

# Bayesian spatio-temporal models for mapping TB mortality risk and its relationship with social inequities in a region from Brazilian Legal Amazon

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**Background:** Reducing TB mortality is a great challenge in Brazil due to its territorial extension, cultural variations and economic and political crises, which impact the health system. This study aimed to estimate in space and time the risk of TB mortality and test its relationship with social inequities.

**Methods:** This was an ecological study that included deaths from TB between 2006 and 2016 in Cuiabá, Brazilian Legal Amazon. Bayesian models based on the integrated nested Laplace approximation approach were used to estimate spatio-temporal RRs. RRs for TB mortality were obtained according to the covariables representative of social inequities.

**Results:** The risk of TB mortality was stable between 2006 and 2016 and high-risk areas were identified throughout the municipality studied. Regarding social inequities, income was an important factor associated with TB mortality risk, as an increase of 1 SD in income resulted in a 35.4% (RR 0.646; CI 95% 0.476 to 0.837) decrease in risk.

**Conclusions:** The results provided evidence of areas with higher TB mortality risks that have persisted over time and are related to social inequities. Advancing social policies and protections in these areas will contribute to achieving the WHO's End TB strategy.

**Keywords:** Bayesian inference, Mortality, Public health, TB

## Introduction

TB is the primary cause of death from infectious diseases in the world, which makes it the perfect expression of unfair suffering and inequality.<sup>1</sup> Even with available medicines, the number of cases and deaths has increased drastically in vulnerable groups and in those living in extreme poverty. The WHO launched the End TB strategy for the post-2015 period, which has the ambitious goal of reducing TB mortality by 95% by 2035.<sup>1</sup>

The economic and political crises in Brazil over the last year have affected the financing of the healthcare system, which

is likely to affect actions addressing TB control, as well as the goal of ending TB. The country has adopted a universal health system, where it has recognised health as a civil right through its constitution promulgated in 1988.<sup>2,3</sup>

The country has a huge territorial extension, with approximately 16 886 km of land bordering 10 countries (Uruguay, Argentina, Paraguay, Bolivia, Peru, Colombia, Venezuela, Guyana, French Guiana and Suriname) and is one of the largest land borders in the world.<sup>4</sup> Another issue is that about 40% of the borders contain the Amazon forest, where infectious disease control is more difficult.<sup>5</sup> Brazil is also one of the countries with

the greatest social inequality in the world, which impacts the quality of healthcare for the population.<sup>6</sup>

Social health inequities emerge when inequalities in social, economic and/or geographical positions lead to differences in access to health among population groups.<sup>7</sup> As seen in the literature, health inequities have been analysed according to structural and intermediary determinants. The structural components are related to macro-policies, cultural and societal values, while the intermediaries are linked to material circumstances such as living conditions, work, sanitation, income, education and psychosocial, behavioural and cultural factors.<sup>7</sup>

Although studies have evidenced the association of social inequities with TB,<sup>8,9</sup> few studies have been developed that consider spatial and temporal dependence,<sup>10</sup> as well as the interaction between space and time. Bayesian hierarchical models have become extremely helpful in the analysis of spatial and spatio-temporal data, mainly to identify variations on smaller geographical scales in Brazilian cities.<sup>11</sup> This method enables the examination of spatio-temporal variation across Brazilian metropolitan regions, even where the data are rarer or sparse. Mortality due to TB is a rarer phenomenon when compared with other diseases, therefore, it is important to use appropriate methodologies with greater accuracy, sensitivity and specificity. This allows one to understand the determinants of TB mortality, which contributes to health professionals and policymakers being able to assess whether resources are adequately allocated. In addition, it allows for the redistribution of resources in more problematic areas in terms of TB, thereby making advancements in health equitable.

Thus, this study aimed to estimate in space and time the risk of TB mortality and to evaluate its relationship to social inequities through spatio-temporal models using a Bayesian approach in an area of the Legal Amazon (LA).

## Materials and methods

### Design and location of study

This was an ecological study with both a spatial and a temporal component that was carried out in Cuiabá, the capital of the state of Mato Grosso in central west Brazil (Figure 1). The municipality is located in LA, a region with economic, political and social problems. LA covers approximately 60% of the national territory and is composed of nine Brazilian states belonging to the Amazon basin, including the state of Mato Grosso.<sup>5</sup>

### Population, sources of information and unit of analysis

Data regarding patients who died due to TB (basic cause according to the International Classifications of Diseases, version 10 - A15.0 to A19.9) between 2006 and 2016 and lived in the urban area of Cuiabá were gathered through the Mortality Information System of the Municipal Health Department.

