Leprosy physical disabilities in the 100 Million Brazilian Cohort

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Abstract

Background

Leprosy continues to be an important cause of physical disability in endemic countries such as Brazil. Knowledge of determinants of these events may lead to better control measures, as targeted interventions may mitigate their impact on affected individuals. This study investigated such determinants among the most vulnerable portion of the Brazilian population.

Methods

A large cohort was built from secondary data originated from a national registry of applicants to social benefit programs, spanning the period 2001 to 2015 and including over 114 million individuals. Data were linked to the Leprosy disease notification system utilizing data from 2007 until 2014. Descriptive and bivariate analyses lead to the multivariate analysis using a multinomial logistic regression model with cluster-robust standard errors. Associations were reported as Odds Ratios with their respective 95% confidence intervals

Results

21,565 new leprosy cases were identified among the original cohort members from the study period. Most of the cases (63.1%) had grade zero disability. Grades 1 and 2 represented 21 and 6%, respectively. Factors associated with increasing odds of grades 1 and 2 disability were age over 15 years old (ORs 2,39 and 1,95 respectively), having less schooling (with a clear dose response effect), being a multibacillary patient (ORs 3,5 and 8,22). Protective factors for both grades were being female (ORs 0,81 and 0,61) and living in a high incidence municipality (ORs 0,85 and 0,65).

Conclusions

Worse socioeconomic conditions might act as barriers to early diagnosis, which increases the risk of developing physical disabilities. Early diagnosis is paramount to decrease the incidence of leprosy-related disability, and our findings point to the need for strengthening these actions in non-endemic areas, where cases may be missed when presented at early stages in disease progression. In addition, data linkage proved to be useful in generating evidence for improving policy target at leprosy control in Brazil.

Background

Chronic infections with *Mycobacterium leprae* have the potential to cause lasting nerve damage and physical disabilities [1, 2]. Among patients with leprosy, physical disabilities arise as a result of late diagnoses and/or insufficient treatments. The incidence of leprosy-associated disabilities among newly

detected cases is, therefore, an important indicator of gaps in population-level leprosy control strategies. Leprosy cases are classified as: Grade 0 disability (G0D) when the muscle strength and the sensitivity of these segments are preserved; Grade 1 (G1D) when there is decreased muscle strength and/or decreased sensitivity; and Grade 2 (G2D) when there are visible deformities in the hands, feet, and/or eyes [3, 4].

As part of the 2016–2020 Global Leprosy Strategy, the WHO has set a target of reducing the rate of newly diagnosed leprosy patients with G2D to be less than 1 per million population [4]. Within Brazil, a country with a high leprosy new case detection rate of 13.7/100,000 population as of 2018, the National Leprosy Disease Program has similarly prioritized reducing the rate of diagnoses with G2D as a primary goal. From 2012 to 2016, the mean rate of leprosy new case detections with G2D in Brazil was 10.5 per 1 million inhabitants, with an average of 2,042 people diagnosed annually with leprosy-related G2D in this period [5]. In the last decades, Brazil has adopted extensive public health measures to improve the assessment and prevention of leprosy-related physical disabilities [6]. Nevertheless, a systematic review conducted by Vieira et al. (2018) [7], indicates that the proportion of leprosy cases involving disability among children < 15 years remains high in Brazil, reflecting active transmission and challenges for case detection.

Although there have been large-scale studies in Brazil studying the social determinants of leprosy incidence and treatment default [8, 9], the risk factors for leprosy-associated disability at the time of diagnosis remain inadequately investigated. Using nationwide linked data from the 100 Million Brazilian Cohort, this study seeks to use large-scale data to identify risk factors for having leprosy-related physical disabilities at the time of diagnosis.

Methods

Study Design and Population

The 100 Million Brazilian Cohort [10, 11] was built by linking the health and administrative records of individuals registered in the *Cadastro Único para Programas Sociais* (CadÚnico), a national registry for social assistance programs in the country. This database was created at the Centro de Integração de Dados e Conhecimentos para Saúde at Oswaldo Cruz Foundation (Cidacs, Salvador, Bahia, Brazil) and is part of the Center's mission to evaluate the impact of social determinants and policies on health. The cohort includes administrative records from over 114 million individuals who applied for social assistance between 2001 and 2015.

