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Spatial analysis of neglected diseases in Brazil, 2007-2009.

Análise espacial de doenças negligenciadas no Brasil, 2007-2009.

Análisis espacial de las enfermedades desatendidas en Brasil, 2007-2009.

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ABSTRACT:This paper aims to describe a set of epidemiological information regarding the spatial distribution of selected neglected diseases in Brazil from 2007 to 2009 and their correlation with health care infrastructure and socio-economic indicators. We performed an ecological study of the spatial analysis, based on the incidence of tuberculosis, visceral leishmaniasis, American cutaneous leishmaniasis, malaria and prevalence of leprosy and schistosomiasis. Maps with the spatial distribution of the prevalence and incidence rates were drawn, as well as cluster detection maps, applying spatial statistical analysis techniques. A thematic map with the total distribution of priority municipalities was developed for each disease. Malaria and schistosomiasis had the highest incidence and prevalence rates respectively. All diseases analyzed showed dependence in the spatial correlation measure. A total of 1,630 Brazilians municipalities (29%) were considered by the Ministry of Health as a priority to receive control actions for at least one of the studied diseases.

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North and Northeast regions concentrate municipalities with at least three simultaneous diseases, which overlap with the lowest socio-economic indicators. Spatial analysis studies may contribute to a better planning and organizing health care and services, aiming to reduce the existent gap regarding scientific knowledge on neglected diseases.
Key words: Neglected Diseases, Spatial Analysis, Brazil, Epidemiological Surveillance

RESUMO: Este trabalho tem como objetivo descrever um conjunto de informações epidemiológicas em relação à distribuição espacial das doenças negligenciadas no Brasil 2007-2009 e infra-estrutura de cuidados de saúde e os indicadores socioeconómicos 2010. Um estudo ecológico da análise espacial, com base na incidência de tuberculose, leishmaniose visceral, leishmaniose cutânea americana, a malária e a prevalência da hanseníase e esquistossomose. Mapas com a distribuição espacial das taxas de prevalência e incidência foram sorteados, bem como mapas de detecção de fragmentação, técnicas estatísticas aplicação da análise espacial. Um mapa temático com a distribuição geral dos municípios prioritários foi desenvolvido para cada doença. Malária e esquistossomose têm as maiores taxas de incidência e prevalência, respectivamente. Todas as doenças analisadas mostraram dependência na medida de correlação espacial. Um total de 1.630 municípios brasileiros (29%) foram considerados pelo Ministério da Saúde como prioridade no recebimento de ações para o controle de pelo menos uma das doenças estudadas. As regiões Norte e Nordeste concentram municípios com pelo menos três doenças simultâneas, que se sobrepõem com os mais baixos indicadores socioeconômicos. Estudos de análise espacial podem contribuir para um melhor planejamento e organização de cuidados e serviços de saúde, mitigando a escassez de conhecimento científico existente sobre as doenças negligenciadas.
Palavras-chave: Doenças Negligenciadas, análise espacial, Brasil, Vigilância Epidemiológica

RESUMEN: Este documento tiene por objeto describir el conjunto de la información epidemiológica sobre la distribución espacial de las enfermedades desatendidas en Brasil entre 2007 y 2009 y la infraestructura de atención de la salud y los indicadores socioeconómicos de 2010. Un estudio ecológico del análisis espacial, basado en la incidencia de la tuberculosis, La leishmaniasis visceral, leishmaniasis cutánea americana, la malaria y la prevalencia de la lepra y la esquistosomiasis. Mapas con la distribución espacial de las tasas de prevalencia e incidencia fueron extraídas, así como mapas de detección de clúster, la aplicación de técnicas de análisis de estadística espacial. El mapa temático con la distribución total de municipios prioritarios fue desarrollado para cada enfermedad. La malaria y la esquistosomiasis tiene la más alta incidencia y prevalencia respectivamente. Todas las enfermedades analizados mostró la dependencia en la medida de correlación espacial. El total de 1.630 municipios brasileños (29%) fueron consideradas por el Ministerio de Salud como una prioridad para recibir las acciones de control es, al menos, una de las enfermedades estudiadas. regiones Norte y Nordeste concentran municipios con al menos tres enfermedades simultáneas, que se solapan con los indicadores socioeconómicos más bajos. Los estudios de análisis espacial puede contribuir a una mejor planificación y organización de la atención y los servicios de salud, con el objetivo de reducir la brecha existente En cuanto a los conocimientos científicos sobre las

enfermedades olvidadas.
Palavras claves: Las enfermedades olvidadas, análisis espacial, Brasil, Vigilancia Epidemiológica

INTRODUCTION

In the group of infectious and parasitic diseases, there is a subgroup denominated "neglected tropical diseases" that have received less attention from society, either because they are more common in developing countries, or because there is a high number of cases among the more vulnerable segments of the population. These Diseases contributes to perpetuate poverty cycles, inequality and social exclusion [1,2]. However, they are not a priority for the pharmaceutical and biotechnology industries, which are responsible for the production of vaccines, medicines and diagnosis kits, lacking of solid and continuous investment in research and development (R&D). Only 1% of new therapeutic products released in the market between 2000 and 2011 addressed treatment for such diseases although representing together 11% of the global burden of disease.[3]

In Brazil, despite the epidemiological transition observed in recent decades, which established the chronic degenerative diseases and injuries as a major cause of mortality, infectious diseases remain a major public health problem and in 2008, these diseases accounted for 13.2% of the total burden of disease, reaching 18.3% in the Brazilian North region.[4]

In 2005, the Ministry of Health of Brazil, the Ministry of Science and Technology [5] and the National Council for Scientific and Technological Development (CNPq) [6] launched a joint program, to support the investigation, technological development and innovation for six infectious diseases, defined as neglected in the Brazilian scenario due it's epidemiologic magnitude, which were: dengue fever, Chagas' disease, leishmaniasis, leprosy, malaria and tuberculosis. In 2008 schistosomiasis was included in this list.[1,7,8]

The governmental incentives for R&D for neglected diseases in Brazil were around R$75 million in 2008[9]. In 2011, a group initiative was established, which had as the main goal to strengthen prevention and control actions for a group of diseases, including neglected diseases, which was ratified also for their inclusion in an action plan for the 2011 to 2015 period.[10]

The results from the most recent study of burden of disease in Brazil, based on the year 2008 confirm the impact of neglected diseases on the population health. The seven diseases, together, accounted for more than 350,000 years of healthy life lost.[4]

As infectious diseases, their occurrence generally is related to the geographic space and its characteristics, such as environmental aspects, population density, poverty, climate and water resources.[11]

Studies that includes in their approach a spatial analysis and morbimortality indicators, could

better contribute to identify the pattern of spatial distribution, focusing understanding the socio-environmental risks as well as the identification of the areas with high disease occurrence and more vulnerable population. The accurate identification of risk areas assure a better efficiency on supporting the decision making process aiming actions and policies to address the neglected diseases optimizing resources.[12,13]

This paper was developed in the context of the Burden of Disease in Brazil - 2008 project[4], and aims to present a set of epidemiologic information about the spatial distribution of neglected diseases considered as priority by the Ministry of Health of Brazil, from 2007 to 2009 and their correlation with health care infrastructure and socio-economic indicators.

