Original article

# Spatial analysis of tuberculosis in children under 15 years of age and socioeconomic risk: an ecological study in Paraíba, Brazil, 2007-2016*

doi: 10.1590/S1679-49742021000300006

**Micheline da Silveira Mendes[1]** – orcid.org/0000-0001-7542-0702
**André Luiz Sá de Oliveira[2]** – orcid.org/0000-0002-2483-550X
**Lílian Maria Lapa Montenegro Pimentel[3]** – orcid.org/0000-0002-4728-2995
**Tânia Maria Ribeiro Monteiro de Figueiredo[4]** – orcid.org/0000-0001-6197-2936
**Haiana Charifker Schindler[3]** – orcid.org/0000-0003-3863-4845

[1]Fundação Instituto Oswaldo Cruz, Departamento de Saúde Coletiva, Recife, PE, Brazil
[2]Fundação Instituto Oswaldo Cruz, Núcleo de Estatística e Geoprocessamento, Recife, PE, Brazil
[3]Fundação Instituto Oswaldo Cruz, Departamento de Imunologia, Recife, PE, Brazil
[4]Universidade Estadual da Paraíba, Departamento de Enfermagem, Campina Grande, PB, Brazil

## Abstract

**Objective:** To analyze spatial distribution of tuberculosis in individuals under 15 years old and socioeconomic factors in Paraíba, Brazil, 2007-2016. **Methods:** This was an ecological study based on data from the Notifiable Health Conditions Information System (SINAN), taking each municipality to be a unit of analysis. Spatial distribution of incidence was performed, the local empirical Bayesian method and Moran's I were applied. Socioeconomic data were crossed-checked to identify areas of social prosperity. **Results:** 426 cases were notified, with average incidence of 4.5/100,000 inhabitants. Moran's I was 0.59 (p=0.010). The Moran Map revealed concentration of cases in children under 15 in 38 high priority municipalities, in clusters with high-high and low-low patterns, in the east and northwest of the state, coinciding with areas of low social prosperity. **Conclusion:** There were clusters with greater tuberculosis transmission, indicating priority areas for addressing tuberculosis.

**Keywords:** Ecological Studies; Health Information Systems; Neglected Diseases.

*Article derived from the Academic Master's Degree dissertation entitled 'Tuberculosis in children under 15 years of age in Paraíba State: spatiotemporal analysis from 2007 to 2016', submitted by Micheline da Silveira Mendes to the Postgraduate Program in Public Health/Academic Master's Degree Course in Public Health/Instituto Aggeu Magalhães/Fundação Instituto Oswaldo Cruz, em 2019.

**Correspondence:**
**Micheline da Silveira Mendes** – Rua Enf. Ana Maria B. de Almeida, No. 1217, Jd. Cidade Universitária, João Pessoa, PB, Brazil.
Postcode: 58052-270
E-mail: micheline_mendes@hotmail.com

## Introduction

Tuberculosis is a communicable disease caused by *Mycobacterium tuberculosis*. It mainly attacks the lungs (pulmonary form), although it can also affect other organs (extrapulmonary form), and despite being such an old, well-known and curable disease, it ranks among the communicable diseases that most kill worldwide: in 2018, 7 million new cases were notified; and notifications among children under 15 years of age grew from less than 400,000 in 2015 to 523,000 in 2019.[1,2]

> ***Knowing the clinical panorama of tuberculosis in the younger population, as well as the patterns of its distribution in the territory and its relationship to social, demographic and epidemiological factors, can produce useful information for decision-making processes.***

As with other diseases of epidemiological importance, sociodemographic aspects are associated with tuberculosis occurrence and geographic distribution, so it is recommended that studies be developed to understand these factors in greater depth, to support decision-making on appropriate and timely public policy interventions.[3]

*M. tuberculosis* infection is directly related to the population's living conditions, with poverty being a determining factor for its symptoms worsening or falling ill with tuberculosis. Occurrence of the disease is associated with socioeconomic indicators, such as housing conditions, urban agglomerations, per capita income, unemployment, education, age, access to health services, food and sanitary conditions, in addition to the presence of comorbidities, especially when these lead to a person being immunocompromised.[4,5]

