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Revisiting area risk classification of visceral leishmaniasis in Brazil

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Abstract

Background: Visceral leishmaniasis (VL) is a neglected tropical disease of public health relevance in Brazil. To prioritize disease control measures, the Secretaria de Vigilância em Saúde of Brazil's Ministry of Health (SVS/MH) uses retrospective human case counts from VL surveillance data to inform a municipality-based risk classification. In this study, we compared the underlying VL risk, using a spatiotemporal explicit Bayesian hierarchical model (BHM), with the risk classification currently in use by the Brazil's Ministry of Health. We aim to assess how well the current risk classes capture the underlying VL risk as modelled by the BHM.

Methods: Annual counts of human VL cases and the population at risk for all Brazil's 5564 municipalities between 2004 and 2014 were used to fit a relative risk BHM. We then computed the predicted counts and exceedence risk for each municipality and classified them into four categories to allow comparison with the four risk categories by the SVS/MH.

Results: Municipalities identified as high-risk by the model partially agreed with the current risk classification by the SVS/MH. Our results suggest that counts of VL cases may suffice as general indicators of the underlying risk, but can underestimate risks, especially in areas with intense transmission.

Conclusion: According to our BHM the SVS/MH risk classification underestimated the risk in several municipalities with moderate to intense VL transmission. Newly identified high-risk areas should be further evaluated to identify potential risk factors and assess the needs for additional surveillance and mitigation efforts.

Keywords: Visceral leishmaniasis, Brazil, Disease mapping, Bayesian, Risk classification

Background

Visceral leishmaniasis (VL) in the Americas is a vector-borne neglected zoonosis caused by the intracellular protozoan *Leishmania infantum* [1, 2]. If left untreated, VL is fatal in more than 90% of cases, within two years of the onset of the disease [3].

Every year approximately 200,000–400,000 new cases of VL are registered worldwide [4]. In 2015, 88.8% of VL cases were reported from six countries: Brazil, Ethiopia, India, Somalia, South Sudan and Sudan [4], Brazil was ranked second, reporting 3289 new cases, 14% of the total

reported worldwide, surpassed only by India [5]. In the Americas, Brazil represents 95% of total occurrences [6].

In Latin America transmission is mediated by the vector *Lutzomyia longipalpis* and *Lutzomyia cruzi* [7–9], a synanthropic sandfly with a wide geographic distribution in Brazil [10], and the domestic dogs as its the main animal reservoir in urban and rural areas. Control measures applied against the vector and the reservoir have shown limited success [11].

The Secretaria de Vigilância em Saúde of Brazil's Ministry of Health (SVS/MH) is responsible for the planning, implementation and evaluation of VL surveillance in Brazil. VL surveillance data is used by the SVS/MH for the classification of municipalities in four VL risk categories. This risk classification is the main pillar for the management of the VL control in the country, and is currently based on the average number of reported cases per municipality in periods of 3-years, without considering human population at

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risk. Such simple classification and ranking approach does not account for uncertainties around the average number of cases and variability around risk metrics, and may be unable to fully recognize and address spatial and spatiotemporal dependencies in the data [12].

In this study, we evaluate the spatiotemporal pattern of VL risk in Brazil and generate alternative risk categories to compare with the current SVS/MH risk-classification. We aim to provide additional insights in the epidemiology of VL in Brazil, and inform how accurately the current risk categories reflect the underlying VL risk at the municipality level.

Methods

Data source and collection

The study area comprised all 5564 municipalities in Brazil as listed by the Instituto Brasileiro de Geografia e Estatística (IBGE) database (IBGE general information <http://www.ibge.gov.br/english/>). Municipality-specific annual counts of VL cases for the period 2004–2014, and the official risk classification status for the period 2008–2014 were provided by the SVS/MH.

Data analysis

In order to account for the population at risk, we computed the municipality-specific standardized incidence ratios (SIR), $SIR_{it} = \frac{y_{it}}{e_{it}}$, where, for municipality i and year t , y_{it} is the count of VL cases and e_{it} the expected number of cases calculated by multiplying the population in municipality i for the t year (based on 2010 national census data) by the incidence of VL in the country.

At the first level of the BHM, the observed number of human VL cases in municipality i and year t (y_{it}) was assumed to follow a Poisson distribution $y_{it} \sim \text{Poisson}(e_{it}, \theta_{it})$, where e_{it} is defined above and θ_{it} is the unknown municipality-specific annual relative risk.

The log of θ_{it} was then decomposed additively into spatial and temporal effects and a space-time interaction term, so that

$$\text{Log}(\theta_{it}) = \alpha + v_i + v_t + \gamma_t + \delta_{it}$$

where α is the intercept, representing the population average risk, v_i and v_t describe respectively the spatially structured and unstructured variation in VL risk, γ_t represents the structured temporal effect, and δ_{it} is a space-time interaction term where given by the Kronecker product $\gamma_t \otimes v_i$. Given the large number of municipalities with zero case counts we explored other parameterizations, specifically a zero inflated Poisson likelihood. We computed the Deviance Information Criterion (DIC) to compare the fit of our models [13].