MATERIALS AND METHODS

The present study is an ecologic study of neglected diseases. The analysis unit considered comprises the 5,562 Brazilian municipalities, one Federal District (Distrito Federal - Brasília) and one State District (Distrito Estadual - Fernando de Noronha) being a total of 5,564 geographic units.

The results are presented at the federative units/municipalities and macro region levels. The macro region, defined by the IBGE – Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística), refers to a set of economic, social and political characteristics that are related to the overall organization of the Brazilian national geographic space [14].

As this paper was developed in the context of the project "Carga de Doença no Brasil, 2008" [4], it used data from the same period, which was from 2007 to 2009.

The Information System on Mandatory Notification Diseases (SINAN - Sistema de Informação de Agravos de Notificação Compulsória) was the source of information for cases of incidence of tuberculosis, visceral leishmaniasis, American cutaneous leishmaniasis and prevalent cases of leprosy. The Malaria Epidemiologic Surveillance System (SIVEP-Malária - Sistema de Vigilância Epidemiológica da Malária) was used to obtain the cases of incidence of malaria, and from the Schistosomiasis Control Programme (PCE - Programa de Controle de Esquistossomose) was obtained the prevalent cases of schistosomiasis. In the present study Dengue haemorrhagic fever incidence cases of were included based on information from the Hospital Admission Information System (SIH/SUS - Sistema de Internações Hospitalares).[15]

Although Chagas' disease (cases with cardiac and digestive complications) are considered a neglected disease, data at the municipality level for these sequels are not available at this level of disaggregation, and because of that the disease was not included in this specific analysis.[16]

Population data used was the estimates in the middle of the period of 2008, census data and it was obtained from IBGE.[14]

Identification and exclusion of repeated entries were conducted on the SINAN data. The repeated entries were identified through a set of steps and a probabilistic method using Reclink III®, based on the name of the patient, mother's name, data birth, gender and municipality of residence. The repetition rates were VL (5.3%) , ACL (2.0%), tuberculosis (1.7%) and leprosy (0.7%) [4].

It was calculated the incidence and prevalence per 100,000 inhabitants, for the selected diseases in each municipality, being the geographic unit of analysis the municipality of residence. It was considered the average number of included cases between 2007 and 2009, and the population in the middle of the period of 2008[4]. This procedure aimed to minimize the random fluctuation that occurs in incidence and prevalence when working with small populations at risk and few events, thus providing for better stabilization of cases [17].

Data analysis

Maps with the spatial distribution of incidence and prevalence rates of the analysed diseases were drawn for the visualization of risk areas, as well as maps for the detection of clusters. The scales of each map were developed based on the distribution of incidence or prevalence and, therefore, they are specific for each disease.

The analytical sequence applied was crude rates and scan statistic. The detection parameter used to identify the clusters was percentage of population at risk applied on the crude rates. The spatial analyses were performed using the *maptools* and *SpatialEpi* library of R® software (version 3.0.2)[18]. Additionally, Excel® 2010 was used to organize the data.

The hypothesis of spatial dependence for the distribution of diseases was assumed to be true. As the incidences and prevalences did not present normal distribution only scan statistics were applied[19].

For detecting concentration areas that differed from the expected for the normal dispersion of the phenomenon (clusters), Kulldorff & Nagarwalla [20] spatial scan method was used, since it is appropriate for identifying statistically significant spatial clusters, and the discrete Poisson probabilistic model was considered for the distribution of the cases.

The method described above was chosen since it considers the relative risk for an event and its location, which is here determined by the geographic coordinates of the centroids, identifying the most probable spatial conglomerate (cluster) that potentially violates the null hypothesis of non-agglomeration. For that purpose, the method superimposes a circular window over the map and allows its centre to move over the study region looking for an excess of cases in any region of the map [21].

In order to better illustrate the Brazilian scenario, it was included socio-economic and health care indicators as follow, the Growth Development Product (GDP), Human Development Index (HDI), the number of health services and doctors per 1000 inhabitants obtained from IBGE.

Additionally, it was identified the linear correlation (Spearman) between the selected indicators and the incidence or prevalence rates of the diseases analysed, considering the municipalities were values differ from zero.

Chart 1. Criteria for the classification of priority municipalities according to the distribution of neglected diseases, Brazil 2011.