The World Health Organization (WHO) recognizes tuberculosis as a Public Health emergency and, in recent decades, has encouraged countries to adopt specific international health policies for the disease, and to include it in national health service management guidelines when it affects children and adolescents. To this end, in 2006, the WHO published the Guidance for National Tuberculosis Programmes on the Management of Childhood Tuberculosis in Children, the first guide to address tuberculosis in childhood globally.[6-8]

Tuberculosis in children occurs mostly in countries where it is endemic. Little is known about it from an epidemiological point of view when compared to assessments made in the adult population. However, monitoring the occurrence of tuberculosis in childhood is a valuable indicator of tuberculosis transmission, especially in high-incidence countries. Identification and examination of contacts of infected children and adolescents is an effective strategy for identifying the index case.[7]

Knowing the clinical panorama of tuberculosis in the younger population, as well as the patterns of its distribution in the territory and its relationship to social, demographic and epidemiological factors, can produce useful information for decision-making processes in building and implementing public policies targeting this health condition in childhood.[9,10]

Use of spatial statistics in Public Health and their relationships with socio-environmental factors allows an understanding of the dimensions involved in ecological level and individual level studies of infection, when using appropriate analysis tools, in addition to supporting surveillance of individual risk and prediction of collective risk, in order to understand - and control - endemic processes.[9,10]

The objective of this article was to analyze spatial distribution of tuberculosis in individuals under 15 years of age and associated socioeconomic factors, in the state of Paraíba, Brazil, from 2007 to 2016.

## Methods

This was an ecological study, with spatial analysis of new cases of tuberculosis in children under 15 years of age notified from 2007 to 2016.

The study was conducted in Paraíba, a state located on the eastern coast of Northeast Brazil. The state has a territorial area of 56,468.435 km², divided into 223 municipalities. In 2010, Paraíba had 3.766,528 inhabitants, of whom 27.5% were under 15 years of age. It had a medium Municipal Human Development Index (HDI-M), a low Social Vulnerability Index (SVI), and high social prosperity, based on the 2010 Demographic Census.[11-14]

The study included all cases notified on the Notifiable Health Conditions Information System (SINAN), aged under 15 years old at the time of diagnosis, of both sexes, and resident in the state during the period analyzed; cases with unknown municipality of residence and change of diagnosis were excluded.

The study variables were obtained from the compulsory notification forms, held on the database of the Endemic Diseases Section of the Paraíba State Health Department. This data was collected in April 2018. The data were cleaned for duplicated records and the names of the cases and the names of their mothers were removed in order to ensure anonymity. Population data were obtained from public domain websites, from the Brazilian Institute of Geography and Statistics (IBGE) and from the Institute for Applied Economic Research, also based on 2010 Census data.[13,14]

The variables used for case selection were: age (in complete years); year (date of case diagnosis); municipality of residence (at the time of diagnosis); and resident population under 15 years of age (inhabitants in this age group, per municipality). HDI-M and SVI were used on order to identify the socioeconomic status of the municipalities, using United Nations Development Program (UNDP) classification parameters, where HDI-M is classified as follows: very low development (0.000 to 0.499); low development (0.500 to 0.599); medium development (0.600 to 0.699); high development (0.700 to 0.799); and very high development (0.800 to 1.000). SVI rates vulnerability as follows: very low (0.000 to 0.200); low (0.201 to 0.300); medium (0.301 to 0.400); high (0.401 to 0.500); and very high (0.500 to 1.000). Overlapping HDI level and SVI level allowed us to identify municipal social prosperity (Figure 1), again using 2010 Census data and the UNDP parameters, according to the model proposed by Ferreira & Pinto.[15]

The incidence coefficient of new cases in the population between zero and 14 years of age was calculated (per 100,000 inhabitants) in order to identify areas of active transmission of the disease, and areas of case concentration (clusters). Average incidence for the period was calculated by taking the sum of new cases divided by the 10 years of the study period; the quotient of this operation, in turn, was divided by the population aged 0-14 years living in the municipalities (2010 Census data), and then multiplied by 100,000. Thus, it was possible to visualize the spatial distribution of this indicator in the state.

