

Spatial clustering, social vulnerability and risk of leprosy in an endemic area in Northeast Brazil: an ecological study

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Abstract

Background: Despite the global decline in the detection of leprosy cases, its incidence has remains unchanged in certain settings and requires the determination of the factors linked to its persistence. We examined the spatial and space-time distribution of leprosy and the influence of social vulnerability on the occurrence of the disease in an endemic area of Northeast Brazil.

Methods: We performed an ecological study of all leprosy cases reported by Sergipe state, Northeast Brazil from 2001 to 2015, to examine the association of the social vulnerability index and the prevalence and persistence of leprosy among the State's municipalities. Socioeconomic and leprosy surveillance information were collected from the Brazilian information systems and a Bayesian Empirical Local model was used to identify fluctuations of the indicators. Spatial and space-time clusters were identified using Scan Spatial statistic tests and to measure the municipalities Relative Risk of leprosy.

Results: Leprosy clusters and burden of disease had a strong statistical association with the municipalities social vulnerability index. Municipalities with a high social vulnerability had higher leprosy incidence, MB leprosy and newly diagnosed cases with grade 2 disability than areas with low social vulnerability.

Conclusion: Social vulnerability is strongly associated with leprosy transmission and maintenance of disease incidence. Leprosy control programs should be targeted to the populations with high social vulnerability.

Keywords: Leprosy; Risk factors; Social vulnerability; Spatiotemporal distribution; Brazil.

Introduction

Despite the global decline in leprosy prevalence due to the widespread use of multidrug therapy and the active search of cases, leprosy is still a public health problem with at least 250,000 incident cases per year. Most leprosy cases occur in tropical regions,^{1,2} with more than 80% reported from Southeast Asia and Brazil.² The distribution within countries is also heterogeneous.^{1,2} Brazil's incident rates are higher in the poor West Central, North and Northeast regions of the country, which report about 50% of cases.^{3,4}

Leprosy incidence has been linked to poor sanitation and housing conditions, crowding and migration.⁵⁻⁷ Although it is known that leprosy mostly affects poor populations, the specific social factors that increase the risk of transmission have not been identified.⁸ Identifying these factors would allow tailoring interventions for the prevention of transmission and the early identification of cases to high risk populations and geographical areas.

This study aimed to examine the spatial and spatiotemporal distribution of leprosy cases and its relationship to the social vulnerability index (SVI) in a leprosy endemic area of Northeast Brazil over a period of 15 years.

Methods

Study design

This was an ecological study with a spatial time-trend analysis of all leprosy cases reported in Sergipe state from 2001 to 2015. The geographic unit of analysis was the municipality, which is the main administrative subdivision of the Brazilian states. We examined the statistical associations between the municipalities' World Health Organization (WHO) leprosy elimination indicators,⁹ their socioeconomic characteristics and their social vulnerability.

Study area

Sergipe state is situated in the Northeast region (Figure 1), and has a population of ~2.3 million, of which 73.5% live in urban areas. The Northeast is one of the poorest regions of the country, with 60% of the population living in poverty. The state has 75 municipalities and a mean population density of 94.3 inhabitants/km².¹⁰

Data sources and measures

The data for the study were collected from several sources. The WHO leprosy elimination indicators were obtained from the National Information System for Notifiable Diseases (SINAN) (<http://sinan.saude.gov.br/sinan>). These included the annual leprosy prevalence per 10,000 population; the detection coefficients of new leprosy cases in the general population and in children <15 years-old; the detection coefficients of new leprosy cases with grade 2 disability at the time of diagnosis (per 100,000 population); the proportion of females among newly diagnosed cases, the proportion with grade 2 disability at time of diagnosis, and of newly detected multibacillary (MB) cases.

We used the Brazilian parameters to establish leprosy endemicity.¹¹ Leprosy detection coefficients in the general population were graded as low (<2.00), moderate: (2.00 to 9.99), high (10.00 to 19.99), very high (20.00 to 39.99) and hyperendemic (≥ 40.00 cases per 100,000 population). Incidence rates in children under 15 years were graded low (<0.50), moderate (0.50 to 2.49), high (2.50 to 4.99), very high (5.00 to 9.99) and hyperendemic (≥ 10.00 cases per 100,000 children).

The Social Vulnerability Index was obtained from the Institute of Applied Economic Research (IPEA) (<http://www.ipea.gov.br>). The index estimates the degree of vulnerability and social exclusion of the population and is composed of 16 social indicators comprising domains of

urban infrastructure, human capital, income and work.¹² The urban infrastructure domain includes the percentage of the population living in households with inadequate water supply, sewage or rubbish collection services; the proportion of households with a per capita income below half the Brazilian minimum salary of households with workers who spend more than one hour commuting to work. The human capital domain includes the infant mortality rate; the percentages of 0-5 and 6-14 year-old children not attending pre-school or school; the illiteracy rate among minors >15 years old; the percentage of mothers heading households or without primary education who have at least one child <15 years of age; the proportion of 10-17 year-old females with children and the percentage of children living in households where none of the residents has completed primary education. The income and work domain includes the proportion of families with a per capita household income below half the minimum salary with workers who spend more than one hour commuting to work; the unemployment rate and the proportions of adults without primary education and in informal employment; the proportion of people in households with income per capita below half the 2010 minimum wage dependent on the elderly and the economic activity of 10-14 year-old children. The SVI is the overall arithmetic mean of the three domains. We did not weight the factors and all domains were given the same importance. The SVI score ranges from 0 to 1 and we classified the municipalities into very low (0 to 0.2), low (>0.2 to 0.3), moderate (>0.3 to 0.4), high (>0.4 to 0.5) and very high SVI (>0.5). Social, demographic and economic data was extracted from the 2010 National Census, available at the Brazilian Institute of Geography and Statistics (IBGE) (<https://www.ibge.gov.br>).

