1 **Spatial analysis of the cure rate for tuberculosis in primary health care in the municipality of**

2 **Rio de Janeiro between 2012 and 2014**

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9 # Abstract

10 Background

11 Tuberculosis (TB) has a high disease burden and the World Health Organization (WHO) states it is a global

12 emergency. TB is the most important cause of death from infectious disease in adults. It is directly related to

13 access to health services and socioeconomic factors. Primary health care (PHC) provides greater linkage of

14 people to health services and greater medication adherence in some chronic diseases. It also provides

15 supervised treatment and more effective search for contactants. The PHC Reform started in 2009 in Rio de

16 Janeiro, increasing coverage from 7% to 46.16% in 2015.

17 **Methodology/Principal findings**

18 This paper aims to evaluate the spatial distribution of new TB cases closed with a cure outcome in dwellers

19 of Rio de Janeiro in the period 2012-2014, according to PHC coverage, controlling socioeconomic,

20 demographic and epidemiological factors. Variables were obtained from the Notifiable Diseases Information

21 System for Tuberculosis (SINAN-TB) and the socioeconomic variables from the 2010 national census at

22 census tract level. The socioeconomic variables were selected from multivariate analysis using main factors

23 analysis technique. The generalized additive model (GAM) was used for the spatial analysis. Association

24 was found between TB cure and variables education, alcoholism, contacts search, HIV serology and elderly.

25 People with family health coverage between 35 and 41 months were 1.64 more likely of cure when

26 compared to people without coverage (95% CI 1.07-2.51). Spatial analysis identified areas with less

27 probability of cure for tuberculosis in the municipality of Rio de Janeiro.

28 **Keywords**: Primary Health Care; Tuberculosis, Family Health; Spatial Analysis.

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Author Summary

Tuberculosis is associated to social and demographic conditions. Lack of access to healthcare contributes to delay in diagnosis and in the beginning of the treatment. Primary health care improve access and adherence to treatment. This study can be useful as a public health policy, since it is possible to prioritize the region in the map to improve TB cure. We found association between tuberculosis cure and the duration of implantation of the primary health care teams. This finding corroborates the importance of treating tuberculosis in this level of care. The spatial analysis of cases of tuberculosis cure showed a significant spatial association with the cure of tuberculosis. The results of this study can contribute reinforcing the policy makers for developing primary health care to improve the access to health services and to reach better TB cure rates. Spatial analysis may be an useful tool for identifying the areas where to prioritize efforts for reaching better results.

Introduction

Tuberculosis (TB) is an infectious disease of great magnitude and importance in the world. It was declared a worldwide emergency disease by the World Health Organization (WHO) in 1993 and is the largest cause of death by infectious diseases in adults [1].

Brazil is one of WHO 22 priority TB control countries and ranked 16th in 2014. These countries together account for 80% of global cases. TB prevalence in Brazil in 2014 was 33.5 / 100,000 inhabitants and mortality rate (MR) was 2.3 deaths / 100,000 inhabitants. Despite this position, an average annual incidence reduction of 2.3% and 0.5 deaths / 100,000 inhabitants has been recorded between 2005 and 2014 [1].

In 2014, the incidence rate in the municipality of Rio de Janeiro was 66.8 / 100,000 inhabitants. The cure rate of smear-positive pulmonary tuberculosis in the city was 69.2%, below that recommended by the WHO, which is 85% [2].

The disease has a direct relationship with the misery and social exclusion, therefore the most socially vulnerable people have a greater probability of developing and proliferating this disease.

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57   Socioeconomic factors hamper people's access to health services [3] which in turn contribute to

58   delayed TB diagnosis and treatment, increasing the possibility of abandoning treatment, one of the

59   main obstacles to control this disease [3].

60   PHC plays a key role in curing tuberculosis because it is the first level of access of a health

61   system, with some basic principles of organization such as longitudinality, comprehensive care and

62   coordination of care within the system itself [4,5]. Therefore, PHC allows greater access and

63   adherence to TB treatment, as well as reaching the most vulnerable populations [4].

64   The countries that adhered to PHC as a health system organizer showed evidence of

65   improvement in care indicators as well as lower health investments when compared to those without

66   structured PHC [4,6,7,8].

67   An association between PHC expanded coverage and reduced treatment abandonment rate

68   and lower mortality due to tuberculosis is described [9].

69   The Municipality of Rio de Janeiro (MRJ) had ESF coverage of approximately 7% up to

70   2008 [10] and only 3.55% coverage of full teams [11,12]. As of 2009, the PHC reform began with

71   expanded coverage to approximately 40% in 2012 and 46.16% in 2015, considering full teams

72   [6,10].

73   Currently, there are two PHC care models: (1) Family Health, with a more comprehensive

74   supply of health services based on PHC principles (access, longitudinality, care coordination and

75   comprehensiveness) [4] with general practitioners and nurses with territorially-defined health

76   responsibility; and (2) Traditional PHC, with medical care based on gender and age (pediatrics,

77   gynecology, medical clinic) [6].

78   Considering that TB is a disease strongly related to socioeconomic factors

79   [13,14,15,16,17,18,19], as well as to access to health services[3,9], it is necessary to evaluate the

80   relationship of expanded PHC coverage in the cure of TB in the municipality.

