011–2019	–1.0 (–2.1 to 0.0)	NA	NA	–1.0 (–2.1 to 0.0)
Maranhão	2011–2019	–0.2 (–2.3 to 1.8)	NA	NA	–0.2 (–2.3 to 1.8)
Piauí	2011–2019	–0.3 (–6.5 to 6.3)	NA	NA	–0.3 (–6.5 to 6.3)
Ceará	2011–2014	–6.9 (–14.7 to 1.7)	2014–2019	2.5 (–1.4 to 6.6)	–1.1 (–3.9 to 1.8)
Rio Grande do Norte	2011–2019	1.0 (–2.2 to 4.3)	NA	NA	1.0 (–2.2 to 4.3)
Paraíba	2011–2019	–1.6 (–6.0 to 2.9)	NA	NA	–1.6 (–6.0 to 2.9)
Pernambuco	2011–2017	2.6 (–0.9 to 6.3)	2017–2019	–8.0 (–25.1 to 13.1)	–0.1 (–4.1 to 4.0)
Alagoas	2011–2019	**–4.8*** (–8.4 to –1.1)	NA	NA	**–4.8*** (–8.4 to –1.1)
Sergipe	2011–2019	–2.9 (–6.1 to 0.5)	NA	NA	–2.9 (–6.1 to 0.5)
Bahia	2011–2019	–2.5 (–5.6 to 0.8)	NA	NA	–2.5 (–5.6 to 0.8)
Southeast	2011–2019	**–1.6*** (–2.3 to –0.9)	NA	NA	**–1.6*** (–2.3 to –0.9)
Minas Gerais	2011–2019	–2.0 (–4.6 to 0.6)	NA	NA	–2.0 (–4.6 to 0.6)
Espírito Santo	2011–2019	0.4 (–2.7 to 3.6)	NA	NA	0.4 (–2.7 to 3.6)
Rio de Janeiro	2011–2019	**–3.5*** (–5.0 to –1.9)	NA	NA	**–3.5*** (–5.0 to –1.9)
São Paulo	2011–2019	–0.1 (–0.9 to 0.7)	NA	NA	–0.1 (–0.9 to 0.7)
South	2011–2019	**2.3*** (0.2 to 4.5)	NA	NA	**2.3*** (0.2 to 4.5)
Paraná	2011–2019	2.2 (–1.7 to 6.2)	NA	NA	2.2 (–1.7 to 6.2)
Santa Catarina	2011–2019	2.6 (–1.2 to 6.6)	NA	NA	2.6 (–1.2 to 6.6)
Rio Grande do Sul	2011–2019	2.1 (–0.6 to 4.8)	NA	NA	2.1 (–0.6 to 4.8)
Central-West	2011–2019	–1.3 (–3.2 to 0.7)	NA	NA	–1.3 (–3.2 to 0.7)
Mato Grosso do Sul	2011–2019	–2.4 (–5.9 to 1.2)	NA	NA	–2.4 (–5.9 to 1.2)
Mato Grosso	2011–2019	–2.2 (–5.4 to 1.2)	NA	NA	–2.2 (–5.4 to 1.2)
Goiás	2011–2019	–1.6 (–4.9 to 1.9)	NA	NA	–1.6 (–4.9 to 1.9)
Distrito Federal	2011–2017	–2.5 (–12.6 to 8.8)	2017–2019	38.3 (–27.7 to 164.4)	6.4 (–6.4 to 21.0)
Brazil	2011–2019	–0.4 (–1.0 to 0.2)	NA	NA	–0.4 (–1.0 to 0.2)

Notes: APC: annual percent change (percentage of annual variation); 95% CI: 95% confidence interval; AAPC: average annual percent change (annual average of percentage change); NA: not applicable; *significant p-value <0.05.
Source: Prepared by the authors based on the results of the study. Source data from the Mortality Information System (SIM) and Brazilian Institute of Geography and Statistics (IBGE).

Another factor that could explain the increase in TB incidence after 2015 is the rollout of a better tool for TB diagnosis in the form of the molecular rapid test (GeneXpert, Cepheid®). Compared to sputum smear microscopy, this diagnostic method has higher sensitivity and specificity for identifying pulmonary TB cases, and its implementation countrywide overlapped with the increase in TB incidence observed in this study (16).

The range of the incidence rate observed in Roraima and Amapá could be explained by the effect of analyzing small numbers. These states, within Amazonas, drive the behavior of the North Region indicators, which presented the highest increase in APC of the incidence rate among all regions. Barriers related to precarious access to services (diagnostic, therapeutic, and clinical follow-up) are factors that hamper TB control and, given the large territory and difficult access of areas of the Amazon rainforest, could intensify the negative impact on morbidity and mortality (5).

Regarding TB mortality, TB is the main cause of death from a single source of infection among people living with HIV. The states with the highest percentages of TB–HIV coinfection are Santa Catarina and Rio Grande do Sul (15.2% in 2019), both in the South Region. The high proportion of TB–HIV coinfection in these states could be related to the high positive APC of the mortality coefficient, being two of the highest values compared to the other federative units (4).