Data analysis

Trends in the WHO leprosy indicators were examined using segmented regression analyses to describe whether they were stable, increasing or decreasing, and the point when the trend had changed. Annual percentage changes (APC) with 95% confidence intervals (CI) were included for all indicators. The analysis was conducted with the Joinpoint Regression software (version 4.5.0.1, National Cancer Institute, USA).

Three coefficients of the WHO leprosy indicators were included with the SVI domains to conduct a spatial analysis (detection of new cases, detection in children <15 years-old and new leprosy cases with grade 2 disability at the time of diagnosis). The WHO leprosy elimination indicators were smoothed using Bayesian Empirical Local modelling to reduce the random variation of small areas or with low numbers of cases. The Moran Global statistic was used to identify spatial autocorrelations, and when these were identified, we used the Local Index of Spatial Association (LISA). Scattering diagrams were generated to position the municipalities in quadrants and calculated the neighbouring municipalities average into Q1 (municipalities with high leprosy rate and high average in the neighbouring municipalities), Q2 (municipalities with low leprosy rates and low average in the neighbouring municipalities), Q3 (municipalities with high leprosy rates and low average in the neighbouring municipalities) and Q4 (municipalities with low leprosy rates and high average in the neighbouring municipalities). Thematic maps were constructed with the Moran diagram using the software Terra View 4.2.2 (Brazilian Space Research Institute, INPE) and QGIS 2.14.11 (Open Source Geospatial Foundation - OSGeo).

We used the Spatial and Space-Time Scan Statistics with Poisson's discrete probability model to identify spatial and spatiotemporal clusters and estimate relative risks. The null hypothesis was that the expected number of cases in each area was proportional to the

population size and the cluster time interval. The scan statistic establishes a flexible circular window in the map, positioned on each of the several centroids and whose radius r is established in 50% of the total population at risk. The flexibility of the window was justified by not knowing the size of the cluster a priori, since the population at risk is not geographically homogeneous.¹³ The test to identify clusters is based on the maximum likelihood method, whose alternative hypothesis is that there is a higher risk inside than outside the window. Monte Carlo simulations with 999 permutations were run with SatScan (version 9.1, National Cancer Institute, Division of Cancer Prevention, Biometry Branch, USA). Space-time clusters were those in which the occurrence of cases was temporarily higher in certain areas. Purely spatial and spatiotemporal variables and clusters with P-values <0.05 were considered statistically significant. Maps were elaborated using the QGIS 2.14.11 software.

Subsequently, the association between the detection coefficients of new leprosy cases in the general population and the SVI was verified using the Ordinary Least Square (OLS) regression according to Anselin et al. (1995) decision criteria.¹⁴ OLS residues were then submitted to the Moran statistic to decide whether to incorporate a spatial component and to select either the Spatial Error or the Spatial Lag Models. In the Spatial Error Model, spatial effects are noises that need to be removed, while the Spatial Lag Model attributes the ignored spatial autocorrelation to the response variable Y . The quality of the model was assessed by observing the Akaike (AIC), Schwarz Bayesian (BIC), R^2 , Log Likelihood and the Moran statistic of the residues.¹⁵ We used the GeoDa 1.10 (Center for Spatial Data Science, Computation Institute, The University of Chicago, USA).

The municipalities were grouped according to their SVI domains. There was a high number of municipalities with no new leprosy cases in children or patients with grade 2 disability. Therefore, we used the general detection coefficient of new leprosy cases for each stratum of social vulnerability and applied the Joinpoint regression model to identify leprosy trends by stratum of social vulnerability.

Ethical considerations

The study did not require research ethics committee approval because it used public-domain aggregate secondary data and no individual patients were identifiable.

Results

A total of 8,238 new leprosy cases were reported in Sergipe state from 2001 to 2015. Of these, 515 had grade 2 disability and 599 were <15 years-old.

Figure 2 describes the trends of the WHO leprosy elimination indicators and Table 1 highlights the inflection points for trend changes. Leprosy prevalence ranged from 4.22 in 2001 to 0.95/10,000 population in 2015, with an annual decrease of -7.8% (95%CI APC: -10.3 to -5.2; $P < 0.001$). The detection coefficient rate of new leprosy cases ranged from 17.33 in 2001 to 16.23/100,000 population in 2015 (APC: -0.3; 95%CI: -4.3 to 3.9; $P = 0.9$), while the leprosy detection rate in children <15 years ranged from 4.12 in 2001 to 3.10/100,000 population in 2015 (APC: -0.6; 95%CI: -8.6 to 8.2; $P = 0.9$). The coefficient of new leprosy cases with grade 2 disability had a stable trend (APC: 2.8; 95%CI: -1.5 to 7.2; $P = 0.2$), whereas the proportion of new leprosy cases with grade 2 disability increased from 5.1% in 2001 to 8.6% in 2015 (APC 5.5; 95%CI: 2.1 to 9.1; $P < 0.001$). There was an increase in the proportion of MB leprosy cases between 2001 and 2015 from 31.4% to 52.5% (APC: 2.5;

95%CI: 1.3 to 3.7; $P < 0.001$), but not in the proportion of women diagnosed with leprosy (APC: -0.3; 95%CI: -0.9 to 0.3; $P = 0.2$).

Figure 3 shows the spatial analysis of the WHO leprosy elimination indicators. Although there was no spatial dependence using the crude indicators, all indicators showed significant spatial dependence when smoothed by the Bayesian Empiric Model. Thirty-two municipalities had high and 37 very high endemicity, of which eleven were considered at greater risk for leprosy transmission (Q1 Moran Map). Using the leprosy detection coefficient in children <15 years old, 40 municipalities had very high-endemicity, with 11 at high risk of leprosy transmission. Sixty-three municipalities had detection coefficients of new leprosy cases with grade 2 disability between 1 and 1.25/100,000 population, of which 13 had a high risk of transmission.

The Spatial and Space-Time Scan Statistics identified spatial and spatiotemporal clusters for the general population, children <15 years-old and for grade 2 disability, as listed in Table 2 and Figure 4.