The indicator was calculated based on the average of the total period (2007 to 2016), aiming to correct random fluctuations and provide better stability, especially in municipalities with very small populations - for example, with fewer than 3,000 inhabitants. The smoothed indicator was also calculated by the local empirical Bayesian method, which uses information from neighboring areas within the same region to estimate risk for the area. The thematic maps of the crude and smoothed coefficients were categorized using the quartile method.[16]

Besides the descriptive analysis, we used: the Box Map (to visualize spatial dependence) and Moran's I on the smoothed indicator, to assess the presence of global spatial dependence and areas of statistical significance, and to ensure the correction of extreme values and silent areas of the disease. In this way it was possible to measure the correlation of a variable with itself, in space, whereby its values were estimated within a range of -1 to +1: positive and negative values of this range indicate positive autocorrelation and negative autocorrelation, respectively; while values close to zero indicate spatial randomness.[17,18]

Existence of local correlation was assessed using local Moran's I (Local Index of Spatial Association), producing a specific value for each municipality, which allowed comparison between neighboring municipalities and visualization of clusters of municipalities with similar values and, therefore, identification of spatial patterns. Interpretation of the quadrants generated though this technique showed the following correlations:

a) municipalities with a high proportion of the indicator, surrounded by other municipalities with high proportions (high-high);

b) municipalities with a low proportion, surrounded by municipalities with a low proportion of the same indicator (low-low), suggesting points of positive spatial association; and

c) municipalities with a high proportion, surrounded by municipalities with a low proportion of this indicator (high-low), and municipalities with a low proportion, surrounded by municipalities with a high proportion of the same indicator (low- high), suggesting points of negative spatial association, representative of transition areas.

Moran Maps were used for the spatial representation of the Moran's mirror diagram, whereby a significance level less than 5% was adopted in the analysis. Areas of high risk for active transmission of the disease and case incidence were considered to be municipalities with high values and neighboring municipalities with the same characteristic.

The georeferenced database used for Paraíba State was obtained from the IBGE online page. It has a vector format, a shapefiles extension (.shp), a geographic coordinate projection system (lat,long) and the SIRGAS 2000 Datum. The open source software QGIS 2.14.8-Essen and TerraView version 5.4.0 were used for data processing, analysis, presentation of cartographic data, calculation of spatial autocorrelation indicator and production of thematic maps.

The research project was approved by the Research Ethics Committee of the Aggeu Magalhães Institute/ Oswaldo Cruz Institute Foundation in Pernambuco: Opinion No. 2.655.809, issued on May 15, 2018.

## Results

In the period from 2007 to 2016, 426 new cases of tuberculosis were diagnosed and notified in the state of Paraíba in individuals under 15 years of age.

The HDI-M data for the state's 223 municipalities were spatially distributed. One hundred and fifty-two (68.2%) municipalities were found have a low development index (Figure 2A). With regard to SVI distribution, 160 (71.7%) municipalities were found to have high or very high vulnerability, especially in the eastern part of the state (Figure 2B). Social prosperity was considered very low in 135 (60.5%) municipalities (Figure 2C).

In the age range under consideration, the average incidence rate was 4.5/100,000 inhab., varying between 3.4 and 5.5/100,000 inhab. when considering the state as a whole. At the municipal level, 91 (40.8%) municipalities had at least one case of tuberculosis in children under 15 years of age in the period analyzed, with incidence varying from 0.9 to 23.9/100,000 inhab. (Figure 3A). The smoothed map, however, revealed an expected incidence rate that varied between 0.19 and 11.03/100,000 inhab. The highest incidence rates were concentrated in municipalities in the eastern part of the state (Figure 3B).