81   This paper aims to evaluate the spatial distribution of new cases of tuberculosis closed with

82   a cure outcome in residents of Rio de Janeiro in the period 2012-2014, by PHC coverage,

83   controlling socioeconomic, demographic and epidemiological factors.

3

84 **Methods**

85   This cross-sectional study was carried out in Rio de Janeiro, correlating TB cure with family

86 health coverage and socioeconomic, demographic and epidemiological variables, and the unit of

87 analysis is made of individuals from newly reported cases of tuberculosis in the period 2012-2014.

88 The municipality is located in the southeast of the country at geographic coordinates 22°44'45.59"

89 to 23°04'58.34" south latitude and 43°05'48.89" to 43°47'43.79" west longitude; it has an area of

90 1,199.82 km^2, a population density of 5,265.82 inhabitants / km^2 and an exclusively urban

91 population estimated at 6,476,631 inhabitants in 2015 [20]. It is divided into 160 neighborhoods, 33

92 administrative regions and 10 health districts (planning areas). Rio shows great economic and social

93 contrasts, with approximately 22% of the population residing in subnormal clusters [21].

94   The study population is comprised of new cases of tuberculosis residing in the MRJ notified

95 in the period 2012-2014. All cases were eligible to be part of the study in order to minimize

96 selection bias.

97   The geo-referencing technique was used from the residence address to identify family's

98 health coverage, assigning a geographical position for each record (latitude and longitude). Thus, it

99 was possible to identify through spatial consultation the family health's coverage polygons to which

100 the point was inserted. The coverage maps were developed by the Municipal Health Secretariat of

101 Rio de Janeiro and correspond to the existing coverage in 2012, 2013 and 2014, with reference to

102 the month of December. Georeferencing of addresses was done using the "Geocode" tool made

103 available by Google Maps through a free Application Programming Interface (API).

104   This process utilized the Google's streets and location base. The accuracy of georeferencing

105 can be evaluated from a score ranging from 0 to 10, (0-not found, 1-country level, 2-state, 3-

106 subregion, 4-city, 5-Zip Code, 6-streets, 7-intersection between streets, 8-address, 9-name of the

107 building or trade, 10-maximum precision). Addresses with a score lower than "5" were considered

108 as losses. Records with scores between "8" and "10" were considered with acceptable accuracy.

109 The remaining records were manually reviewed. Of the 14,384 georeferenced records, the precise

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110 geographic coordinates of 3,484 records (24.22%) could not be determined, characterizing losses of

111 the georeferenced sample. The total number of georeferenced records was 10,900 new closed cases.

112   The outcome variable considered in this study was the "closed with a cure outcome" (yes /

113 no) obtained from the SINAN-TB and the exposure variable was "family health coverage",

114 expressed by the "time of implantation of the teams until TB diagnosis (in months)".

115   The selection of variables was based on the theoretical TB cure model (Fig 1) based on the

116 realms "environment", "individual factors", "access to health service" and "social status". The

117 model includes demographic, social, epidemiological, access and use of health services variables.

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121 **Fig 1. Model of analysis for the cure of tuberculosis [a].**

122 [a] To cure tuberculosis, an individual with the disease must have been diagnosed and treatment performed. The

123 environment, individual factors, access to health services and social condition (agglomeration, income, education,

124 household conditions and demographic factors) of the individual influence the transmission, diagnosis and treatment of

125 tuberculosis. Proper treatment results in the cure of tuberculosis.

126

127   The variable "family health teams implantation time" reflects access to health service and

128 was obtained from data from the National Registry System of Health Establishments of the Ministry

129 of Health (SCNES). For the purpose of classifying family health coverage, all records located in

130 polygons of areas with family health coverage whose diagnosis was given after 3 months of

131 implantation of the team were considered with coverage and all other cases without family health

132 coverage. The 3-month period was used as cut-off point because it is the minimum reasonable time

133 for a new family health team to carry out all registration of people residing in its health territory and

134 produce an initial health diagnosis.

135   The variables selected from the SINAN-TB were: age; gender; race / color (white / non-

136 white); schooling; "HIV coinfection" (yes / no); "alcohol abuse history" (yes / no); "Contact

137 search" (yes / no); "serology for HIV" (positive, negative, not performed); "supervised treatment"

138 (yes / no).

139   Considering that there is a large number of socioeconomic variables from the 2010

140 demographic census (IBGE, 2011)[22], a multivariate analysis was performed using the main

141 components analysis technique. Thus, the TB cure-related realms ("agglomeration", "household

142 conditions", "demographic", "schooling", "income") were established from the theoretical model

143 related to the "social condition" (Fig 1) and for each realm, the variables that, to a lesser extent,

144 represent the other variables of that realm were selected.

145   The socioeconomic and demographic variables resulting from this analysis were: "average

146 monthly income of the person in charge (R$)"; "average number of residents per household";

147 "population density in the census sector"; "Density of dwellers/rooms"; "proportion of permanent

148 private households with bathrooms for the exclusive use of residents or water closet and sanitary

149 sewage via general sewer or rainwater network"; "Proportion of permanent households with

150 electricity"; "average number of toilets per permanent private residence"; "aging rate".