Five purely spatial clusters were detected for the general detection coefficient of new leprosy cases and four were statistically significant. *Cluster 1* included the municipalities of Itabaiana and Campo do Brito, with the highest relative risk (RR= 2.28; $P < 0.001$) and detection coefficient (56.2/100,000 population). *Cluster 2* included the municipalities of São Cristóvão, Nossa Senhora do Socorro, Barra dos Coqueiros and Aracaju, within Aracaju metropolitan area. This cluster had the lowest relative risk and the lowest general detection coefficient but had the largest population and thus the highest number of new leprosy cases ($n = 3,928$). Five spatial clusters were identified for the detection coefficient of new leprosy cases in children <15, with *Clusters 3 and 4* having the highest relative risks (RR= 4.30 and

5.35; $P= 0.01$ for both). One cluster, composed of Itabaiana and Campo do Brito municipalities, was statistically significant for the coefficient of new leprosy cases with grade 2 disability ($RR= 2.07$; $P <0.001$).

Two spatiotemporal clusters were identified for the general population. *Cluster 1* was identified between 2004 and 2009, and included four municipalities (Aracaju, São Cristóvão, Nossa Senhora do Socorro e Barra dos Coqueiros), which included 1,862 cases, resulting in a detection rate of 38.7 cases/100,000 population and a relative risk of 1.72 ($P = 0.001$).

Cluster 2 occurred between 2007 and 2012 and included two municipalities (Itabaiana e Campo do Brito), with a detection rate of 68.2/100,000 population and relative risk of 2.72 ($P = 0.001$). Two space-time clusters were identified for children <15 years-old, with *Cluster 1* (2004-2009 period) having a detection rate of 11.8 cases/100,000 population and relative risk of 2.36 ($P = 0.001$); and *Cluster 2* (2007-2012 period) with a detection rate of 80.8/100,000 population and relative risk of 12.98 ($P = 0.001$). Three space-time clusters (*cluster 1* in 2013-2015 and *clusters 2 e 3* in 2004-2006 period) were identified for the coefficient of new leprosy cases with grade 2 disability, with *Clusters 2 and 3* having the highest relative risks ($RR= 17.4$ and 5.09 ; $P= 0.001$ for both).

The SVI spatial analysis is shown in figure 5. Eight of 75 municipalities had high SVI, 45 very high and one low SVI. The vulnerability was high and very high in the income and work domains of 33 (44.0%) and 38 (50.6%) municipalities, respectively. Most municipalities had very low ($n=18$) or low ($n=28$) vulnerability for the infrastructure domain, with only five having high vulnerability. For the human capital domain, most municipalities ($n = 48$) were considered to have very high vulnerability.

The multivariate regression analysis showed that the detection coefficients of new leprosy cases per 100,000 general population were independently associated with the SVI and all its domains over the entire study period (Table 3). The Moran statistic and Lagrange multiplier tests indicated there was no spatial influence of the components evaluated (I Moran 0.051; $P = 0.17$).

The largest reduction in leprosy detection was reported in the municipalities with the lowest SVI and leprosy detection was stationary in municipalities with high social vulnerability (Table 4).

Discussion

Several studies have described the geographic distribution of leprosy,^{16–20} but few have explored how social, economic and demographic features are associated with the risk of leprosy transmission. In this study, we describe the spatiotemporal distribution of leprosy cases and their relationship with social vulnerability. In Sergipe, leprosy has a heterogenous geographic distribution, with well-defined spatiotemporal clusters which are mostly located in areas with a high degree of social vulnerability.

Overall, leprosy reports in Sergipe increased between 2001 and 2003, with a substantial decrease after 2006, remaining stable in subsequent years. The 2001-2003 increase was likely due to Brazil joining the leprosy elimination initiative in 2000, with the adoption of active case finding, multidrug therapy, contact tracing associated and population awareness campaigns. The 2006 decrease followed the lower prevalence reported from other regions in Brazil and is likely a reflection of the removal of long standing cases by the elimination initiative.^{18,21,22}

Despite the elimination initiative, leprosy transmission and incidence have continued in the community, and other factors, such as living conditions and socioeconomic factors, are likely to play a role facilitating its persistence.

We found a strong relationship between the municipalities' social vulnerability and the burden of leprosy, with leprosy clusters detected in municipalities with high social vulnerability. In other words, the more heterogeneous the distribution of resources in a municipality, the higher the odds that the municipality would report leprosy as an important health problem.

Social and financial deprivation affect people's lives in complex ways. Areas with large income inequalities often have the worse living conditions, poor sanitation, inadequate housing, crowding and difficult access to education and health services²³⁻²⁵. This study identified that these areas have a higher proportion of patients with advanced forms of leprosy, *vis a vis* MB leprosy and individuals with grade 2 disability, likely reflecting a late diagnosis and barriers to access health services. Brazil,^{5,17,22,26,27} Bangladesh¹⁶ and India²⁸⁻³⁰ have long reported the well-established relationship between poverty and the occurrence of advanced forms of leprosy and that patients in areas with good primary health care services are diagnosed earlier.^{22,31,32} Socioeconomic differences influence not only access, but also the quality and utilization of health services.⁶

Our findings also highlight that leprosy has not declined over time in municipalities with high social vulnerability, despite major efforts to eradicate leprosy with active case detection and contact tracing. Areas with higher social vulnerability also have slightly more cases in children, indicating a continued transmission in the population and the potential of remaining undetected leprosy cases in the community.³³

The literature describes leprosy as a disease of predominantly rural areas.^{28,30} However, our results indicate that many cases are being reported in small and medium towns of rural and urban areas, as reported by others.^{5,16,34,35} Other factors can play an important role as disease determinants, such as selective migration towards small towns,^{36,37} which may result in an unplanned urbanization and informal settlements with precarious infrastructure, which in turn is closely related to poor social indicators and inequity.³⁵ Further studies with greater granularity in these urban centres are needed to verify whether the disease is further concentrated in the neighbourhoods with the greatest social vulnerability.