By analyzing the Box Map we identified 86 priority municipalities for monitoring occurrence of tuberculosis cases (Figure 4A). After statistical analysis, overall Moran's I for the smoothed coefficients for the whole period was 0.594 (p-value=0.010). The Moran Map revealed concentration of cases in children under 15 years of age in 38 high priority municipalities, in clusters of sectors characterized by high-high and low-low patterns identified in the eastern and northwestern parts of the state, respectively (Figure 4B).

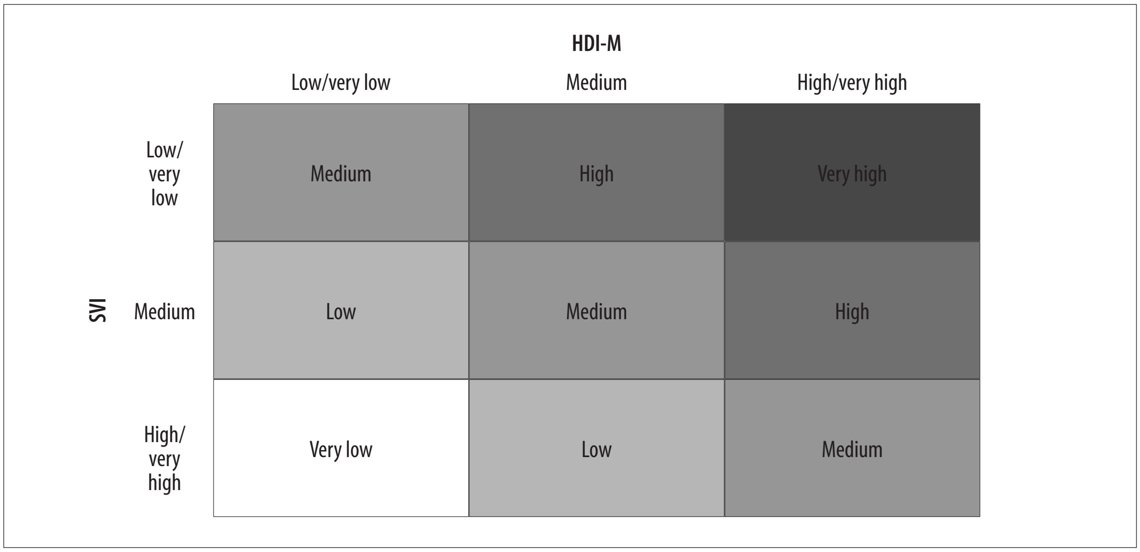
## Discussion

Among the municipalities in Paraíba, the areas with the highest incidence rates of tuberculosis in childhood coincided with scenarios of social inequality, with low HDI-M and high or very high SVI. None of the municipalities were assessed as having a very low or very high HDI-M, or a very low SVI.

When analyzing the municipalities with the highest average incidence of tuberculosis among people under 15 years of age in the period selected for the study, we found high social vulnerability, low to medium HDI-M, and low or very low social prosperity in most of these municipalities. These data differ from those found in studies that analyzed all the Brazilian municipalities in 2000 and 2010, when the results for country's social prosperity as a whole were better. This difference can be explained by the heterogeneity of the Brazilian territory, which is significant between its macro-regions. For example, 84% of the municipalities in the Southern region of Brazil were within the two highest social prosperity ranges, while in the Northeast region, only 3% were in those strata.[15,19]

Returning to present study in the state of Paraíba, distribution of new cases of tuberculosis in children under 15 years of age showed spatial heterogeneity, analysis of which identified municipalities at high risk of active transmission of the disease. Moreover, we found clusters of municipalities in need of priority interventions. However, when the Bayesian methods and the local Moran index were used, an even greater number of municipalities in need of tuberculosis interventions focused on the youngest were found.