A non-informative normal distribution with mean 0 and variance σ_v^2 was used as prior distribution for the

spatially unstructured random effect v_i , while the spatially structured effect v_i was assigned a conditional autoregressive structure as previously described [14]. Briefly, v_i was assumed to follow a normal distribution with mean conditional to the neighboring municipalities v_j , where neighborhood is defined in terms of geographical adjacency, and variance σ_v^2 dependent on the number of neighboring municipalities n_i ,

$$v_i | v, j \text{ neighbor of } i \sim N\left(\frac{1}{n_i} \gamma \sum_{j=1}^{n_i} v_j, \frac{\sigma_v^2}{n_i}\right)$$

Finally, γ_t was assigned a random walk type 1 (RW1) $\gamma_t \sim N(\gamma_{t-1}, \sigma_\gamma^{-1})$. Exponential priors (3, 0.01) were assigned to all the standard deviations of the random effects [15]. In addition, we investigated also the sensitivity of our results to other less informative priors with larger ranges. Model posterior parameters were estimated using Integrated Nested Laplace Approximation (INLA), and fitted using the R-INLA package [16] conducted in R [17]. Results were visualized using ArcGIS 10.4 (ESRI ArcMap, 2016).

Risk classification

The actual MH risk classification is based upon the most recent three-year moving average of the number of VL human cases registered in each municipality. This classification is updated every June. Municipalities are classified as no transmission (class 0, no cases reported), sporadic transmission (class 1, moving average < 2.4), moderate transmission (class 2, moving average in the interval [2.4–4.4]), and intense transmission (class 3, moving average ≥ 4.4 cases) [18, 19].

In order to compare the current risk classification SVS/MH with the results of the BHM, we computed the posterior estimates of the ‘exceedence’ probability of risk $\text{Prob}(\theta_{it} > 1) | y$ [20–22] further categorized into 4 categories (0, 1, 2, 3) if $\text{Prob}(\theta_{it} > 1)$ assumed < 0.5, 0.5–0.75, 0.75–0.95 and > 0.95, respectively. Exceedence categories were compared with the four SVS/MH risk classes via the weighted Kappa correlation test. Finally, the correspondent three-year moving average of the annual number of cases per municipality predicted by the model BHM (\hat{y}_{it}) was used to create a third risk classification in which municipalities were classified as no transmission (class 0, no cases predicted); sporadic transmission (class 1, \hat{y}_{it} predicted moving average < 2.4); moderate transmission (class 2, \hat{y}_{it} predicted moving average in the interval 2.4–4.4) and intense transmission (class 3, \hat{y}_{it} predicted moving average ≥ 4.4) to compare with the SVS/MH classification based on observed cases (y_{it}). The agreement between this classification and that of the SVS/MH was also compared via the weighted Kappa correlation test.

Results

Descriptive results

From January 2004 to December 2014, a total of 37,405 VL cases were registered by the SINAN/SVS/MH Brazil. The annual average case count by municipality is shown in Fig. 1. The annual case count of VL during the study period (2004–2014), for the entire country, ranged between 2947 and 3713 cases (Fig. 2).

Five municipalities (0.09%) accounted for almost 20% of the total number of cases reported during the period of study: Fortaleza (state of Ceará) 1865 (4.98%), Campo Grande (state of Mato Grosso do Sul) 1520 (4.06%), Araguaína (state of Tocantins) 1294 (3.45%), Belo Horizonte (state of Minas Gerais) 1176 (3.14%), and Teresina (state of Piauí) 961 (2.57%).

Bayesian hierarchical model

The BHM with Poisson likelihood had the lowest DIC value (Table 1), and included spatial (structured and unstructured), temporal random effects, and interaction term. Models were robust to different choices of priors.

The posterior estimates of the spatially structured random effect u_i were higher for municipalities located in the central and eastern part of Brazil, while the non-spatially structured were scattered throughout the country (Fig. 3). The average standard deviation was calculated for all municipalities and v_i shown to be 2.5 times larger than that of v_i (6.96 versus 2.76), suggesting that a higher proportion of the unexplained risk of VL (not attributable to the size of the population at risk) was partially explained by factors with a spatial structure (Fig. 3). Finally, the