For this study, we extracted a de-identified dataset including exposure data related to geographic factors (i.e. region, urbanicity, and residence in a 'high-burden cluster'), household living conditions (i.e. household density, housing materials, water source, electricity source, sewage disposal, and waste disposal), family per capita income (i.e. relative to the Brazilian minimum wage), and individual socioeconomic indicators (i.e. sex, age, self-identified race/ethnicity, literacy, educational attainment, and employment status). For children younger than 18 years, education and employment were reported as the

education level and employment status of the head of the family (here defined as the oldest member of the family). Among the geographic factors examined, we investigated risks within clusters of higher incidence, as defined by Penna et al. (2009) [12] based on epidemiological data from 1980 until 2007. These clusters were described as 29 spatial clusters comprising 789 municipalities and were devised to facilitate decision-making for leprosy control in Brazil. Although these were defined more than ten years ago, a recent study [13] analyzed the spatial distribution of leprosy in selected endemic regions of the country comparing the periods 2001–2003 versus 2010–2012 and concluded that there is significant overlap of clusters comparing both time periods.

As previously described [8, 9, 14, 15] the data from the 100 Million Brazilian Cohort was then linked to leprosy notification records from 2007 to 2014 in the national notifiable disease system, *Sistema de Informação de Agravos de Notificação*, SINAN-leprosy. Additional variables from the SINAN data included the operational classification of leprosy (i.e. paucibacillary or multibacillary [PB or MB]), the number of skin lesions, and the grade of disability at diagnosis.

The study population for this investigation included members of the 100 Million Brazilian Cohort followed from 1 January 2007 and 31 December 2014. Cohort members were excluded if they: (i) were diagnosed with leprosy prior to registration in CadÚnico, (ii) belonged to family units without one member aged over 15 years (i.e., children registered separately from their families), (iii) had less than one day of follow-up, (iv) were relapsed leprosy cases or (v) did not have information on grade of disability at diagnosis.

Statistical Analysis

Descriptive analysis was performed to assess the distribution of the independent variables, followed by bivariate analysis with the outcome (presence of any degree of disability) to assess the strength of association between independent variables and grade of disability at diagnostic. Those with a p-value less than 0.1 were considered eligible for the multivariate model.

For the multivariate analysis, a multinomial logistic regression model with cluster-robust standard errors (i.e., accounting for familial clustering of covariates) to estimate the adjusted odds ratios (OR) was used, with grade zero disability cases used as the reference category.

All analyses were performed using Stata, version 15.0 (Stata Corp LLC, College Station, Texas, USA).

Ethics

This study was performed under the international (Helsinki), Brazilian and UK research regulations and was approved by the Three Ethics Committee of Research: (i) University of Brasília (1.822.125), (ii) Instituto Gonçalo Muniz - Fiocruz (1.612.302) and (iii) London School of Hygiene and Tropical Medicine's Research Committee (10580–1).

Role of Funding Source

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Results

The study included 21,565 new leprosy cases, from the original cohort of 33,905,423 individuals (Fig. 1). At the time of diagnosis, 15,095 (63.1%) cases had G0D, while grades 1 and 2 represented 21% (5,026) and 6% (1,444), respectively. In the multivariate model, 16,376 cases were included, as missing values for some variables prevented a number of cases from being included.

In the study population, the mean age of newly detected leprosy cases was 37.6 years old, varying by the grade of disability (G0D 34.9; G1D 43.4; G2D 45.7) (Table 1). Overall, cases were equally distributed by sex, and 49.6% of the cases were female. The majority of the cases identified as mixed race (“pardo”) (72.1%), had up to 4 years of schooling (61%) and were literate (79.3%). Almost half (49.1%) were employed. Although 81.8% earned up to 0.5 minimum wage, 11.3% reported no source of income. Most lived in urban areas (79.5%), and the regions with the highest percentage of cases were the Northeast (40.4%) and the North (23.6%). The majority (69.3%) lived in brick or cement-made dwellings, with publicly provided water, garbage collection and electricity. However, 67% of reported using a homemade tank as a sewage disposal system. The majority of the cases lived in municipalities that belonged to the epidemiologically-defined high incidence clusters (63.8%) There were more MB cases than PB (59.2 vs 40.8%) at time of diagnosis (Table 1).

Regarding G1D, individuals aged over 15 years showed higher odds of presenting with disability (OR 2.39; 95%CI 2.06–2.77), as well as having less schooling with a clear dose-response effect (ORs for no schooling, $\leq$ 10 years of education, $>$ 10 and $\leq$ 14 years were respectively 1.64, 1.48 and 1.28, all p-values $<$ 0.05). Being unemployed also increased the chance of G1D (OR 1.19; 95%CI 1.06–1.32). Living in rural areas (OR 1.14; 95%CI 1.04–1.26), presenting as multibacillary (OR 3.50; 95%CI 3.13–3.92) and having lesions (OR 1.12; 95%CI 1.02–1.24) also had the same effect. Factors that showed to be protective against grade included being female (OR 0.81; 95%CI 0.75–0.88). In addition, increasing household density and living in a cluster municipality was protective against this outcome as well (OR 0.85; 95%CI 0.78–0.93) (Table 2).