151   The variables obtained from the Demographic Census represent the averages and

152 proportions of each census tract. These values were repeated for each individual resident in the

153 same census tract, since these variables in this level of aggregation show high homogeneity. The

154 other variables were analyzed from the individual level.

155   Data descriptive analysis was performed using the R software (R Development Core Team,

156 2016)[23,24] through bivariate logistic regression (gross analysis).

157   During TB spatial exploratory analysis, we observed the distribution of points and

158 identification of possible clusters through the point density estimation technique, defined as Kernel

159 density estimation, which consists of generating a point density surface within a region of influence,

160 weighted by the distance of each from the location of interest, for the visual identification of "hot

161 areas" on the map. Bandwidths from 500m to 3,000m were tested, with 250m increments. A matrix

162 of 500x500 points and a radius of 2,500 m was used because it was considered the most appropriate

163   for highlighting strategic areas. We generated maps with estimates of TB incidence rate through the

164   kernel ratio between reported cases of TB and the kernel of the population.

165   Spatial analysis was based on the generalized additive model (GAM), which can be

166   considered an extension of generalized linear models, with the inclusion of a non-parametric

167   element by smoothing functions. The model has the great advantage of being more flexible and

168   relatively simple to interpret [25]. The Thin Plate Regression Splines smoothing technique was

169   used.

170   The construction of the generalized additive models was performed through manual

171   selection, based on the essential factors of the theoretical framework (Fig 1), not only considering

172   the statistically significant variables in the bivariate analysis, but also those of epidemiological

173   importance.

174   We did not only consider the p-value of each association, but the importance previously

175   described of each variable and the impact on the explanatory power of the model. Only those

176   variables with a clear negative impact under the explanatory power of the model, observed through

177   deviance, were removed.

178   The software for constructing family health coverage maps and spatial data queries was

179   ArcGIS, version 10.2.2 [26] in Latlong/WGS84 projection, available in the shapefile extension.

180   R software [23] was used with RStudio software [24], version 0.99.893 for the exploratory

181   analysis, multivariate analysis, kernel estimation and spatial analysis. During the analyses, the

182   following additional packages of R were used: car [27], mgcv [28], descr [29], sp [30], sdep [31],

183   maptools [32], splancs [33], fields [34], RColorBrewer [35], ggplot2 [36].

184   This work was funded by the authors. The Ethics Committee of the Municipal Health

185   Secretariat of Rio de Janeiro approved the study, under opinion Nº 1.389.137 and CAAE protocol

186   52493216.5.0000.5279, in compliance with the recommendations contained in Resolution 466/12 of

187   the National Health Council. All data analyzed were anonymized.

188

189   **Results**

190 During the years 2012 to 2014, 16,363 new TB cases of MRJ residents were identified. Of

191 these, 905 cases were excluded from the study due to lack of closure in addition to 161 cases of

192 street population and other 913 records of institutionalized persons, since these individuals cannot

193 be classified in terms of family health coverage, leaving out 14,384 records for the study.

194 The closing percentage for this period was 94.47%. The cure rate was 71.57% (11,063 new

195 cases) of the total cases closed. The mean incidence rate was 84.91 cases / 100,000 inhabitants. In

196 the same period, there were 725 cases of death by TB resulting in a mean specific mortality rate of

197 3.76 cases per 100,000 inhabitants, and the case fatality rate was 4.69% among new cases closed.

198 Median age was 38 years.

199 The estimation of the incidence rate from the Kernel ratio (Fig 2) shows that the "hot areas"

200 are mainly concentrated in the southern zone (Rocinha), followed by the northern zone (Complexo

201 do Alemão, Acari, Pavuna) and the western zone (Senador Camará, Realengo).

202

203 **Fig 2. Kernel ratio among new cases of tuberculosis and population. Municipality of Rio de Janeiro (RJ), Brazil,**

204 **from 2012 to 2014.**

205 **Source**: **Cartographic data: IPP, Epidemiological data: SINAN-TB. Projection GCS. Datum WGS84**

206

207 Of the new TB cases between 2012 and 2014 that were part of the study (n = 14,384), most

208 cases occurred in males (n = 8,919; 62.0%), of non-white race / color = 7,839, 54.5%) and illiterates

209 (n = 4,493, 31.2%).

210 An association with several variables was found (Table 1) from the crude bivariate analysis

211 of TB cure with socioeconomic and demographic variables. In relation to age, there is a lower

212 probability of cure in the age range > 25 to 50 years (OR 0.86, 95% CI 0.78-0.94) compared to the

213 reference category (0 to 25 years). Among individuals aged > 80 years, the probability of cure

214 decreases even further (OR 0.44, 95% CI 0.32-0.59). Women were 1.51 times (95% CI 1.39-1.63)

215 more likely to be cured than men. Non-white people were less likely to be cured (OR 0.68, 95% CI

216 0.62-0.73) than white people. The higher the level of schooling, the greater the probability of cure

217 compared to illiterate people. The higher the average monthly income of the person responsible, the

218 greater the probability of cure. On the other hand, the higher the average number of residents in

219 permanent private households, the lower the probability of cure. The greater the percentage of

220 permanent private households with electricity and the average number of bathrooms per household,

221 the greater the probability of a cure. The higher the aging rate of the census tract of the individual,

222 the greater the probability of cure, evidencing an apparent paradox with findings in the age groups

223 measured at the individual level.