Rio de Janeiro and Alagoas showed a significantly decreasing trend in the TB mortality rate. There are no known studies that establish possible causal factors on the mortality rate trends observed in these states. It is, therefore, a finding that deserves further investigation in order to better understand this phenomenon.

Amazonas and Roraima registered a significant increasing trend in the mortality rate. The impressive variation observed in the state of Roraima may be linked to the potential inaccuracy in analyzing small numbers. These states have an important flow

of immigrants, from Guyana and Venezuela (17), and a sizeable Indigenous population (18) in their territory. These populations are more vulnerable to becoming ill with TB (3) through factors that contribute to worsening of the disease and progression to death (18, 19).

The underreporting of TB cases interferes with the measurement of incidence and mortality coefficients, impairing the data collection that supports decision-making regarding the development of public policies, guidelines, clinical guidelines, and direction of actions toward the achievement of TB control goals proposed by WHO (20). Factors that may explain the underreporting of cases in the country's surveillance system include the structural and organizational problems of health services, such as the deficit of professionals in the Primary Health Care (PHC) system (21).

Furthermore, the literature points to potential factors that aggravate the progression of incident TB cases to death from TB, such as smoking (22) and HIV coinfection (23). Resistance to first- and second-line drugs is also a factor in unfavorable TB outcomes (24), especially when linked to pathologies such as diabetes mellitus (25) and lung, respiratory, hematological, and head and neck cancers (26), which are diseases that have been showing an upward trend annually, with a capacity to boost TB incidence and mortality in the coming years (26, 27).

The COVID-19 pandemic has caused a change in the situation of TB control in Brazil, and it is necessary to monitor these impacts (10). In view of this, PHC is indicated as a potential and necessary area to reduce the negative effects of the COVID-19 pandemic on TB incidence and mortality (28).

A study carried out in Brazil identified an association between the impact of PHC and a reduction in the TB incidence coefficient equivalent to 0.78 (95% CI [0.72, 0.84]), mortality of 0.72 (95% CI [0.55, 0. 94]), and an increase of the disease cure rate corresponding to 1.04 (95% CI [1.00, 1.08]) (29). This scenario highlights the importance of adopting efficient measures in TB control, with the scope of optimizing indicators in Brazil, especially in the PHC network that favors the decentralization of the management of the service network, in addition to conducting reorganization of the actions of health for different scenarios (30, 31).

That said, considering the evidence presented in this study, it can be inferred that even with the increasing trend of the incidence coefficient in Brazil, the number of deaths remained stationary. This suggests that the increase in cases may be linked to factors such as expansion of diagnostic access, implementation of new policies such as articulation with the prison system for TB testing/diagnosis in incarcerated people, and strengthening of laboratories in border areas for diagnosis in migrants; such policies favor early diagnosis and reduce the chances of death (32).

It is important to note that the risk of developing the active form of TB is higher in homeless people, people living with HIV, and in Indigenous populations. These factors likely contribute to the differences in TB incidence among Brazilian states. Besides these are socioeconomic scenarios such as increased poverty, political crisis, unemployment rate, race, and education, but studies that establish their real association are lacking (33).

The present research has the potential to support future investigations aimed at understanding the disease, in which it meets the interests of public health by systematizing the trend of the main indicators related to TB, from the understanding of changes in inflection points. It also favors the production of timely and potential information to guide federal, state, and municipal governments in decision-making and in the planning of strategies that drive public health related policies, in addition to the care of health professionals and managers, with a scope in the achievement of goals for TB control.

Regarding limitations of this study, the underreporting of TB cases stands out as a factor that could influence the trend analysis. Research carried out by estimation, through modeling (34), shows significant underreporting of TB cases in the states of the North and Northeast, which can interfere with time series analyses. Furthermore, underreporting of TB deaths and/or incorrect classification of causes of death also have the potential to influence the total number of deaths, calculation of coefficients, and similarly, for incidence, trend analysis (35). Also, this study used secondary routine data for the analysis.

Conclusion

During the interval analyzed, a decreasing trend of incidence was observed between 2011 and 2015 and an increasing trend for the period 2015–2019. On the other hand, no change in mortality trend was found in Brazil. When verifying the temporal trend analysis of these indicators in the states and regions, it was possible to recognize the main territories that need more attention, in particular the North and South regions. Regarding the states, Amazonas was the only state with an increase in the AAPC for the incidence and mortality rates over the years; and in Rio de Janeiro state, an increasing inflection was observed for incidence and a decreasing AAPC in the mortality coefficient.

The investigation by inflection points in the incidence and mortality curves makes it possible to identify trends in different segments of the period analyzed. This analysis provides elements for a deeper understanding of the behavior of the indicators, supporting the integrated planning at the national, state, and municipal levels of strategic actions aimed at TB control in these territories. Therefore, from the results of this study, it appears there is a need to change this scenario through the implementation of the technical recommendations included in the MoH national guidelines, such as the strengthening of diagnosis and timely treatment for populations, with a view to improving the TB control situation in the country.

Consequently, further studies are needed to investigate the characteristics of the regions and states with the highest coefficients, in order to corroborate the identification of the reasons behind the rise of the indicators addressed.

