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**Comparing Trends in Tuberculosis Mortality and Vaccination Rates in Brazil:
Before, During, and After the COVID-19 Pandemic**

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LISTA DE ABREVIATURAS

TB	Tuberculosis
WHO	World Health Organization
BCG	Bacillus Calmette-Guerin
COVID-19	Coronavirus disease
SARS-CoV-2 virus	severe acute respiratory syndrome coronavirus2
DATASUS	Department of Informatics of the Unified Health System (Departamento de Informática do Sistema Único de Saúde)
IBGE	Brazilian Institute of Geography and Statistics
SUS	Unified Health System (Sistema Único de Saúde)



ABSTRACT

MA, G.H. **Comparing Trends in Tuberculosis Mortality and Vaccination Rates in Brazil: Before, During, and After the COVID-19 Pandemic.** 2023. Completion work of the Pharmacy-Biochemistry Course at the School of Pharmaceutical Sciences of the University of Sao Paulo, 2023.

Key-words: Tuberculosis, COVID-19, Brazil, Pandemic Impact, Public Health Trends

INTRODUCTION: Tuberculosis (TB) is a deadly infectious disease caused by *Mycobacterium tuberculosis*, affecting millions of people worldwide. Despite significant progress in TB control, the COVID-19 pandemic introduced new challenges, including disruptions in healthcare services. This study examines the impact of the pandemic on TB incidents, mortality, and vaccination rates in Brazil, shedding light on critical public health trends. **OBJECT:** The objective of this study is to analyze trends in TB incidents, mortality, and vaccination rates in Brazil before, during, and after the COVID-19 pandemic. Using publicly available up-to-date demographic data, the research aims to understand how the pandemic affected TB control efforts and to provide insights into the broader public health context. **MATERIALS AND METHODS:** This descriptive ecological study analyzed data from January 2011 to December 2022, drawing from public domain databases provided by the Department of Informatics of the Unified Health System (DATASUS) and the Brazilian Institute of Geography and Statistics (IBGE). Key data points include BCG vaccination coverage, TB incidents, TB-related deaths, and population size. Furthermore, Microsoft Office Excel software was used for data management and analysis. A descriptive analysis of the variables was carried out through graphical plots. **RESULTS:** BCG vaccination coverage in Brazil declined from 2011 to 2018 but drastically dropped from 2018 to 2021. A slight recovery was observed in 2022, but concerns remain about falling vaccination rates. TB incidence remained stable until 2016, followed by a significant increase until 2019. There was a noticeable decrease in TB incidence in 2020, followed by a sharp increase in 2021 and 2022, reaching a six-figure number of new cases in 2022. TB mortality rates gradually decreased until 2020 but surged significantly in 2021, with approximately 9% more deaths compared to the previous year. **CONCLUSION:** The study reveals the profound impact of the COVID-19 pandemic on TB control efforts in Brazil. The drop in TB notifications during the pandemic indicates potential delays in diagnosis and treatment, and prevention is vital to protect public health and work towards global TB elimination. Further research is needed to explore specific factors contributing to the changes in TB incidence and mortality during the pandemic and to develop targeted strategies for mitigating such crises' impact on TB control. In the face of evolving public health challenges, a continued commitment to TB control is essential to ensure the health and well-being of the population in Brazil and globally.



RESUMO

MA, G.H. **Comparando tendências de mortalidade por tuberculose e taxas de vacinação no Brasil: antes, durante e depois da pandemia de COVID-19.** 2023. Trabalho de Conclusão de Curso de Farmácia-Bioquímica – Faculdade de Ciências Farmacêuticas – Universidade de São Paulo, São Paulo, 2023.

Palavras-chave: Tuberculose, COVID-19, Brasil, Impacto da Pandemia, Tendências em Saúde Pública.

INTRODUÇÃO: A tuberculose (TB) é uma doença infecciosa mortal causada pelo *Mycobacterium tuberculosis*, afetando milhões de pessoas em todo o mundo. Apesar dos progressos significativos no controle da TB, a pandemia de COVID-19 introduziu novos desafios, incluindo perturbações nos serviços de saúde. Este estudo examina o impacto da pandemia nos incidentes de TB, mortalidade e taxas de vacinação no Brasil, lançando luz sobre tendências críticas de saúde pública.