This study has some limitations. The data were obtained from routine information systems and represents information on patients who sought treatment. Consequently, missing and undetected cases in poor communities could have influenced the detection rates, as higher underreporting is expected in areas with poor access to health services. These factors may bias differently the study indicators and trends. Secondary data in ecological studies are also unsuitable to establish disease causality and therefore the study only provides evidence of statistically significant associations between leprosy, poverty and social vulnerability.

In conclusion, this study identified a strong relationship between the degree of social vulnerability and the burden of leprosy. Social vulnerability is an important determinant of disease transmission and its maintenance in this population. The geographical distribution of exposure to leprosy could be used to focus interventions for the early identification of cases and to prevent transmission. Our results provide potential avenues to improve control programs by targeting interventions to populations with high social vulnerability, since they have the highest risk of infection. Programs aiming to eliminate leprosy as a public health problem should include interventions that reduce social inequality.

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Figure 1. Geographic location of the study area, Sergipe-Brazil.

Figure 2. Detection rate of new leprosy cases in the general population, in children under 15 years old and in patients with grade 2 disability (A) and proportion of newly detected MB leprosy cases with grade 2 disability (B).

Figure 3. Spatial distribution of the coefficients of detection of new leprosy cases per 100,000 general population, children under 15 years old and grade 2 disability.

Figure 4. Spatial and space-time clusters of new leprosy cases per 100,000 general population, children under 15 years old and grade 2 disability.

Figure 5. Spatial distribution and Moran Map of the Social Vulnerability Index.

Table 1. Trend of leprosy elimination indicators. Sergipe, Brazil, 2001-2015.

| Indicator | Period | Annual Percentage Change (95%CI*) | Trend |
|---|-----------|-----------------------------------|------------|
| Annual leprosy prevalence rate per 10,000 population | 2001-2015 | -7.8 (-10.3 to -5.2) | Decreasing |
| General detection coefficient rate per 100,000 population | 2001-2003 | 35.6 (-0.5 to 84.7) | Stable |
| | 2003-2015 | -5.4 (-7.0 to -3.5) | Decreasing |
| | 2001-2015 | -0.3 (-4.3 to 3.9) | Stable |
| Detection coefficient rate in children <15 years-old per 100,000 population | 2001-2003 | 43.9 (-23.7 to 171.3) | Stable |
| | 2003-2015 | -6.5 (-9.9 to -2.9) | Decreasing |
| | 2001-2015 | -0.6 (-8.6 to 8.2) | Stable |
| Detection coefficient of newly diagnosed leprosy cases with grade 2 disability at diagnosis | 2001-2015 | 2.8 (-1.5 to 7.2) | Stable |
| Percentage of patients with grade 2 disability at diagnosis | 2001-2015 | 5.5 (2.1 to 9.1) | Increasing |
| Percentage of cases with MB leprosy | 2001-2015 | 2.5 (1.3 to 3.7) | Increasing |
| Percentage of female cases | 2001-2015 | -0.3 (-0.9 to 0.3) | Stable |

*95%CI: Confidential interval 95%

Table 2. Purely spatial and spatiotemporal clusters of the detection coefficients of new leprosy cases per 100,000 general population, children under 15 years old and with grade 2 disability.

| Purely spatial scan statistic | | | | | |
|--------------------------------------|----------------------------|------------------------|--|----------------------|----------------|
| Cluster | Number of locations | Number of cases | Annual cases per 100,000 population | Relative Risk | p-value |
| General population | | | | | |
| 1 | 02 | 877 | 56.2 | 2.28 | <0.001 |
| 2 | 04 | 3928 | 31.7 | 1.40 | <0.001 |
| 3 | 02 | 294 | 44.3 | 1.71 | <0.001 |
| 4 | 03 | 79 | 41.3 | 1.58 | 0.032 |
| 5 | 01 | 37 | 42.8 | 1.63 | 0.499 |
| Children under 15 years old | | | | | |
| 1 | 01 | 66 | 17.3 | 2.85 | <0.001 |
| 2 | 06 | 319 | 8.5 | 1.64 | <0.001 |
| 3 | 01 | 12 | 27.6 | 4.30 | 0.01 |
| 4 | 01 | 9 | 34.5 | 5.35 | 0.01 |
| 5 | 01 | 15 | 11.6 | 1.79 | 0.95 |
| Grade 2 disability | | | | | |
| 1 | 02 | 51 | 3.3 | 2.07 | 0.001 |
| 2 | 03 | 44 | 2.7 | 1.66 | 0.26 |
| 3 | 02 | 12 | 3.8 | 2.34 | 0.62 |
| 4 | 05 | 24 | 2.7 | 1.63 | 0.89 |
| 5 | 03 | 17 | 2.9 | 1.79 | 0.91 |
| Space-time scan statistic | | | | | |
| General population | | | | | |
| 1 | 04 | 1862 | 38.7 | 1.72 | 0.001 |
| 2 | 02 | 433 | 68.2 | 2.85 | 0.001 |
| Children under 15 years old | | | | | |
| 1 | 20 | 218 | 11.8 | 2.36 | 0.001 |
| 2 | 1 | 9 | 80.8 | 12.98 | 0.001 |

| Grade 2 disability | | | | | | |
|--------------------|----|-----|------|------|-------|--|
| 1 | 50 | 174 | 5.4 | 2.79 | 0.001 | |
| 2 | 1 | 9 | 39.4 | 17.4 | 0.001 | |
| 3 | 4 | 20 | 11.4 | 11.4 | 0.001 | |

Table 3. Ordinary Least Square regression using the detection coefficients of new leprosy cases per 100,000 general population as dependent variable.