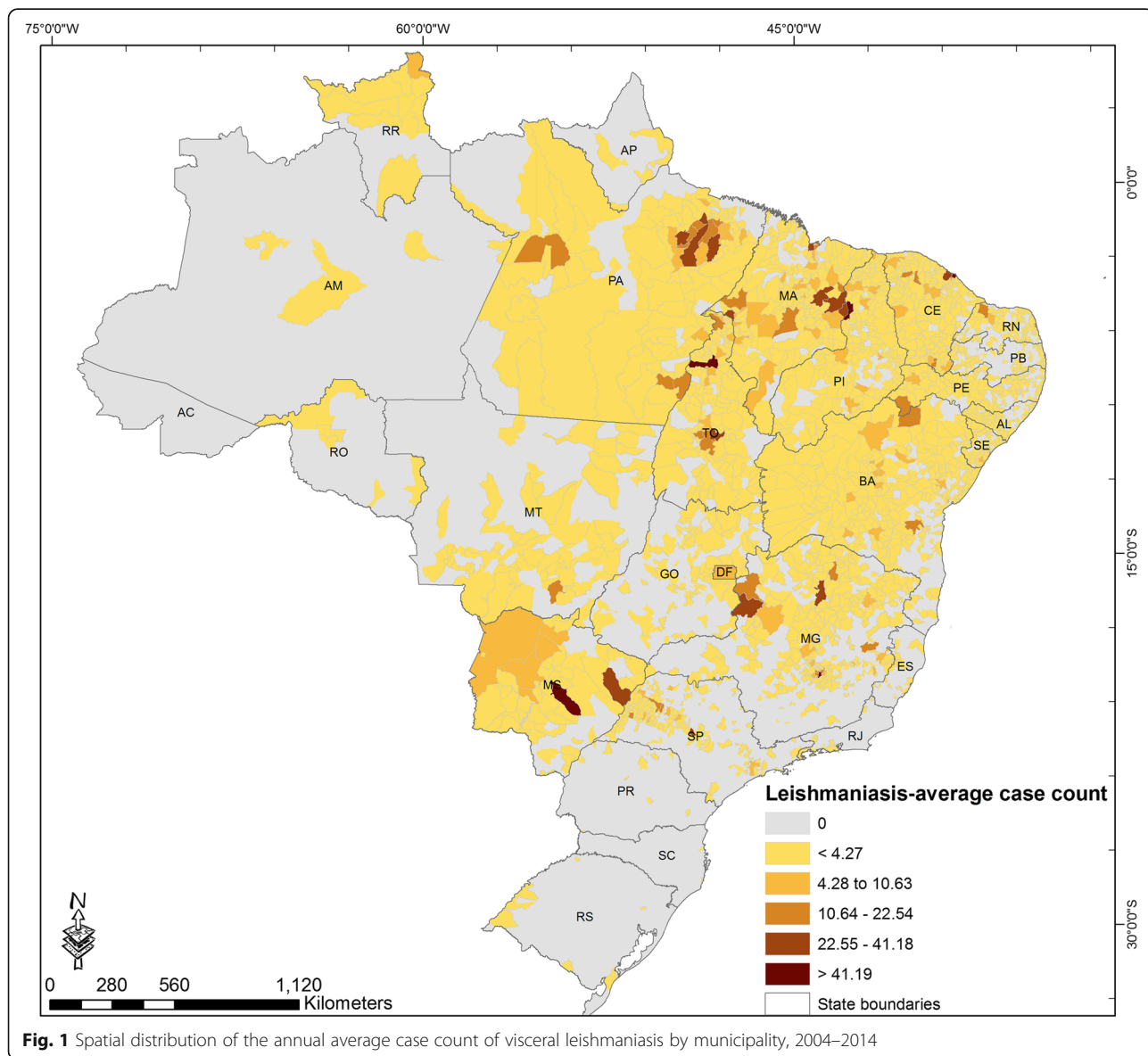


Fig. 1 Spatial distribution of the annual average case count of visceral leishmaniasis by municipality, 2004–2014

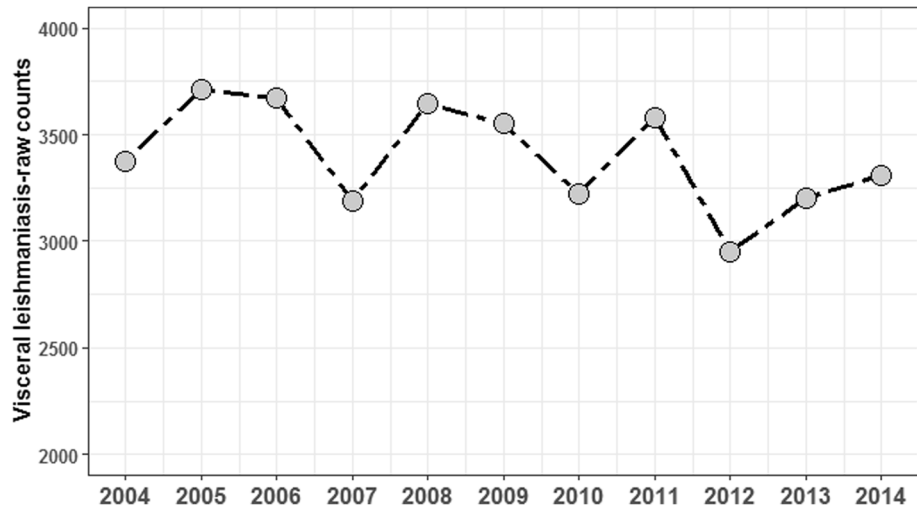


Fig. 2 Number of cases of visceral leishmaniasis reported in Brazil over 11 years (2004 to 2014)

proportion of the marginal variances were calculated for each parameter in the final model: the major contributors were the spatial effects ν (32.8%), υ (57.8%), with less variance explained by the temporal γ (1%) and spatial temporal interaction δ (9.3%).

Comparisons of the risk classifications

The proportion of municipalities that were classified in the same category by both the BHM via computation of the exceedence probabilities and the SVS/MH classification was 79.84%, very similar to the results obtained when the SVS/MH classification was compared with results using the predicted cases [78.05%, see Additional file 1: Figure S1 and Additional file 2: Figure S2]. This comparison (Table 2) revealed that the classifications based on the BHM (via exceedence probabilities or

