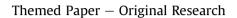
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Leprosy in Brazil: an analysis of the Global Burden of Disease estimates between 1990 and 2019



RSPH

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ABSTRACT

Objective: To analyze the occurrence of leprosy in Brazil and its states between 1990 and 2019, according to Global Burden of Disease (GBD) estimates, and its correlation with development status. *Study design:* A descriptive and analytical ecological epidemiological study.

Methods: Rates of incidence, prevalence, and years lived with disability (YLD) due to leprosy, standardized by age, per 100,000 inhabitants, were analyzed. The trend analysis consisted of the joinpoint regression model and the average annual percentage change. The correlation between the incidence rate and the sociodemographic index (SDI) was investigated (Spearman test) at a 5% significance level. Incidence, prevalence and YLD rates were presented by country's states, sex, and age.

Results: There was an average percentage decrease of -1.1% per year (P < 0.001) in the incidence rate in the country and, between 1990 and 2019, a decline from 4.8 to 3.5 per 100,000 inhabitants; prevalence from 26.1 to 22.2, and YLD from 1.1 to 1.0. The incidence rate was higher among men and the elderly. Maranhão (7.0 in 1990; 4.2 in 2019), Alagoas (6.6 in 1990; 4.1 in 2019), Acre (6.1 in 1990; 4.0 in 2019), Mato Grosso (5.2 in 1990 and 3.7 in 2019), and Mato Grosso do Sul (4.8 in 1990 and 3.7 in 2019) presented the highest incidence rates. A negative correlation was observed between SDI levels and leprosy incidence rates in 1990 (R = -0.71; P < 0.0001) and 2019 (R = -0.81; P < 0.0001).

Conclusions: Despite the decrease in the rates of leprosy incidence, prevalence, and YLDs over the analyzed period, Brazil has a long way towards achieving its eradication. The greater burden of the disease in males stands out. The estimated risk of the disease was higher in the states with the lowest SDI levels. Therefore, interventions must consider the heterogeneity of the disease burden geographically and between sociodemographic groups.

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Introduction

Leprosy is a neglected tropical disease caused by *Mycobacterium leprae*. It primarily affects the skin and progresses to peripheral neuropathy, with potential long-term disability. Stigma and discrimination are associated with leprosy, especially when visible physical disabilities are present.^{1–3}

The 2030 Agenda for Sustainable Development addresses all neglected tropical diseases.^{4,5} The Sustainable Development Goals (SDGs), especially SDG-03 (health and well-being), SDG-10

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(reduced inequalities), and SDG-17 (partnerships and means of implementation) have great potential to achieve the goals of the Global Leprosy Strategy 2021–2030 – 'Towards zero leprosy'.⁶ This strategy, seeking to drive rapid and sustainable progress in all leprosy-endemic countries, combines the WHO Roadmap for Neglected Tropical Diseases 2021–2030² with the goals of Agenda 2030.^{4,5} It also brings together countries with different contexts and levels of endemicity for leprosy, into two groups of global goals for 2030: (i) 120 countries with an interruption of transmission (zero new autochthonous cases) and (ii) other countries must contribute to a 70% reduction, by 2030, in the annual number of new detected cases, 90% of the rate (per million inhabitants) of new cases with grade 2 physical disability, and 90% of the rate (per million children) of new cases in children.⁷

Brazil is among the global priority countries for leprosy, comprising 23 nations with the highest leprosy burdens.⁸ From 2011 to 2021, Brazil ranked second in the number of newly detected cases, following India and preceding Indonesia. In 2021, Brazil accounted for nearly 92% (18,318 out of 19,826) of the total number of new cases detected in the Americas.⁶

The Brazilian Ministry of Health (MS), in recent years, has promoted actions to increase the detection of new cases, prevent disabilities, and strengthen the leprosy surveillance system, integrating it with health care actions.⁹ In view of the above, the present study aimed to analyze the burden of leprosy in Brazil and its states, based on estimates from the Global Burden of Disease (GBD) study between 1990 and 2019 and its correlation with the sociodemographic index (SDI).

Methods

Study design

This epidemiological, descriptive and analytical ecological study examines the Global Burden of Disease (GBD) morbidity metrics for leprosy in Brazil from 1990 to 2019. The analysis is stratified by age groups, sex, and geographic distribution across the country. The political-administrative division of Brazil into Federative Units and Regions is illustrated in Supplementary Fig. 1.