As far as G2D is concerned, those older than 15 years old were more likely to present it (OR 1.95; 95%CI 1.51–2.50) and having less education also showed a similar association, with a clear dose response gradient (ORs for no schooling, $\leq$ 10 years of education, $>$ 10 and $\leq$ 14 years were respectively 1.91, 1.64, 1.31, all p-values $<$ 0.05). Being a multibacillary patient was also a risk factor (OR 8.22; 95%CI 6.51–10.38). On the other hand, being female (OR 0.61; 95%CI 0.53–0.70), and living in a high incidence municipality (OR 0.67; 95%CI 0.58–0.78) decreased the odds of presenting G2D at diagnosis (Table 2). Other protective factors included living in the north, Northeast and centre-west region.

Discussion

This study investigated factors associated with leprosy-related disability in a large Brazilian set of cases. Among 16,376 new cases of leprosy analysed, were less likely to present grade 1 or grade 2 physical disabilities women, those living in the North, Northeast and Center-West regions or in high incidence clusters, in urban areas and with greater household crowding. In contrast, being over 15 years of age, with a lower level of schooling, not working and being multibacillary increased the chances of presenting grade 1 or grade 2 physical disabilities.

The higher likelihood of leprosy-related disabilities found among those older than 15 years is similar to previous studies. In a hyperendemic area of the Center-West region of Brazil, the estimated risk ratio of grade 2 disability was 5.3 times higher among patients aged ≥ 45 years [16]. In the state of Minas Gerais, a retrospective study showed that age above 15 years was an important risk factor for the development of physical disability in leprosy patients [17]. A study of patients residents in the state of Maranhão showed a progressive increase in the chances of developing physical disability among those older than 15 years, ranging from 3 to 10.4 times more [18]. Considering the duration of the disease is directly related to age and, given the chronic profile of leprosy effects, increasing age may result in more advanced disabilities [17, 19].

Regarding gender, some studies did not identify an association between gender and the level of disability [20–22]. However, as in this study that used data from all over Brazil, other studies report higher grades of physical disability among male individuals with leprosy [17, 23].

Men are generally more exposed to *M. leprae* and have reduced contact with health care, which may delay diagnosis and increases the risk of developing physical disabilities [24]. Data from the Ministry of Health for the general population show that between 2012 and 2016 the detection rate of new cases with physical disability grade 2 was much higher in males with 15.2 cases per 1 million men, while the rate in women was 6.1 cases per 1 million women [5]. Cultural factors may explain the difference between the studies because women may be more likely to seek health assistance than men [18], while men go when the disease is in a more advanced stage.

Our study also suggests that higher levels of education were negatively associated with the presence of physical disabilities at diagnosis, which is consistent with the literature [16, 17]. Higher education may be associated with a better understanding of the disease and, consequently, better access and utilization of health services. Regular treatment and evaluation, as well as self-care, are aspects that prevent the worsening of leprosy cases [17, 25].

The fact that cases from the Northeast and the North regions were less likely to present G1D and G2D contrasts the findings from Freitas and colleagues (2016) [13], which showed greater proportions of G2D in municipalities with higher incidence rates of leprosy. They hypothesize that “in these municipalities, at least in the short term, a consequence of increased surveillance actions may be the initial increase in the ‘detected’ cases of the disease. In turn, this increase may lead to increased tracing of people who have

had contact with it and greater detection of cases with grade 2 disability, which previously were not identified. This hypothesis may explain the finding that municipalities with a greater proportion of cases presenting with grade 2 disability also had higher average leprosy incidence rates". However, the areas with higher endemicity do not have a better structure surveillance and care system, as they are systematically poorer. The clusters are located in areas that are more vulnerable.

Therefore, we hypothesize that this fact is likely due to a more sensitive health staff and surveillance system to case detection, therefore more capable of detecting leprosy cases earlier. Assuming that disability is a marker for late diagnosis, it is expected that regions of high endemicity will show a lower chance of patients presenting with grades 1 and 2 disability. G2D, as already mentioned may indicate a late diagnosis and a suboptimal surveillance system. According to Penna et al. (2009) [12], access to primary health care units has improved mainly in rural areas and small towns, improving the diagnosis of leprosy in the first decade of this century. However, as her work emphasizes, "the diagnosis of skin diseases depends on the cultural importance given to skin lesions, as well as health-seeking habits among the population."