Disease	Criteria
Haemorrhagic dengue fever	Since there are no official criteria (published by the Ministry of Health) for the classification of the risk areas for this disease, the last incidence quintile was chosen as the cut-off point for the classification of priority municipalities (235 municipalities).
Schistosomiasis	The criteria from Portaria 2,556 from October 28, 2011 were used for the classification of priority municipalities. It considers as priority the municipalities with prevalence equal to or larger than 10% and populations in areas of extreme poverty (79 municipalities).
Leprosy	The criteria from Portaria 2,556 from October 28, 2011 were used for the classification of priority municipalities. 1. Municipalities with a detection coefficient higher than 20 per 100,000 inhabitants and located in higher risk areas according to the study by the Ministry of Health; and, b) Minimum of 20 new cases (662 municipalities); 2. For the municipalities outside the risk areas, were also included municipalities with 50 new cases if at least 5 cases are in patients under 15 years of age (5 municipalities); 3. All of the capitals (27 municipalities); 4. Municipalities from metropolitan regions with 50 new cases, being at least 5 cases in patients under 15 years of age (67 municipalities); 5. Those listed as high risk municipalities by the Ministry of Health in the following States: Mato Grosso, Goiás, Piauí, Tocantins, Maranhão, Pará and Rondônia, witht a detection coefficient equal to or higher than 20 per 100,000 inhabitants; and, b) with a minimum of 10 new cases, being at least 1 case in patients under 15 years of age (426 municipalities).
American cutaneous leishmaniasis	Municipalities that have notified one or more cases of ACL in the last 10 years. According to the Ministry of Health (2000), even with a simplified concept for risk area, the use of this indicator better assesses the risk of contracting the disease (2,355 municipalities).
Visceral leishmaniasis	According to the Ministry of Health, the classification of the areas for surveillance and control of visceral leishmaniasis is as described below, based on the number of cases in the 3 former years: (http://portal.saude.gov.br/portal/saude/profissional/visualizar_texto. cfm?idtxt=34340): 1. Areas with no transmission: do not present cases in humans in the mean of the former 3 years; 2. Areas with sporadic transmission: mean < 2.4; 3. Areas with moderate transmission: mean ≥ 2.4 and < 4.4; 4. Areas with intense transmission: mean ≥ 4.4. Municipalities with intense transmission rates were considered as priority from 2007 to 2009 period (298 municipalities).
Malaria	Municipalities are included in the classification by the Secretaria de Vigilância em Saúde do Ministério da Saúde (SVS), according to the risk of transmission of malaria as: A) High risk (annual parasite incidence higher than 49.9 cases/1,000 inhabitants), Medium risk (annual parasite incidence between 10 and 49.9 cases/1,000 inhabitants), Low risk (annual parasite incidence lower than 9.9 cases/1,000 inhabitants) (Brazil, 2009). Municipalities with high transmission were considered as priority municipalities (558 municipalities).
Tuberculosis	Technical Note no. 15 from October 07, 2011 was used for the classification of priority municipalities from 2007 to 2009 period: These criteria are: 1 – Capitals (27 municipalities); 2 – Municipalities with population equal to or lower than 100,000 inhabitants (266 municipalities); 3 – Incidence rate > 80% of the national rate (32 new cases per 100,000 inhabitants) (3,146 municipalities); 4 – Mortality rate by tuberculosis higher than the national rate (2.5 deaths per 100,000 inhabitants) (1,084 municipalities).

Source: Núcleo de Pesquisa em Métodos Aplicados aos Estudos de Carga Global de Doença, ENSP/Fiocruz

Brazil's Ministry of Health indicates priority municipalities according to the pattern of occurrence of some diseases and these locations are prioritized for integration measures and enhancement of actions of monitoring and control of the diseases, according to the criteria presented on Chart 1. Considering this prioritization incentive, an analysis of the municipalities ranked according to the criteria of each disease analysed in this study was conducted. Thematic maps were developed showing the distribution of the total number of priority municipalities per disease for such analysis. The distribution of these municipalities expressed as a percentage per disease and by federative units was included.

The present study was developed in the context of the Burden of diseases in Brazil-2008 project. The data was obtained at the National Management of the SINAN system after the signature of the term of concession and confidentiality by the coordination of the project Carga de Doença. The project was submitted and approved by the Research Ethics Committee of the National School of Public Health, (CAAE: 0054.0.031.000-11), according to the terms of the resolution CNS nº 466/2012.

RESULTS

Table 1. Mean, median, minimum and maximum values and total of priority municipalities for the control of dengue hemorrhagic fever, schistosomiasis, leprosy, leishmaniases, malaria and tuberculosis. Brazil, 2007 to 2009.

Disease	Measures	Incidence/Prevalence (100,000 inhabitants)	Priority Municipalities
Haemorrhagic dengue fever	Mean	5.7*	235
	Mediana	3.0	
	Min - Max	1.0 – 150	
Schistosomiasis	Mean	502.9**	78
	Mediana	36.0	
	Min - Max	1.0 – 115,415	
Leprosy	Mean	63.6**	794
	Mediana	34.0	
	Min - Max	1.0 e 1,690	
Americana Cutaneous Leishmaniasis	Mean	100.3*	2,355
	Mediana	26.0	
	Min - Max	1.0 – 5,330	
Visceral Leishmaniasis	Mean	20.0*	298
	Mediana	12.0	
	Min - Max	1.0 – 363.0	
Malaria	Mean	2,346.7*	556
	Mediana	142.0	
	Min - Max	1.0 – 74,103	
Tuberculosis	Mean	52.7*	244
	Mediana	42.0	
	Min - Max	4.0 – 1,095	

Source: Núcleo de Pesquisa em Métodos Aplicados aos Estudos de Carga Global de Doença, ENSP/Fiocruz.

Notes: (*) incidence (**) prevalence

In terms of incidence, the highest values were observed for malaria (2,346.7 cases per 100,000 inhabitants), American cutaneous leishmaniasis (100.3 cases per 100,000 inhabitants) and

tuberculosis (52.7 cases per 100,000 inhabitants). The highest prevalence rate was observed for schistosomiasis (502.9 cases per 100,000 inhabitants) (Table 1).

Figure 1. Spatial distribution of incidence/prevalence of Dengue hemorrhagic fever, American Cutaneous Leishmaniasis (ACL), Visceral Leishmaniasis (VL), Malaria and Tuberculosis and prevalence of Schistosomiasis and Leprosy. Brazil, 2007 to 2009.