Social variables were collected from the Atlas of Human Development in Brazil, which contains variables about population size, education, housing, health, work, income and vulnerability.<sup>12</sup> The units of analysis were Human Development Units (HDUs), which are located in metropolitan areas, have at least 400 permanent homes and have a greater homogeneity of socioeconomic con-

ditions.<sup>12</sup> The municipality of Cuiabá has 89 urban HDUs, which were included in this study.

### Study variables

TB mortality risk was defined as an effect or outcome of the study. According to the theoretical framework, variables related to the intermediate determinants and structural components associated with social health inequities were selected (Table 1).<sup>7</sup> The resident population of the municipality, as well as gender and age, were obtained through the Brazilian Institute of Geography and Statistics.<sup>13</sup> The variables consisted of education, income, longevity, marital status, skin colour, occupation, schooling, housing and basic sanitation.<sup>7</sup> In addition, time and space random effects were added into the study.

For database construction, TB deaths were distributed according to HDU and the year. The variables were obtained from the 2010 Demographic Census, which were repeated for all years studied according to each HDU. For analysing the spatial dependence, an identifier (1 to 89) was inserted into the database for each HDU, as well as another one to represent the temporal dependence ID (1 to 11), also by year. For measuring the spatio-temporal interaction, an ID was included, which represented each HDU and year (1 to 979).

### Data analysis

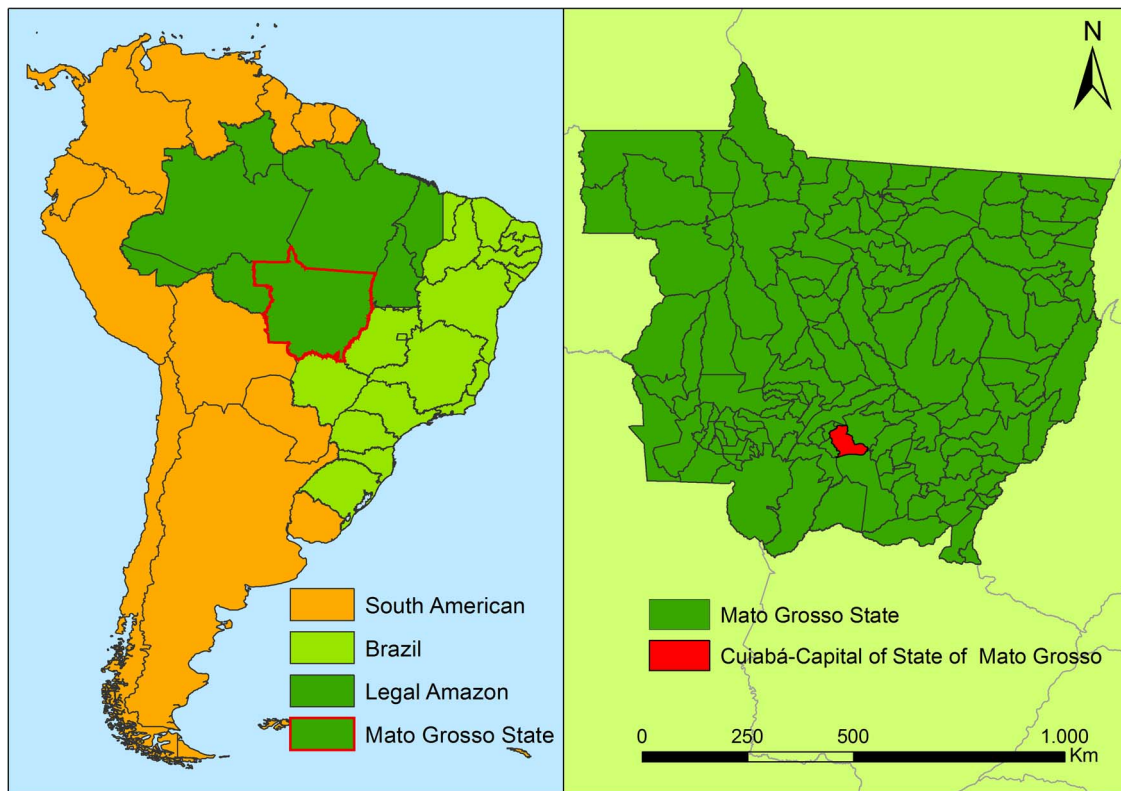
Initially, the global TB mortality rate was calculated considering the total deaths that occurred during the study period and the total population living in urban areas of the municipality. Then mortality rates were calculated according to gender, skin colour, age, marital status and education. For this, we considered the deaths and the population according to each group.