OBJETIVO: O objetivo deste estudo é analisar tendências nos incidentes de TB, mortalidade e taxas de vacinação no Brasil antes, durante e depois da pandemia de COVID-19. Utilizando dados demográficos atualizados publicamente disponíveis, a investigação visa compreender como a pandemia afetou os esforços de controle da TB e fornecer conhecimentos sobre o contexto mais amplo da saúde pública.

MATERIAIS E MÉTODOS: Este estudo ecológico descritivo analisou dados de janeiro de 2011 a dezembro de 2022, provenientes de bases de dados de domínio público disponibilizadas pelo Departamento de Informática do Sistema Único de Saúde (DATASUS) e pelo Instituto Brasileiro de Geografia e Estatística (IBGE). Os principais dados incluem a cobertura da vacinação BCG, incidentes de TB, mortes relacionadas com TB e tamanho da população. Além disso, foi utilizado o software Microsoft Office Excel para gerenciamento e análise de dados. Foi realizada análise descritiva das variáveis por meio de gráficos.

RESULTADOS: A cobertura da vacinação BCG no Brasil diminuiu de 2011 a 2018, mas caiu drasticamente de 2018 a 2021. Uma ligeira recuperação foi observada em 2022, mas permanecem preocupações sobre a queda nas taxas de vacinação. A incidência de TB permaneceu estável até 2016, seguida de um aumento significativo até 2016, seguida de um aumento significativo até 2019. Houve uma diminuição notável na incidência de TB em 2020, seguida de um aumento acentuado em 2021 e 2022, atingindo um número de seis dígitos de novos casos em 2022. Mortalidade por TB as taxas diminuíram gradualmente até 2020, mas aumentaram significativamente em 2021, com aproximadamente 9% mais mortes em comparação com o ano anterior.

CONCLUSÃO: O estudo revela o profundo impacto da pandemia de COVID-19 nos esforços de controle da TB no Brasil. A queda nas notificações de TB durante a pandemia indica potenciais atrasos no diagnóstico e tratamento, e a prevenção é vital para proteger a saúde pública e trabalhar no sentido da eliminação global da TB. É necessária mais investigação para explorar fatores específicos que contribuem para as mudanças na incidência e mortalidade da TB durante a pandemia e para desenvolver estratégias específicas para mitigar o impacto dessas crises no controle da TB.

Diante da evolução dos desafios de saúde pública, um compromisso contínuo com o controle da TB é essencial para garantir a saúde e o bem-estar da população no Brasil e no mundo.



1. Introduction

Tuberculosis (TB) is one of the deadliest infectious and communicable diseases worldwide, which affects, primarily, the lungs and other organs. TB is caused by *Mycobacterium tuberculosis* bacteria, which is also known as Bacilo de Koch. The transmission is mainly between people by droplet infection when small drops of saliva, which hold infectious agents, are expelled by the sick and are aspirated by other individuals. (1) According to the World Health Organization (WHO), around 10.6 million individuals worldwide were diagnosed with TB in 2021, which is equal to a rate of 134 cases per 100,000 people, whereas in Brazil around 104,000 individuals were diagnosed, which is equal to a rate of 48 per 100,000 people. Moreover, only in 2021, there were an estimated 1.6 million deaths from TB worldwide, and until the COVID-19 pandemic, TB remained the leading cause of death from a single infectious agent. (2)

Bacillus Calmette-Guerin (BCG), a live attenuated strain of *Mycobacterium bovis* (*M. bovis* is part of the *M. tuberculosis* complex and responsible for cattle TB), is the first TB vaccine and was developed a century ago, in 1921 in exact. (3) In fact, this medicine has a wide range of usage, however, this is the only vaccine used to prevent TB. For the prevention of TB, the vaccine is administered through a single intradermal injection after birth, mostly before completing a year.