The study by Freitas et al. (2016) [13] looked at risk factors, estimated rate ratios (RR), and identified a high NCDR in the Midwest and North regions compared to the South, large cities and greater urbanization, median and high illiteracy rate, income inequality (Gini index), domiciles' agglomeration, worse sanitation condition, and percentage of cases with grade 2-disability.

Although we found similar evidence that individuals living in urban areas were at a greater risk of leprosy detection than individuals living in rural areas, we did not find evidence of an association of household density with leprosy risk in the full cohort. It is, however, noteworthy that in subgroup analyses increased household density (more than one resident per two rooms) was associated with an increased leprosy risk in children, a group indicative of active transmission [8].

The association between the proportion of multibacillary leprosy and presentation of G2D has been shown in the past [16, 26, 27]. Studies conducted in some Brazilian cities indicate that at the time of diagnosis, the educational level variables and operational classification are statistically associated with the development of physical disabilities ($p < 0.05$). It is emphasized that multibacillary individuals are twice as likely to develop sequelae as paucibacillary individuals [28].

Our study has several strengths: the large sample size and extensive follow up period allowed us to evaluate determinants of disability to the extent that is rarely possible. This study linked data from over 100 million individuals and was able to assess factors associated with physical disability in an unprecedented way, also as we were able to evaluate a wider range of variables present in CadÚnico. Unlike other studies, we analyzed the most vulnerable fraction of the Brazilian population, as this is the profile of individuals enrolled in CadUnico.

Nevertheless, our study has some limitations. The use of secondary data originated from routine surveillance activities always brings the issue of completeness of information. We did not have complete

information on disability evaluation at diagnosis (n = 1,557) and at discharge. The latter was poorly collected to an extent that does not permit to analyze. Efforts should be undertaken to stress the importance of performing this evaluation at discharge and record it in the information systems. Other factors associated with disability were not available in our database and therefore, could not be assessed, such as health services characteristics and patients' perception and knowledge about leprosy.

Conclusion

Our study indicated that worse socioeconomic conditions might act as barriers to early diagnosis, which increases the risk of developing physical disabilities. Our findings suggest the need for early and qualified diagnosis of leprosy in endemic regions and especially in regions considered non-endemic that may present high rates of hidden prevalence. Focus could be given to younger patients, which reflect recent and active transmission. It is imperative to train staff in less endemic areas to become sensitive to leprosy, aiming at reducing under detection. In addition, data linkage proved a powerful tool to shed more light on identifying potential causal factors of disabilities among the poorest Brazilian population.

There is a need for further studies on GIF-related socioeconomic and clinical factors at the end of treatment, issues we could not address in our study. Future research should also explore if the findings found in this work will replicate among relapses or reinfections; considering we focused exclusively on new cases. Besides early diagnosis and timely treatment, social protection policies and initiatives are key to lead us to effective leprosy control - evidence that has been put forth a century ago[29] and yet remains valid.

Declarations

Ethics approval and consent to participate

This study was performed under the international (Helsinki), Brazilian and UK research regulations and was approved by the Three Ethics Committee of Research: (i) University of Brasília (1.822.125), (ii) Instituto Gonçalo Muniz - Fiocruz (1.612.302) and (iii) London School of Hygiene and Tropical Medicine's Research Committee (10580 – 1).

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study are available from Center of Data and Knowledge Integration for Health (Cidacs – https://cidacs.bahia.fiocruz.br/) but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Cidacs.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

- MNS participated in the study conceptualization, investigation, formal analysis and visualization, writing of the original draft, interpretation of the results and revision and editing of the final version of the manuscript.
- JSN participated in the study conceptualization, investigation, formal analysis and visualization, writing of the original draft, interpretation of the results and revision and editing of the final version of the manuscript. She also participated in the supervision and funding acquisition.
- JMP participated in the investigation, formal analysis and visualization, interpretation of the results and revision and editing of the final version of the manuscript.
- AAM participated in the investigation, formal analysis and visualization, interpretation of results and revision and editing of the final version of the manuscript.
- MYI participated in the investigation, interpretation of results and revision and editing of the final version of the manuscript.
- CSST participated in formal analysis and visualization, interpretation of the results and revision and editing of the final version of the manuscript.
- MLFP participated in the interpretation of the results and revision and editing of the final version of the manuscript. She also participated in the supervision and funding acquisition.
- LS participated in the interpretation of the results and revision and editing of the final version of the manuscript.
- LCR participated in the study conceptualization, interpretation of the results and revision and editing of the final version of the manuscript. She also participated in the supervision and funding acquisition.
- MLB participated in the study conceptualization, interpretation of the results and revision and editing of the final version of the manuscript. He also participated in the supervision and funding acquisition.
- EBB participated in the study conceptualization, investigation, formal analysis and visualization, interpretation of the results and revision and editing of the final version of the manuscript.

