Factors associated with cure when treating tuberculosis in the state of Rio de Janeiro, Brazil, 2011-2014*

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Abstract

Objective: to analyze factors associated with cure when treating tuberculosis (TB) in the state of Rio de Janeiro, Brazil, from 2011 to 2014. **Methods**: this was a cross-sectional study with data from the Notifiable Diseases Information System (SINAN); logistic regression was used for data analysis. **Results**: of the 57,142 cases reported, 49,691 (86.96%) were included in the study; schooling ≥13 years (*odds ratio* (OR) 3.48; 95%CI 2.74;4.41) and residing in rural areas (OR 2.27; 95%CI 1.38; 3.73) were factors associated with a higher chance of cure; being male (OR 0.71; 95%CI 0.66;0.76) and brown skin color/race (OR 0.73; 95%CI 0.68;0.78) stood out as factors associated with less chance of cure. **Conclusion**: social and economic determinants were identified that influence the treatment outcome, evidencing the need for social support and guaranteed access to health services.

Keywords: Tuberculosis; Public Policy; Social Vulnerability; Cross-Sectional Studies.

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Introduction

Tuberculosis (TB) is considered one of the most long-standing infectious diseases affecting mankind, with TB deaths having been recorded for at least five thousand years.[1] In the 21st century, TB is still a public health problem worldwide, due to wide geographical dispersion, the existence of multidrug-resistant cases and co-infection with the human immunodeficiency virus (HIV).[2] 9.6 million cases and 1.5 million deaths from TB were estimated for the year 2014. The estimated incidence of TB-HIV co-infection for the same year was 1.2 million cases, with 400,000 deaths.[3]

Tuberculosis is related to poverty, social exclusion and deprivation, this being a very common scenario in developing countries where TB continues at considerable levels,[4] given the intense social inequality, increasing poverty, uncontrolled urban and population growth which, in turn, are reflected in social inequalities in health.[5] In 2016, Brazil was in 18th place among the 22 countries accounting for 80% of TB cases worldwide.[6]

A year later, in 2015, there were 63,189 new cases of the disease in Brazil, representing an incidence coefficient of 30.9 cases per 100,000 inhabitants.[6] In the state of Rio de Janeiro in 2015, the TB incidence rate was 54.5 cases per 100,000 inhabitants, and the TB mortality rate was 5.1 per 100,000 inhabitants.[6] However, this distribution is not homogeneous.[7] The highest concentration of cases is observed in poorer regions and affects, in particular, some of the most vulnerable groups, characterized by individual and collective susceptibility resulting from the social and economic situation in which they find themselves.[4,8]

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In 2012, a model was proposed capable of linking the social determinants of TB, taking account of the multicausality of disease and three dimensions of this vulnerability: (i) individual; (ii) programmatic or institutional; and (iii) social or contextual.[9] Looking at vulnerability from these three dimensions enables different forms of analysis, ranging from proximal to distal determinants, and from the individual level to the institutional and collective level.[10]

In Brazil, studies 11-13 have demonstrated how these factors affect the outcome of TB treatment, in particular comorbidities (alcoholism and HIV/AIDS), education level, sex, age, income, occupation and family support. The state of Rio de Janeiro is marked by social contrasts: in 2012, it was considered to be the seventh most unequal Federative Unit in Brazil as measured by the Gini coefficient. This reflects the high levels of both income and poverty in the region.[8,14] Studies on factors associated with the outcome of TB treatment in Rio de Janeiro can be useful for identifying more vulnerable groups.

The objective of this study was to analyze factors associated with cure when treating tuberculosis (TB) in the state of Rio de Janeiro, Brazil, from 2011 to 2014.

Methods

This was a cross-sectional study using data on reported tuberculosis (TB) cases held on the Notifiable Diseases Information System (SINAN).

Rio de Janeiro state covers an area of 43,781,566km² containing 92 municipalities. In 2015 it had an estimated population of 16,550,024 inhabitants[15] distributed between nine health microregions.

The dependent variable was the outcome of treatment, with cure being considered to be a favorable outcome. Unfavorable outcomes were considered to be: abandonment, primary abandonment (non-adherence within the first 30 days), death from TB, drug-resistant tuberculosis (TBDR) and treatment failure.