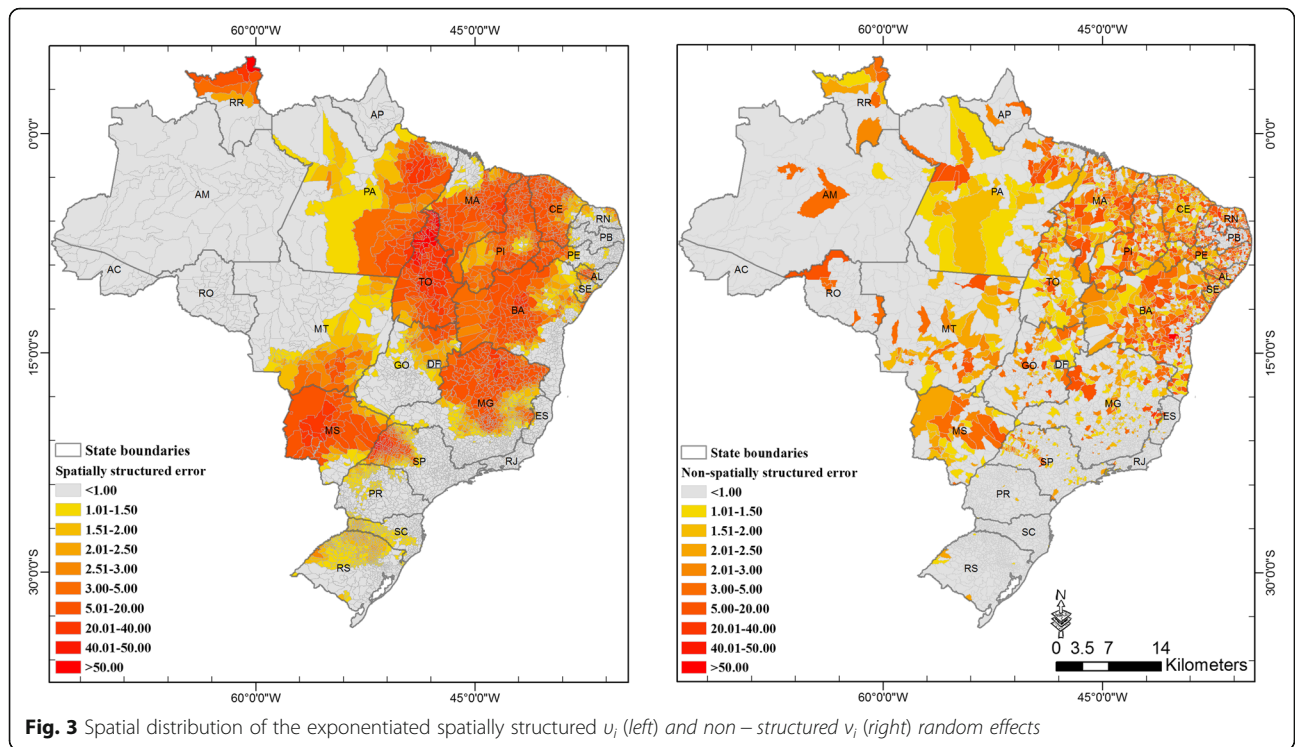
predicted cases) allocated a higher proportion of municipalities to categories two and three (moderate and intense transmission). Specifically, the classification based on the exceedence probabilities categorized between two and four times more municipalities as category three than the SVS/MH risk classification. Conversely, the current SVS/MH risk classification identified almost four times more municipalities as class one than the classification based on the posterior estimates of the exceedence probabilities. The average agreement between both classifications over the seven years was considered good (weighted Kappa = 0.69) [further information on yearly agreement is provided in Additional file 3: Table S1]. A good agreement (weighted Kappa = 0.63) on average was also obtained when the SVS/MH classification was compared with the one based on the predicted number of cases (\hat{y}_{it}) [see Additional file 4: Table S2 for yearly agreement]. However, if the lower risk category (0) was excluded from the comparison the agreement was much lower (0.17 and 0.12 when the SVS/MH classification was compared to the exceedence probabilities and predicted cases from the BHM, respectively), revealing most of the discordant results were obtained in municipalities with some risk as determined by both proposed classification [Table 2 and Additional file 1: Figure S1 to Additional file 2: Figure S2].

We have explored the spatial distribution for the comparison among all classifications, we demonstrate the scenario for the 2014 pattern, where SVS/MH, BHM-exceedence and BHM-predictions for intense transmission (class 3) are mapped in Fig. 4 [see Additional file 5: Figure S3, Additional file 6: Figure S4, Additional file 7: Figure S5, Additional file 8: Figure S6, Additional file 9: Figure S7, Additional file 10: Figure S8 for the 2008 to 2013

Table 1 Composition of eight different models, description of likelihood and for model diagnostics DIC is reported

Model components	Likelihood ^a	DIC (pD)
$\text{Log}(\theta_{it}) = a + u_i + v_i + \gamma_t$	Poisson	59,537.50 (2709.0)
	Zero-inflated negative binomial	74,771.96 (946.49)
	Negative Binomial	75,834.50 (1,8235.2)
	Zero inflated Poisson	78,936.66 (1058.7)
$\text{Log}(\theta_{it}) = a + u_i + v_i + \gamma_t + \delta_{it}$	Poisson	49,770.9 (6802.5)
	Zero-inflated negative binomial	75,837.0 (2756.1)
	Negative Binomial	83,372.3 (1,7720.3)
	Zero inflated Poisson	72,654.0 (3166.4)

^aAdditional information about the used likelihood options can be find elsewhere (<http://www.r-inla.org/models/latent-models>)



maps], showing that discordant municipalities were located throughout the country.

Discussion

VL is endemic in Brazil, and has been historically distributed across multiple states, especially in the North and Northeast regions of the country. However, recent reports indicate that the disease is expanding within Brazil and is reaching neighboring countries like Argentina and Uruguay [23–25]. Recently affected areas in Brazil include states located in the South (such as Rio Grande do Sul) and in the Midwest region [10]. For the study period, municipalities

that presented higher number of cases were mostly located in the states of Tocantins, Minas Gerais, Mato Grosso do Sul, Ceará and Piauí (Fig. 1), supporting the results observed in previous studies that had also identified the above states as high-risk areas [26–30]. For the 11 years studied here less than 10% of the municipalities reported at least one case of VL in any given year (mean of municipalities with one or more VL cases during 2004–2014 = 437, min = 380, max = 492). However, VL incidence varied largely in those affected municipalities.