In efforts to control TB, in 2014, the End TB Strategy was created by the WHO and approved by the Sixty-seventh World Health Assembly. This strategy aims to eliminate TB worldwide, with no deaths or suffering caused by the disease, by setting a goal to completely eradicate the global TB epidemic by 2035, aiming to reduce TB patients by 90% and TB-related deaths by 95%. (4) In addition, the average annual decline in global TB incidence rate was about 2% in 2015 and the primary goal is to push down the rate to 10% by 2025, through the optimized use of current and new tools. (4)



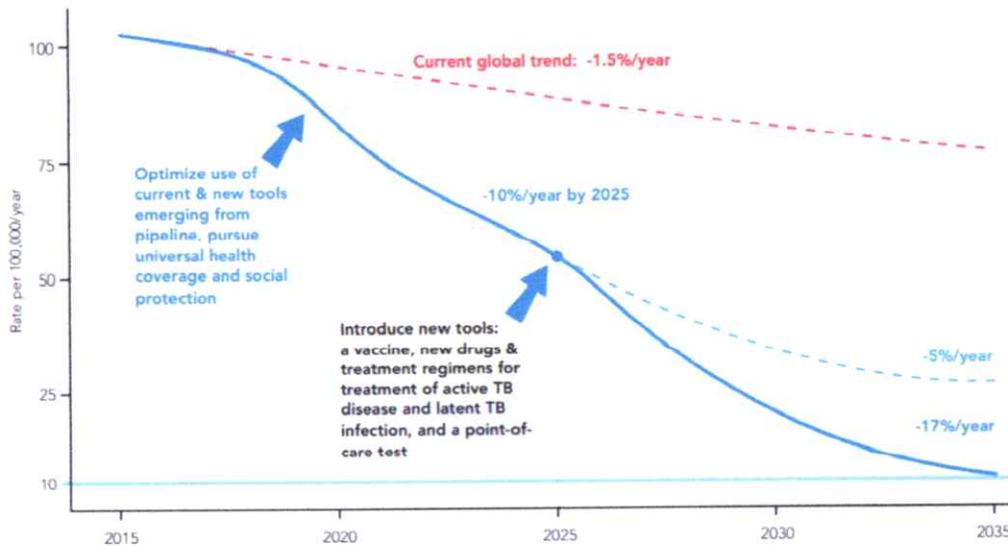


Figure 1: Desired decline in global TB incidence rates to reach the 2035 targets.

Source: The end TB strategy. Available from:

<https://www.who.int/publications/i/item/WHO-HTM-TB-2015.19>

The Coronavirus disease (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus2 (SARS-CoV-2 virus). Detecting its first case in China in December 2019, the disease spread exponentially across the world, which led WHO to characterize the outbreak as a pandemic on 11 March 2020. (5) Since then, as of today, September 10, 2023, there have been 770,437,327 confirmed cumulative cases of COVID-19, with 6,956,900 confirmed cumulative deaths globally. And as a preventive effort to control COVID-19, a total of 13,500,122,024 vaccine doses have been administered. (6)

Since COVID-19 and TB have similar symptoms, including fever and respiratory symptoms, these clinical similarities have had a damaging impact on access to TB diagnosis, treatment, and prevention. As consequence, progress made in the years up to 2019 has slowed, stalled, or reversed, and global TB targets are off track. (7) (8) The study relating the notification rate of COVID-19 is correlated with low rates of notification and death from TB. (9)

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According to data released by the WHO, among the countries where 84% of TB cases are concentrated, there was a 21% drop in TB notifications from 2019 to 2020, and in Brazil the number decreased by 10.9% (10)