The exposure variables analyzed were:
- sex (male; female);
- age (by age groups: under 20; 20 to 39; 40 to 60; over 60);
- ethnicity/skin color (white; black; brown; other [yellow and indigenous]);
- education level (in years of schooling: illiterate; 1 to 4; 5 to 8, 9 to 12; 13 or more);
- area of residence (urban, rural);
- occupational disease (yes; no);
- institutionalized (no; prison; asylum; orphanage; psychiatric hospital; another);
- HIV/AIDS (yes; no);
- alcoholism (yes; no);

- smoking (yes; no);
- diabetes (yes; no);
- other comorbidities (yes; no);
- type of notification (new case; recurrence; return after dropout; unknown, referral);
- supervised treatment (yes; no);
- clinical form (pulmonary, extra-pulmonary, pulmonary + extra-pulmonary);
- X-ray (normal; suspect);
- smear microscopy, 1st sample (negative; positive); and
- sputum culture (negative; positive)

All cases recorded as being finalized were considered to meet the inclusion criterion. All cases that were not conclusively finalized were excluded (information missing, unknown or with change of diagnosis). It is of note that cases with a recorded outcome did not necessarily receive treatment; for example, the outcome 'death from TB' includes both treated cases and those not treated initially.

The initial database, formed by the eligible cases, was processed by using filters, with the goal of eliminating duplicates. To this end, was used the Statistical Package for the Social Sciences, version 20.0 (SPSS Inc, Chicago, IL, USA) was used.

The first step taken was to checkthe completeness of two new variables included on the SINAN system: (i) street people (yes; no); and (ii) beneficiary of government income transfer program (yes; no).A descriptive analysis of the variables of interest for the study was then performed (absolute number and frequency). In the crude analysis, we used the Pearson chi-squared test. In the analysis adjusted by non-conditional multiple logistic regression,[9] we used a conceptual hierarchical model.

The hierarchical model used was that proposed by Maciel in 2012.[9] In this model, the social determinants of TB are classified by level of vulnerability. In the present study, level 1 considered the sex, education level, ethnicity/skin color and age variables; level 2, area of residence, institutionalization, disease related to work; and level 3, smoking, HIV/AIDS, diabetes, and other comorbidities, mental illness and alcoholism. Level 4 was comprised of the analysis of the type of admission, X-ray, sputum culture, clinical form and directly observed treatment.

The Pearson chi-squared test was used to identify the variables significantly associated with the outcome (p<0.05) in the crude analysis, initially input to the non-conditional multiple logistic regression hierarchical model. As the variables lost significance (p>0.05) at each level of regression – from the most distal to the most proximal - they were removed from the model. *Odds ratio* (OR) and confidence intervals of 95% (95%CI) were calculated, with the help of Stata software version 14. Adjustment of the final model was done using the Hosmer-Lemeshow goodness of fit test.[16]

The study project was submitted to the Ethics Committee of the Sergio Arouca National School of Public Health, Oswaldo Cruz Foundation (Fiocruz), and approved on 16 September 2016 by Opinion No. 1727131.

Results

The initial database was comprised of 57,142 notifications. After the use of filters to eliminate duplicates and delete cases with change of diagnosis from the database, 49,691 cases remained (Figure 1). 8,416 cases with no outcome were discarded. The final study sample was comprised of 41,279 cases of tuberculosis, divided between 32,607 having cure as their outcome (79.0%) and 8,672 with an unfavorable outcome (21%).

Regarding the incompleteness of the two new variables included on the SINAN-TB system, regarding street people, 44,302 (89.2%) records were found with no information and 2,353 (4.7%) filled in as unknown; and with regard to the beneficiaries of the government Income Transfer Program, 44,422 (89.4%) records with no information and 3,776 (7.6%) with unknown information were found (data not shown in Tables or Figures).

Table 1 describes the characteristics of the cases: the majority were males(65.0%), aged between 40 and 59 years (34.5%), with 5 to 8 years of schooling (35.1%), diagnosed with the pulmonary form of the disease (85.0%), recorded as new cases (82.8%), with suspected X-ray (95.3%) and positive sputum smear microscopy (69.6%).

Table 2 presents the results of the crude and adjusted analyses of the hierarchical logistic regression model. On level 1, the male sex was associated with a lower chance of a favorable outcome (OR 0.71; 95%CI 0.66;0.76), when compared to females. We observed a greater chance of a favorable outcome among those with 9-12 years of schooling (OR 2.04; 95%CI 1.68;2.47) and 13 or more years of schooling (OR

3.48; 95%CI 2.74;4.41), compared to the illiterate. Black race/skin color (OR 0.62; 95%CI 0.57;0.67) and brown skin color (OR 0.73; 95%CI 0.68;0.78) were also associated with the lowest chance of cure, compared to those of white race/skin color; the same association was observed in the 20-39 age range (OR 0.65; 95%CI 0.58;0.73).