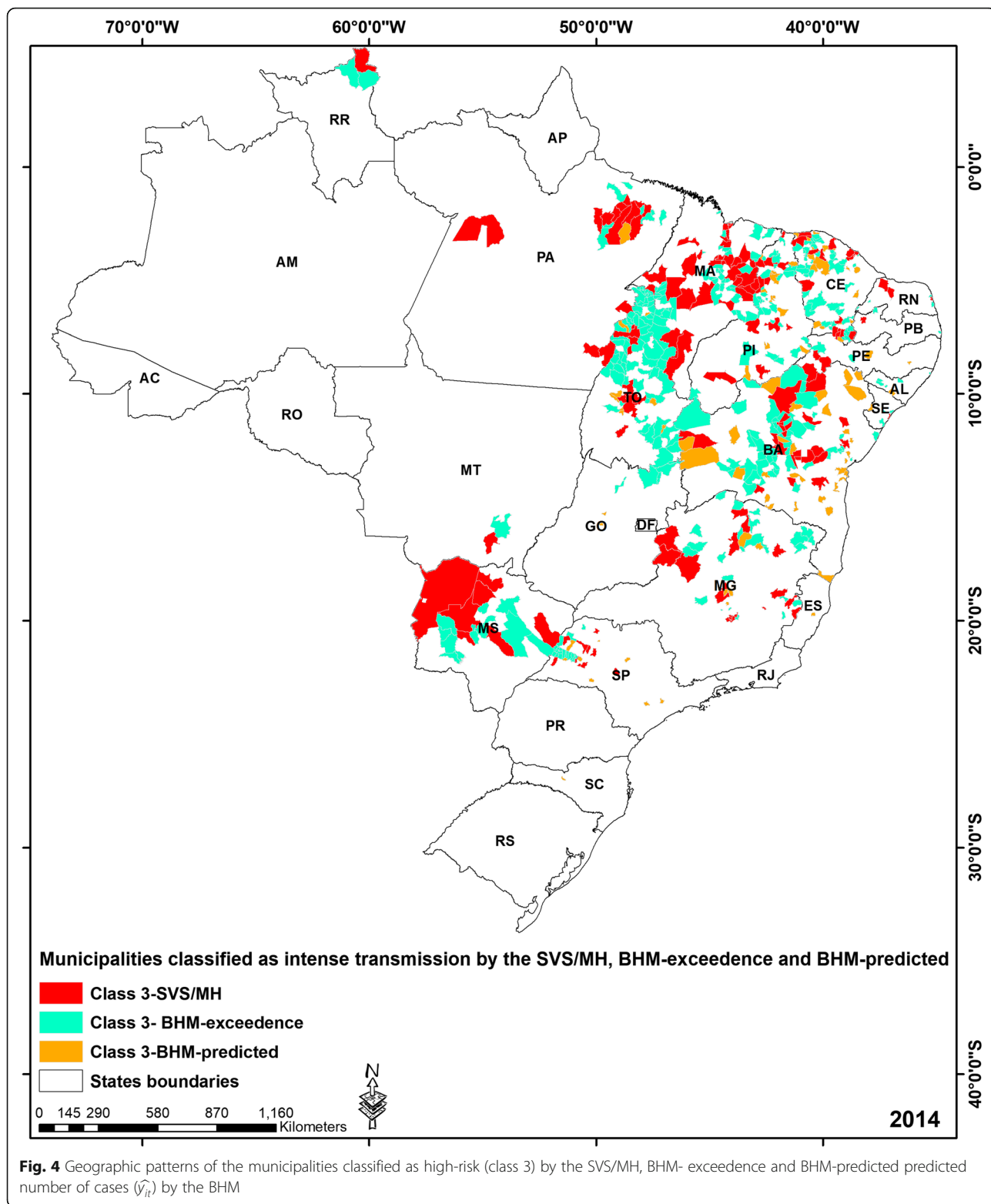
The inclusion of both spatially structured and unstructured random effects in the model allowed a better

Table 2 Comparison of the number of municipalities allocated to the different risk levels depending on the classification followed (BHM or SVS/MH classification)

Year	Risk class 0			Risk class 1			Risk class 2			Risk class 3		
	^a exceedence	^b SVS/MH	\hat{y}_{it}	exceedence	^b SVS/MH	\hat{y}_{it}	exceedence	^b SVS/MH	\hat{y}_{it}	exceedence	^b SVS/MH	\hat{y}_{it}
2008	4691	4307	5032	244	1040	16	233	88	242	396	129	272
2009	4659	4329	5033	259	1006	17	243	99	227	403	130	285
2010	4626	4312	5012	266	1016	21	252	98	230	420	138	299
2011	4614	4289	5003	266	1003	15	259	129	230	425	143	309
2012	4619	4259	4994	265	1060	22	252	146	240	426	99	301
2013	4604	4275	4985	263	1034	21	234	105	232	463	150	321
2014	4527	4273	4949	272	1026	12	271	119	247	494	146	354

^aNumber of municipalities classified as 0, 1, 2, and 3 based on the posterior estimates of exceedence probabilities (0: < 0.5, 1: 0.5–0.75, 2: 0.75–0.95 and 3: > 0.95).

^bNumber of municipalities classified as 0- zero case reported; 1-sliding average lower than 2.4; 2-sliding average was between [2.4 to 4.4); and 3- sliding average above or equal to 4.4 cases by the MH according to the current national regulations



understanding of how the risk was directly explained by the population at risk across the country. The exponentiated posterior estimates for the spatially structured random effect term were above one in multiple regions

including Central-Western, Northeast and especially north of Roraima state (Fig. 3-left). High values of u_i indicate a positive association between the spatially structured effects and VL in Brazil, signaling the presence of

additional risk factors that are not directly related with VL occurrence and that have a spatial component. This spatially-dependent risk may be in part related with the local density of infected reservoirs (dogs), in line with previous studies that described a positive spatial dependency between the occurrence of human and canine VL cases [31]. Therefore, larger concentrations of infected dogs per inhabitants in certain municipalities could lead to increased risk, since dogs are considered the main reservoir of the disease in Latin America and in Brazil in particular [27, 32, 33].