The geographic coordinates (latitude and longitude) of each residential address were located through Google Earth Pro Version 9.3.104.2 (Google Inc., Mountain View, CA). The geo-referencing was performed using ArcGIS Version 10.6 (Environmental Systems Research Institute, Redlands, CA, USA). We constructed a file with shapefile extension, which was plotted together with a Cuiabá HDU map.<sup>12</sup>

After the geo-referencing of deaths, mortality rates were calculated for each HDU, which were standardised by gender and age, considering the age groups 0–14, 15–59 and  $\geq 60$  y. These rates were calculated by the direct method, considering the deaths for each HDU throughout the study period. The standard population used was the population of the urban area of Cuiabá, also according to gender and age. For this study, the total population of the municipality and the populations of the HDUs were gathered from the 2010 census.<sup>13</sup>

The number of TB deaths per HDU and year was considered as the dependent variable in models using latent Gaussian Bayesian models, Poisson probability distribution and a spatio-temporal structure.<sup>14</sup>

To interpret the coefficients obtained in the modelling as RRs in relation to the mortality rate of the entire urban area of Cuiabá and the entire study period, the expected deaths by indirect standardisation were calculated. Mortality rates were calculated for the entire urban area of Cuiabá and throughout the study period by gender and age (0–14, 15–59 and  $\geq 60$  y). From these



**Figure 1.** Geographical location of the selected municipality of the Legal Amazon, Brazil.

rates, and considering the age and gender structure of each HDU and year, the expected deaths for each HDU and year were obtained, which were considered as offsets in the modelling.

Two analytical approaches were constructed. In the first model, the TB mortality log-risks by HDU and year were fitted in space and time by a spatio-temporal effects model without covariables. The second one modelled the TB mortality log-risks by HDU for each year using a model with spatio-temporal effects and covariables representative of social inequity.

An exploratory analysis was performed to identify outliers and collinearity among the covariables, which would be inserted in the model. A collinearity analysis was performed using the variance inflation factor (VIF). The variables with VIF >3 were diagnosed as collinear.<sup>15</sup> The covariables included in the last model were standardised by subtracting their mean values and then dividing by their respective SDs.

To estimate the spatio-temporal dependence, different random effects were considered. Spatial dependence was considered by a Besag-York-Mollié model composed of structured and unstructured random effects models, parameterised as proposed by Simpson et al.<sup>16</sup> The temporal dependence was modelled considering an unstructured random effect and a structured order of 1 random walk. The spatio-temporal interaction was modelled considering unstructured random effects on time and space (type I space-time interaction), unstructured on space and structured on time (type II), unstructured on time and structured on space (type III) and structured on space and time (type IV).<sup>14</sup> The deviance information criterion (DIC) was calcu-

lated as an adjustment measure for selecting the most suitable models.

The models were performed according to the integrated nested laplace approximation (INLA) approach, an approximate method for Bayesian inference in latent Gaussian models.<sup>17</sup> Non-informative priors for the fixed effects were assumed. For the precision parameters of the random effects, priors with penalised complexity were adopted.<sup>16,17</sup> Thematic maps were elaborated with the presentation of the standardised mortality rates for each HDU and entire period, spatio-temporal RRs for HDU and year and respective probabilities that these risks were greater than unity. The RRs for the covariables considered in the modelling were also obtained.

### Software used

Space operations and thematic maps were developed using ArcGIS software version 10.6. Statistical analyses were performed in R version 3.4.1 (R Core Team 2017)<sup>18</sup> and package R\_INLA version 0.0-1 432 754 561 ([www.r-inla.org](http://www.r-inla.org)) (see [Supplementary Data 1](#)).

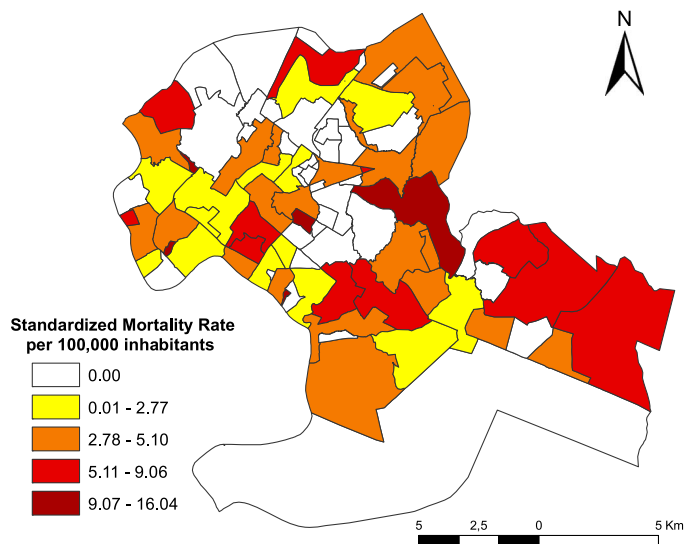
### Results

From 2006 to 2016, there were 225 deaths from TB, of which 77.8% were of the pulmonary clinical type. [Figure 2](#) shows the distribution of the standardised mortality rate by gender and age for the HDUs in the municipality.