224

225 **Table 1. Gross cure analysis of new cases of tuberculosis with socioeconomic variables (N = 14,384). Municipality**

226 **of Rio de Janeiro (RJ), Brazil, 2012-2014.**

Variables (N=14,384)	Cure						OR	CI 95%	p-value
	Yes		No		Total				
	n	%	N	%	N	%			
Age									
0 to 25 years	2,759	26.2%	926	24.0%	3,685	25.6%	1.00		
>25 to 50 years	4,865	46.2%	1,908	49.5%	6,773	47.1%	0.86	0.78-0.94	<0.001[b]
>50 to 80 years	2,745	26.1%	923	23.9%	3,668	25.5%	1.00	0.9-1.11	0.975
>80 years	96	0.9%	74	1.9%	170	1.2%	0.44	0.32-0.59	<0.001[b]
Ignored	65	0.6%	23	0.6%	88	0.6%	0.95	0.59-1.53	0.839
Sex									
Male	6,264	59.5%	2,655	68.9%	8,919	62.0%	1.00		
Female	4,264	40.5%	1,199	31.1%	5,463	38.0%	1.51	1.39-1.63	<0.001[b]
Race/color									
White	4,243	40.3%	1,169	30.3%	5,412	37.6%	1.00[a]		
Non-white	5,570	52.9%	2,269	58.9%	7,839	54.5%	0.68	0.62-0.73	<0.001[b]
Ignored	717	6.8%	416	10.8%	1,133	7.9%	0.47	0.41-0.54	<0.001[b]
Schooling									
Illiterate	3,186	30.3%	1,307	33.9%	4,493	31.2%	1.00[a]		
Primary school	1,747	16.6%	496	12.9%	2,243	15.6%	1.44	1.28-1.63	<0.001[b]
Secondary school	1,923	18.3%	389	10.1%	2,312	16.1%	2.03	1.79-2.3	<0.001[b]
Higher education	619	5.9%	100	2.6%	719	5.0%	2.54	2.04-3.17	<0.001[b]
Ignored	3,055	29.0%	1,562	40.5%	4,617	32.1%	0.80	0.73-0.88	<0.001[b]

	OR	CI 95%	p-value
Monthly average income of the responsible person (R$)	1.001	1.001-1.004	<0.001[b]
Average number of residents in permanent private households	0.77	0.69-0.85	<0.001[b]
Percentage of permanent households with electricity	2.16	0.57-8.06	<0.001[b]
Average number of restrooms per household	1.33	1.20-1.48	<0.001[b]
Aging rate	5.87	2.77-12.43	<0.001[b]

227 SOURCE: Municipal databases of SINAN (DATASUS/MS) and IBGE, 2010. Updated 10/01/2016.

228 Abbreviations: n, sampling size; OR, odds ratio; SD, standard deviation; p-value, significance level.

229 [a] reference category; [b] statistical significance p<0.05

230

231 An association between cure of new tuberculosis cases and some epidemiological variables

232 was found (Table 2). People without AIDS coinfection were 3.46 (95% CI: 3.07-3.91) times more

233 likely of being cured when compared to people with coinfection. Similarly, people with negative

234 HIV serology were 3.67 (95% CI 3.28-4.12) times more likely of being cured compared to people

235 with positive serology. On the other hand, people with unsupervised treatment were less likely to be

236 cured (OR 0.65, 95% CI 0.60-0.70) compared with those whose treatment was supervised, and

237 people whose cases had no search for contactants were also less likely to be cured (OR 0.36, 95%

238 CI 0.33-0.39) compared to those who did. In relation to the Family Health coverage, a slightly

239 higher probability of cure is perceived the higher the coverage, but without statistical significance.

240

241 **Table 2. Gross cure analysis of new cases of tuberculosis with epidemiological and healthcare variables (N =**

242 **14,384). Municipality of Rio de Janeiro (RJ), Brazil, 2012-2014.**

Variables (N=14,384)	Cure						OR	CI 95%	p-value
	Yes		No		Total				
	n	%	N	%	N	%			
AIDS Coinfections									
Yes	606	8.0%	643	23.1%	1,249	12.1%	1.00		
No	6.977	92.0%	2,139	76.9%	9,116	87.9%	3.46	3.07-3.91	<0.001[b]
HIV test performed									
Positive	744	7.1%	707	18.3%	1,451	10.1%	1.00		
Negative	7.573	71.9%	1,960	50.9%	9,533	66.3%	3.67	3.28-4.12	<0.001[b]
Not performed	2.213	21.0%	1,187	30.8%	3,400	23.6%	1.77	1.56-2.01	<0.001[b]