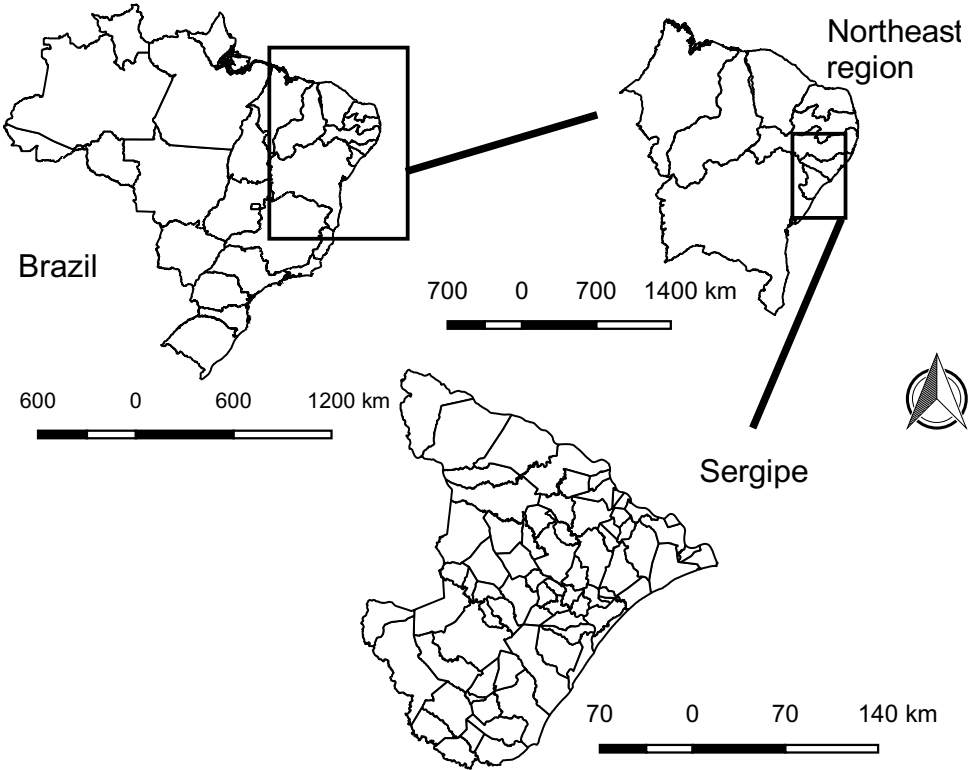
| Social Vulnerability Index | Coefficient | Std. Error | t-statistic | P-value |
|--------------------------------------|--------------------|-------------------|--------------------|----------------|
| Social Vulnerability Index (overall) | -1.0406 | 0.281627 | -3.69496 | <0.001 |
| Infrastructure domain | -0.332195 | 0.144266 | -2.30265 | 0.02 |
| Income and work domain | -0.792017 | 0.27277 | -2.90361 | 0.004 |
| Human capital domain | -0.652378 | 0.262851 | -2.48193 | 0.01 |

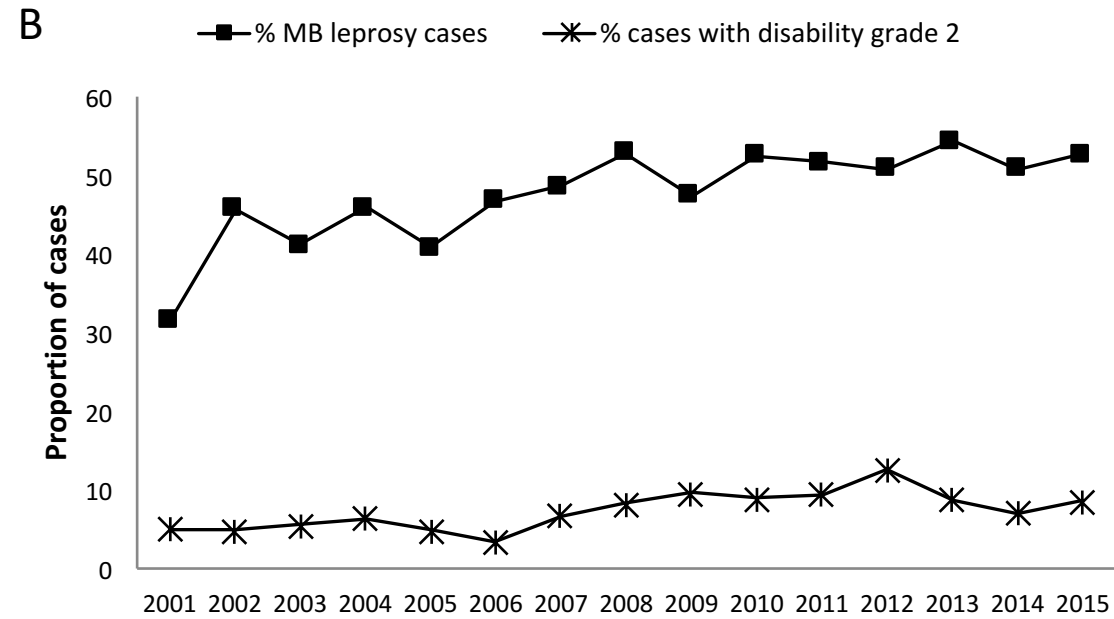
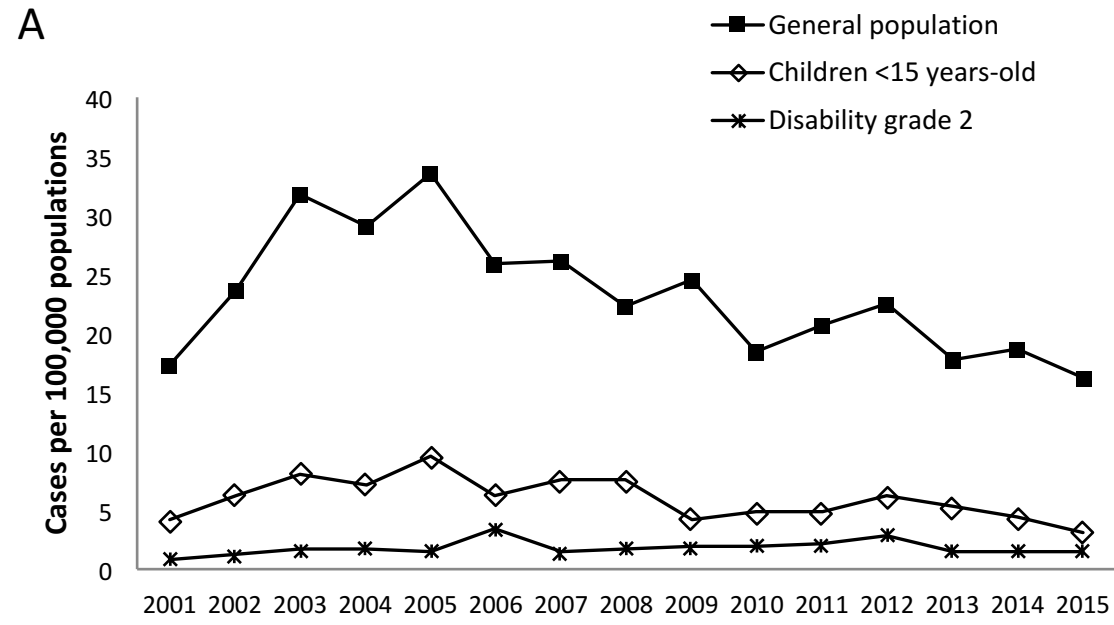
Table 4. Trend of the general detection coefficient per 100,000 population by the Social Vulnerability Index.