**Table 1.** Proxy variables of structural and intermediary social determinants of health in the municipality of Legal Amazon

Variable	Definition
Percentage of people in households with inadequate water supply and sewage	Ratio among people living in households whose water supply does not come from the general network and whose sanitary sewage is not carried out by sewage collection system or septic tank and the total population living in permanent private households, multiplied by 100. Only permanent private households are considered
Percentage of people in households without electricity	Ratio among people living in households without electricity and total population residing in permanent private households, multiplied by 100
Average per capita household income	Ratio between the sum of the income of all individuals living in permanent private households and the total number of these individuals
Average household income per capita of the poor	Average per capita household income of people with per capita household income equal to or less than R\$ 140.00 monthly, in August prices of 2010. The universe of individuals is limited to those living in permanent private households
Average household income per capita of those who are vulnerable to poverty	Average per capita household income of people with per capita household income equal to or less than R\$ 255.00 per month, at August 2010 prices. The universe of individuals is limited to those living in permanent private households
Illiteracy rate of the population aged $\geq 25$ y	Ratio of the population aged $\geq 25$ y who cannot read or write a simple note and the total of people in this age group, multiplied by 100
Unemployment rate of population aged $\geq 18$ y	Percentage of the economically active population in this age group that was unoccupied, that is, was not occupied in the week prior to the date of the census but had sought work during the month prior to the date of this survey
Ageing rate	Ratio between the population aged $\geq 65$ y and the total population multiplied by 100
Proportion of blacks	Proportion of residents self-declared as black
Proportion married	Spouses or partners of different gender

Source: Brazilian Institute of Geography and Statistics (2010). United Nations Development Program: Atlas of Human Development in Brazil (2013).



**Figure 2.** Standardized mortality rate by sex and age in a municipality of the Legal Amazon (2006-2016).

The general mortality rate for the municipality was 3.4 deaths per 100 000 inhabitants, and it was verified that the deaths registered in the period of study were distributed heterogeneously, and that the mortality rates ranged between 0 and 16.0 deaths per 100 000 inhabitants.

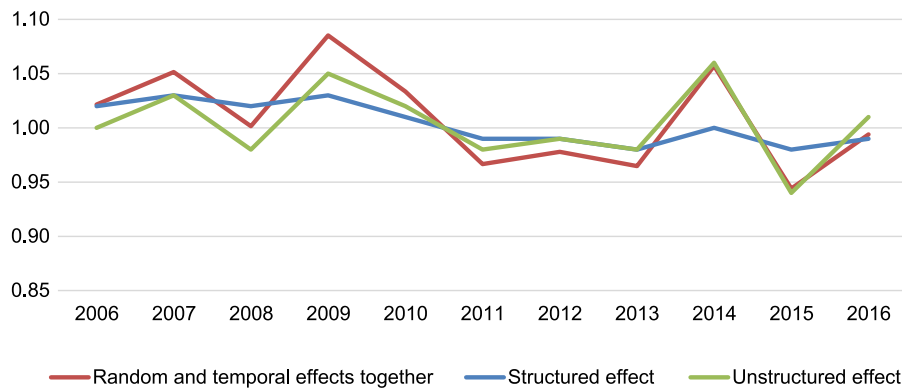
Mortality rates were 5.6 deaths per 100 000 inhabitants for men and 1.9 deaths per 100 000 inhabitants for women. Patients with brown skin colour had higher mortality rates (4.7 deaths per 100 000 inhabitants), followed by those with black skin colour (3.4 deaths per 100 000 inhabitants) and white skin colour (2.0 deaths per 100 000 inhabitants).

Regarding age, the findings revealed that TB mortality was higher among those  $\geq 60$  y (22.5 deaths per 100 000 inhabitants); patients aged from 15 to 59 y had a mortality rate of about 2.7 deaths per 100 000 inhabitants. In addition, the mortality rate was 3.4 deaths per 100 000 inhabitants among people who were single and 8.8 deaths per 100 000 inhabitants in people with no schooling or with up to 7 y of schooling.