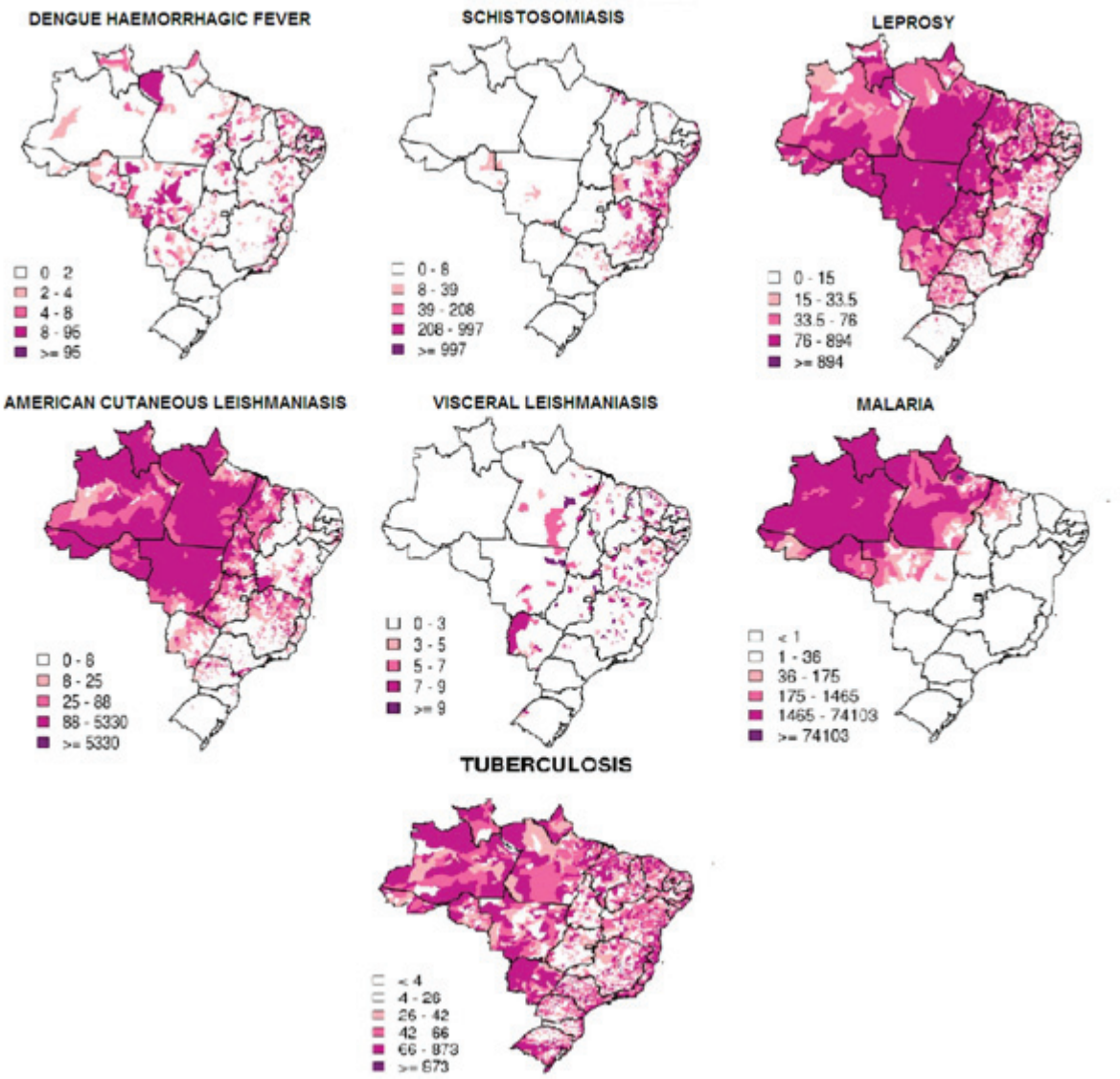


Figure 1 shows the spatial distribution of the incidences of Dengue haemorrhagic fever, ACL, VL, malaria and tuberculosis and prevalence of schistosomiasis and leprosy.

Dengue haemorrhagic fever was present in 21.2% of the municipalities, with an average incidence of 3 cases per 100,000 inhabitants. The highest incidence was found in the state of Rio de Janeiro (8 cases per 100,000 inhabitants).

Around of 29% of the Brazilian municipalities presented cases of Schistosomiasis and it is concentrated in the coast of Northeast and Southeast macro-regions. Its prevalence in the Northeast

was 122 cases per 100,000 inhabitants, and in the Southeast, 65 cases per 100,000 inhabitants. The State of Alagoas had the highest prevalence, 492 cases per 100,000 inhabitants, followed by Sergipe with 418 cases per 100,000 inhabitants.

Leprosy was detected in all Brazilian States, being detected in 71.3% of municipalities being the highest rates in the Centre-West macro-region.

ACL was found in 50% of the municipalities in the country, majority in the North macro-region, with sparse concentrations in the Centre-West and in the states of Bahia and in Minas Gerais. These two macro-regions have, respectively, a detection rate of 53 and 24 cases per 100,000 inhabitants in the 2007-2009 period. The VL was present in 19% of the Brazilian municipalities, concentrated in the Northeast macro-region and in the states of Pará, Tocantins, Mato Grosso, Mato Grosso do Sul and Minas Gerais, with incidences varying from 3 to 5 per 100,000 inhabitants.

During the period studied, malaria showed a high concentration in the Amazon region, which accounted for 96% of the cases, scattered on the states: Acre, Amapá, Amazonas, Pará, Rondônia and Roraima.

Mycobacterium tuberculosis was notified in 83.6% of the Brazilian municipalities. The highest incidence (71 cases per 100,000 inhabitants) was detected in Rio de Janeiro, followed by Amazonas state (68 cases per 100,000 inhabitants). The highest incidences per macro-region were observed for the North and the Southeast macro-region with, respectively, 46 and 41 cases per 100,000 inhabitants.

Figure 2 shows the primary clusters, which are the cluster detection for the neglected diseases investigated, territorial agglomerates with higher probability ratio of occurrence, as well as secondary clusters with a strong probability ratio that were identified from the spatial scan analysis.

Rio de Janeiro is a primary cluster for Dengue hemorrhagic fever, while the States of Mato Grosso, Pará, Tocantins, Roraima and Rio Grande do Norte, which presented a strong probability ratio, were considered as secondary clusters.

For schistosomiasis, a strong prevalence structure was found in the Northeast and Southeast macro-regions, being considered as primary clusters.

Primary clusters for leprosy were found in the North and Centre-West macro-regions, and with special relevance to the following States: Amazonas, Goiás, Mato Grosso, Mato Grosso do Sul, Pará, Rondônia, Tocantins and a small portion of Maranhão.

For ACL, the spatial scan analysis showed primary clusters in the North macro-region, in the state of Mato Grosso and in western Maranhão. Regarding the distribution of VL cases, with a primary cluster concentrated in the Northeast macro-region and in the States of Pará and Tocantins.

Specifically for malaria, the spatial scan analysis showed that the Amazon region is an endemic area in Brazil. Finally, many tuberculosis clusters were identified, and the State of Rio de Janeiro is the single State with a primary cluster.

Socio demographic characteristics are an important determinant of neglected diseases, because of its relevance, it was analyzed human development indicators, human resources and installed capacity in health, which were selected in order to better characterize the regions affect by these diseases.

Figure 2. Identification of clusters of Dengue hemorrhagic fever, ACL, VL, Malaria and Tuberculosis and prevalence of Schistosomiasis and Leprosy. Brazil, 2007 to 2009.