Increased risk may be also explained by other factors. For example, in some areas with high VL incidence like Teresina (Northeastern Brazil) a correlation between VL incidence and more limited urban infrastructures and poorer living conditions has been previously described [26, 34, 35]. Future analysis can expand on our models by incorporating covariates explaining local development as one example. Changes in the environment, such as deforestation due to expansion of the road networks, have been also shown to have a major effect on the risk of VL and other vector-borne diseases [36]. Indeed, the expanding habitat of the vector may be associated to some extent with the increase in VL incidence in areas traditionally considered non-endemic in Brazil, especially in the South and Midwest regions, a situation that may become more concerning in the future [25].

The nearly 80% agreement between the SVS/MH and BHM-exceedence and predicted risk classifications when all risk categories are considered suggests that the current strategy for the classification of municipalities may provide an acceptable approach in a significant proportion of the municipalities in the country. However, when results from municipalities classified in categories 1–3 (i.e., ‘some risk’) by the three approaches were compared, the agreement dropped largely [Table 2, Additional file 1: Figure S1 and Additional file 2: Figure S2], and major disagreements were identified particularly regarding to the category of higher risk (class 3) as classified by the BHM, that were evident throughout the study period [Additional file 3: Table S1, Additional file 4: Table S2, Fig. 4 and Additional file 5: Figure S3, Additional file 6: Figure S4, Additional file 7: Figure S5, Additional file 8: Figure S6, Additional file 9: Figure S7, Additional file 10: Figure S8 for the 2008 to 2013 maps]: a considerable proportion of these high risk municipalities (between 58% in 2012 and 82% in 2013) were identified to have lower risk according to the SVS/MH classification. The SVS/MH classification seemed to be more sensitive to year-to-year changes (for example, there was a 30% drop in the number of municipalities classified as high risk between 2011 and 2012), which could be due to surveillance artifacts since the risk of VL would not be expected to change so drastically in such a short time-span. The classification yielded by

the BHM, on the other hand, provided a more stable risk landscape over time and space due to the smoothing stemming from the inclusion of spatial effects in the model [Fig. 4 and Additional file 5: Figure S3, Additional file 6: Figure S4, Additional file 7: Figure S5, Additional file 8: Figure S6, Additional file 9: Figure S7, Additional file 10: Figure S8]. This is obvious from a close look at the municipalities classified differently by the two approaches, showing that these were typically located neighboring others with a large spatially structured random effect term (v_i). The implications in the control of VL may be relevant if municipalities stop the application of control measures without accounting for the risk in neighboring municipalities (Fig. 4).

Both “moderate” and “intense transmission” municipalities according to SVS/MH (categories 2 and 3) are subjected to the same disease control measures in terms of resources and active surveillance activities. However, the BHM results suggest that a substantial underestimation may take place when only focusing on numerator data, since every year an average of 131 and 288 additional municipalities were classified as moderate (class 2) and intense (class 3) transmission areas, respectively, using this approach. This highlights the importance of incorporating information on the population at risk as well as spatial and temporal effects most related to the risk of infectious diseases. The comparison between the SVS/MH classification and those based on the exceedence probabilities or the predicted number of cases (\hat{y}_{it}) revealed that even though agreement was good (weighted Kappa min:0.66-max:0.69) discordances were not only found in municipalities classified as higher risk [Additional file 3: Table S1, Additional file 4: Table S2]. Our current analyses allow the identification of municipalities with higher VL risk that could have been previously inadequately classified according to the methodology adopted by the SVS/MH. The new classification proposed in this study may help to identify municipalities that, despite not presenting high morbidity, are under a high risk of disease transmission, and should therefore be subjected to improved surveillance.

Finally, the limitations of this study are mainly associated to the lack of information on neighboring countries for municipalities located at the edge of the study area (Paraguay, Argentina and Bolivia). In addition, location of cases were based on where the notification took place, and may not indicate where the infection actually occurred. However, we suggest that the modeling the incidence ratio and inclusion of spatial and temporal effects and the smoothing technique we used helped to remove the effects of the variation of count cases used by the current MHS risk classification, and hence provide a better approximation of the municipality-level risk.

Conclusions

The comparison between the VL risk classification currently in use by the SVS/MH and that obtained through a BHM revealed that raw case counts of VL may be sufficient to indicate disease risk in a large proportion of the municipalities in Brazil, but may underestimate the risk in others, particularly those neighboring high risk areas. Our results identified “hot” areas where disease clustered, and where control and surveillance efforts could be implemented in order to prevent further spread of VL in the country. Resources to support increased measures in those hot areas could come from the many more areas classified as “1” (sporadic transmission) by the SVS/MH compared to those identified by our models.

Additional files

Additional file 1: Figure S1. Proportion of municipalities classified by the BHM model exceedence probabilities and the SVS/MH classification. (TIFF 26367 kb)

Additional file 2: Figure S2. Proportion of municipalities classified by the BHM model-predicted risk class and the SVS/MH classification. (TIFF 26367 kb)

Additional file 3: Table S1. Weighted Kappa between BHM model-exceedence probabilities and the SVS/MH classification. (DOCX 18 kb)

Additional file 4: Table S2. Weighted Kappa between BHM model-predicted risk class and the SVS/MH classification. (DOCX 18 kb)

Additional file 5: Figure S3. The spatial distribution of all classifications SVS/MH, BHM-exceedence and BHM-predictions for 2008. (TIF 26986 kb)

Additional file 6: Figure S4. The spatial distribution of all classifications SVS/MH, BHM-exceedence and BHM-predictions for 2009. (TIF 26986 kb)

Additional file 7: Figure S5. The spatial distribution of all classifications SVS/MH, BHM-exceedence and BHM-predictions for 2010. (TIF 26986 kb)