10

Supervised treatment									
Yes	6.181	65.2%	1,895	54.9%	8,076	62.4%	1.00		
No	3.300	34.8%	1,556	45.1%	4,856	37.6%	0.65	0.6-0.7	<0.001[b]
Search for contactants									
Yes	8.572	81.4%	2,359	61.2%	10,931	76.0%	1.00		
No	1.958	18.6%	1,495	38.8%	3,453	24.0%	0.36	0.33-0.39	<0.001[b]
Alcohol abuse									
Yes	769	8.7%	524	17.2%	1,293	10.9%	1.00		
No	8.066	91.3%	2,517	82.8%	10,583	89.1%	2.18	1.94-2.46	<0.001[b]
FH coverage									
4 to 18 months	1.211	26.8%	417	25.8%	1,628	26.6%	1.00		
>18 to 35 months	1.766	39.1%	680	42.0%	2,446	39.9%	0.89	0.78-1.03	0.115
>35 to 41 months	418	9.3%	124	7.7%	542	8.8%	1.16	0.92-1.46	0.207
>41 months	1.118	24.8%	397	24.5%	1,515	24.7%	0.97	0.83-1.14	0.717

243 SOURCE: Municipal databases of SINAN (DATASUS/MS) and IBGE, 2010. Updated 10/01/2016.

244 Abbreviations: n, sampling size; OR, odds ratio; SD, standard deviation; p-value, significance level.

245 [a] reference category; [b] statistical significance p<0.05

246 The spatial Generalized Additive Model (GAM) enabled the building of a TB cure

247 probability map. Thus, it was assumed that cases were all newly reported cases of tuberculosis in

248 MRJ in the period from 2012 to 2014 that were not closed due to cure outcome (non-cure), and

249 controls those records closed due to cure outcome (Fig 3).

250

251 **Fig 3. Map of probability of cure of tuberculosis using the Generalized Additive Model – GAM for cases (not**

252 **cured) and controls (cure). Rio de Janeiro, 2012 to 2014.**

253 **Source**: Cartographic data: IPP, Epidemiological data: SINAN-TB. Projection GCS. Datum WGS84

254 It is possible to observe that people residing within the blue contours in the west and south

255 zones (right and left ends of the map) represent areas with an OR significantly above 1, that is,

256 people residing in those areas tend to have more tuberculosis cure, whereas those living in the north,

257 surrounded by the red contour (central contour of the map) tend to have less probability of cure.

258 The final model of the spatial analysis of new TB cases in MRJ in the years 2012 to 2014 for

259 TB cure and the socioeconomic, demographic and epidemiological variables using the generalized

260 additive model is presented in Table 3.

11

261 **Table 3. Final model of spatial analysis of new cases of tuberculosis with socioeconomic, demographic and**

262 **epidemiological variables using the generalized additive model - GAM (N = 14,384). Municipality of Rio de**

263 **Janeiro (RJ), Brazil, 2012-2014.**

Variable	Coefficient	Error	OR	CI 95%	*p*-value
Coverage 4 to 18 months	0.3101913	0.1337	1.36	1.04-1.77	0.020*
Coverage >35 months to 41 months	0.4972078	0.2178	1.64	1.07-2.51	0.022*
Coverage >41 months	0.0982589	0.1378	1.10	0.84-1.44	0.476
Alcohol abuse (yes)	-0.7423219	0.1556	0.47	0.35-0.64	<0,001*
Primary School	0.1327906	0.1345	1.14	0.87-1.48	0.323
Secondary School	0.5474371	0.1454	1.72	1.30-2.29	<0,001*
Higher Education	0.4809512	0.2641	1.61	0.96-2.71	0.068.
Search for contactants (yes)	0.6972460	0.1273	2.00	1.56-2.57	<0,001*
Positive serology for HIV (yes)	-1.1426839	0.1470	0.31	0.23-0.42	<0,001*
Supervised treatment (yes)	0.1781498	0.1271	1.19	0.93-1.53	0.160
Age 0 to 25 years	0.0005724	0.1332	1.00	0.77-1.29	0.996
Age > 50 to 80 years	0.3062125	0.1339	1.35	1.04-1.76	0.022*
Age > 80 years	-1.1596947	0.5508	0.31	0.10-0.92	0.035*
Aging rate	2.2402193	1.1253	9.39	1.03-85.26	0.046*

264 SOURCE: Municipal databases of SINAN (DATASUS/MS) and IBGE, 2010. Updated 10/01/2016.

265 Deviance: 9.16%; AIC/UBRE: -0.049082

266 Abbreviations: OR, odds ratio; CI 95%, 95% confidence interval; p-value, significance level.

267 * Statistical significance p<0.05

268   The family health coverage variable, measured here as time lapse of teams implantation at

269 the time of diagnosis, was significant for the categories "4 to 18 months" and "> 35 months to 41

270 months". People covered by family health tend to cure more for tuberculosis the longer the team's

271 time of implantation: OR 1.36 (95% CI 1.04-1.77) and OR 1.64 (95% CI 1.07-2 , 51), respectively.

272 People with a history of alcohol abuse had almost half the probability of cure (OR 0.47, 95% CI

273 0.35-0.64) when compared to people with no history of alcohol abuse. There was a positive trend in

274 the association between the educational level and the probability of TB cure, especially in the case

275 of secondary school students, with 1.72 times the probability of cure (95% CI 1.30-2.29) compared

276 to illiterate people. People where the search for contactants occurred were 2.00 (95% CI 1.56-2.57)

277 times more likely of achieving cure. People who had positive HIV serology were 0.31 (95% CI

12

278 0.23-0.42) times less likely of achieving cure. On the other hand, people residing in census tracts

279 with higher aging rates were 9.39 (95% CI 1.03-85.26) times more likely of achieving cure. The

280 figure below illustrates the same final spatial model through a chart with the odds ratio of the

281 variables.