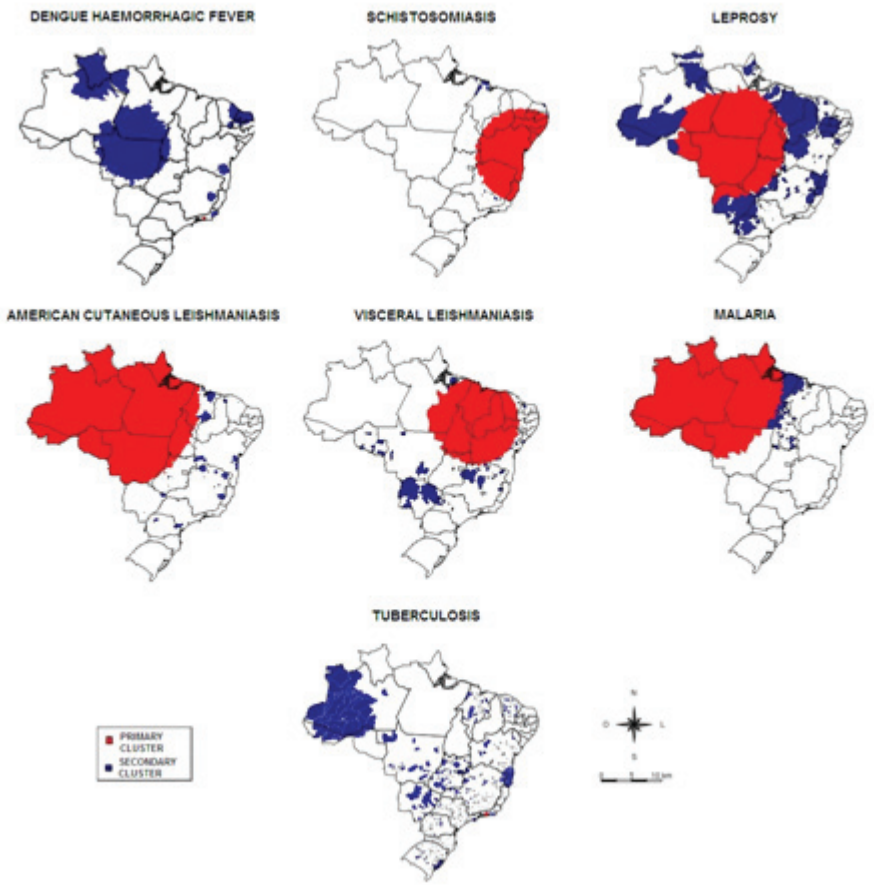
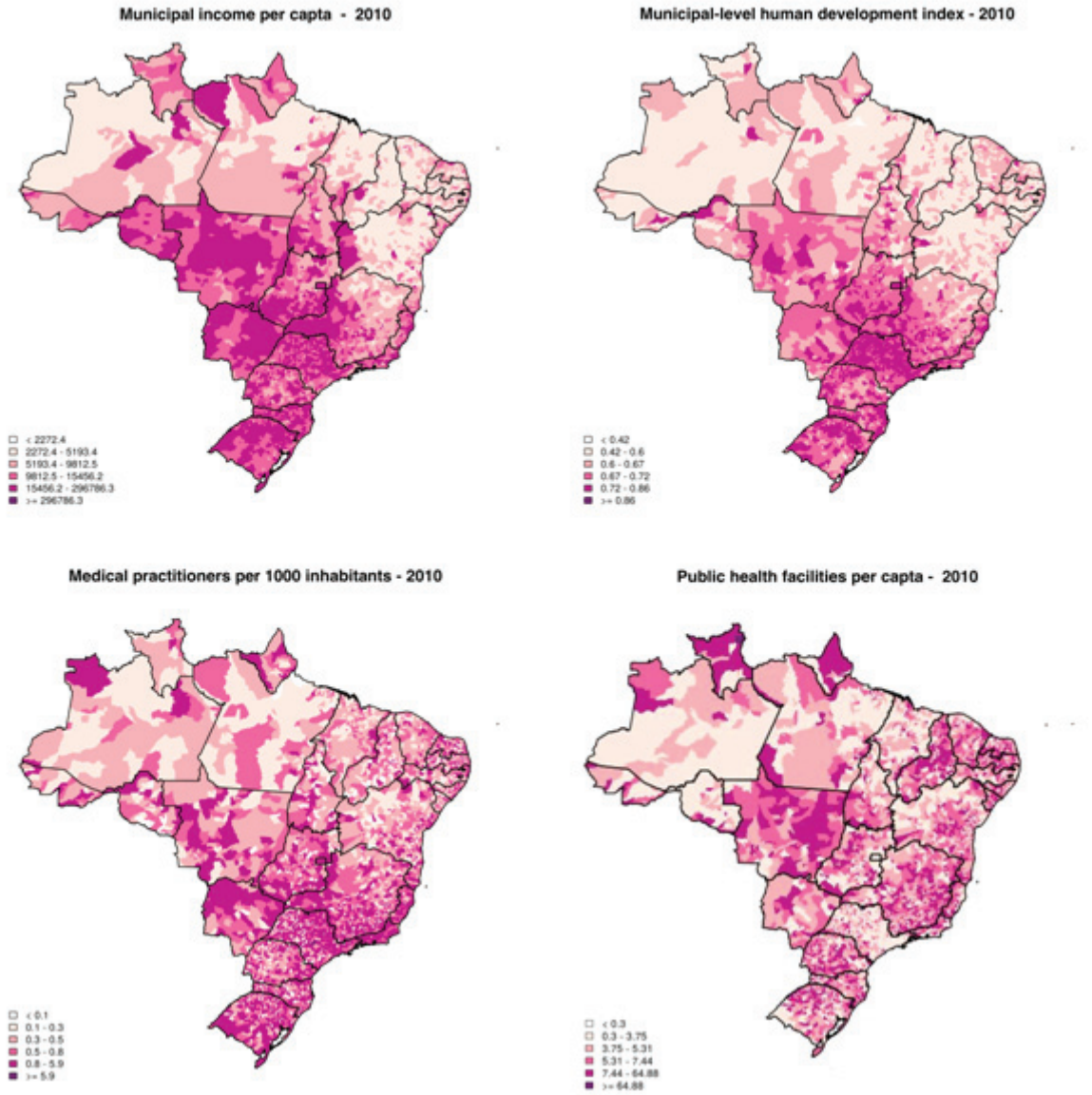


Figure 3. Spatial distribution of municipalities according to selected development indicators. Brazil, 2007 to 2009.



In general, these indicators are better in South, Southeast and Center-West macro-regions, which are wealthier, more urbanized, industrialized and have better health care infrastructure. The macro-regions North, Northeast is mostly rural and less populated, and usually shows a lower performance (Figure 3).