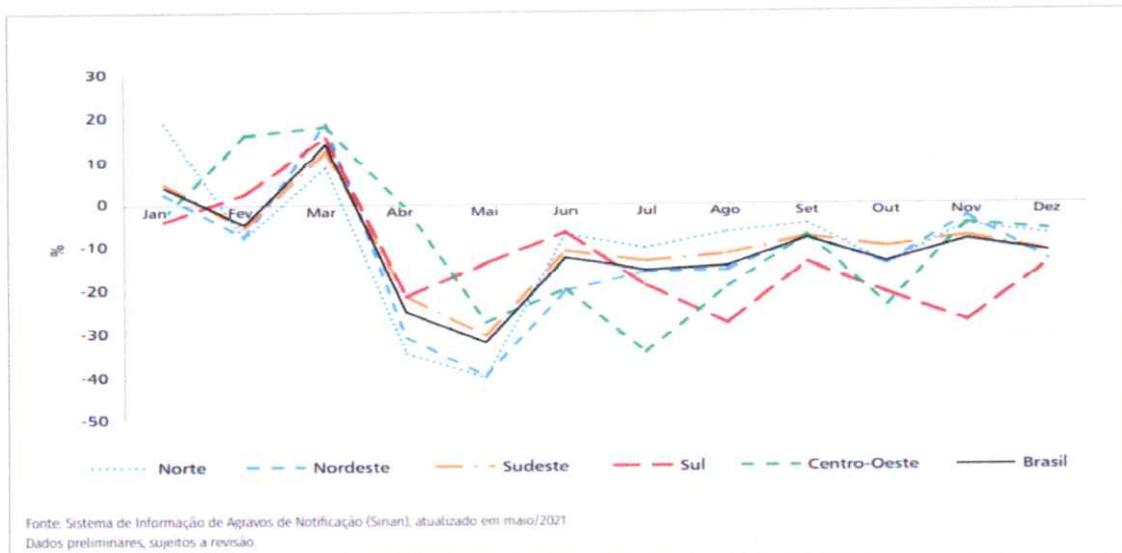


Figure 2: Percentage difference between the number of tuberculosis notifications, in Brazil and regions, comparing the years 2019 and 2020.

Source: BRASIL. Ministério da Saúde. Secretaria de Vigilância em Saúde Boletim Epidemiológico 22-Indicadores operacionais da tuberculose no Brasil e a COVID-19: Análise comparativa dos anos de 2019 e 2020. 4p. 2021 Available online: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/edicoes/2021/boletim_epidemiologico_svs_22-2.pdf

These findings suggest that it is possible that the TB data is hidden by the critical COVID-19 pandemic, and global and national TB strategies have fallen back and are at risk in many countries.

2. OBJECTIVES

The objective of this study is to examine the trends in tuberculosis incidents, mortality, and vaccination rates in Brazil before, during, and after the COVID-19 pandemic, using the XIII General Census of Brazil from IBGE and the public domain database TABNET. The study aims to examine the impact of the COVID-19 pandemic on TB control efforts in Brazil and to identify any changes in TB mortality and vaccination rates that may have occurred as a result. Moreover, by performing this ecological research, the study can provide information on how much the COVID-19 pandemic pushed back the public health policies regarding tuberculosis. Overall, the objective of the study is to contribute to the knowledge and understanding of TB control efforts in Brazil, particularly in the context of the COVID-19 pandemic.

3. MATERIALS AND METHODS

3.1 Study Design and Strategy

The research for this descriptive ecological study has been performed through 2 public domain databases to analyze and forecast the trends regarding tuberculosis disease from January 2011 to December 2022. It consists of all information, including BCG vaccination number (11), BCG vaccination coverage (12), tuberculosis incident (13), death notifications (14), and the size of the population, during the period. Data were collected from the databases of the Department of Informatics of the Unified Health System (DATASUS) of the Ministry of Health and the Brazilian Institute of Geography and Statistics (IBGE).



3.2 Data for Analysis

The data referring to the number of BCG vaccinations and notifications were based on the public domain database TABNET, which is an easy-to-use data search tool developed by DATASUS for public use of health information within the scope of the Unified Health System (SUS). The figures shown through TABNET are derived from related public domain databases, the National Immunization Program Information System, Disease Notification System (SINAN), and Mortality Information System (SIM).

The number of populations used for the study derived from the results of the XIII General Census of Brazil, also known as Census 2022 (Censo 2022) (16), a national periodic demographic research operated by IBGE. The population from 2011 to 2021 (marked as * in Table 1) has been estimated using the two latest demographic researches, Censo 2010 and Censo 2022, which gave a result of 190,755,799 residents in 2010 and 203,062,512 in 2022. The figures were calculated assuming that there has been a regular increase between those years.

Moreover, the figures for New Case Incidents and Death Incidents were computed per 100,000 habitats. The summary of the data is described in Table 1 and overall data collection has been revised by September 14, 2023.