We also found proximity between municipalities with low incidence rates and others with high rates, which did not form clusters. We also found municipalities with notifications of tuberculosis in the age group studied surrounded by others with no occurrence of the disease. Municipalities having crude incidence rates equal to zero may indicate underreporting of cases. A similar situation was found in the state of Espírito Santo between 2000 and 2007, namely crude incidence rates indicating municipalities with zero incidence of childhood tuberculosis bordering municipalities with an incidence rate of 85 cases per 100,000 inhabitants, suggesting centralization of case diagnosis in some cities and case underreporting in their cities of origin.[20]




Source: Adapted from Ferreira & Pinto.[15]

**Figure 1 – Levels of social prosperity, based on the ratio between the levels of the Municipal Human Development Index (HDI-M) and the Social Vulnerability Index (SVI)**

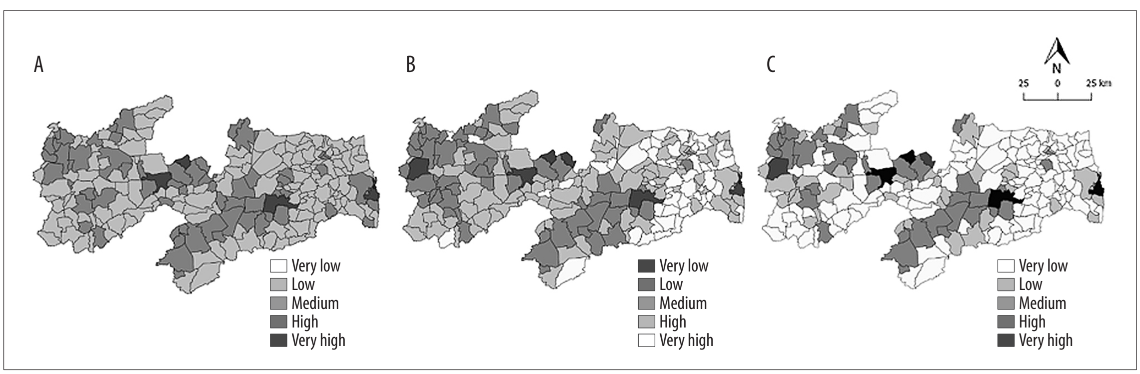



**Figure 2 – Spatial distribution of the Municipal Human Development Index (HDI-M) (A), Social Vulnerability Index (SVI) (B) and social prosperity(C) of Paraíba's municipalities**

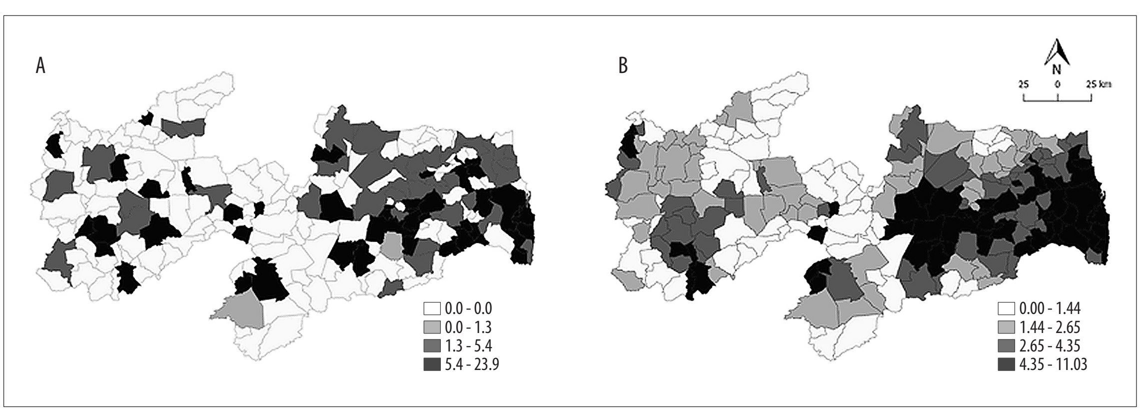



**Figure 3 – Spatial analysis of the new tuberculosis case incidence coefficient among children under fifteen years of age (per 100,000 inhab.), crude coefficient (A) and coefficient smoothed using the local empirical Bayesian method (B), Paraíba, 2006-2017**