- GOP participated in the study conceptualization, interpretation of the results and revision and editing of the final version of the manuscript. He also participated in the supervision and funding acquisition.

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Tables

Table 1. Characteristics of leprosy cases evaluated for physical disabilities. The 100 Million Brazilian Cohort, 2007-2014.

Variables	Physical Disabilities			Total
	Grade 0 (N=15,095) n(%)	Grade 1 (N=5,026) n(%)	Grade 2 (N=1,444) n(%)	n(%)
Individual characteristics				
Age (Mean [SD])	34.9 (19.2)	43.4 (18.6)	45.7 (19.0)	37.6 (19.5)
Sex				
Male	6,984 (46.3)	2,915 (58.0)	965 (66.8)	10,864 (50.4)
Female	8,111 (53.7)	2,111 (42.0)	479 (33.2)	10,701 (49.6)
Ethnicity				
White	2,645 (17.9)	1,076 (21.8)	330 (23.2)	4,051 (19.2)
Black	1,178 (8.0)	412 (8.4)	132 (9.3)	1,722 (8.1)
Asian	49 (0.3)	19 (0.4)	1 (0.1)	69 (0.3)
Mixed (brown)	10,879 (73.5)	3,406 (69.0)	956 (67.3)	15,241 (72.1)
Indigenous	48 (0.3)	20 (0.4)	1 (0.1)	69 (0.3)
Ignored/Missing				455 (0.02)*
Literacy				
Yes	12,182 (81.5)	3,714 (74.6)	1,028 (71.6)	16,924 (79.3)
No	2,760 (18.5)	1,262 (25.4)	407 (28.4)	4,429 (20.7)
Ignored/Missing				234 (0.01)*
Schooling				
No education/Pre-school	2,266 (17.0)	1,060 (23.3)	362 (26.8)	3,688 (19.2)
Primary School (ages 5 to 10)	5,346 (40.1)	2,034 (44.6)	595 (44.1)	7,975 (41.5)
Junior High School (ages 11 to 14)	3,981 (29.9)	1,101 (24.1)	302 (22.4)	5,384 (28.0)
Senior High School	1,677 (12.6)	350 (7.7)	89 (6.6)	2,116 (11.0)
Higher Education	48 (0.4)	14 (0.3)	2 (0.2)	64 (0.3)
Ignored/Missing				2,566 (0.1)*
Work condition				
Employed	6,801 (50.6)	2,073 (46.1)	562 (44.2)	9,436 (49.1)
Unemployed	3,211 (23.9)	1,309 (29.1)	421 (33.1)	4,941 (25.7)
Unemployed but currently studying	3,434 (25.5)	1,112 (24.8)	288 (22.7)	4,834 (25.2)
Ignored/Missing				2,615 (0.1)*
Per capita income				
No income	1,682 (11.1)	577 (11.5)	173 (12.0)	2,432 (11.3)
0 - 0.25 minimum wage	8,580 (56.8)	2,428 (48.3)	681 (47.2)	11,689 (54.2)
0.25 - 0.5 minimum wage	2,440 (16.2)	835 (16.6)	241 (16.7)	3,516 (16.3)
0.5 - 1 minimum wage	1,910 (12.7)	961 (19.1)	285 (19.7)	3,156 (14.6)
>1 minimum wage	482 (3.2)	225 (4.5)	64 (4.4)	771 (3.6)
Ignored/Missing				1 (0.0)*
Household characteristics				
Region of residence				
North	3,636 (24.1)	1,164 (23.2)	298 (20.6)	5,098 (23.6)
Northeast	6,401 (42.4)	1,822 (36.2)	497 (34.4)	8,720 (40.4)
Southeast	1,966 (13.2)	814 (16.2)	297 (20.6)	3,107 (14.4)