This project only involves the use of data made available by the Ministry of Health, which are in the public domain. Following the Brazilian regulation, this study does not require assessment and approval by the Research Ethics Committee, as stated by the resolution of the National Health Council n. 510, April 07, 2016. (16)

Year	Vaccination Doses	Vaccinal Coverage (%)	New Cases (NC)	Deaths (D)	Brazil Population	NC Incidents	D Incidents
2011	3,108,763	107.94	87,813	4,563	*191,781,358	45.79	2.38
2012	3,044,007	105.69	86,183	4,421	*192,806,918	44.70	2.29
2013	3,129,807	107.54	86,208	4,617	*193,832,477	44.48	2.38
2014	3,116,296	107.28	85,213	4,467	*194,858,037	43.73	2.29
2015	3,049,524	105.08	85,452	4,610	*195,883,596	43.62	2.35
2016	2,843,993	95.55	86,207	4,483	*196,909,156	43.78	2.28
2017	2,915,403	97.98	90,594	4,614	*197,934,715	45.77	2.33
2018	2,846,012	99.72	94,735	4,531	*198,960,274	47.62	2.28
2019	2,532,544	86.67	96,184	4,532	*199,985,834	48.10	2.27
2020	2,254,471	77.14	86,414	4,569	*201,011,393	42.99	2.27
2021	2,135,015	74.97	91,776	5,120	*202,036,953	45.43	2.53
2022	2,458,339	90.06	101,806		203,062,512	50.14	
Total	33,434,174		1,078,585	50,527			

Table 1: Demographic characteristics concerning tuberculosis, Coverage and Incidents in 100k

3.3 Statistical Analysis

Microsoft Office Excel software was used for data management and analysis. A descriptive analysis of the variables was carried out through graphical plots.

4. RESULTS

During the 12 years studied, 1,078,585 cases of tuberculosis were reported in Brazil. According to the available data, more than 50,000 people died of tuberculosis in Brazil from 2011 to 2021.

Figure 3 demonstrates the trends of BCG vaccination throughout the research period. From 2011 to 2018, even with the slight constant reduction in doses applied and vaccinal coverage (from 107.94% in 2011 to 99.72% in 2018), including a sudden decrease of approximately 10% from 2015 to 2016 (105.08% to 95.55%) and then followed by slight increases until 2018 reaching 99.72%, the coefficient of the vaccinal coverage per 100,000 children below 1-year-old has maintained above 95%. Then, from 2018, both the number of BCG doses applied in new-born and the vaccinal coverage level started to drop drastically reaching their lowest in 2021 (99.72% in 2018, 86.67% in 2019, 77.14% in 2020, and 74.97% in 2021), an average decline of approximately 8% as the year went on. Yet, there was some recovery of figures in 2022 (90.06%), which was about a 15% increase compared to 2021. (Figure 3)