On level 2, living in the rural zone was associated with a greater chance of an unfavorable outcome (OR 2.27; 95%CI 1.38;3.73). However, being institutionalized in an asylum (OR 0.35; 95%CI 0.15;0.83) and in other establishments except prisons, asylums, orphanages and psychiatric hospitals (OR 0.40; 95%CI 0.32;0.49) had lower chances of a favorable outcome, when compared to not being institutionalized.

None of the variables considered on level 3 (smoking, alcoholism and comorbidities) showed a statistically significant association with the outcome.

On level 4, all types of admission, when compared to new cases, showed a lower chance of cure: recurrence (OR 0.55; 95%CI 0.43;0.72), return after dropout (OR 0.21; 95%CI 0.16;0.28) and referral (OR 0.41; 95%CI 0.28;0.60). Similarly, there was an association with positive sputum smear microscopy (OR 0.73; 95%CI 0.59;0.91) and with positive sputum culture (OR 0.58; 95%CI 0.47;0.71), both when compared to the negative results (Table 2). The final model showed a good fit, as indicated by the model adjustment test: chi-squared test value of 7.03 and p-value equal to 0.533.

Discussion

The results found in this study enabled identification of factors associated with the outcome of tuberculosis treatment in the state of Rio de Janeiro between 2011 and 2014. Being of the male sex, having low schooling, having black or brown skin color, being a young adult, living in an urban area, being institutionalized, having a suspect chest X-ray result, having positive 1st sample smear and positive sputum culture results, were factors associated with lower chance of cure. These data demonstrate the relationship between tuberculosis and precarious living conditions.[17]

Being of the male sex was associated with a lower chance of curing tuberculosis. This corroborates the findings of a retrospective cohort study conducted in Cuiabá, MT, between 1998 and 2000, when predictive factors for the abandonment of TB treatment were analyzed.[18] A similar result was found in a case-control study performed in Manaus, AM, and Fortaleza, CE, between 2006 and 2008 as to factors associated with abandonment of TB treatment in Primary Health Care
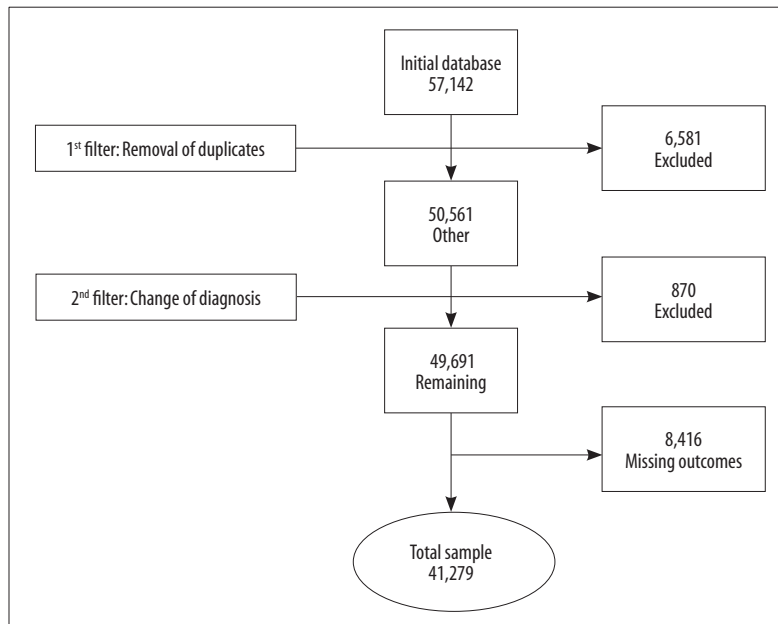

Figure 1 – Flow diagram of the sample of tuberculosis cases taken from the Notifiable Diseases Information System, Rio de Janeiro state, 2011-2014

Table 1 – Characteristics of notified cases of tuberculosis, Rio de Janeiro state, 2011-2014