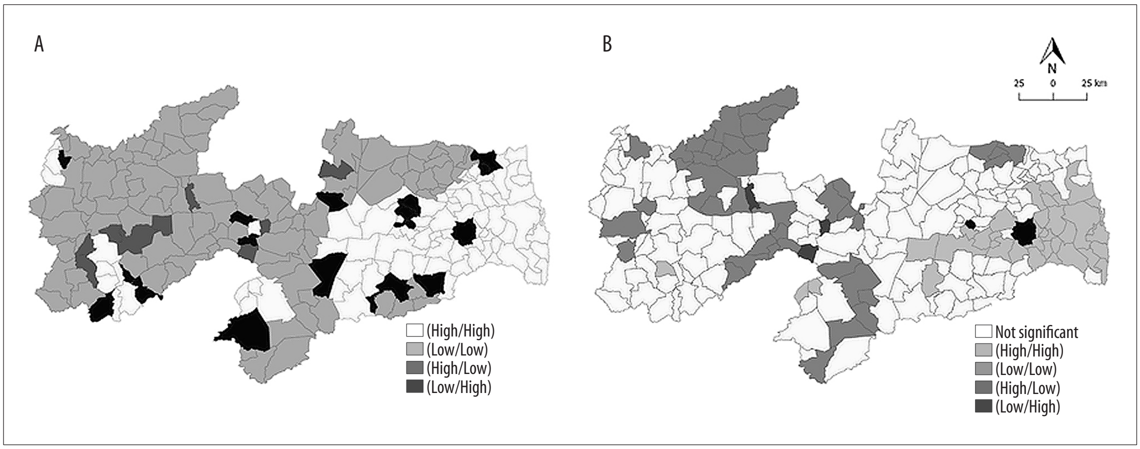



**Figure 4 – Spatial analysis of the new tuberculosis case incidence coefficient among children under fifteen years of age (per 100,000 inhab.), Box Map (A) and Moran Map (B), Paraíba, 2006-2017**

It is noteworthy that the distribution of crude incidence reveals a set of municipalities with high incidence rates of childhood tuberculosis around the metropolitan regions of João Pessoa and Campina Grande, the largest urban centers in the state. These findings echo those of Fortaleza, from 2000 to 2011, and São Paulo, from 2001 to 2010, regarding the spatial distribution of the disease.[10,21]

Although crude incidence rates show the spatial distribution of the disease, their instability and presence in places with small populations can lead to incorrect conclusions. In order to obtain more reliable results, studies have used spatial analysis based on smoothed incidence rates. This is the case of research on leprosy that, by using the local empirical Bayesian method, has achieved a better understanding of spatial implications due to cases in neighboring municipalities, visualization of the spatial pattern of the disease, risk sites, and the influence of small populations.[17,20-23]

In this study, analysis of the autocorrelation of the smoothed coefficients provided incidence indicators that were more stable, as well as identification of clusters of more critical areas, covering more than half of the municipalities in the state, with more well-defined clusters in the *Zona da Mata* and in the Agreste regions of Paraíba. This scenario reflects how serious tuberculosis is in the state, considering that areas with tuberculosis cases in children denote recent transmission of the disease.[10]

In this study, it was possible to identify areas with statistically significant risk of the disease, contributing to the delineation of priority areas for health intervention. Four clusters were found, the largest formed by 22 municipalities, concentrated in the eastern part of the state. This finding demonstrated spatial association in these areas, and corroborated findings of other investigations that used Moran's I and found areas of spatial autocorrelation and clusters of active transmission, evidenced by the Moran Map, identifying priority locations for disease control.[17,20,21]

The possible limitations of this research may be related to the use of secondary data retrieved from the SINAN system. Although they are official data widely used in technical and scientific studies, they are subject to inconsistencies with regard to the quantity, quality and processing of information. Therefore, we chose to use the municipalities as the units of analysis in order to avoid loss of quality, since this is a mandatory SINAN field. There is no way of quantifying underreporting, which is expected to be low as in Paraíba provision of medication is conditioned to case notification. Nor is it possible to quantify duplicated records, or even check for their existence in the database, although the State Health Department did provide the data after eliminating duplicates and cases with change of diagnosis. Another possible limitation of the study is that in epidemiological terms tuberculosis in this age group is quite low, proportionally, in relation to other age groups.