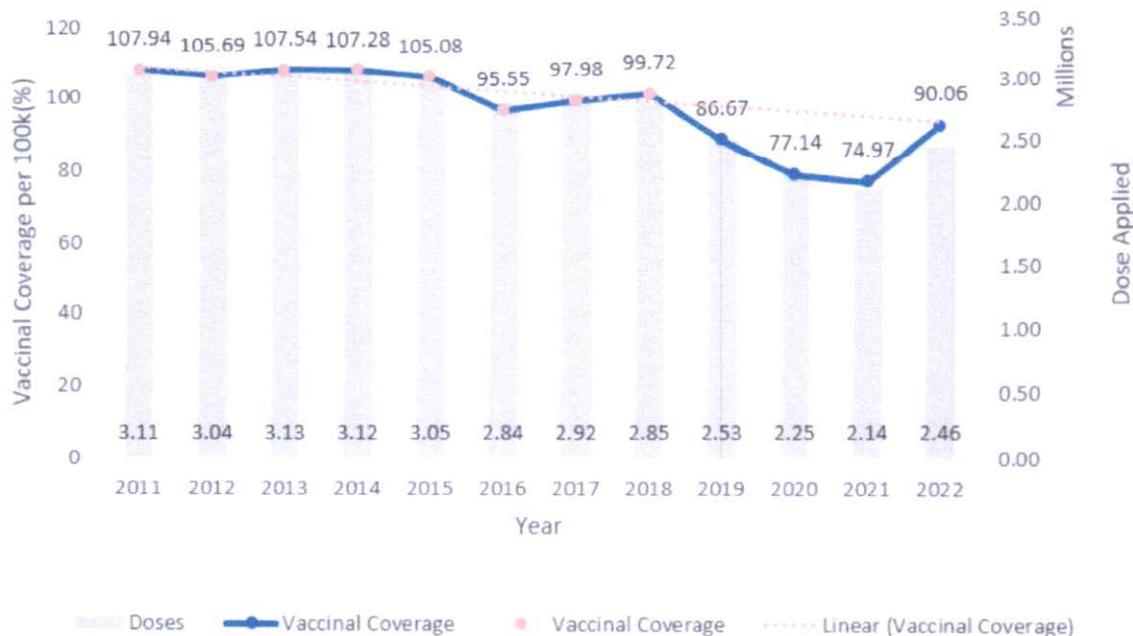


Figure 3: BCG vaccination trend from 2011 to 2022

There also was a slight constant decrease in the incidence of tuberculosis, however, only until 2016 (45.49 cases/100,000 inhabitants in 2011 to 43.78 cases/100,000 inhabitants in 2015). Then, from that year on, there was a high

increase in new case notifications until 2019 (48.10 cases/100,000 inhabitants in 2019), followed by an abrupt fall by 2020 (42.99 cases/100,000 inhabitants). From then on, there has been even greater regular elevation of the new TB notification until 2022 (42.99 in 2020, 45.48 in 2021, and 50.14 cases/100,000 inhabitants in 2022), reaching the first 6-figure cases (101,810 new incidents in 2022) in more than 10 years. (Figure 4)

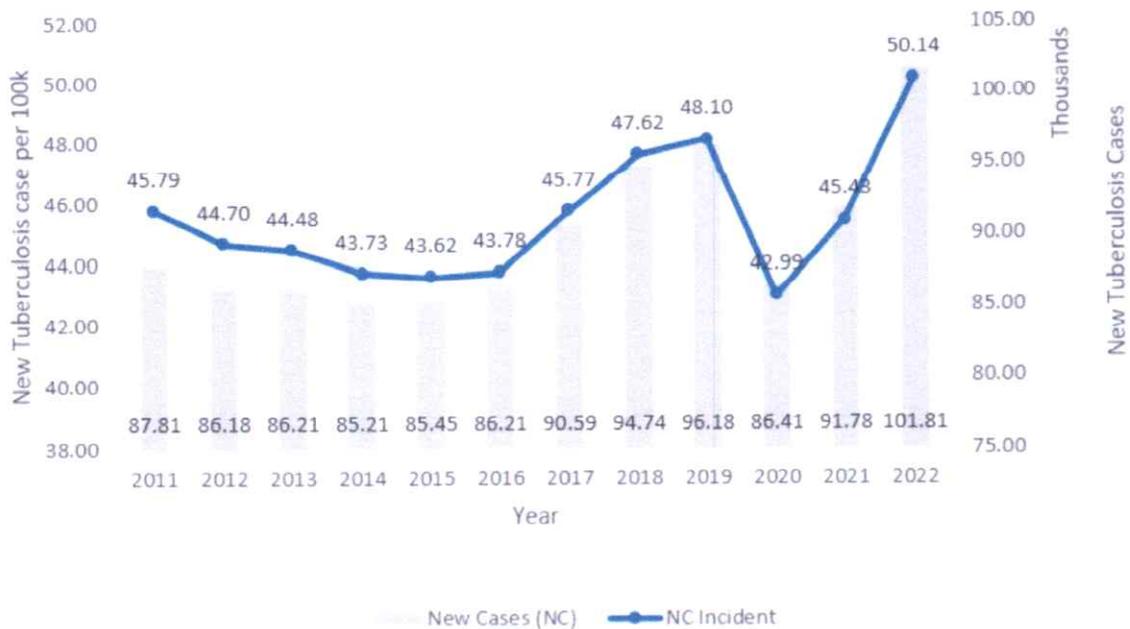


Figure 4: Tuberculosis incident trend from 2011 to 2022

Over time, in Brazil, the coefficient of mortality by TB has been decreasing slowly until 2020, from 2.38 deaths per 100,000 inhabitants in 2011 to 2.27 deaths per 100,000 inhabitants in 2020. However, this nature of reduction came to an end in 2021 registering more than 5,000 deaths by TB, which is 2.53 deaths per 100,000 inhabitants. This is approximately 9% more deaths in 2021 than compared to the previous year.