Variables	n	%
Sex (n=41,275)		
Male	26,634	65.0
Female	14,641	35.0
Age in years (n=41,279)		
<20	4,059	9.9
20-39	18,180	44.0
40-59	14,244	34.5
≥60	4,796	11.6
Race/skin color (N=37,430)		
White	14,506	39.0
Black	8,111	22.0
Brown	14,438	38.0
Other	375	1.0
Schooling, in years of study (n=28,656)		
Illiterate	696	2.4
1-4	7,366	25.7
5-8	10,066	35.1
9-12	8,135	28.4
≥13	2,396	8.4
HIV/AIDS (n=27,901)		
Yes	3,184	13.6
No	24,717	86.4
Alcoholism (n=34,156)		
Yes	4,597	13.5
No	29,559	86.5
Diabetes (n=33,751)		
Yes	2,745	8.1
No	31,006	91.9
Smoker (n=3,541)		
Yes	332	9.4
No	3,209	90.6
Occupational disease (n=27,717)		
Yes	738	2.7
No	26,979	97.3
Clinical form (n=41,279)		
Pulmonary	35,067	85.0
Extra-pulmonary	4,879	11.8
Pulmonary + extrapulmonary	1,333	3.2
Place of residence (n=39,002)		
Rural	424	1.1
Urban	38,578	98.9

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Table 1 – Characteristics of notified cases of tuberculosis, Rio de Janeiro state, 2011-2014

Variables	n	%
Institutionalized (n=36,709)		
No	34,153	93.0
Prison	1,290	3.5
Nursing home	59	0.2
Orphanage	72	0.2
Psychiatric hospital	89	0.2
Other	1,046	2.9
Type of admission (n=41,278)		
New case	34,192	82.8
Recurrence	2,794	6.8
Return after abandonment	2,422	5.9
Unknown	204	0.5
Referral	1,666	4.0
X-rays (n=37,685)		
Suspected	35,901	95.3
Normal	1,784	4.7
Sputum smear microscopy, 1st sample (n=31,175)		
Positive	21,708	69.6
Negative	9,467	30.4
Sputum culture (n=6,056)		
Positive	3,808	62.9
Negative	2,248	37.1
Supervised treatment (n=36,902)		
Yes	16,047	44.1
No	20,345	55.9

services, according to which individuals of the male sex had a 1.78 greater chance of abandoning treatment, when compared to those of the female sex.[19] This difference according to sex may be explained by the fact of lower demand for health services by men:[20] women are believed to be more concerned about their health than men and as such they tend to use these services with greater frequency.[20] Furthermore, the priorities of health service programmatic activities are directed towards maternal and child health, such as family planning, clinical gynecological and obstetric care, the post delivery period and the menopause, among other health care issues.

Low schooling was associated with a lower chance of cure. This reflects an adverse economic and social situation, which contributes to making individuals susceptible to illness and an unfavorable treatment outcome.[19] Low schooling was also associated with treatment dropout in a study conducted in the municipality of Porto Alegre, RS.[21]

In the present study, the 20-39 age range also showed a lower chance of a favorable outcome. This finding is in keeping with a study on factors associated with TB treatment abandonment in Londrina, PR, in 2006, which found that being a young adult was a risk factor for treatment dropout.[22] Individuals in this age group comprise the largest portion of alcohol users, smokers and illicit drug users, especially in large urban centers.[23-25] The contribution of these factors to TB treatment failure has already been demonstrated in other studies. The same reasoning can be applied to the condition of residing in urban areas, where the incidence of TB is greater in poor outskirts which are known for their social vulnerability,[17] as is the case of the metropolitan region of Rio de Janeiro.

Table 2 – Distribution and factors associated with tuberculosis outcome according to the hierarchical model of dimensions of vulnerability,[a] Rio de Janeiro State, 2011-2014