Tuberculosis in individuals under 15 years of age in Paraíba was distributed spatially, enabling identification of clusters of incidence in the state. This confirmed that spatial analysis can be an important tool in identifying locations of cases of childhood tuberculosis. In this context, this study can be considered to be pioneer in analyzing occurrence of tuberculosis among children under 15 years of age and its spatial distribution in a Northeast Brazilian state.

The results obtained indicate that further research should be conducted, including in other Brazilian states, in order to contribute to the monitoring of areas of active transmission of the disease and to provide information for the National Tuberculosis Control Program and its actions focused on children and adolescents. Future studies may also assist in the planning of local territorial-based activities and the technical, political and operational monitoring of actions to combat the disease and promote health, with tuberculosis in childhood and adolescence as a sentinel event of recent transmission of the infection.

## Authors' contributions

Mendes MS and Schindler HC took part in the concept and planning of the study, data analysis and interpretation and final drafting of the manuscript. Oliveira ALS took part in planning the study, data analysis and interpretation and critically reviewing the manuscript. Pimentel LMLM and Figueiredo TMRM took part in reviewing the manuscript. All the authors have approved the final version of the manuscript and declare themselves to be responsible for all aspects thereof, guaranteeing its accuracy and integrity.

## References


1. Cano APG, Romaneli MTN, Pereira RM, Tresoldi AT. Tuberculose em Pacientes Pediátricos: Como tem sido feito o diagnóstico? Rev Paul Pediatr.2017; 35(2):165-70. doi: https://doi.org/10.1590/1984-0462/;2017;35;2;00004.
2. World Health Organization. Global tuberculosis report: 2020. Geneva: WHO; 2020.297 p.
3. Almeida MG, Barbosa DRM, Almeida DFS. Epidemiologia e distribuição espacial da tuberculose multirresistente (TBMR) no Brasil notificada através do SINAN, 2008-2012. Rev Epidemiol Control Infec 2013;3(4):117-22. doi: http://dx.doi.org/10.17058/reci.v3i4.3564
4. Pereira AGL, Medronho RA, Escosteguy CC, Valencia LIO, Magalhães MAF. Distribuição espacial e contexto socioeconômico da tuberculose, Rio de Janeiro, Brasil. Rev. Saude Publica. 2015; 49(48). doi: https://doi.org/10.1590/S0034-8910.2015049005470.
5. Santos MLSG, Vendramini SHF, Gazetta CE, Oliveira SAC, Villa TCS. Pobreza: caracterização socioeconômica da tuberculose. Rev Lat-Am Enfermagem. 2007; 15(n.spe):762-7. doi: https://doi.org/10.1590/S0104-11692007000700008.
6. Duarte R, Silva DR, Rendon A, Alves TG, Rabahi MF, Centis R et al. Eliminação da tuberculose na América Latina: considerações. J Bras Pneumol. 2018;44(2):73-6. doi: https://doi.org/10.1590/s1806-37562017000000449.
7. World Health Organization. Guidance for national tuberculosis programmes on the management of tuberculosis in children. 2nd ed. Geneva, WHO;2014.146 p.
8. Sant'anna CC, Hijjar MA. Recente contribuição da Organização Mundial de Saúde para o controle da tuberculose na infância. Rev Saude Publica. 2007; 41(sppl.1):117-20. doi: https://doi.org/10.1590/S0034-89102007000800016.
9. Silva LB Análise Espacial dos casos de tuberculose na Rocinha, no período de 2007 a 2013, Rio de Janeiro. [dissertação]. [Rio de Janeiro]: Universidade Federal do Estado do Rio de Janeiro.
10. Venâncio TS, Tuan TS, Nascimento LFC. Incidência de tuberculose em crianças no estado de São Paulo, Brasil, sob enfoque espacial. Cienc Saude Colet 2015; 20(5):1541-47. doi: http://dx.doi.org/10.1590/1413-81232015205.14672014.
11. Brandão ICA, Martiniano CS, Monteiro AI, Marcolino EC, Brasil SKD, Sampaio J. Análise da organização da rede de saúde da Paraíba a partir do modelo de regionalização. Rev Bras Cienc. Saude. 2012; 16(3):347-52.
12. Instituto Brasileiro de Geografia e Estatística. Coordenação de população e indicadores sociais–COPIS: projeção da população. Brasília, DF: IBGE; [data desconhecida] [acesso 17 nov.2018]. Disponível em: https://www.ibge.gov.br/ geociencias/organizacao-do-territorio/malhas-territoriais.html.