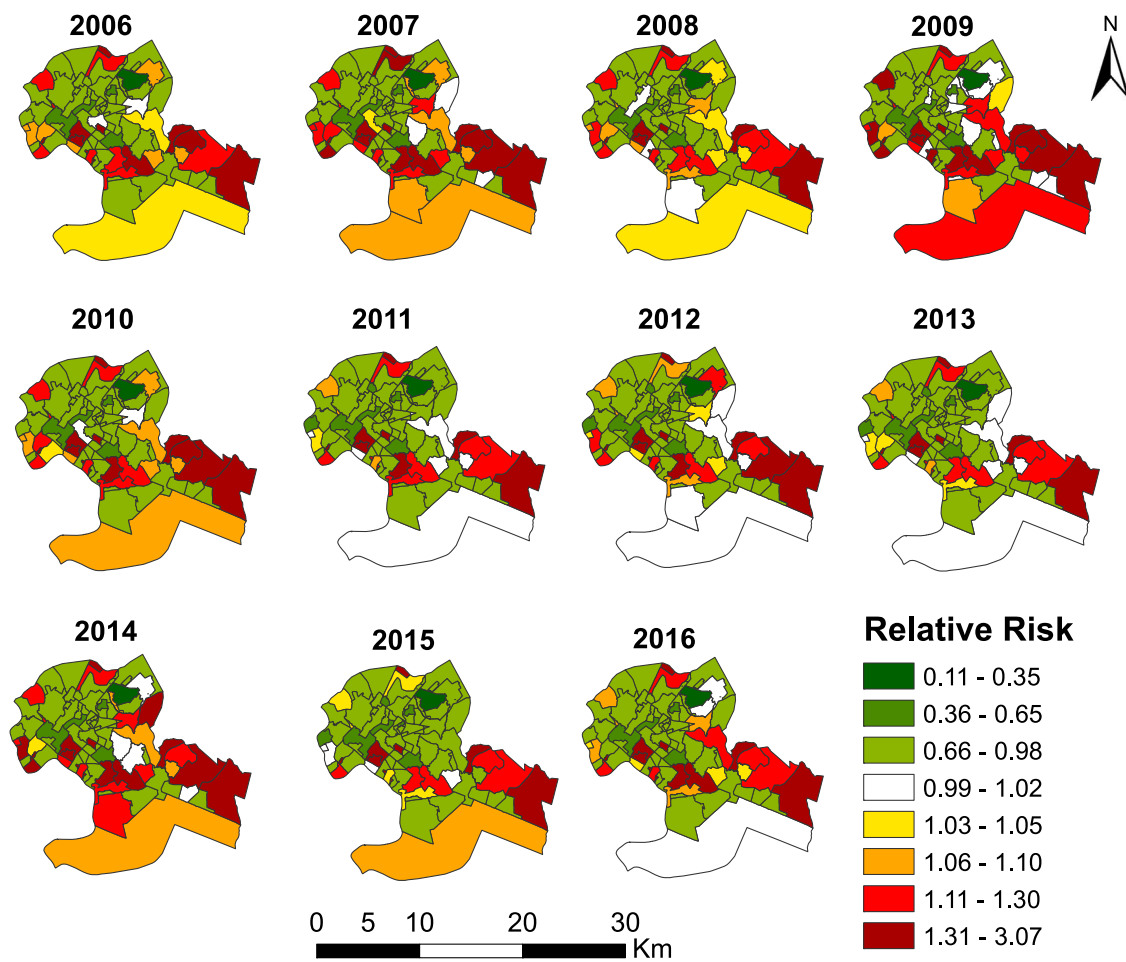
Of the total cases, 208 (92.4%) were geo-referenced by address; 17 could not be geo-referenced because of address inconsistencies (5.4%) or the absence of an address on the death certificate (2.2%).

First, we ran the models without covariables, considering the four types of space-time interactions, and the best model was the one with unstructured random effects on time and space (type I) (see [Supplementary Data 2](#)). [Figure 3](#) shows the results obtained with this model and highlights the posterior means of the temporal RRs of mortality by TB in the period 2006–2016, adjusted by space. Although the figure shows a drop in RR over this period, it can be stated that the mortality risk showed stable behaviour during the study period, given the small reduction detected.





**Figure 3.** Posterior means of the temporal RRs of TB mortality adjusted for space in a municipality of the Legal Amazon (2006–2016).