Data sources and indicators

This study used data from GBD 2019, coordinated by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington. The GBD produces estimates of morbidity and mortality for specific causes, on exposure to risk factors, and for various health indicators in time series, beginning from 1990, by age, sex, and country, including subnational units of some countries, such as Brazil, enabling comparability in time and space. It is important to note that the GBD makes use of data sources available in all countries and applies methodologies for adjustment, standardization, and validation of estimates. More details on GBD are available in other publications.^{10–12}

The GBD uses data sources on leprosy available around the world and from each specific country to calculate its estimates. The sources used are described on the following website: https://ghdx. healthdata.org/gbd-2019/data-input-sources. Regarding Brazil, the GBD prepares estimates based on data from various years of the Notifiable Diseases Information System (*Sistema de Informação de Agravos de Notificação* – SINAN), a national system for reporting diseases and illnesses, as well as mandatory public health events.¹³ Additionally, the Health Survey of the Municipality of São Paulo (ISA Capital) is also utilized.

In the present study, three morbidity metrics were used to characterize the burden of leprosy: incidence, prevalence, and Years Lived with Disability (YLD) rates, per 100,000 inhabitants and age standardized. The incidence rate was considered a proxy for the detection rate of new cases. The YLD metric can also be described as years lived in suboptimal health. This metric results from multiplying the number of individuals who present this outcome by the weight of the disability of a given sequelae. Disability weights, which reflect the severity of the health loss associated with the outcome, are defined through surveys with the general public and range from 0 (equivalent to a state of full health) to 1 (equivalent to death).¹²

Another GBD metric used in this study was the sociodemographic index (SDI), which identifies, on a scale of 0–1, where countries or smaller geographic areas, such as Brazil's Federative Units are located in the development spectrum. A site with an SDI of 0 would have a theoretical minimum level of health-relevant development, while a site with an SDI of 1 would have a theoretical maximum level. The SDI was prepared by the GBD based on three measures: i) per capita income; ii) average years of schooling from the age of 15; and iii) total fertility rate (TFR) for women under 25 years of age. For example, a higher SDI value will be attributed to a country or location with higher per capita income, higher average years of schooling, and lower TFR when compared to other countries.¹⁴

Data analysis

To analyze the trend of the leprosy incidence rate in Brazil from 1990 to 2019, the joinpoint regression model was used, using the Joinpoint software (version 4.9.1.0). The joinpoint analysis identifies the times at which the trend changes and estimates the annual percentage change (APC)¹⁵ for each segment of time. The average annual percentage change (AAPC) in incidence rates was calculated to identify the trend over the entire period studied. AAPC is the weighted average of the slopes of the regression line, with different weights according to the length of each segment over the entire range from 1990 to 2019. An increase or decrease in the trend is significant when different than zero ($P \le 0.05$). During the period studied, the incidence rates were also analyzed according to sex and age groups.

Furthermore, in those years, the existence of a correlation between the leprosy incidence rate and the SDI, according to the country's states, was analyzed using Spearman's correlation, considering a significance level of 5%.¹⁶ For 1990 and 2019, the agestandardized incidence, prevalence, and YLD rates per 100,000 inhabitants were presented according to the country's states.

The data used in this study were obtained from IHME's Global Health Data Exchange (GHDx) and are available at the following electronic addresses: https://ghdx.healthdata.org/gbd-2019 (morbidity metrics) and https://ghdx.healthdata.org/record/ihmedata/gbd-2019-socio-demographic-index-sdi-1950-2019 (SDI).

Ethical aspects

This study meets the requirements of Resolution 466/2012, of the Brazilian National Health Council,¹⁷ as the data used come from secondary databases in the public domain and do not allow for the identification of individuals.

Results

In Brazil, over the 30-year period (1990–2019), leprosy incidence rates showed a decreasing trend, with an average annual percentage change drop of -1.1% per year (P < 0.001) (Fig. 1). Supplementary Table 1 provides a detailed overview of the trends in leprosy incidence rates by sex, as determined by the joinpoint