Table 2. Significant Spearmen correlations between the diseases rates and the economic and health indicators.

Diseases*	GDP	HDI	Doctors per 100,000 inhabitants	Health facilities per 100,000 inhabitants
Dengue haemorragic fever	-0,109	-0,086	0,108	-0,100
Schistosomiasis	-0,131	-0,135	0,102	-0,058
Leprosy	-0,143	**-0,183**	-0,041	-0,088
American Cutaneous Leishmaniasis	-0,121	**-0,180**	-0,073	-0,111
Visceral Leishmaniasis	**-0,231**	**-0,187**		-0,109
Malaria	**-0,171**	**-0,250**	**-0,161**	-0,148
Tuberculosis	-0,070	-0,050	0,123	**-0,165**

* Correlation is significant at the 0.05 level (2-tailed).

Among the selected indicators, HDI showed the strongest negative associations (protector effect) with the majority of the investigated diseases, especially leprosy, ACL and AVL. Despite of statistically significant, the correlations between the diseases rates and the economic and health indicators had o low magnitude. (Table 2)

For each of the neglected diseases investigated, the criteria for the classification of priority municipalities for control actions, according to the Ministry of Health, are presented in Chart 1. Considering this aspect of the analysis, it could be observed that ACL accounted for the highest number of municipalities considered as priority (2,355 – 42.3%), followed by leprosy (794 – 14.3%), malaria (556 –10 .0%), Dengue hemorrhagic fever (235 – 4.2%), VL (298 – 5.4%), tuberculosis (244 – 4.4%) and, finally, schistosomiasis (78 – 1.4%) (Chart 1 and Table 3).

Table 3. Proportion of municipalities defined as priority by the Ministry of Health per Unit of the Federation and per disease, Brazil 2008.

UF	Dengue hemorrhagic fever	Leprosy	Schistosomiasis	ACL *	VL **	Malaria	Tuberculosis
North							
Rondônia	0.9	4.2	-	2.2	-	9.3	0.8
Acre	-	0.6	-	0.9	-	3.8	0.4
Amazonas	-	1.6	-	2.5	-	11.1	0.8
Roraima	-	0.3	-	0.6	-	2.7	0.4
Pará	3.8	13.4	-	5.9	3.0	24.7	4.1
Amapá	-	0.3	-	0.7	-	2.9	0.4
Tocantins	3.8	5.2	-	5.0	7.0	5.7	0.8
Northeast							
Maranhão	3.4	13.2	3.8	8.0	13.4	28.3	3.3
Piauí	0.9	3.4	-	1.9	8.4	-	0.8
Ceará	5.5	5.3	-	4.5	14.8	-	3.3
Rio Grande do Norte	28.9	0.3	1.3	0.3	3.0	-	1.2
Paraíba	8.1	1.5	1.3	1.3	1.7	-	1.2
Pernambuco	4.3	4.9	6.3	3.6	4.7	-	4.1
Alagoas	-	1.0	19.0	1.2	1.3	-	0.8
Sergipe	0.9	0.9	17.7	0.7	2.0	-	0.8
Bahia	11.1	6.8	3.8	9.5	16.8	-	6.1
Southeast							
Minas Gerais	8.1	4.2	44.3	15.4	8.1	-	7.8
Espírito Santo	0.9	3.0	2.5	1.9	0.7	-	3.7
Rio de Janeiro	4.3	2.9	-	1.7	-	-	10.7
São Paulo	0.9	2.5	-	9.3	5.0	-	27.9
South							
Paraná	0.4	3.0	-	6.9	-	-	6.1
Santa Catarina	-	0.1	-	1.3	-	-	3.7
Rio Grande do Sul	-	0.1	-	0.6	0.3	-	7.4
West Center							
Mato Grosso do Sul	0.4	1.4	-	2.4	4.7	-	0.8
Mato Grosso	11.1	9.9	-	5.9	1.3	11.5	1.6
Goiás	2.6	9.9	-	5.8	3.7	-	0.8
Distrito Federal	-	0.1	-	-	-	-	-
Brazil	100	100	100	100	100	100	100
Total of priority municipalities (N=2,899)	235	794	78	2,355	298	556	244
Percentage of priority municipalities ***	4.2%	14.3%	1.4%	42.3%	5.4%	10.0%	4.4%

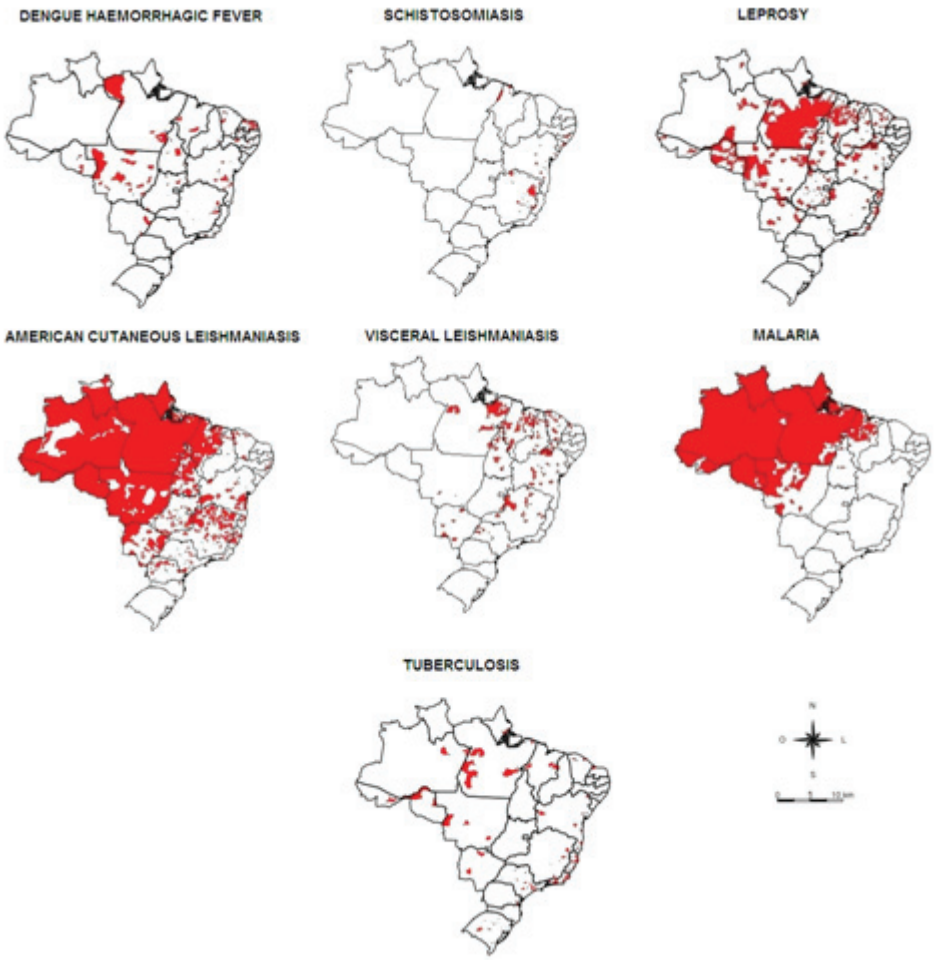
Source: Núcleo de Pesquisa em Métodos Aplicados aos Estudos de Carga Global de Doença, ENSP/Fiocruz. Data obtained from SINAN, 2007 to 2009 and from the Plano de Ações Estratégicas 2011 – 2015, from the Ministry of Health.