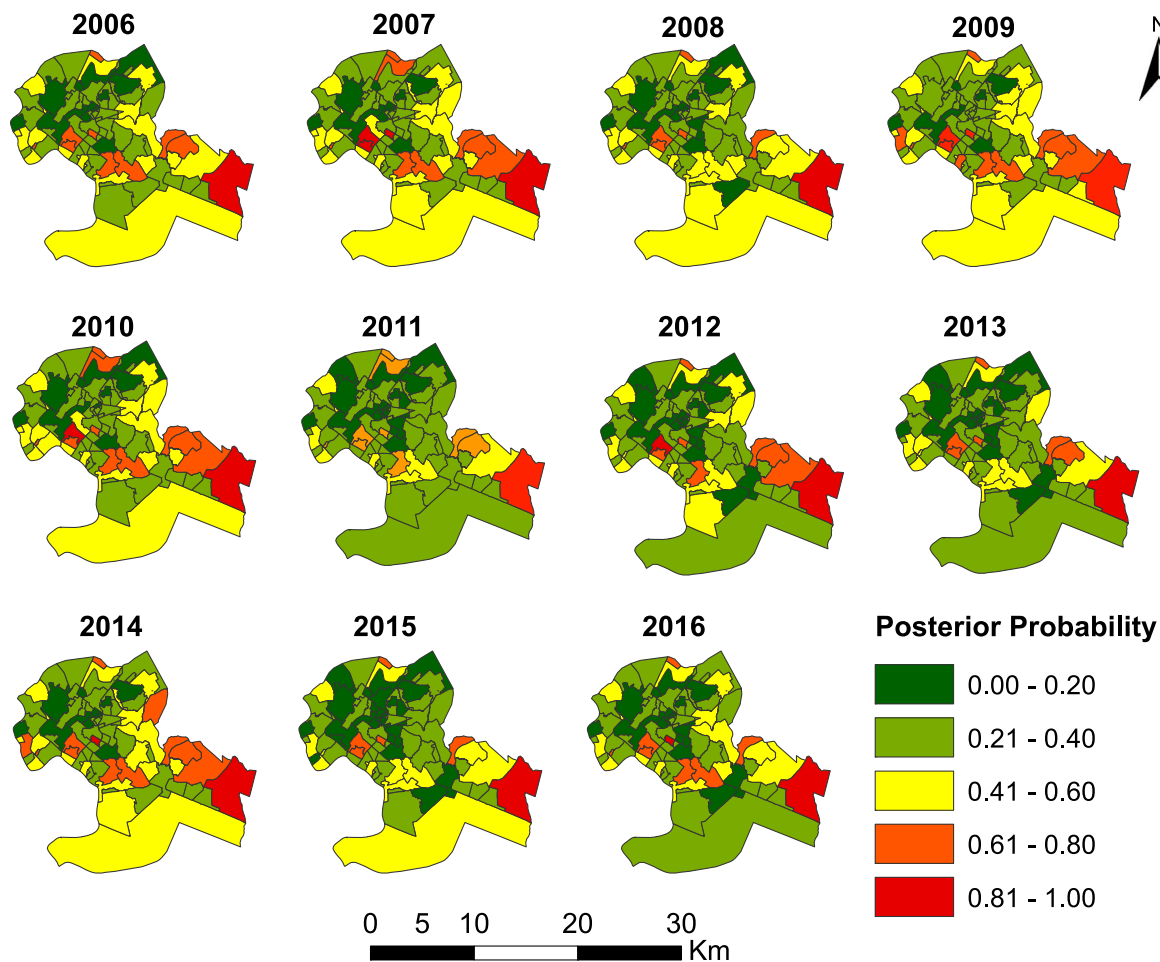


**Figure 4.** Posterior means of the spatio-temporal RRs for TB mortality in the period from 2006 to 2016 in a municipality of the Legal Amazon.

Figure 4 shows maps with the posterior means of the spatio-temporal RRs for TB in the period from 2006 to 2016 according to HDUs. In Figure 4, darker colours represent the areas of highest risk. From Figure 4 we observed a decreased risk in various HDUs when we compared the initial year of 2006 with the final year of 2016. Although RRs have decreased, there are still high-risk areas for TB that have remained over time, possibly indicating

the presence of factors at those sites that are involved in the occurrence of TB deaths.

Figure 5 shows the posterior probabilities of spatio-temporal RRs to be higher than unity for each year. The HDUs located in the south and east regions stand out because they have the highest concentration of high-risk areas for TB mortality in the period of study.



**Figure 5.** Posterior probability that the RRs are  $> 1$  in the period from 2006 to 2016 in a municipality of the Legal Amazon.

Second, we ran the models with all covariables, considering the four types of space-time interactions and, again, the best one was the type I model (see [Supplementary Data 2](#)). For the model with covariables, 10 variables of social inequity were considered, as presented in [Table 1](#). The variables 'Illiteracy rate of population  $\geq 25$  y' and 'Proportion of blacks' presented VIF values of 3.74 and 8.18, respectively, so they were excluded from the analysis by collinearity (see [Supplementary Data 3](#)).

[Table 2](#) shows the results of this model, quantifying the posterior means of the RRs of fixed effects (representative covariables of social inequities) and 95% credible intervals (95% CI). Among the covariables investigated, only household income per capita was considered important; an increase of 1 SD in income was accompanied by a decrease of 35.5% in the risk of mortality from TB. The spatio-temporal model that considered the effect of covariables representative of social inequality presented a lower DIC value (928.8) compared with the model without those covariables (929.2).