Author contributions. JNBSJ conceived the original idea. JNBSJ, RMC, DAS, and KBA developed the methodology. RMC and DAS contributed data analysis software. JNBSJ, RMC, and DAS analyzed the data. JNBSJ and LCA contributed resources. PB contributed funding. JNBSJ and PB contributed project administration. DMP, KBA, and PB provided supervision. JNBSJ wrote the original draft. All authors reviewed and edited the manuscript. All authors read and approved the final manuscript for submission.

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Tendencias de los coeficientes de incidencia y mortalidad por tuberculosis en Brasil, 2011-2019: análisis por puntos de inflexión

RESUMEN

Objetivo. Analizar la tendencia temporal de las tasas de incidencia y mortalidad por tuberculosis en Brasil entre el 2011 y el 2019.

Métodos. Este fue un estudio ecológico de series temporales de las tasas de incidencia y mortalidad por tuberculosis en Brasil entre el 2011 y el 2019. Los datos se obtuvieron del Sistema de Información sobre Enfermedades de Notificación Obligatoria y del Sistema de Información sobre Mortalidad, y las estimaciones de población proceden del Instituto Brasileño de Geografía y Estadística. Las tendencias se analizaron mediante el programa de regresión Joinpoint, que reconoce los puntos de inflexión para el análisis temporal.

Resultados. La tasa promedio de incidencia de tuberculosis en Brasil para el periodo fue de 35,8 casos por 100 000 habitantes. Entre el 2011 y el 2015, este coeficiente experimentó una variación porcentual anual del -1,9% (intervalo de confianza [IC] del 95% [-3,4, -0,5]), seguida por un aumento del 2,4% (IC 95% [0,9, 3,9]) hasta el 2019. La tasa de mortalidad promedio entre el 2011 y el 2019 fue de 2,2 muertes por cada 100 000 habitantes, con una variación porcentual promedio anual del -0,4% (IC del 95% [-1,0, 0,2]). El estado de Amazonas fue el único que a lo largo de los años presentó un aumento de la variación porcentual promedio anual de la tasa de incidencia (3,2%; IC del 95% [1,3, 5,1]) y de la tasa de mortalidad (2,7%; IC del 95% [1,0, 4,4]), en tanto que, entre el 2014 y el 2019, el estado de Río de Janeiro presentó una inflexión creciente de la incidencia (2,4%; IC del 95% [1,4, 3,5]) y una variación porcentual promedio anual decreciente (-3,5%; IC del 95% [-5,0, -1,9]).

Conclusiones. Durante el periodo analizado, se observa una tendencia decreciente de la incidencia entre el 2011 y el 2015, y una tendencia creciente para el periodo comprendido entre el 2015 y el 2019. En cambio, no se encontró ningún cambio en la tendencia de la mortalidad en Brasil.

Palabras clave Tuberculosis; epidemiología; estudios de series temporales; incidencia; mortalidad; Brasil.

Tendências nos coeficientes de incidência e mortalidade por tuberculose no Brasil, 2011-2019: análise por pontos de inflexão

RESUMO

Objetivo. Analisar a tendência temporal das taxas de incidência e mortalidade por tuberculose no Brasil entre 2011 e 2019.

Métodos. Estudo ecológico de série temporal das taxas de incidência e mortalidade por tuberculose no Brasil entre 2011 e 2019. Os dados foram extraídos do Sistema de Informação de Agravos de Notificação e do Sistema de Informação sobre Mortalidade, e as estimativas populacionais foram obtidas do Instituto Brasileiro de Geografia e Estatística. As tendências foram analisadas por regressão *joinpoint*, que reconhece pontos de inflexão para análise temporal.

Resultados. A taxa média de incidência da tuberculose no Brasil no período foi de 35,8 casos por 100 mil habitantes. O coeficiente teve uma variação percentual anual de –1,9% (IC 95% [–3,4; –0,5]) de 2011 a 2015, seguida de um aumento de 2,4% (IC 95% [0,9; 3,9]) até 2019. A taxa média de mortalidade entre 2011 e 2019 foi de 2,2 óbitos por 100 mil habitantes, com uma variação percentual anual média de –0,4% (IC 95% [–1,0; 0,2]). Ao longo dos anos, o Amazonas foi o único estado com aumento na variação percentual anual média na taxa de incidência (3,2%; IC 95% [1,3; 5,1]) e na taxa de mortalidade (2,7%; IC 95% [1,0; 4,4]). Já o estado do Rio de Janeiro teve inflexão crescente na incidência de 2014 a 2019 (2,4%; IC 95% [1,4; 3,5]) e média anual de variação percentual decrescente (–3,5%; IC 95% [–5,0; –1,9]).

Conclusões. Durante o período analisado, foi observada uma tendência decrescente na incidência entre 2011 e 2015 e crescente entre 2015 e 2019. Por outro lado, não foi encontrada nenhuma mudança na tendência de mortalidade no Brasil.

Palavras-chave Tuberculose; epidemiologia; estudos de séries temporais; incidência; mortalidade; Brasil.