| Social Vulnerability Index | Number of municipalities | Period | Annual Percentage Change | (95%CI*) | Trend |
|-------------------------------|--------------------------|-----------|--------------------------|----------------|------------|
| Very low | 0 | - | - | - | - |
| Low | 1 | 2001-2003 | 32.3 | 2.4 to 70.9 | Increasing |
| | | 2003-2015 | -7.8 | -9.2 to -6,4 | Decreasing |
| Moderate | 21 | 2001-2003 | 48.1 | -17.9 to 167.0 | Stable |
| | | 2003-2015 | -4.2 | -7.5 to -0.8 | Decreasing |
| High | 45 | 2001-2005 | 19.9 | 5.8 to 35.8 | Increasing |
| | | 2005-2015 | -5.9 | -8.7 to -3,0 | Decreasing |
| Very high | 8 | 2001-2015 | -0.5 | -6.3 to 5.6 | Stable |
| Infrastructure domain | | | | | |
| Very low | 18 | 2001-2009 | 7.9 | -0.4 to 16.8 | Stable |
| | | 2009-2015 | -11.6 | -21.8 to -0.1 | Decreasing |
| Low | 28 | 2001-2003 | 57.7 | -3.4 to 157.6 | Stable |
| | | 2003-2015 | -5.4 | -8.1 to -2.7 | Decreasing |
| Moderate | 20 | 2001-2015 | -1.3 | -4.3 to 1.8 | Stable |
| High | 4 | 2001-2003 | 81.7 | -25.1 to 340.9 | Stable |
| | | 2003-2015 | -2.5 | -7.4 to 2.8 | Stable |
| Very High | 5 | 2001-2015 | 1.2 | -7.0 to 10.1 | Stable |
| Income and work domain | | | | | |
| Very low | 0 | - | - | - | - |
| Low | 1 | 2001-2003 | 32.2 | 2.4 to 70.9 | Increasing |
| | | 2003-2015 | -7.8 | -9,2 to -6,4 | Decreasing |
| Moderate | 3 | 2001-2015 | -1.0 | -3.7 to 1.8 | Stable |
| High | 33 | 2001-2003 | 43.5 | -15.5 to 143.5 | Stable |
| | | 2003-2015 | -5.9 | -8.8 to -2,9 | Decreasing |
| Very high | 38 | 2001-2003 | 56.7 | -4.0 to 155.9 | Stable |
| | | 2003-2015 | -1.8 | -4.6 to 1.1 | Stable |
| Human capital domain | | | | | |
| Very low | 0 | - | - | - | - |
| Low | 0 | - | - | - | - |
| Moderate | 1 | 2001-2003 | 32.3 | 2.4 to 70.9 | Increasing |

| | | | | | |
|-----------|----|-----------|-------|----------------|------------|
| High | 26 | 2003-2015 | -7.8 | -9.2 a -6.4 | Decreasing |
| | | 2001-2003 | 55.5 | -14.5 to 182.9 | Stable |
| Very high | 48 | 2003-2015 | -4.6 | -7.9 to -1.1 | Decreasing |
| | | 2001-2006 | 11.9 | 0.2 to 24.9 | Increasing |
| | | 2006-2015 | -10.0 | -10.0 to -1.6 | Decreasing |

*95%CI: Confidential interval 95%



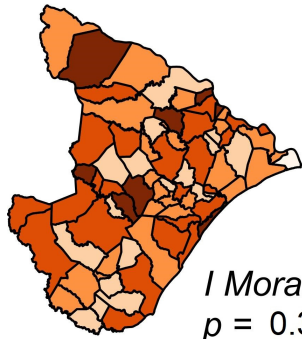


Crude rate

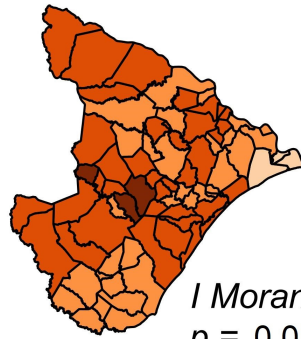
Smoothed indicator by Empirical Bayesian Model

Moran Map (Smoothed indicator)