South	346 (2.3)	202 (4.0)	88 (6.1)	636 (3.0)
Central-west	2,716 (18.0)	1,024 (20.4)	264 (18.3)	4,004 (18.6)
Area of residence				
Urban	12,100 (80.2)	3,894 (77.6)	1,128 (78.3)	17,122 (79.5)
Rural	2,984 (19.8)	1,125 (22.4)	312 (21.7)	4,421 (20.5)
Ignored/Missing				22 (0.0)*
Household density				
≤ 0.5 inhab/room	5.014 (33,67)	2.141 (43,22)	619 (43,65)	7.774 (36,56)
0.5 - 0.75 inhab/room	2.802 (18,82)	848 (17,12)	230 (16,22)	3.880 (18,25)
0.75 - 1.00 inhab/room	3.320 (22,30)	970 (19,58)	253 (17,84)	4.543 (21,37)
>1.00 inhab/room	3.754 (25,21)	995 (20,08)	316 (22,28)	5.065 (23,82)
Ignored/Missing				338 (0.01)
Construction material				
Bricks/Cement	10,429 (70.0)	3,347 (67.5)	975 (68.7)	14,751 (69.3)
Wood/Taipa/Others	4,473 (30.0)	1,610 (32.5)	444 (31.3)	6,527 (30.7)
Ignored/Missing				318 (0.01)*
Water supply				
Public network (tap water)	10,171 (68.3)	3,311 (66.8)	978 (68.9)	14,460 (68.0)
Well/Natural source/Others	4,731 (31.7)	1,646 (33.2)	441 (31.1)	6,818 (32.0)
Ignored/Missing				318 (0.01)*
Electricity				
Electricity with counter	13,566 (91.0)	4,468 (90.1)	1,278 (90.1)	19,312 (90.8)
Electricity without counter	1,336 (9.0)	489 (9.9)	141 (9.9)	1,966 (9.2)
Ignored/Missing				318 (0.01)*
Waste disposal system				
Public network/Septic tank	4,823 (32.8)	1,588 (32.6)	506 (36.5)	6,917 (33.0)
Homemade tank/Ditch/Others	9,864 (67.2)	3,285 (67.4)	879 (63.5)	14,028 (67.0)
Ignored/Missing				705 (0.03)*
Garbage disposal				
Public collection system	11,409 (76.6)	3,654 (73.7)	1,070 (75.4)	16,133 (75.8)
Burned/Buried/Outdoor disposal/Others	3,494 (23.4)	1,303 (26.3)	349 (24.6)	5,146 (24.2)
Ignored/Missing				317 (0.01)*
High-burden cluster municipality				
No	5,148 (34.1)	1,987 (39.5)	679 (47.0)	7,814 (36.2)
Yes	9,947 (65.9)	3,039 (60.5)	765 (53.0)	13,751 (63.8)
Clinical characteristics				
WHO operational classification				

Paucibacillary	7,698 (51.0)	968 (19.3)	128 (8.9)	8,794 (40.8)
Multibacillary	7,396 (49.0)	4,058 (80.7)	1,316 (91.1)	12,770 (59.2)
Ignored/Missing				3 (0.0)*
Presence of lesions				
No	9,123 (60.44)	1,862 (37.05)	432 (29.92)	12,419 (51.94)
Yes	5,940 (39.35)	3,135 (62.38)	1,004 (69.53)	11,419 (47.76)
Ignored/Missing	32 (0.21)	29 (0.58)	8 (0.55)	73 (0.31)*

*The percentage of ignored/missing data refers a part of the total.

Table 2. Univariate and adjusted analyses for grade of physical disabilities. The 100 Million Brazilian Cohort, 2007-2014.