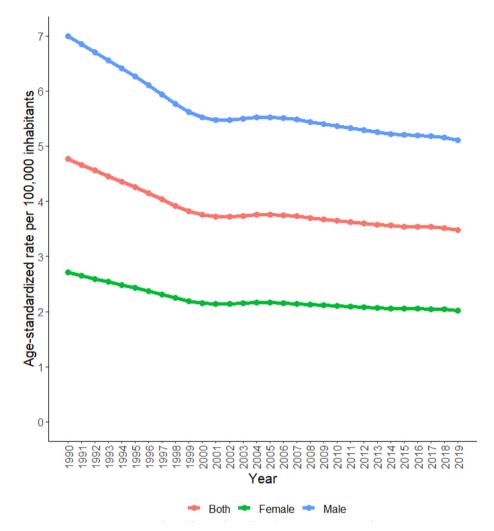


Fig. 1. Leprosy incidence rates according to sex, Brazil, 1990–2019. Source: produced by authors based on GBD 2019 estimates. Note: average annual percentage reductions in incidence rates (P < 0.001): both sexes (-1.1%); female (-1.1); male (-1.1).

analysis for the period 1990–2019. Similar patterns were observed for both males and females. The most significant downward trend in rates was noted until 2000 (Supplementary Table 1).

In Table 1, estimates of the three morbidity metrics used to characterize the burden of leprosy in Brazil and respective percentages of decrease between 1990 and 2019 are presented. The age-standardized incidence rate declined, respectively, from 4.8 to 3.5 per 100,000 inhabitants, prevalence decreased from 26.1 to 22.2 per 100,000 inhabitants, and the rate of YLDs went from 1.1 to 1.0 per 100,000 inhabitants. During this period, the percent changes for these metrics were, respectively: -26.9%; -15.0%; and -7.8%.

The burden of leprosy was substantially higher among males: the relative risk, prevalence ratio, and YLD ratio were more than double the values estimated for females in 1990 and 2019 (Table 1). In these years, new cases of leprosy were estimated in all age groups from 5 years of age onwards. The incidence of leprosy in children and adolescents between 5 and 14 years of age stands out (Fig. 2).

Supplementary Fig. 2 illustrates the spatial distribution of incidence, prevalence, and YLD rates of leprosy across Brazil's Federative Units. Fig. 3 ranks these metrics using a color scale that transitions from the darkest blue (indicating the lowest value) to the darkest red (indicating the highest value). The distribution of age-standardized leprosy incidence rates per 100,000 inhabitants shows the highest rates in the North, Northeast, and Midwest regions (Supplementary Fig. 2). It is noteworthy that the states of Maranhão (7.0 in 1990; 4.2 in 2019) and Alagoas (6.6 in 1990; 4.1 in 2019) in the Northeast Region, and Acre (6.1 in 1990; 4.0 in 2019) in the North Region, in this order, presented the three highest rates in the country in both evaluated years. In the Midwest region of the country, the state of Mato Grosso showed the highest incidence rates (5.2 in 1990 and 3.7 in 2019), followed by Mato Grosso do Sul (4.8 and 3.7) and Goiás (4.7 and 3.5), while the Federal District showed the lowest rates in the country, both in 1990 (3.9) and in 2019 (2.8) (Fig. 3).

Prevalence rates were also higher in the North, Northeast, and Midwest regions (Supplementary Fig. 2). In 1990 and 2019, the highest rates were estimated for Maranhão (58.6 and 33.9, respectively), Alagoas (50.0 and 31.4), and Acre (42.1 and 29.3). In these years, the prevalence rates in Mato Grosso, Mato Grosso do Sul, and Goiás were much higher than the rates in the Federal District, which presented the lowest rates in the country, of 17.5 and 14.5 per 100,000 inhabitants, respectively (Fig. 3).

In 1990 and 2019, YLD rates were also higher in Maranhão (3.0 and 1.7, respectively), Alagoas (2.5 and 1.6), and Acre (2.0 and 1.4) (Fig. 3). Regarding YLDs in absolute numbers, that is, the number of years lived with some level of health loss associated with leprosy,

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Table 1

Incidence, prevalence, and YLD^a rates^b for leprosy and percentage variation of these rates, according to sex, Brazil, 1990 and 2019.