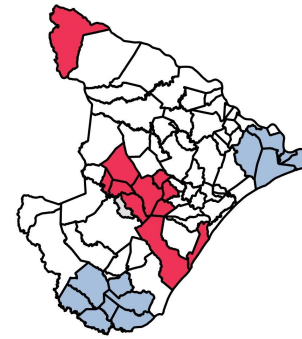
General population



I Moran 0.03
p = 0.3



I Moran 0.434
p = 0.01



Legend

Endemic by general population and < 15 years-old

- Low
- Moderate
- High
- Very High
- Hyperendemic

Moran Map by general population and <15 years-old

- No Significant
- Q1
- Q2
- Q4

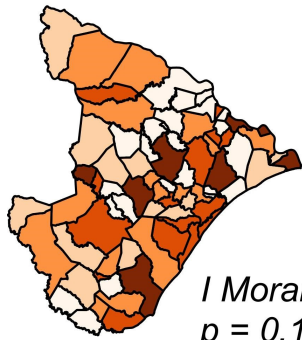
Coefficient of disability Grade 2

- < 1
- 1 a 2.5
- 2.6 a 3.5
- 3.6 a 4.5
- >4.5

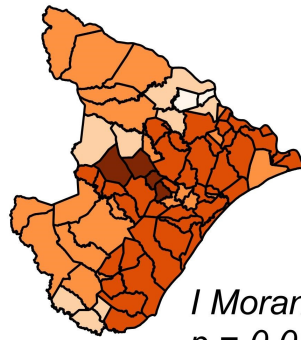
Moran Map

- No Significant
- Q1
- Q2
- Q3

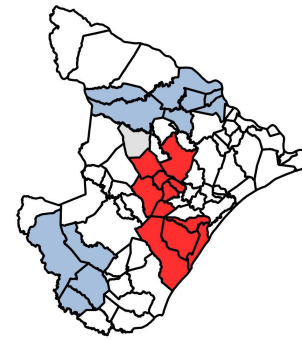
Children < 15 years-old



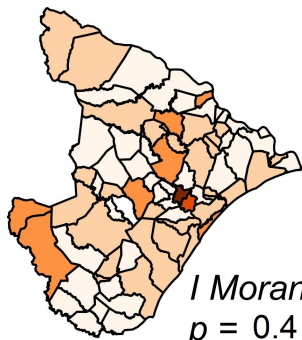
I Moran -0,03
p = 0,1



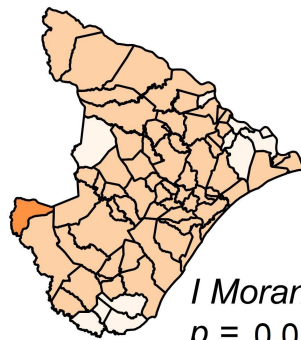
I Moran 0,451
p = 0,01



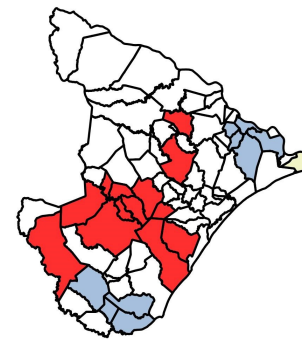
Disability Grade 2



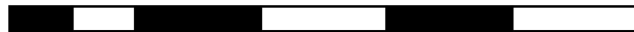
I Moran 0.02
p = 0.4



I Moran 0.517
p = 0.01



80 0 80 160 240 320 km



Detection coefficient of new cases per 100,000 population

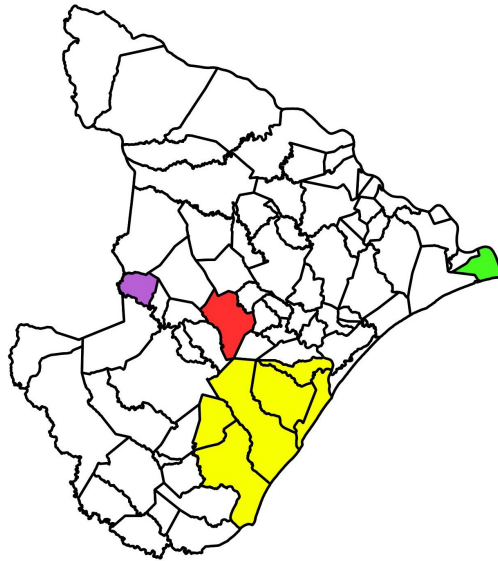
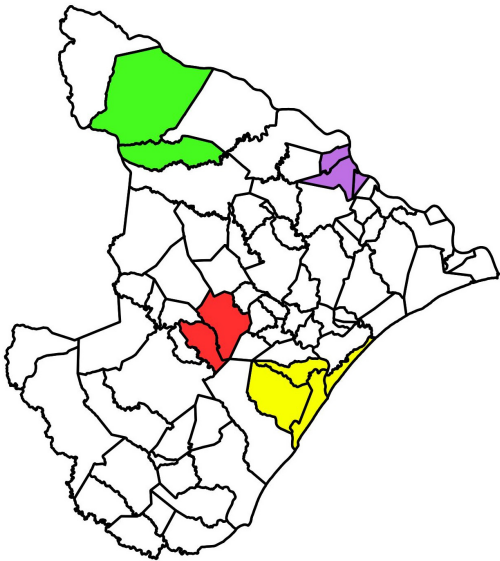
Detection coefficient of new cases per 100,000 inhabitants