Characteristics	Unfavorable outcome[b] n (%)	Favorable outcome[c] n (%)	OR[d] crude (95%CI)[e]	P Value[f]	OR[d] adjusted (95%CI)[e]	P-Value adjusted[g]
LEVEL 1						
Sex						
Female	2,439 (16.6)	12,202 (83.4)	1.00	<0.001	1.00	<0.001
Male	6,230 (24.0)	20,404 (76.0)	0.65 (0.62;0.69)		0.71 (0.66;0.76)	
Education level (in years of schooling)						
Illiterate	167 (24.0)	529 (76.0)	1.00	<0.001	1.00	<0.001
1-4	1,729 (23.0)	5,637 (77.0)	0.28 (0.22;0.34)		1.08 (0.90;1.31)	
5-8	2,363 (23.0)	7,703 (77.0)	0.28 (0.24;0.33)		1.11 (0.92;1.33)	
9-12	1,161 (14 .0)	6,974 (86.0)	0.28 (0.24;0.33)		2.04 (1.68;2.47)	
≥13	192 (8.0)	2,204 (92.0)	0.52 (0.44;0.61)		3.48 (2.74;4.41)	
Race/skin color						
White	2,251 (16.0)	12,255 (84.0)	1.00	<0.001	1.00	<0.001
Black	2,095 (26.0)	6,016 (74.0)	1.06 (0.80;1.40)		0.62 (0.57;0.67)	
Brown	3,308 (23.0)	11,130 (77.0)	0.56 (0.42;0.74)		0.73 (0.68;0.78)	
Other	61 (16.0)	314 (84.0)	0.65 (0.49;0.86)		1.03 (0.73;1.46)	
Age (in years)						
<20	670 (17.0)	3,389 (83.0)	1.00	<0.001	1.00	<0.001
20-39	4,321 (24.0)	13,859 (76.0)	1.15 (1.03;1.28)		0.65 (0.58;0.73)	
40-59	2,792 (20.0)	11,452 (80)	0.73 (0.67;0.79)		0.97 (0.86;1.10)	
≥60	889 (19.0)	3,907 (81)	0.93 (0.86;1.01)		1.08 (0.93;1.25)	
LEVEL 2						
Place of residence						
Urban	8,139 (21.0)	30,439 (79.0)	1.00	<0.001	1.00	<0.001
Rural	46 (11.0)	378 (89.0)	0.45 (0.33;0.62)		2.27 (1.38;3.73)	
Institutionalized						
No	6,895 (20.0)	27,258 (80.0)	1.00	<0.001	1.00	<0.001
Prison	273 (21.0)	1,017 (79.0)	2.36 (2.08;2.68)		1.04 (0.80;1.34)	
Nursing home	25 (42.0)	34 (58.0)	2.23 (1.86;2.68)		0.35 (0.15;0.83)	
Orphanage	19 (26.0)	53 (74.0)	0.81 (0.48;1.38)		0.67 (0.29;1.55)	
Psychiatric hospital	8 (9.0)	81 (91.0)	1.66 (0.97;2.85)		3.50 (0.82;14.9)	
Other	391 (37.0)	655 (63.0)	6.04 (2.89;12.63)		0.40 (0.32;0.49)	
Occupational Disease						
No	5,536 (21.0)	21,443 (79.0)	1.00	0.001	1.00	0.116
Yes	116 (16.0)	622 (84.0)	1.38 (1.13;1.69)		1.24 (0.95;1.63)	
LEVEL 3						
HIV/AIDS						
No	4,547 (18.0)	20,170 (82.0)	1.00	<0.001	1.00	0.260
Yes	1,290 (41.0)	1,894 (59.0)	0.33 (0.30;0.36)		0.73 (0.42;1.27)	
Alcoholism						
No	5,339 (18.0)	24,220 (82.0)	1.00	<0.001	1.00	0.123
Yes	1,539 (33.0)	3,058 (67.0)	0.44 (0.41;0.50)		0.65 (0.38;1.12)	
Smoking						
No	684 (21.0)	2,525 (79.0)	1.00	<0.001	1.00	0.081
Yes	134 (40.0)	198 (60.0)	0.40 (0.32;0.51)		0.50 (0.23;1.09)	

Table 2 – Distribution and factors associated with tuberculosis outcome according to the hierarchical model of dimensions of vulnerability,[a] Rio de Janeiro State, 2011-2014