Notes: (*) American cutaneous leishmaniasis

(**) Visceral leishmaniasis

……(***) Total of Brazilian municipalities 5564

Figure 4. Distribution of priority municipalities for Dengue hemorrhagic fever, ACL, VL, Malaria and Tuberculosis and prevalence of Schistosomiasis and Leprosy. Brazil, 2007 to 2009.



Regarding the distribution of the municipalities considered as priority for dengue haemorrhagic fever, 51% were identified in three States: Rio Grande do Norte (29%), Bahia (11%) and Mato Grosso (11%) (Figure 4). As for leprosy, the highest concentration was found in the States of Pará (13.4%), Maranhão (13.2%), and Mato Grosso (9.9%)

The State of Minas Gerais had the highest number of municipalities considered as priority for schistosomiasis (44.3%), followed by Alagoas (19.0%) and Sergipe (17.7%).

The priority municipalities for ACL were concentrated in the states of Minas Gerais (15.4%), Bahia (9.5%), Maranhão (8.0%), Paraná (6.9%) account for 40% in this disease. VL concentrated around 40% in three states, Bahia (16.8%), Ceará (14.8%) and Maranhão (13.4%), all in the Northeast macro-region.

Five states concentrated more than 80% of the priority municipalities in Brazil for malaria, namely: Maranhão (28.3%), Pará (24.7%), Mato Grosso (11.5%), Amazonas (11.1%) and Rondônia

(9.3%).

Regarding the municipalities considered as priority for tuberculosis, 27.9% are located in the State of São Paulo, 10.7% in Rio de Janeiro and 7.4% in Rio Grande do Sul, adding up to 46% of the total for the country.

Figure 5. Spatial distribution of municipalities according to the total of diseases defining them as priority for neglected diseases. Brazil, 2007 to 2009.

In Brazil, 1,630 municipalities (29%) were considered as priority for at least one of the seven diseases investigated. The Northeast macro-region accounted for the highest number of such municipalities, 578, (35.5%), followed by the North macro-region with 384 (23.6%), the Southeast with 331 (20.3%), Centre-West with 241 (14.8%) and South with 96 (5.9%) (Figure 5).

The observation of the internal distribution of priority municipalities in the region indicates that in the North macro-region 86% of the municipalities were considered as priority, followed by the Centre-West macro-region with 52%.

In the Northeast and North macro-regions are located the municipalities that concentrate the highest number of diseases, with some them being a priority for more than five diseases simultaneously (Figure 5).

DISCUSSION

One of the main findings of the present study was the concentration in the North and Northeast regions of municipalities with at least three (or more) simultaneous diseases, and these regions also presented the lower values for socio-economic and health care indicators. It suggests that there are common aspects among them such as: the natural environment of the vectors associated to each disease, which makes the region to become naturally endemic; the expansion of territorial occupation; less favored life conditions; poverty; lack of adequate health services structure, which could act as a support system to identify, prevent and treat neglected diseases.

The North and Northeast regions in Brazil present significant inequalities expressed by means of social and urban infrastructure indicators. The population in vulnerable situation represents up to 85% in the North and 80% in the Northeast, for reasons as need, income or a combination of both, which expresses the multidimensional character of poverty [22]. In 2010, the Northeast was the second most populated region in Brazil, accounting for 28% of the total population of the country, while the North region accounted for 8.3% [23]. From the total Brazilian population residing in urban areas, 7.2% are located in the North and 24% in the Northeast. The proportion of households covered by the piped water supply network was at around 4.6% in the North and 24.2% in the Northeast, whereas 12.1% in the North and 76.9% in the Northeast did not have a bathroom or a restroom. Only 5.9% of households in the North and 22.3% in the Northeast had

garbage collection services and an adequate sewage system was present only 3.4% in the North and in 17.6% in the Northeast [23].

Five out of seven diseases analyzed in the present study, dengue hemorrhagic fever, malaria, ACL, VL and schistosomiasis, share similarities in terms of required climate conditions and the need of a vector to be transmitted, usually characterized by a hematophagous insect or an intermediate host. Additionally, these five diseases have the social and economic factors as a strong determinant factor in their prevalence or incidence, as well as sanitary conditions, water supply, income, education and housing.[24] .

However, environmental and social issues are no longer only seen as characteristics that by themselves would determine the occurrence of neglected diseases. Other relevant aspects that perpetuate the presence of these diseases are currently considered, such as: the lack of scientific knowledge, the cost of drugs and vaccines, poor management in public health regarding inadequate planning of actions [25].

The identification of environmental factors associated to this set of diseases, as well as the burden attributable to these factors, may contribute to a better planning and organization of actions and of health services, besides bridging the still existing gap in scientific knowledge.

Considering the dengue hemorrhagic fever, studies indicate its association to factors related to the urban structure such as basic sanitation, garbage collection and education [26]. The first case in Brazil was identified in Rio de Janeiro, caused by the serum-type of virus 2 (DEN-2), in 1990. From that date on, the number of hospitalizations showed an upward trend and, in 2008, Brazil accounted for over 60% of the notifications in the Americas [27]. During the period 2000–2010, the incidence of dengue disease in the country varied substantially, reaching a peak in 2010 of .1 million cases (538/100,000 inhabitants) and the lowest value was approximately 72,000 cases in 2004 (63.2/100,000 inhabitants).[28]

Approximately 200 million people are infected by Schistosomiasis in the world . This disease may be found mainly in Africa, Latin America, the Middle East, Asia and in the Caribbean. The Brazil, where the only existing species is the *Schistosoma mansoni, is* the most heavily affected country in the Americas, with about 2.5 million–6 million infected persons and 700–800 deaths are reported annually.[29]. However, in this country there has been a reduction of 50% in the occurrence and in the severity of this disease, and a reduction of 90% of hospital admissions from 1999 to 2009 [30].