General population

Children < 15 years-old

Disability Grade 2

Space Scan Statistic



Legend

Spatial Cluster

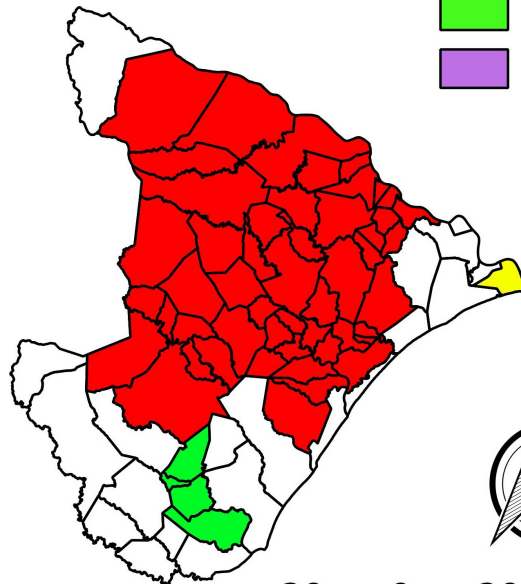
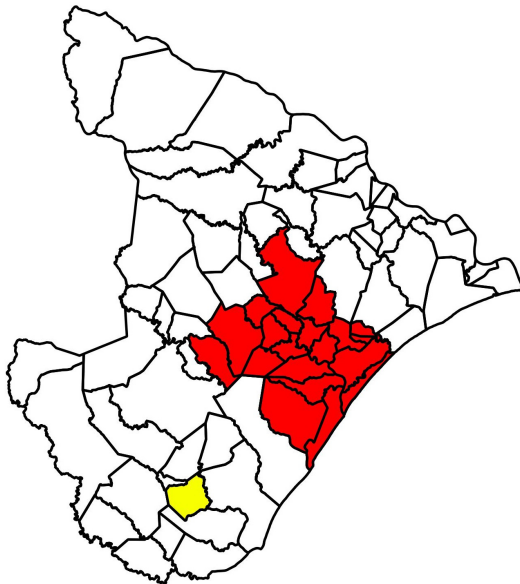
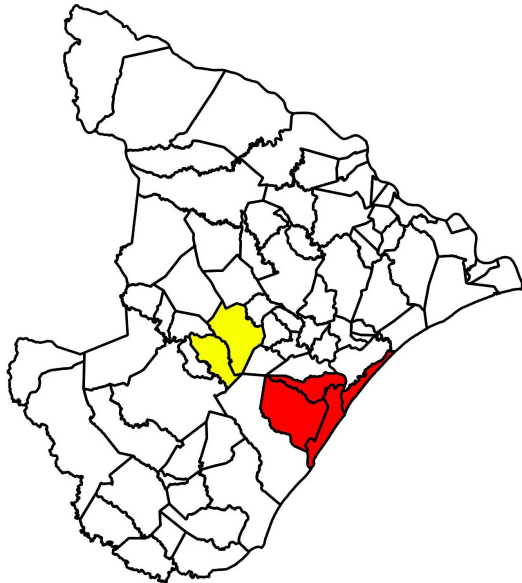
Cluster 01

Cluster 02

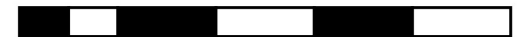
Cluster 03

Cluster 04

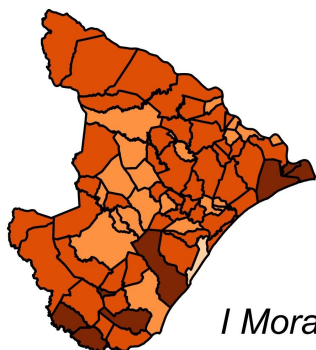
Space-Time Scan Statistic



20 0 20 40 60 80 km

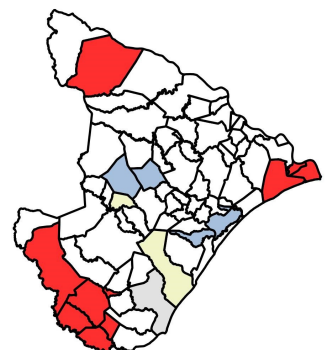


General SVI

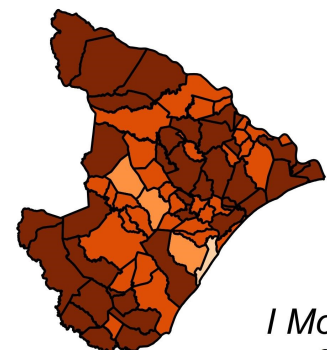


I Moran 0.265
 $p = 0.01$

General SVI
 Moran Map

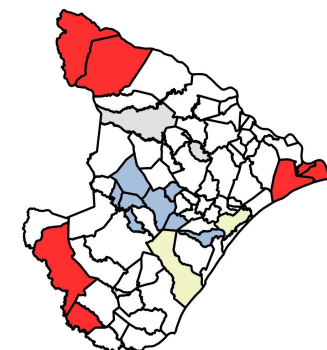


Income and work SVI

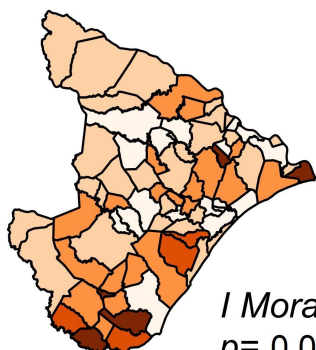


I Moran 0,226
 $p = 0.01$

Income and work SVI
 Moran Map

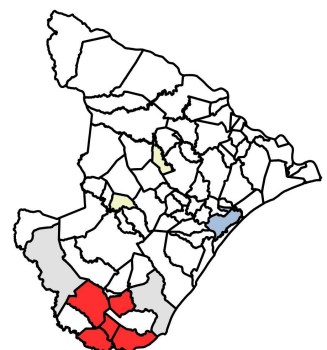


Infrastructure SVI

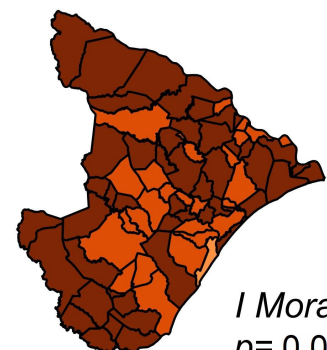


I Moran 0.232
 $p = 0.01$

Infrastructure SVI
 Moran Map

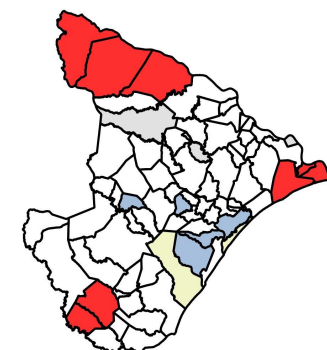


Human capital SVI



I Moran 0.266
 $p = 0.01$

Human capital SVI
 Moran Map



- Legend
- SVI Strata
- Very Low
 - Low
 - Moderate
 - High
 - Very High

- Moran Map
- No Significant
 - Q1
 - Q2
 - Q3
 - Q4