	Grade 1		Grade 2	
	OR[1] (95%CI) (N=16,376)	OR_{adj}[2,3] (95%CI) (N=16,376)	OR[1] (95%CI) (N=16,376)	OR_{adj}[2,3] (95%CI) (N=16,376)
Individual characteristics				
Age				
Up to 15 years old	1.00	1.00	1.00	1.00
> 15 years old	3.41 (3.01-3.87)	2.39 (2.06-2.77)	3.28 (2.63-4.11)	1.95 (1.51-2.50)
Sex				
Male	1.00	1.00	1.00	1.00
Female	0.62 (0.58-0.66)	0.81 (0.75-0.88)	0.48 (0.38-0.48)	0.61 (0.53-0.70)
Schooling				
No education/Pre-school	1.60 (0.86-2.94)	1.64 (1.40-1.93)	3.83 (0.93-15.88)	1.91 (1.44-2.53)
Primary School (ages 5 to 10)	1.30 (0.71-2.38)	1.48 (1.28-1.70)	2.67 (0.65-11.04)	1.64 (1.27-2.12)
High School (ages 11 to 14)	0.95 (0.52-1.74)	1.28 (1.10-1.48)	1.82 (0.44-7.55)	1.31 (1.00-1.72)
Senior High School	0.72 (0.39-1.32)	-	1.27 (0.30-5.34)	-
Higher Education	1.00	1.00	1.00	1.00
Work condition				
Employed	1.00	1.00	1.00	1.00
Unemployed	1.06 (0.98-1.16)	1.19 (1.06-1.32)	1.01 (0.86-1.18)	1.47 (1.23-1.74)
Unemployed but currently studying	1.34 (1.23-1.45)	1.13 (1.03-1.24)	1.59 (1.39-1.81)	1.15 (0.98-1.35)
Household characteristics				
Region of residence				
North	0.55 (0.46-0.66)	0.91 (0.72-1.15)	0.32 (0.25-0.42)	0.53 (0.39-0.72)
Northeast	0.49 (0.41-0.58)	0.81 (0.64-1.01)	0.31 (0.24-0.39)	0.53 (0.39-0.71)
Southeast	0.70 (0.58-0.85)	1.06 (0.84-1.33)	0.58 (0.45-0.76)	0.80 (0.59-1.08)
South	1.00	1.00	1.00	1.00
Central-west	0.65 (0.54-0.78)	0.86 (0.68-1.09)	0.38 (0.29-0.49)	0.50 (0.36-0.68)
Area of residence				
Urban	1.00	1.00	1.00	1.00
Rural	1.17 (1.08-1.27)	1.14 (1.04-1.26)	1.12 (0.98-1.28)	1.05
Household density				
≤ 0.5 inhab/room	1.00	1.00	1.00	1.00
0.5 - 0.75 inhab/room	0.71 (0.65-0.78)	0.87 (0.78-0.98)	0.66 (0.57-0.78)	0.96 (0.80-1.16)
0.75 - 1.00 inhab/room	0.68 (0.63-0.75)	0.87 (0.78-0.97)	0.62 (0.53-072)	0.85 (0.71-1.03)
>1.00 inhab/room	0.62 (0.57-0.68)	0.79 (0.71-0.88)	0.68 (0.59-0.79)	1.04 (0.87-1.23)
High-burden cluster municipality				
No	1.00	1.00	1.00	1.00
Yes	0.79 (0.74-0.85)	0.85 (0.78-0.93)	0.58 (0.52-0.65)	0.67 (0.58-0.78)
Clinical characteristics				
WHO operational classification				
Paucibacillary	1.00	1.00	1.00	1.00

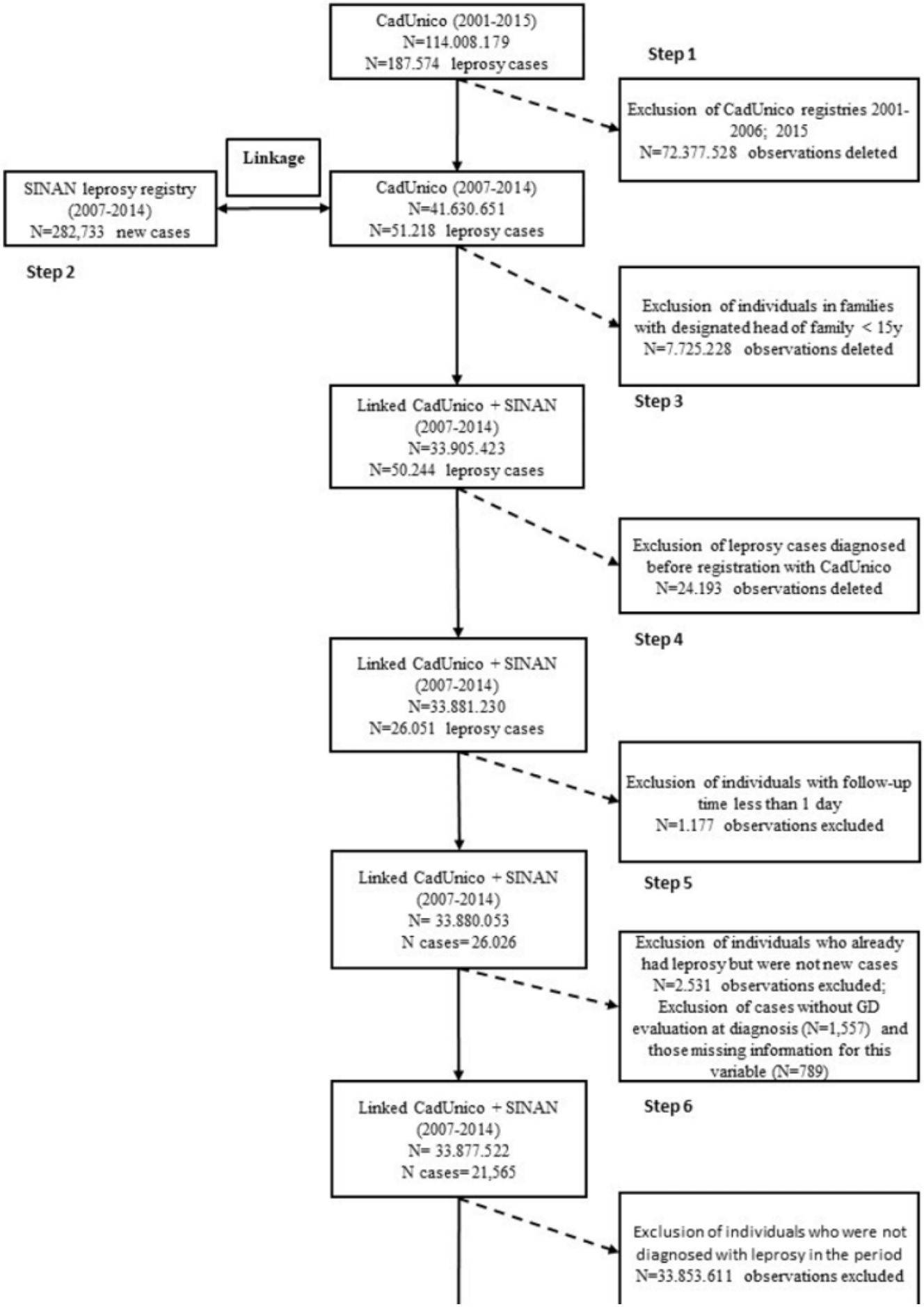
Multibacillary	4.36 (4.04-4.71)	3.50 (3.13-3.92)	10.7 (8.9-12.87)	8.22 (6.51-10.38)
Presence of lesions				
No	1.00	1.00	1.00	1.00
Yes	2.56 (2.38-2.76)	1.12 (1.02-1.24)	3.44 (3,015-3.93)	1.03 (0.88-1.20)