282

283 **Fig 4. Final spatial analysis model using the generalized additive model - GAM for non-cure of tuberculosis. Rio**

284 **de Janeiro, 2012 to 2014**

285   The final spatial model map can be visualized in Fig 5. It is the smoothed spatial component,

286 adjusted for the other socioeconomic, demographic and epidemiological variables of the final

287 model. Significant spatial association was found (p = 0.0219). The areas surrounded by green dotted

288 lines had positive spatial correlation for cure, whereas red dotted lines had inverse spatial

289 correlation with cure.

290

291 **Fig 5. Final spatial analysis model using the generalized additive model - GAM for tuberculosis cure - smoothed**

292 **spatial component adjusted for the other covariates. Rio de Janeiro, 2012 to 2014.**

293

294

295 **DISCUSSION**

296   In Brazil, there are few studies on the spatial distribution of endemic diseases, such as TB, in

297 urban areas [15]. The information about the spatial and temporal spread of these diseases allows to

298 understand the occurrence of these events in the territory. In addition, the description and

299 visualization of the spatial distribution of the event facilitate the identification of its association with

300 local characteristics, such as socioeconomic conditions.

301   The cure rate of 71.57% was lower than the value found in other studies conducted in other

302 regions of the country, such as Silva et al (2014)[17], who found 90.9% of the cases closed due to

303 cure in Maranhão. However, it is better than in Crato (CE), where Pinto et al (2015)[18] found a

304 cure rate of 47.2%.

13

305   Spatial analysis demonstrated a significant spatial association with TB cure. In addition, the

306   TB cure probability map shows that the southern and western zones were more likely to be cured

307   from tuberculosis while residents living in the north were less likely to be cured. This result can be

308   useful as a public health policy, since it is possible to prioritize this region to improve TB cure in

309   MRJ. Possibly, the regions with the greatest probability of cure are associated with greater coverage

310   of the family health strategy, such as in the western part of the municipality, covering more than

311   90% since 2010, in addition to Rocinha with 100% coverage since 2012. On the other hand, for the

312   rest of the southern zone and the Tijuca region, it is probably due to much easier access to other

313   health facilities, better socioeconomic situation and retention of physicians with good qualification.

314   From the spatial analysis, it was possible to perceive, as expected, an association between

315   tuberculosis cure and better socioeconomic conditions such as educational level and income.

316   Despite the association between race / color and cure in bivariate analysis, no association was found

317   in the final spatial analysis model. Possibly, this variable has bad data entry problems. The spatial

318   model demonstrated that the higher the educational level, the better the probability of cure, which is

319   consistent with that expected from the literature [17,19].

320   There was an apparent paradox between the lower probability of cure among the elderly,

321   when analyzing the variable age at the individual level and the higher probability of cure the higher

322   the aging rate at the level of the census tract. This may be due to the fact that, at the individual level,

323   older patients have lower adherence to treatment due to intrinsic factors, leading to more adverse

324   effects, increased drug interaction, forgetfulness of taking medication and less immunity. On the

325   other hand, those patients residing in census tracts with higher rates of aging have a greater

326   likelihood of cure, probably because this variable represents more structured communities from the

327   socioeconomic viewpoint, which could have a longer life expectancy, and from a temporal

328   viewpoint, because they are possibly older migration communities and with a larger social support

329   network that would favor a better treatment and consequently a better probability of cure. It is worth

330   noting that the aging rate was the variable that showed the highest probability of cure (OR 9.39),

331   albeit with the greatest variability (95% CI 1.03-85.26), evidencing the importance of the social

14

332   context for TB cure. The positive serology for HIV and alcohol abuse variables were associated

333   with a lower probability of TB cure. In addition to the expected lower immunity, these patients may

334   show less adherence, due to drug interaction and greater occurrence of medication side effects

335   [37,38].

336   The search for contactants was associated with a greater likelihood of cure for tuberculosis.

337   Possibly, those cases whose professionals have made active search for contactants are the well-

338   cared patients, receiving the greatest attention from the professionals.

339   It can be observed that the longer the implantation time of family health teams since the

340   diagnosis of the disease, the greater the probability of TB cure, except for the category of 41 months

341   or more, which evidenced the worst probability of cure among the categories. Data of this study are

342   insufficient to explain this phenomenon, since it would be expected that teams with 41 months or

343   more would be more likely to cure. One possible explanation is that the first family health teams in

344   the MRJ were deployed in very vulnerable regions and, despite SMS-Rio efforts, some of them

345   remained for a long time without being complete due to lack of doctors. This type of study does not

346   allow a correlation between cause and effect and the external validity may not be reached. Other

347   studies are necessary to confirm or not the results founded.

348

349   **Conclusion**

350   The spatial analysis of cases of tuberculosis cure in the years 2012 to 2014 showed a

351   significant spatial association with the cure of tuberculosis. In addition, regions in the municipality

352   with more probability of cure were evidenced, which favors the manager to implement more

353   efficient TB control measures. Regarding PHC coverage, a significant association was found

354   between TB cure and time of family health implantation when the socioeconomic variables were

355   controlled. This finding corroborates the importance of treating tuberculosis in this level of care.