13. Costa MA, Marguti BO, editores. . Atlas da vulnerabilidade social nos municípios brasileiros. Brasília, DF: Ipea: 2015 [acesso 17 nov. 2018]. Disponível em: https://www.ipea.gov.br/portal/index.php?option=com_content&view=article&id=26118.

14. Instituto Brasileiro de Geografia e Estatística [homepage na internet]. Geociências, organização do território, malhas territoriais. Brasília, DF: IBGE; [data desconhecida] [acesso 17 nove. 2018]. Disponível em: http:www.ibge.gov.br

15. Ferreira GS, Pinto CVS. Desenvolvimento humano, vulnerabilidade e prosperidade social no Rio Grande do Sul: uma visão inter e intrarregional por meio dos Coredes. In: Marguti BO, Costa MA, Pinto CVS, organizadores. Brasília, DF: Ipea; 2017:297-332.

16. Assunção RM, Barreto S, Guerra HL, Sakurai E. Mapas de taxas epidemiológicas: uma abordagem Bayesiana. Cad Saude Publica. 1998; 14(4):713-23. doi: https://doi.org/10.1590/S0102-311X1998000400013.

17. Barbosa CC. Padrões espaciais dos casos novos da hanseníase no estado de Pernambuco, Brasil, 2016 [dissertação]. [Recife]: Instituto Aggeu Magalhães, Fundação Oswaldo Cruz. 2017.

18. Santos SM, Souza WV. organizadores. Introdução à estatística espacial para a saúde pública.. Brasília, DF: MS, Fundação Oswaldo Cruz, 2007.

19. Costa MA, Marguti BO. Atlas da vulnerabilidade social nos municípios brasileiros. IPEA (Instituto de Pesquisa Econômica Aplicada). [internet] 2015.

20. Sales CMM, Figueiredo TAM, Zandonade E, Maciel ELN. Análise espacial da tuberculose infantil no estado do Espírito Santo, 2000 a 2007. Rev Soc Bras Med Trop. 2010;43(4):435-9. doi: http://dx.doi.org/10.1590/S0037-86822010000400020.

21. Lima MS. Padrões espaço-temporais da mortalidade relacionada à coinfecção tuberculose e HIV/AIDS no Brasil, 2000 –2011 [dissertação]. [Fortaleza]: Faculdade de Medicina, Universidade Federal do Ceará. 2015. 116 f.

22. Lorena DM, Martins-Melo FR, Brito AL, Alencar CH, Heukelbach J. Spatial patterns of leprosy in a hyperendemic state in Northern Brazil, 2001-2012. Rev Saude Publica.2015; 49:84. doi: https://doi.org/10.1590/S0034-8910.2015049005866.

23. Magalhães MAFM, Medronho RA. Análise espacial da Tuberculose no Rio de Janeiro no período de 2005 a 2008 e fatores socioeconômicos associados utilizando microdado e modelos de regressão espaciais globais. Cienc Saude Colet, 2017;22(3):831-40. doi: https://doi.org/10.1590/1413-81232017223.24132015.


**Received on 06/12/2020**
**Approved on 05/02 /2021**

Associate Editor: Bárbara Reis-Santos – orcid.org/0000-0001-6952-0352
Scientific Editor: Taís Freire Galvão – orcid.org/0000-0003-2072-4834
Editor-in-chief: Leila Posenato Garcia – orcid.org/0000-0003-1146-2641