Because the DIC values of the models without covariables were very close to the models with all covariables, we finally ran models with only the household income per capita covariable and, again, the type I model proved to be the best (see [Supplementary Data 2](#)). [Table 3](#) shows the spatio-temporal mod-

elling results using only the household income per capita covariable. The posterior means of the RRs of fixed effects remained practically unchanged, but the model presented a narrower CI (mean 0.646; 95% CI 0.476 to 0.837; DIC 922.5) and a pronounced decrease in the value of the DIC (from 929.2 to 922.5), which confirms the association of this covariable with the risk of mortality from TB.

[Figure 6](#) shows the spatial distribution of household income per capita according to minimum wages. Accordingly, a correspondence was observed between the HDUs with higher estimated RRs of TB death ([Figure 4](#)) with lower per capita incomes.

## Discussion

This study aimed to estimate in space and time the risk of TB mortality and evaluate its relationship with social inequities through a spatio-temporal Bayesian approach in an area of the LA.

Through the spatio-temporal models, the findings revealed that the risk of TB mortality between 2006 and 2016 remained practically unchanged. The results of the spatio-temporal models provided evidence of areas with higher TB mortality risk that have

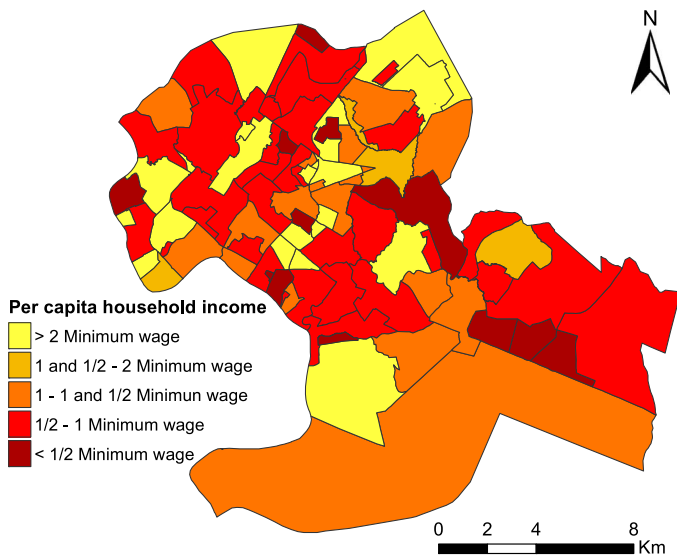
**Table 2.** Posterior means of the fixed effects (RRs for the covariables representative of social inequity) and 95% CI intervals for TB mortality in spatiotemporal modelling with covariables, in a municipality in the Legal Amazon (2006–2016)

Covariables	95% CIs		
	mean	0.025 quant	0.975 quant
(Intercept)	0.674	0.518	0.847
Ageing rate	1.077	0.750	1.510
Average per capita household income	0.645	0.390	0.980
Average household income per capita of the poor	1.007	0.806	1.241
Average household income per capita of those who are vulnerable to poverty	1.117	0.827	1.482
Percentage of people in households with inadequate water supply and sewage	1.098	0.887	1.336
Percentage of people in households without electricity	1.160	0.856	1.531
Unemployment rate of population aged ≥18 y	0.899	0.651	1.200
Proportion married	1.021	0.702	1.470

**Table 3.** Posterior means of the fixed effects and 95% CIs for TB mortality in spatial modelling with household income per capita, in a municipality in the Legal Amazon (2006–2016)

Covariables*	95% CIs		
	mean	0.025 quant	0.075 quant
(Intercept)	0.704	0.558	0.866
Average per capita household income	0.646	0.476	0.837

\*Model with type I space-time interaction



**Figure 6.** Spatial distribution of per capita household income in a municipality of the Legal Amazon.

persisted over time and suggest that social inequities accounted for part of the TB mortality in those regions. The covariable, household income per capita, was an important factor in the risk of mortality due to TB.

A limitation of this study is the use of secondary information sources, which do not exclude the possibility of incompleteness of data. However, the mortality information system is recognised for its precision and is considered the gold standard among Brazilian information systems.<sup>19</sup> The Atlas of Human Development, the source of social variables, consists of data that meet the requirements of statistical analyses.<sup>12</sup>

Although the risk of mortality from TB declined during the period under investigation, this reduction was minimal and can be considered negligible. Moreover, many HDUs that presented with high risk in 2006 maintained this condition over time, especially HDUs located in the south and east regions of the municipality.

In order for interventions to be more effective and have a real impact on the reality of TB morbidity and mortality, it is necessary to take actions in areas of greater vulnerability.<sup>20</sup> Therefore, the regions that presented a persistent risk of death due to TB over the years are priorities for investment in surveillance and control of the disease.