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465

Supporting Information Legends

467   **S1 Checklist: STROBE Checklist**

468   **S2 Fig 3. Model of analysis for the cure of tuberculosis .** To cure tuberculosis, an individual with the disease must

469   have been diagnosed and treatment performed. The environment, individual factors, access to health services and social

470   condition (agglomeration, income, education, household conditions and demographic factors) of the individual

471   influence the transmission, diagnosis and treatment of tuberculosis. Proper treatment results in the cure of tuberculosis.

472

473   **S3 Fig 4. Kernel ratio among new cases of tuberculosis and population. Municipality of Rio de Janeiro (RJ),**

474   **Brazil, from 2012 to 2014.** Source: Cartographic data: IPP, Epidemiological data: SINAN-TB. Projection GCS. Datum
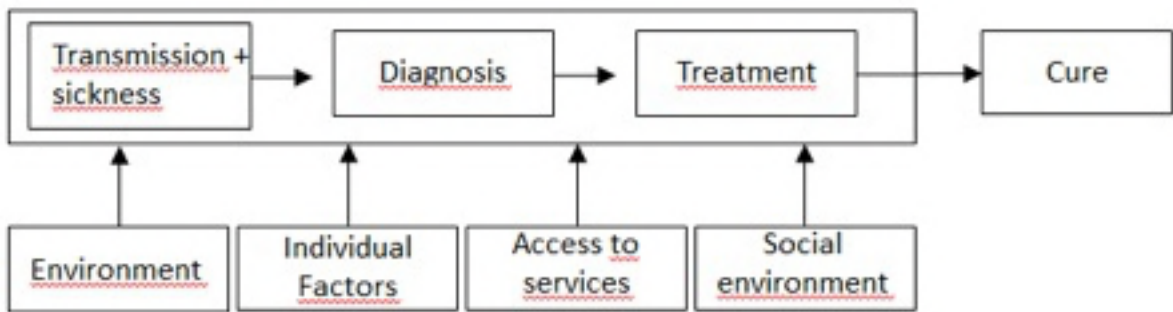
475   WGS84

476

477   **S4 Fig 3. Map of probability of cure of tuberculosis using the Generalized Additive Model – GAM for cases (not**

478   **cured) and controls (cure). Rio de Janeiro, 2012 to 2014.** Source: Cartographic data: IPP, Epidemiological data:

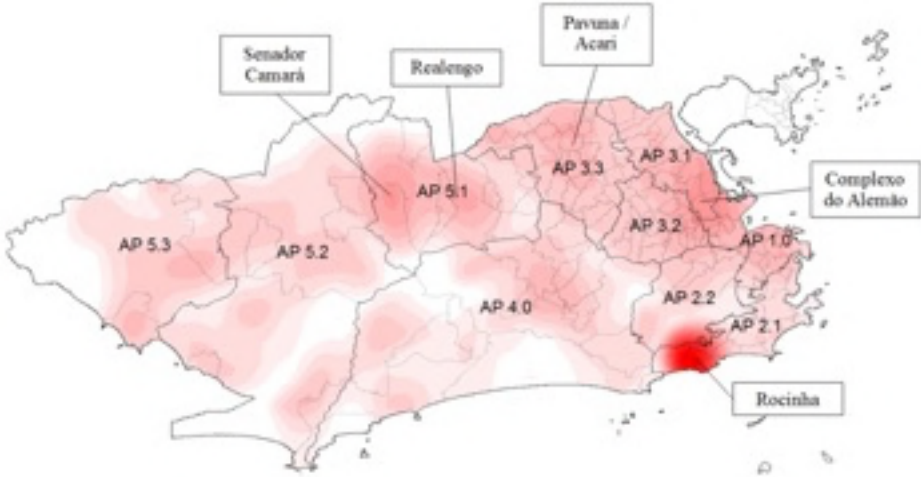479   SINAN-TB. Projection GCS. Datum WGS84
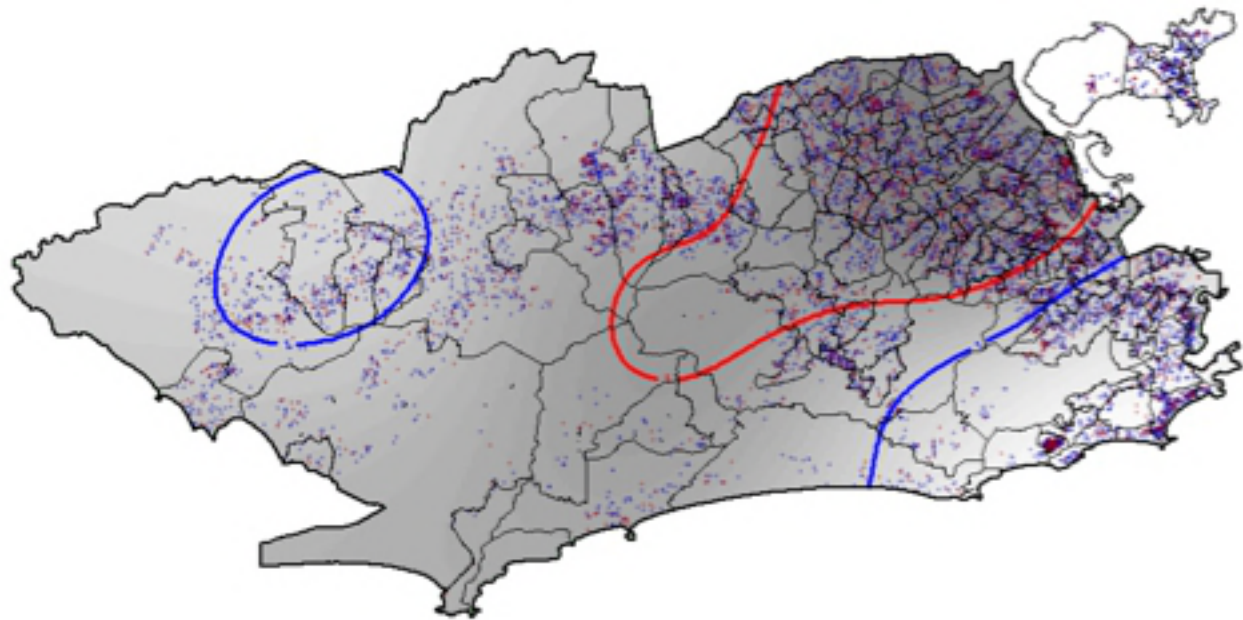
480