Metrics	Year	Rate reduction ^c			
	1990		2019	1990×2019	
	No. of cases	Rate (95% UI) ^d	No. of cases	Rate (95% UI)	%
Incidence					
Both sexes	5601	4.8 (3.9-5.8)	8370	3.5 (2.9-4.2)	-26.9
Female	1635	2.7 (2.2-3.3)	2548	2.0 (1.7-2.5)	-25.4
Male	3966	7.0 (5.7-8.6)	5822	5.1 (4.2-6.2)	-26.9
Male/female relative risk	-	2.6	-	2.6	-
Prevalence					
Both sexes	28,452	26.1 (22.5-30.4)	53,434	22.2 (19.0-26.0)	-15.0
Female	8951	15.9 (13.6–18.7)	17,526	13.7 (11.6–16.1)	-14.3
Male	19,502	37.4 (32.2-43.4)	35,908	32.0 (27.4-37.5)	-14.5
Male/female relative risk	-	2.4	-	2.3	-
YLDs					
Both sexes	1213	1.1 (0.7–1.7)	2515	1.0 (0.7-1.5)	-7.8
Female	397	0.7 (0.5-1.0)	848	0.7 (0.4–1.0)	-7.8
Male	817	1.6 (1.0-2.3)	1667	1.5 (0.9-2.2)	-7.0
Male/female relative risk	-	2.3	-	2.1	-

^a YLDs: Years Lived with Disability.

^b Age-standardized (per 100,000 inhabitants).

^C Estimated reduction by 1–2019 rate/1990 rate, based on rates with 03 decimal places.

^d 95% UI: 95% uncertainty interval.

Source: Produced by authors based on GBD 2019 estimates

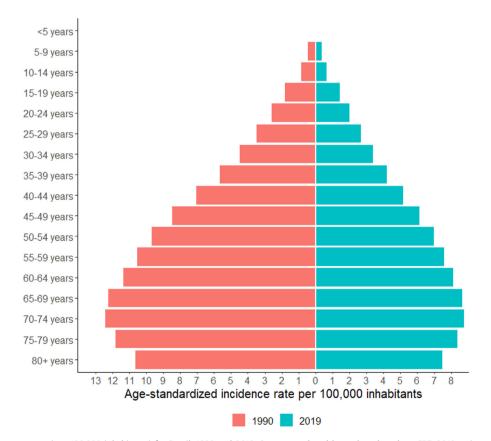


Fig. 2. Incidence rates* by age group (per 100,000 inhabitants) for Brazil, 1990 and 2019. Source: produced by authors based on GBD 2019 estimates. *Age-standardized (per 100,000 inhabitants).

including disabilities, corresponded to 1213 years in 1990 in Brazil. In 2019, this total was estimated at 2515 years (Table 1).

A strong negative correlation was observed between leprosy incidence rates and SDI levels in the Brazilian states in 1990 (R = -0.71; P < 0.0001) and 2019 (R = -0.81; P < 0.0001).

In both years, the estimated risk of the disease was higher in the states with the lowest SDI levels (Fig. 4). The states in the North, Northeast, and Midwest regions had the highest leprosy incidence rates and the lowest SDI levels in both evaluated years.

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_	1990	2019	_	1990	2019		1990	2019	
	Incidence			Prevalence			YLDs		
Brazil -	4.76	3.48		26.1	22.2		1.13	1.04	
Acre -	6.12	4.04		42.1	29.3		2.04	1.45	
Amazonas -	5.21	3.8		29.2	25.7		1.29	1.24	
Amapá -	4.44	3.83		22.5	25.6		0.92	1.23	
Pará -	5.51	4.03		33.4	28.9		1.54	1.43	
Rondônia -	5.85	3.79		35.1	25.4		1.6	1.21	
Roraima -	5.51	3.87		31.3	26.1		1.38	1.26	
Tocantins -	5.17	3.73		31.6	25.3		1.45	1.21	
Alagoas -	6.63	4.09		50	31.4		2.52	1.58	
Bahia -	5.38	3.85		33.2	27.3		1.54	1.34	
Ceará -	4.77	3.51	-	28	23.6		1.26	1.13	
Maranhão -	6.98	4.23	-	58.6	33.9		3.04	1.73	
Paraíba -	4.73	3.59		28.2	25		1.27	1.22	
Pernambuco -	5.64	3.88		35.9	27.5		1.68	1.36	
Piaui -	4.93	3.88		31.3	29		1.47	1.45	
Rio Grande do Norte	4.61	3.51	-	26.1	23.2		1.14	1.11	
Sergipe -	5.3	3.79		31.9	26.5		1.46	1.29	
Distrito Federal -	3.92	2.78		17.5	14.5		0.66	0.6	
Mato Grosso -	5.21	3.68		29.3	23.7		1.28	1.11	
Mato Grosso do Sul -	4.78	3.71		25.2	24.2		1.06	1.15	
Goiás -	4.73	3.46		25.5	21.9		1.09	1.02	
Espírito Santo -	4.64	3.4		24.2	20.8		1.02	0.96	
Minas Gerais -	3.4	4.71		24.7	21.2		1.04	0.98	
Rio de Janeiro -	4.65	3.42		22.9	20.6		0.94	0.95	
São Paulo -	4.22	3.17		19.9	18.2		0.77	0.81	
Paraná -	4.73	3.42		24.5	21.1		1.03	0.97	
Rio Grande do Sul	3.99	3.16		18.3	18.3		0.7	0.82	
Santa Catarina -	4.17	3.12		19.7	17.8		0.77	0.79	