Additional file 8: Figure S6. The spatial distribution of all classifications SVS/MH, BHM-exceedence and BHM-predictions for 2011. (TIF 26986 kb)

Additional file 9: Figure S7. The spatial distribution of all classifications SVS/MH, BHM-exceedence and BHM-predictions for 2012. (TIF 26986 kb)

Additional file 10: Figure S8. The spatial distribution of all classifications SVS/MH, BHM-exceedence and BHM-predictions for 2013. (TIF 26986 kb)

Abbreviations

BHM: Bayesian hierarchical model; DIC: Deviance Information Criterion; IBGE: Instituto Brasileiro de Geografia e Estatística; INLA: Integrated Nested Laplace Approximation; RW1: Random walk type 1; SIR: Standardized incidence ratios; SVS/MH: Secretaria de Vigilância em Saúde of Brazil's Ministry of Health; VL: Visceral leishmaniasis

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Availability of data and materials

Data of reported cases are available through the Secretaria de Vigilância em Saúde of Brazil's Ministry of Health (SVS/MH) upon request and can also be retrieved from the National Information System of Health of the Ministry of Health (Sistema de Informação de Agravos de Notificação [SINAN] do Ministério da Saúde [MS]- <http://portalsinan.saude.gov.br/doencas-e-agravos>)

Authors' contributions

GM, JA, VJDRVB and AP authors reviewed the literature, and contributed to the conception and design of the study. VJDRVB, LED, FEFLJ and RVA acquired the leishmaniasis data. GM wrote the code for the spatiotemporal and prior sensitivity analysis. GM, JA and HCB reviewed and improved the codes. GM, JA, VJDRVB, AP, LED, FEFLJ, HCB and RVA interpreted and discussed the results, wrote the manuscript, and revised it critically. All authors read and approved the final manuscript.

Ethics approval and consent to participate

N/A

Consent for publication

N/A

Competing interests

The authors declare that they have no competing interests.

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References

- Harhay MO, Olliaro PL, Costa DL, Costa CHN. Urban parasitology: visceral leishmaniasis in Brazil. *Trends Parasitol.* 2011;27(9):403–9 PubMed PMID: WOS:000295207500007.
- Malaviya P, Picado A, Singh SP, Hasker E, Singh RP, et al. Visceral Leishmaniasis in Muzaffarpur District, Bihar, India from 1990 to 2008. *PLOS ONE.* 2011;6(3):e14751.
- WHO. WHO neglected tropical disease 2014. Available from: http://www.who.int/neglected_diseases/diseases/en/.
- WHO. First WHO report on neglected tropical diseases 2010. Available from: http://www.who.int/neglected_diseases/2010report/en/.
- WHO. Number of cases of visceral leishmaniasis reported data by country 2017. Available from: <http://apps.who.int/gho/data/node.main.NTDLEISH?lang=en>.
- PAHO. Informe Epidemiológico das Américas. Leishmanioses 2017. Available from: <http://iris.paho.org/xmliui/handle/123456789/34113>.
- Lainson R, Rangel EF. *Lutzomyia longipalpis* and the eco-epidemiology of American visceral leishmaniasis, with particular reference to Brazil - A Review. *Mem I Oswaldo Cruz.* 2005;100(8):811–27 PubMed PMID: WOS: 000235006100001.
- Missawa NA, Veloso MA, Maciel GB, Michalsky EM, Dias ES. Evidence of transmission of visceral leishmaniasis by *Lutzomyia cruzi* in the municipality of Jaciara, state of Mato Grosso, Brazil. *Rev Soc Bras Med Trop.* 2011;44(1): 76–8 PubMed PMID: 21340413.