Characteristics	Unfavorable outcome[b] n (%)	Favorable outcome[c] n (%)	OR[d] crude (95%CI)[e]	P Value[f]	OR[d] crude (95%CI)[e]	P-Value adjusted[g]
LEVEL 3						
Diabetes						
No	6,324 (20.0)	24,682 (80.0)	1.00	<0.001	1.00	0.111
Yes	473 (17.0)	2,272 (83.0)	1.23 (1.11;1.36)		0.56 (0.28;1.14)	
Other comorbidities						
No	3,960 (18.0)	17,532 (82.0)	1.00	<0.001	1.00	0.895
Yes	1,511 (30.0)	3,447 (70.0)	0.51 (0.48; 0.55)		1.04 (0.56;1.96)	
LEVEL 4						
Notification Type						
New case	5,939 (17.0)	28,253 (83.0)	1.00	<0.001	1.00	<0.001
Recurrence	733 (26.0)	2,061 (74.0)	1.87 (1.67;2.09)		0.55 (0.43;0.72)	
Return after abandonment	1,390 (57.0)	1,032 (43.0)	1.10 (0.96;1.27)		0.21 (0.16;0.28)	
Unknown	139 (68.0)	65 (32.0)	0.29 (0.25;0.33)		0.69 (0.03;13.9)	
Referral	470 (28.0)	1,196 (72.0)	0.18 (0.13;0.25)		0.41 (0.28;0.60)	
Supervised Treatment						
No	4,227 (21.0)	16,118 (79.0)	1.00	0.001	1.00	0.307
Yes	3,110 (19.0)	12,937 (81.0)	1.09 (1.04;1.15)		0.91 (0.75;1.10)	
Clinical form						
Pulmonary	7,650 (22.0)	27,417 (78.0)	1.00	<0.001	1.00	0.624
Extra-pulmonary	642 (13.0)	4,237 (87.0)	1.43 (1.26;1.61)		1.22 (0.67;2.23)	
Pulmonary + extrapulmonary	380 (29.0)	953 (71.0)	2.63 (2.28;3.04)		0.84 (0.51;1.39)	
X-rays						
Normal	257 (14.0)	1,527 (86.0)	1.00	<0.001	1.00	0.207
Suspected	7,454 (21.0)	28,447 (79.0)	0.64 (0.56;0.73)		1.51 (0.80;2.84)	
Sputum smear microscopy (1st)						
Negative	1,762 (19.0)	7,705 (81.0)	1.00	<0.001	1.00	0.005
Positive	4,731 (22.0)	16,977 (78.0)	0.82 (0.77;0.87)		0.73 (0.59;0.91)	
Sputum culture						
Negative	367 (16.0)	1,881 (84.0)	1.00	<0.001	1.00	<0.001
Positive	1,073 (28.0)	2,735 (72.0)	0.50 (0.44;0.57)		0.58 (0.47;0.71)	

a) Level 1: Sex + race/color + age + schooling.
Level 2: Level 1 (significant) + place of residence + institutionalized + occupational disease.
Level 3: Level 2 (significant) + HIV/AIDS + alcoholism + smoking + diabetes + mental illness + comorbities.
Level 4: Level 3 (significant) + admission type + sputum smear (1st sample) + sputum culture + x-ray + supervised treatment.
b) Unfavorable outcomes were considered to be: abandonment, primary abandonment, death from TB, drug-resistant tuberculosis and failure.
c) Favorable outcome: Cure.
d) OR: *odds ratio*.
e) 95%CI: 95% confidence interval.
f) p-value in the non-adjusted analysis.
g) P-value in the adjusted analysis.

In Recife, PE, between 2005 and 2010, when analyzing factors associated with the outcome of tuberculosis treatment, the crude analysis found association between type of admission and outcome;[26] return after abandonment showed 7.2 times more chance of abandoning treatment, while recurrence showed 1.9 times more chance. The study conducted in Recife also found that return after abandonment was associated with a 79% higher chance of an unfavorable outcome, and a 45% higher chance of recurrence. Positive sputum smear microscopy and positive sputum culture were also associated with an unfavorable outcome. It is possible that this finding is associated with more severe clinical TB, related to cavitary disease, which hinders treatment of the disease.[27]

A limitation of the present study includes issues related to the incompleteness of the variables, including individuals without information on TB treatment outcome and individuals with unknown or inconsistent information for some variables analyzed. These are limitations found in other studies based on SINAN system data and are to be expected when using secondary databases.[28,29] However, due to sample size, this study has sufficient statistical power to detect differences between the groups.

Conducted in the state of Rio de Janeiro, this study allowed us to identify factors determining the outcome of TB treatment in a state with the highest burden of TB in the country. The outcome of tuberculosis treatment has proven to be associated with the clinical characteristics of TB and sociodemographic factors, corroborating the theoretical model proposed here of dimensions of vulnerability.[9]

Rio de Janeiro state is marked by social inequalities, especially in large urban centers. In terms of public policies, measures are needed to ensure universal access to services and, especially, social protection, in order to modify these social and economic determinants that influence the outcome of treating tuberculosis. As to surveillance actions, the importance of the complete filling in of the notification form is emphasized, considering the considerable incompleteness we found, especially in relation to the new SINAN-TB system variable: being a beneficiary of the government income transfer program.

Authors' contributions

Santana JN, Sales CM and Maciel EL participated in the conception and design of the study, analysis and interpretation of the results, writing and critical review of the manuscript. Prado TN contributed to the analysis and interpretation of results, writing and critical review of the content of the manuscript. All authors approved the final version of the manuscript and declared themselves to be responsible for all aspects of the study, ensuring its accuracy and integrity.

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