481   **S5 Fig 4. Final spatial analysis model using the generalized additive model - GAM for non-cure of tuberculosis.**

482   **Rio de Janeiro, 2012 to 2014**

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| Transmission + sickness | → | Diagnosis | → | Treatment | → | Cure |

Environment → Transmission + sickness

Individual Factors → Diagnosis

Access to services → Treatment

Social environment → Treatment

Senador Camará

Realengo

Pavuna / Acari

Complexo do Alemão

AP 5.1

AP 3.3

AP 3.1

AP 3.2

AP 1.0

AP 5.3

AP 5.2

AP 4.0

AP 2.2

AP 2.1

Rocinha

Variables (y-axis, top to bottom):
- Aging rate
- Search for contacts (yes)
- Secondary school
- Coverage >35 months to 41 months
- Higher education
- Coverage 4 to 18 months
- Age >50 to 80 years
- Supervised treatment (yes)
- Primary school
- Coverage >41 months
- Age 0 to 25 years
- Alcohol abuse (yes)
- Positive serology for HIV (yes)
- Age >80 years

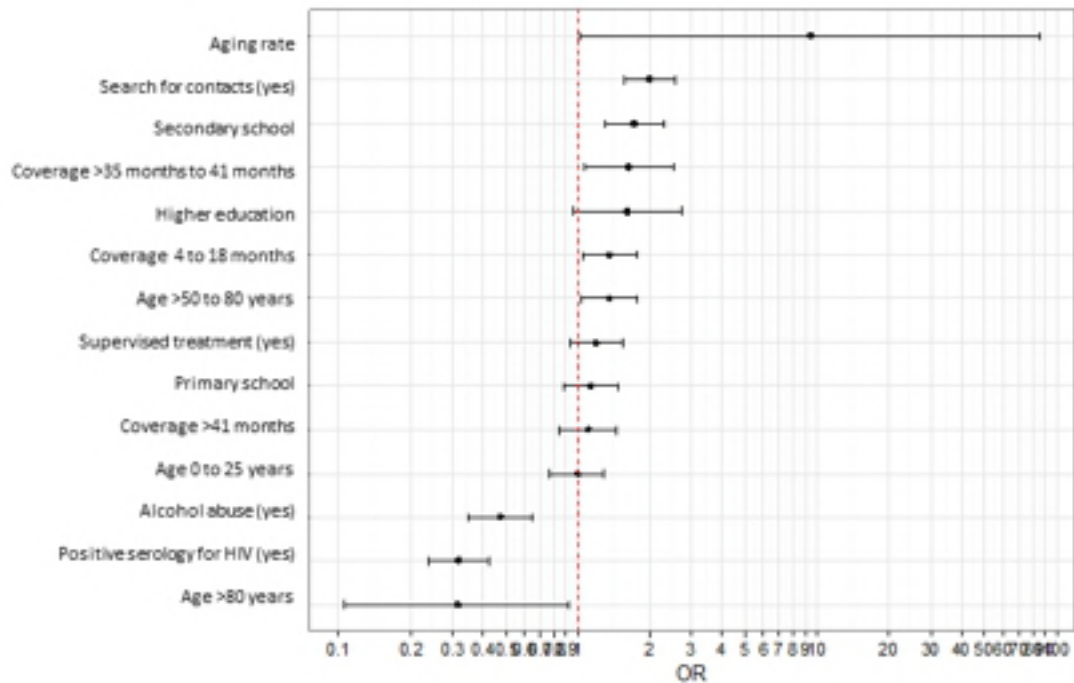OR (x-axis): 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1 2 3 4 5 6 7 8 9 10 20 30 40 50 60 70 80 90 100

Modelo espacial final Cura de Tuberculose - GAM