[1]Univariate logistic regression model accounting for household cluster.

[2]Final model of multinomial logistic regression accounting for household cluster with exclusion of the missing data.

[3]For all the tests and for permanence of the variables in the final model was used the significance level of 5%.

Figures


CadUnico (2001-2015)
N=114.008.179
N=187.574 leprosy cases
Step 1
Exclusion of CadUnico registries 2001-2006; 2015
N=72.377.528 observations deleted
Linkage
SINAN leprosy registry (2007-2014)
N=282,733 new cases
Step 2
CadUnico (2007-2014)
N=41.630.651
N=51.218 leprosy cases
Exclusion of individuals in families with designated head of family < 15y
N=7.725.228 observations deleted
Step 3
Linked CadUnico + SINAN (2007-2014)
N=33.905.423
N=50.244 leprosy cases
Exclusion of leprosy cases diagnosed before registration with CadUnico
N=24.193 observations deleted
Step 4
Linked CadUnico + SINAN (2007-2014)
N=33.881.230
N=26.051 leprosy cases
Exclusion of individuals with follow-up time less than 1 day
N=1.177 observations excluded
Step 5
Linked CadUnico + SINAN (2007-2014)
N= 33.880.053
N cases=26.026
Exclusion of individuals who already had leprosy but were not new cases
N=2.531 observations excluded;
Exclusion of cases without GD evaluation at diagnosis (N=1,557) and those missing information for this variable (N=789)
Step 6
Linked CadUnico + SINAN (2007-2014)
N= 33.877.522
N cases=21,565
Exclusion of individuals who were not diagnosed with leprosy in the period
N=33.853.611 observations excluded

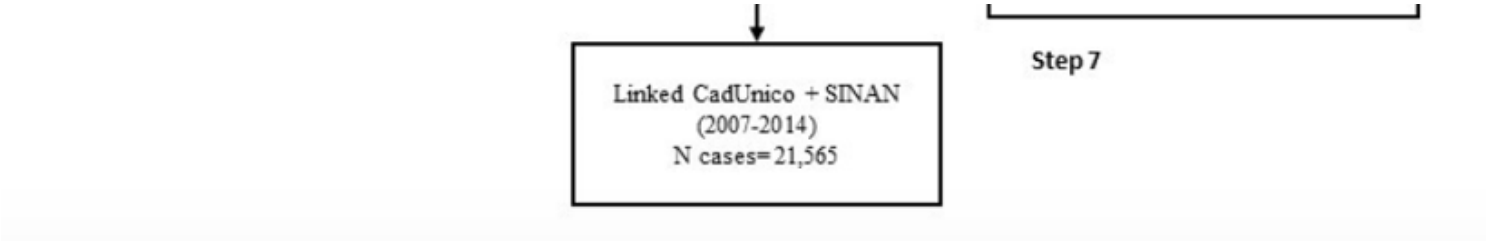


Figure 1

Study population selection flowchart from the 100 Million Brazilian Cohort.