Figure 5: Number of deaths by TB and its count per 100,000 inhabitants

5. DISCUSSION

The results of the present study show that there were recognizable changes in the vaccination, incident, and mortality rates associated with tuberculosis in Brazil, around the time of the COVID-19 pandemic.

The decline in reported cases and decreased testing for TB diagnosis in Brazil in the aftermath of the COVID-19 pandemic can be ascribed to a variety of factors. These include delays in inputting data into the information system, reduced healthcare services, the reassignment of healthcare personnel for COVID-related activities, diminished demand for healthcare services among symptomatic individuals, and a decrease in the administration of laboratory tests. Additionally, the drop in TB notifications during 2020 and 2021 suggests an increase in the number of undiagnosed and untreated TB cases. Consequently, an immediate rise in TB-related deaths was anticipated in the initial year of the COVID-19 pandemic,

but this only became evident in Brazil 2021. This phenomenon might be attributed to an overestimation of the surveillance system's ability to accurately classify TB tests during the pandemic and whether such causes of death were adequately documented on death certificates, particularly when COVID-19 took precedence. (17)

Moreover, when we exclude the years impacted by the pandemic from consideration, we can observe a continuous decline in TB diagnosis testing, approximately -1.6% each year, and a significant uptick in the occurrence of TB cases, approximately 1.278 per 100,000 inhabitants of TB incident increase. Consequently, TB mortality is expected to increase significantly in response to these trends.

Figure 6 and Figure 7 are identical research published by the Secretariat of Health and Environment Surveillance (SVS) of the Ministry of Health. However, it is important to note that these numbers differ from those of Figure 4 because they do not correspond to the same data extraction periods. It is noted in DATASUS that the data for Figure 4 was updated in April 2023, and obtained in September 2023, which is after the publication of the report card. Additionally, Figures 5 and 7 share the same method and source, however, the numbers are unlike due to the source of the population size. The population data for Figure 4 has been derived from the most recent demographic study, the Census 2022 conducted by IBGE. In contrast, the population data for Figure 7 was obtained from the 2018 IBGE estimates in the "Projection of the Populations of Brazil and Federation Units by sex and simple age: 2010-2060". (18)



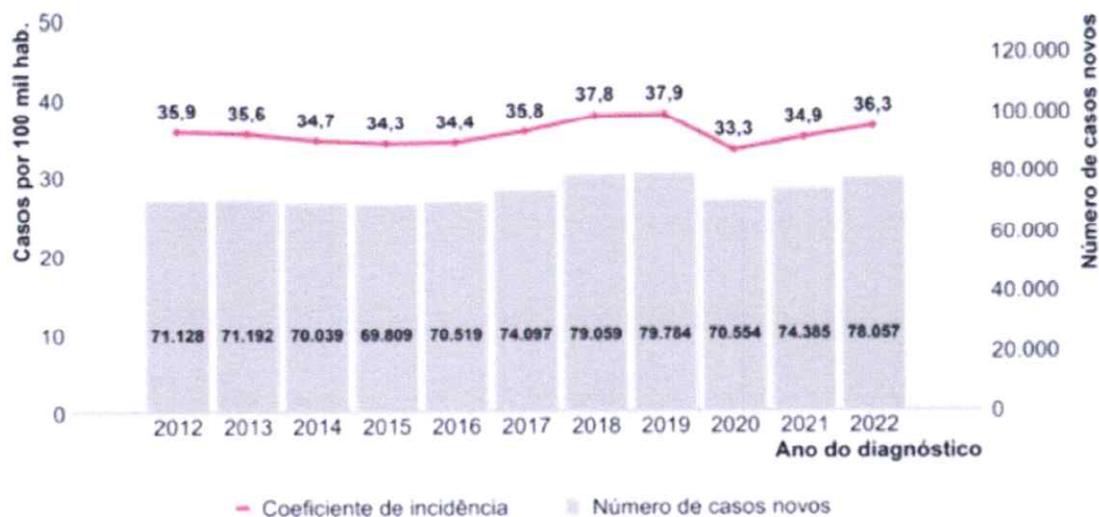


Figure 6: Incidence coefficient (cases per 100 thousand inhabitants) and number of new cases of tuberculosis. Brazil, 2012 to 2022. Source: Boletim Epidemiológico da Tuberculose (17)