Fig. 3. Prevalence, incidence, and YLD rates* for leprosy, Brazil and states, 1990 and 2019. Source: produced by authors based on GBD 2019 estimates. *Age-standardized (per 100,000 inhabitants). Note: the color scale transitions from the darkest blue (lowest value) to the darkest red (highest value).

Discussion

The present study highlights that, over a period of 30 years (1990–2019), the occurrence of leprosy remained high in Brazil, one of the countries with the highest burden of the disease in the world,⁶ despite the decrease in incidence, prevalence, and YLDs. Although present in all states of the country, the disease had a heterogeneous distribution, with the highest incidence rate estimates appearing in the North, Northeast, and Midwest regions. The greater burden of the disease in males and the incidence of the disease in all age groups from 5 years of age and over stood out. This epidemiological scenario maintains leprosy as a severe public health problem in the country and perpetuates the challenge of reducing the burden of this disease, as recommended by the Global Leprosy Strategy 2021–2030 – 'Towards zero leprosy'.⁷

The trend towards a significant decrease in incidence rates, from 1990 to 2019 in Brazil, was also observed in previous studies that associate such a decrease with the introduction of multidrug therapy at the beginning of the 1980s.^{18–23}

According to the metrics presented, the burden of leprosy was higher in males. Globally, the proportion of new cases among women has remained at less than 40% over the last 10 years.²³ In this context, some studies suggest the underreporting of leprosy cases in females associated with gender inequality and a greater burden of stigma, including self-stigmatization.^{24,25} The greater risk of leprosy among females, such as contacts in household clusters, especially multibacillary cases, also stood out.²⁶

The states in the North, Northeast, and Midwest regions of Brazil, which have the lowest SDIs, presented greater risks for the disease in the country in 1990 and 2019. The occurrence of leprosy, much like that of other neglected tropical diseases, is often related to worse socioeconomic conditions.^{27,28} Furthermore, the burden of disease among the population also contributes to the rise in poverty.^{2,7,29,30} The Federal District has the highest SDI in Brazil, which partly explains the lower values of its morbidity metrics for leprosy.

In the evaluated years, the incidence of leprosy was observed in all age groups of 5 years of age and over and proved to be higher in elderly individuals. The detection of new cases in children and

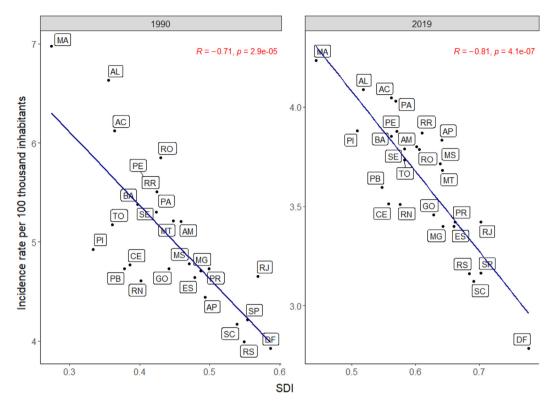


Fig. 4. Scatter diagram and Spearman correlation analysis between leprosy incidence rates and the sociodemographic index (SDI), in the Brazilian states, 1990 and 2019. Source: produced by authors based on GBD 2019 estimates. Note: • North region: seven states, Acre (AC), Amapá (AP), Amazonas (AM), Pará (PA), Rondônia (RO), Roraima (RR) and Tocantins (TO); • Northeast region: nine states, Alagoas (AL), Bahia (BA), Ceará (CE), Maranhão (MA), Paraíba (PB), Pernambuco (PE), Piauí (PI), Rio Grande do Norte (RN) and Sergipe (SE); • Southeast region: four states, Espírito Santo (ES), Minas Gerais (MG), Rio de Janeiro (RJ) and São Paulo (SP); • South region: three states, Paraná (PR), Rio Grande do Sul (RS) and Santa Catarina (SC); • Midwest region: the Federal District (DF) and the states of Goiás (GO), Mato Grosso (MT) and Mato Grosso do Sul (MS).