Actions addressed towards TB mortality control should overtake the health sector and include multi-sectoral initiatives to provide quality care, equitable access to health services and an approach to managing the determinants of the disease.<sup>7,20</sup>

The municipality is marked by social inequalities, mainly in relation to income distribution, a factor that was associated with a higher risk of mortality due to TB in this study.<sup>12</sup> In the municipality, 63.5% of all income produced is concentrated among the richest fifth of the population, and the Gini Index indicates that

income differences between the richest and poorest have not improved significantly since the 1990s.<sup>12</sup>

Low income is a factor that compromises the quality of life and health of the population and should be strongly considered in the context of TB control actions. Income restrictions can reduce the perception of the magnitude of the disease, contribute to failure in treatment and limit the use of health services.<sup>9</sup>

LA has unfavourable social indicators, with high levels of extreme poverty, overcoming the national average, and the lowest percentage of coverage of basic sanitation services in the country.<sup>21</sup> In addition, the region has an extensive area of international borders, which makes it unique in relation to socio-spatial dynamics and hampers the implementation of health policies.<sup>21</sup>

It is important to highlight that the variables included in the model were able to explain only part of the risk of TB mortality. This suggests that there are other factors that permeate the reality of this region that may be influencing the occurrence of death from TB. Thus, future studies that consider other factors of health inequities may contribute to the clarification of the reasons for TB mortality in these areas. In addition, variables related to the quality of and access to health services need to be investigated because they are part of the dynamics of the origin of health inequities.<sup>7</sup>

The WHO emphasises that to progress in equity in health and elimination of TB it is necessary to implement social and health policies that comprise determinants of the disease.<sup>7</sup> Social protection policies are fundamental for equity in health and are efficient measures for the control of the disease. Implementing these policies simultaneously with diagnostic innovations, quality of treatment and improvement of health services may be the key to elimination of the disease.<sup>22</sup>

Brazil has adopted social protection policies, such as the *Bolsa Familia* Program, which is articulated with the Unified Health System and has been a positive experience in TB control.<sup>23</sup> However, it is necessary to consider the effect of the recent economic crisis and social policies in Brazil that have threatened investment in and advancement of these policies.<sup>24,25</sup> The effects of the economic recession and fiscal austerity policies may be especially severe for the Brazilian health system and put at risk the right to health, especially among the most vulnerable groups.<sup>3</sup>

Another issue is that the flow of refugees has increased considerably in the country, especially in border regions such as LA.<sup>26</sup> The failure of public policies to accommodate these immigrants increases the social vulnerability of this group due to the extremely iniquitous conditions of survival and the difficulties of access to adequate sanitary conditions, social protection programmes and health services.<sup>26</sup> This condition of social inequity may consequently increase the risk of TB death in this population.

The literature is still limited regarding studies that investigate the health conditions of the Amazon region, mainly in relation to TB; although some studies have investigated the incidence and abandonment of treatment,<sup>27</sup> little is known about the mortality of the disease. Thus, the present study advances knowledge in that it identified inequities related to the risk of deaths due to TB in this area of LA.

The main strength of this study is based on the search for explanations for the risk of TB deaths using Bayesian modelling

through the INLA approach. This method allowed us to estimate the risk of death due to TB in the Amazon region, considering the spatial and temporal effects and the interactions with social inequities.

In addition, this study is aligned with global efforts to control TB, as it is consistent with one of the pillars of the End TB strategy, which advocates the intensification of research with the incorporation of new technologies to eliminate the disease.

## Conclusions

It was possible to show, through the Bayesian approach, the existence of high-risk areas for TB mortality in LA, which have persisted for more than a decade. Social inequities explain part of the deaths evidenced in this study and improvement in income could change this reality.

Considering the socio-spatial complexity of the LA region, it is evident that health equity, as well as the reduction of TB deaths by 95%, according to the End TB strategy, represents a great challenge for this region. Thus, interventions aimed at eliminating TB are needed and should be directed mainly towards areas that have a high and persistent risk of mortality from TB.

## Supplementary data

Supplementary data are available at *Transactions* online.

**Authors' contributions:** JDA, FCN and RAA contributed to study design and data analysis as well as data discussion; DTS, LSA, TZB and ACVR participated in the systematic protocol and data collection; LTC, ASB and ISA reviewed the manuscript and contributed to the data analysis; JDA, CN, FCN, RAA, LHA and MAMA applied the data analysis as well as data interpretation and a final review of the work; LHA, MAMA, RCF, PSG and FCN critically reviewed the manuscript in terms of content and its theoretical framework. All authors approved the manuscript.

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**Competing interests:** None declared.

**Ethical approval:** In accordance with the Guidelines and Norms Regulating Research on Human Beings established in Brazilian Resolution No. 466/2012, the research project was approved by the Research Ethics Committee of the Ribeirão Preto College of Nursing (66365517.5.0000.5393).

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