9. Dos Santos SO, Arias J, Ribeiro AA, Hoffmann MD, De Freitas RA, Malacco MAF. Incrimination of *Lutzomyia cruzi* as a vector of American Visceral Leishmaniasis. *Med Vet Entomol*. 1998;12(3):315–7 PubMed PMID: WOS: 000075782800013.
10. Souza GD, dos Santos E, Andrade JD. The first report of the main vector of visceral leishmaniasis in America, *Lutzomyia longipalpis* (Lutz & Neiva) (Diptera: *Psychodidae: Phlebotominae*), in the state of Rio Grande do Sul, Brazil. *Mem I Oswaldo Cruz*. 2009;104(8):1181–2 PubMed PMID: WOS: 000274413300017.
11. Romero GAS, Boelaert M. Control of Visceral Leishmaniasis in Latin America- A Systematic Review. *Plos Neglect Trop D*. 2010;4(1) PubMed PMID: WOS: 000274179500012.
12. Courtemanche C, Soneji S, Tchernis R. Modeling Area-Level Health Rankings. *Health Serv Res*. 2015;50(5):1413–31. <https://doi.org/10.1111/1475-6773.12352> PubMed PMID: 26256684; PubMed Central PMCID: PMC4600354.
13. Spiegelhalter DJ, Best NG, Carlin BR, van der Linde A. Bayesian measures of model complexity and fit. *J R Stat Soc B*. 2002;64:583–616 PubMed PMID: WOS:000179221100001.
14. Knorr-Held L, Besag J. Modelling risk from a disease in time and space. *Stat Med*. 1998;17(18):2045–60 PubMed PMID: WOS:000075939000002.
15. Simpson D, Håvard R, Martins GT, Riebler A, Sørbye GS. Penalising model component complexity: A principled, practical approach to constructing priors. *Statistical Science*. 2015;arXiv:1403.4630.
16. Martino S, Havard R. Implementing approximate Bayesian inference using integrated nested Laplace approximation: a manual for the inla program. NTNU, Norway: Department of Mathematical Sciences; 2009.
17. Team RDC. R : a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2010.
18. Brasil Ministério da Saúde SdVeS. Manual de Vigilância e Controle da Leishmaniose Visceral. 2007.
19. Saúde Md. Guia de Vigilância em Saúde 2016 [cited 1]. Available from: <http://portal.arquivos.saude.gov.br/images/pdf/2016/novembro/18/Guia-LV-2016.pdf>.
20. Lawson AB. Bayesian disease mapping: hierarchical modeling in spatial epidemiology. New York: CRC Press; 2013.
21. Richardson S, Thomson A, Best N, Elliott P. Interpreting posterior relative risk estimates in disease-mapping studies. *Environ Health Persp*. 2004;112(9): 1016–25 PubMed PMID: WOS:000222315800011.
22. Rotejanaprasert C, Lawson A, Bolick-Aldrich S, Hurley D. Spatial Bayesian surveillance for small area case event data. *Stat Methods Med Res*. 2016; 25(4):1101–17 PubMed PMID: WOS:000382871200003.
23. Salomon OD, Basmajdian Y, Fernandez MS, Santini MS. *Lutzomyia longipalpis* in Uruguay: the first report and the potential of visceral leishmaniasis transmission. *Mem Inst Oswaldo Cruz*. 2011;106(3):381–2 PubMed PMID: 21655832.
24. Salomon OD, Quintana MG, Bruno MR, Quiriconi RV, Cabral V. Visceral leishmaniasis in border areas: clustered distribution of phlebotomine sand flies in Clorinda, Argentina. *Mem Inst Oswaldo Cruz*. 2009;104(5):801–4 PubMed PMID: 19820846.
25. Peterson AT, Campbell LP, Moo-Llanes DA, Travi B, Gonzalez C, Ferro MC, et al. Influences of climate change on the potential distribution of *Lutzomyia longipalpis* sensu lato (*Psychodidae: Phlebotominae*). *Int J Parasitol*. 2017. <https://doi.org/10.1016/j.ijpara.2017.04.007> PubMed PMID: 28668326.
26. Neto JC, Werneck GL, Costa CHN. Factors associated with the incidence of urban visceral leishmaniasis: an ecological study in Teresina, Piauí State, Brazil. *Cad Saude Publica*. 2009;25(7):1543–51 PubMed PMID: WOS: 000267705400012.
27. Ashford DA, David JR, Freire M, David R, Sherlock I, Eulalio MC, et al. Studies on control of visceral leishmaniasis: impact of dog control on canine and human visceral leishmaniasis in Jacobina, Bahia, Brazil. *Am J Trop Med Hyg*. 1998;59(1):53–7 PubMed PMID: 9684628.
28. Vieira CP, Oliveira AM, Rodas LA, Dibo MR, Guirado MM, Chiaravalloti NF. Temporal, spatial and spatiotemporal analysis of the occurrence of visceral leishmaniasis in humans in the City of Birigui, state of Sao Paulo, from 1999 to 2012. *Rev Soc Bras Med Trop*. 2014;47(3):350–8 PubMed PMID: 25075487.
29. Margonari C, Freitas CR, Ribeiro RC, Moura ACM, Timbo M, Gripp AH, et al. Epidemiology of visceral leishmaniasis through spatial analysis, in Belo Horizonte municipality, state of Minas Gerais, Brazil. *Mem I Oswaldo Cruz*. 2006;101(1):31–8 PubMed PMID: WOS:000236054000007.
30. Antonialli SAC, Torres TG, Paranos AC, Tolezano JE. Spatial analysis of American Visceral leishmaniasis in Mato Grosso do Sul State, Central Brazil. *J Infection*. 2007;54(5):509–14 PubMed PMID: WOS:000246442900016.
31. Teixeira-Neto RG, da Silva ES, Nascimento RA, Belo VS, de Oliveira CD, Pinheiro LC, et al. Canine visceral leishmaniasis in an urban setting of Southeastern Brazil: an ecological study involving spatial analysis. *Parasite Vector*. 2014;7 PubMed PMID: WOS:000348547300001.
32. de Araujo VEM, Pinheiro LC, Almeida MCD, de Menezes FC, Morais MHF, Reis IA, et al. Relative Risk of Visceral Leishmaniasis in Brazil: A Spatial Analysis in Urban Area. *Plos Neglect Trop D*. 2013;7(11) PubMed PMID: WOS: 000330378400025.
33. Souza VA, Cortez LR, Dias RA, Amaku M, Ferreira Neto JS, Kuroda RB, et al. Space-time cluster analysis of American visceral leishmaniasis in Bauru, Sao Paulo state, Brazil. *Cad Saude Publica*. 2012;28(10):1949–64 PubMed PMID: 23090174.
34. de Almeida AS, Medronho RD, Werneck GL. Identification of Risk Areas for Visceral Leishmaniasis in Teresina, Piauí State, Brazil. *Am J Trop Med Hyg*. 2011;84(5):681–7 PubMed PMID: WOS:000290365100006.
35. Werneck GL, Costa CHN, Walker AM, David JR, Wand M, Maguire JH. Multilevel modelling of the incidence of visceral leishmaniasis in Teresina, Brazil. *Epidemiol Infect*. 2007;135(2):195–201 PubMed PMID: WOS: 000244652800003.
36. Seva AD, Mao L, Galvis-Ovallos F, Tucker Lima JM, Valle D. Risk analysis and prediction of visceral leishmaniasis dispersion in Sao Paulo State, Brazil. *PLoS Negl Trop Dis*. 2017;11(2):e0005353. <https://doi.org/10.1371/journal.pntd.0005353> PubMed PMID: 28166251; PubMed Central PMCID: PMC5313239.

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