adolescents (<15 years of age) indicates early exposure of the population to the bacillus, which is associated with a high prevalence in the general population. Therefore, the incidence in children under 15 years of age is a robust indicator of high transmission and insufficient quality of control programs.^{31–37} It is worth adding that global efforts to improve diagnostic and therapeutic techniques have focused on leprosy in adults, while childhood leprosy has still been relatively neglected.³⁸

The estimates presented herein highlight the number of years lived with worse health (YLDs), which, in the case of people affected by leprosy, can represent different degrees of disability. Leprosy is a chronic disease with long-term biopsychosocial impacts and is one of the main causes of preventable physical disabilities. Stigma and discrimination are associated with the disease, especially when visible physical disabilities are present.^{1,2,25,38}

Although much has been achieved in combating leprosy around the world, challenges persist. Brazil, like other countries endemic for leprosy, needs to strengthen investments in health systems, aiming to expand medical care and achieve health goals.³⁹ The development of better diagnostic and therapeutic methods for leprosy continues to be a significant challenge.³⁸ In the absence of an effective vaccine, early diagnosis and treatment of affected people, as well as the prevention of patient contact with leprosy, are important in order to interrupt the transmission of the bacillus, reduce the risk of physical disabilities and deformities, and decrease the physical and psychosocial burden and economic risk associated with the disease.^{18,40–43}

Regarding prevention of patient contact with leprosy, it is important to highlight the strategy of immunoprophylaxis with BCG and the use of a single dose of rifampicin. A randomized clinical trial showed a 57% efficacy in preventing the incidence of leprosy in contacts in the first two years after intervention with a single dose of rifampicin.⁴⁴ The combination of a single dose of rifampicin and BCG vaccination showed an additional protective effect, approaching 80%.⁴³

It is important to highlight the Brazilian conditional income transfer program, entitled The Family Grant Program (*Programa Bolsa Família* – PBF), a poverty reduction policy, which was associated with a decrease in the incidence of leprosy in families living in municipalities with a high incidence of the disease.⁴⁵ Furthermore, being a beneficiary of the PBF, which facilitates income transfers and improves access to healthcare, was associated with greater adherence to polychemotherapy for leprosy and cure in multibacillary cases.⁴⁶

Specific studies on spatial analysis, which used SINAN as a data source and municipalities as a geographic unit of analysis, identified main clusters of municipalities with the highest incidence of leprosy in the North, Northeast, and Midwest regions of the country in different periods.^{47,48} By contrast, the present study considered the Brazilian Federative Units, larger geographic units, to describe the spatial distribution of the disease throughout the country based on GBD estimates.

This work have certain limitations. The present study did not analyze more specific indicators, such as the rate of new cases with grade 2 physical disability per million inhabitants, established in the Global Leprosy Strategy 2021–2030 – 'Towards zero leprosy'.⁷ Such a metric would indicate late diagnosis and weaknesses in disease surveillance. Additionally, the disability weights related to leprosy proposed by the GBD may be underestimated, as suggested by Chandran et al.,⁴⁹ which would impact the value of the YLD estimates. On the other hand, the GBD uses the SINAN database to calculate its estimates, and this system is crucial to supporting the monitoring and evaluation of health actions, as well as the planning of strategies to reduce the burden of diseases, such as leprosy in Brazil.

In Brazil, the National Strategy for Combating Leprosy 2019–2022⁹ was guided by the following pillars: strengthening the management of the leprosy program in the three spheres of government; tackling leprosy and its complications, including monitoring drug resistance; and promoting social inclusion by combating stigma and discrimination, including access to social and financial support services and programs.^{45,46} Therefore, prioritizing the reduction of the burden of leprosy is designed as a strategic action in Brazil, considering the existence of different sociodemographic contexts, the availability of scientific knowledge on the prevention of the transmission of the bacillus, as well as for the diagnosis and treatment of cases, and reduction of physical disability.

Author statements

Acknowledgments

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Ethical approval

The study was conducted with secondary data of public access, without nominal identification, and therefore does not require approval from a Bioethics Committee, in accordance with Brazilian standards of ethics for the use of data in research.

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Competing interests

The authors declare no conflicting interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2024.07.035.

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