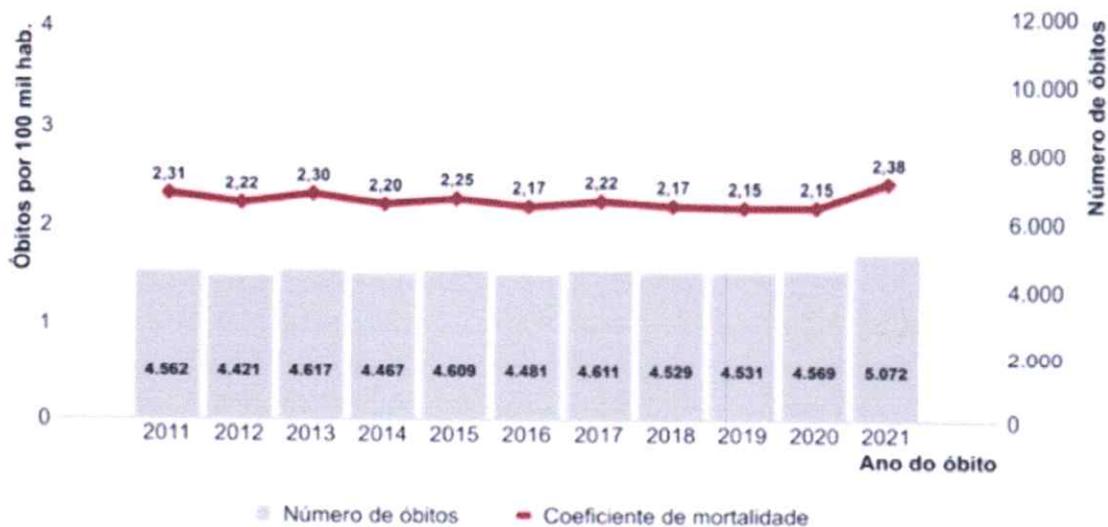


Figure 7: Tuberculosis mortality rate (deaths per 100 thousand inhabitants). Brazil, 2011 to 2021. Source: Boletim Epidemiológico da Tuberculose (17)

6. CONCLUSIONS

This study provides a comprehensive analysis of tuberculosis (TB) incidents, mortality, and vaccination rates in Brazil before, during, and after the COVID-19 pandemic. The findings reveal a dynamic landscape marked by significant shifts in public health indicators.

The impact of the COVID-19 pandemic on TB control efforts in Brazil is evident. The decline in reported TB cases and reduced testing during the pandemic raised concerns about undiagnosed and untreated TB cases, potentially leading to delayed treatment and unfavorable patient outcomes. The disruption of healthcare services and the reassignment of healthcare personnel for COVID-related activities played a role in this phenomenon.

Vaccination coverage, particularly for BCG, showed a troubling decline, coinciding with an increase in TB incidence. Ensuring adequate vaccination coverage remains crucial for TB prevention, and efforts should be made to improve coverage rates.

When considering the years unaffected by the pandemic, a consistent decline in TB testing and a significant uptick in TB incidence was observed. This suggests that TB mortality may rise in response to these trends if not addressed promptly.

Data variability between different sources and extraction periods underscores the importance of data accuracy and consistency in drawing meaningful conclusions.

Overall, this study highlights the importance of maintaining TB control efforts even during global health emergencies. The COVID-19 pandemic has shown how clinical similarities between diseases can impact diagnosis and treatment,



potentially causing setbacks in TB control. Strategies for TB diagnosis, treatment, and prevention should be strengthened to safeguard public health and work towards the global goal of eliminating TB.

Further research is warranted to delve deeper into the specific factors contributing to the changes in TB incidence and mortality during the pandemic and to develop targeted strategies for mitigating the impact of such crises on TB control.

In the face of evolving public health challenges, a continued commitment to TB control efforts is essential to ensure the health and well-being of the population in Brazil and around the world.



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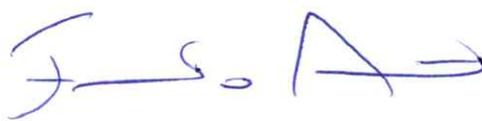
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ANEXOS

Data e assinatura do aluno(a)

SP 16/10/2023



Data e assinatura do orientador(a)

S.O. 16/10/2023

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