Leprosy is an infectious disease associated to standards of living and poverty, low levels of education and poor housing and hygiene conditions favor its onset [31]. Its elimination, until the year of 2015 by reaching less than 1 case per 10,000 inhabitants is one of the goals of the Ministry of Health [32]. Brazil is the second country in the world with the largest number of new notified cases

and accounts for 92% of total new cases in the Americas.[33]

Between 2007 and 2009, detection in Brazil was of 2.23 cases per 10,000 inhabitants. The estimated prevalence in the world is of 0.4 million people, mainly in India, sub-Saharan Africa, Latin America and the Caribbean. From these, India and Brazil are among the 20 countries most affected [34].

ACL is a public health problem in 88 countries spread around four continents (the Americas, Europe, Africa and Asia), and is considered by the WHO as one of the six most important infectious diseases because of its high detection coefficient and its capacity to produce deformities. It is estimated that 350 million people around the world are exposed to the risk of infection. In Brazil, approximately 2 million new cases of its different clinical forms are notified per year [35].

Although its origin has been in the Amazon region, further investigation about the geographical distribution of ACL in Brazil showed that this disease may have different epidemiologic patterns. It may occur both in forest locations due the deforestation related with economic activities as well as in the outskirts of large urban centers where the adaptation of parasites and vectors to the environmental changes makes domestic animals into new reservoirs [36].

Regarding visceral leishmaniasis, the first evidence of its existence in Brazil was found in the Northeast region, specifically in the State of Ceará. However, its communication cycle has expanded from the original rural areas and now reaches urban areas [37,38]. Among the factors that have influenced the fast expansion of VL in the urban centers are deforestation, the expansion of the agricultural borders, extractivism, rural settlements, mining fields, electrical dams and constant migration flows[39]. Changes in the ecology and biology of the vector may explain the urbanization process of VL [40], but not all involved mechanisms regarding its urbanization have been completely elucidated [41].

The increase in the incidence of VL and the expansion of transmission areas has been a reason for concern since 70% of all the cases in South America take place in Brazil. Between 2007 and 2009, more than 8% of Brazilian municipalities reported autochthonous cases and the average incidence for the period was of 1.7 cases [42].

Malaria is recognized as a serious health problem in the world, affecting almost 50% of the population, in more than 109 countries and territories. In Brazil, approximately 300,000 new cases are reported each year. However, after the beginning of the disease eradication program in the early 1960s, numbers have been going down [24]. It is estimated that there are 300 million new cases and 1 million deaths per year, especially in children under 5 years of age and pregnant women in Africa [43].

In Brazil, 99% of the malaria cases are concentrated in the Legal Amazon region. 407,995 cases were reported in 2003, 70% of P. vivax, 29% of P. falciparum and 1% of P. malariae [44].

The Amazon region is considered as the endemic area for malaria in the country. Even in the endemic area there is no uniform risk of contracting the disease. This risk is measured by the Annual Parasite Incidence (API), which is used for the classification of the infection risk of different areas as high, medium and low according to the number of cases per 1,000 inhabitants [43]. Environmental factors such as water quality, and the socio-economic level have been nationally and internationally accepted as important risk factors for malaria, as well as the type of economic activity pursued by the household members [45–47].

Although tuberculosis is a very old disease, it continues to be a public health concern. One third of the world population is infected or at risk of developing it [48]. In the present study, tuberculosis was found in practically all of the country, with slightly higher incidences in the North and Centre-West regions. Infection is still significant in Brazil, and the factors that most affect its maintenance include individual characteristics, co-infections, nutrition and socio-economic and environmental characteristics such as poverty, family income, education, sanitary conditions and household density [49].

Considering the hypothesis of spatial autocorrelation was true for all of the studied diseases. This hypothesis is confirmed by other spatial analysis studies on neglected diseases [12,26,50,51].

The ministry of health has defined high-priority municipalities based on specific criteria, which overlaps mostly those who had presented high prevalence/incidence of the studied diseases. Despite the fact that the objective of this paper was not discuss or propose new criteria to define high-priority municipalities, We believe that the knowledge on the simultaneous occurrence of diseases and its geographical distribution could be used as an important tool, to confirm, analyze and re-orient the necessary actions to control the diseases under the scope of this study.

The limitations of the present study concern the use of secondary data subject to underreporting and, therefore, to the possibility of not accurately representing the true incidence in the municipalities studied. The National Information System of Diseases Notification (SINAN), used in this study, still presents problems regarding the coverage of cases reported and the quality of the information on the report forms is still one of the factors that influence on the assurance of the quality of the information. Nevertheless, in order to minimize the influence of the quality of the case reporting, the present study removed repeated entries and considered only the confirmed cases of the investigated diseases from the incidence/prevalence estimates.

FINAL CONSIDERATIONS

The innovative approach by priority municipalities considering the simultaneous occurrence of diseases, as well as the results of the research, have contributed to the knowledge of the spatial

distribution of the analyzed diseases in Brazil and in its macro-regions, highlighting the importance of the space as a methodological alternative for helping in planning, monitoring and assessing actions in health, guiding interventions towards disease control.

According to the results presented in this study, the predisposing factors for the maintenance of incidence/prevalence of the studied diseases would be, generally speaking, issues related to sanitary conditions, garbage collection, education, poverty, poor housing conditions, hygiene, deforestation, expansion of borders, migration flows, individual immunity, demographic and household density, and planning of public health actions.

Although the present study does not aim to analyze the relationship between the diseases and conditions of life, the spatial patterns of cases indicate a concentration of more than one type of disease in poorer locations. The overlapping of diseases affecting these locations may be a consequence of the accumulation of problems related to the inefficient solution of structural aspects of sanitation and urban organization which result in the continuation of precarious conditions of living, as well as a consequence of the treatment of diseases, which requires more resources and technological investments, even if it implies an increase in costs for the health system. Finally, is necessary that prevention and treatment policies are articulated among the different sectors, considering that often their impact might yield uneven results in society.

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