

Bushmaster bites in Brazil: ecological niche modeling and spatial analysis to improve human health measures

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ABSTRACT

In 2017, the World Health Organization has included snakebites in category A on the list of neglected tropical diseases, i.e., with a high impact on world health, not receiving the necessary attention. It is fundamental to prevent this health issue through the cooperation among different areas of knowledge. Our goals here were to identify the potential geographical distribution of the largest venomous American snake *Lachesis muta* (the Bushmaster), to support the planning of antivenom distribution in Brazil and mitigate this disease, once this species may cause serious accidents with a high risk of death. Occurrence records of the species were obtained from scientific collections. Data on antivenom distribution were obtained from the Ministry of Health and State Secretaries of Health. Our results showed climatic suitability for *L. muta* in 60% of the Brazilian territory, including the Amazon and the Atlantic Forest. The highest incidence rates and suitability values were recorded for the northern region, which is a priority for the mitigation of this disease. Our results may help planning efficient antivenom distribution. We also encourage mapping the distribution of other venomous species to identify areas of occurrence and improve human health measures.

Key words: Anti-botropic-laquetic serum, Maximum entropy modeling of species, Ophidian accidents, Prevalence, Venomous snake.

Introduction

Venomous snakes occur in most parts of the world, consequently there are snakebites, which can lead to serious public health problems, with high morbidity and mortality (Gutiérrez *et al.* 2006; 2010; Uetz *et al.*, 2018). Annually, about 2 million people are affected by snakebites, mostly in poor communities and in developing countries in tropical regions (Kasturiratne *et al.*, 2008; Harrison *et al.*, 2009). More than a

half of the victims need specific medical treatment, such as the administration of antivenom (WHO, 2018), often monospecific antivenom (e.g., Habib and Warrel, 2013).

Antivenom is safe and effective to minimize mortality and morbidity caused by snakebites (WHO, 2018). The crisis in the production, deployment, and accessibility of this product is a concern

in many parts of the world (e.g., Theakston and Warrell, 2000). Antivenoms are costly, often scarce and poorly distributed in areas where they are most needed (Gutiérrez *et al.*, 2006; Michael *et al.*, 2018; Schioldann *et al.*, 2018). Building an operating system by organizing local epidemiological data and anticipating the occurrence of accidents can be the first step to decrease public health problems (Chippaux, 2017). This operating system is relevant for the appropriate distribution of antivenoms since the distribution of these products should be guided by the species' distribution ranges and epidemiological data (Gutiérrez *et al.*, 2009). Currently, the distribution of antivenom to Brazilian States of the federation is done by the Ministry of Health just based on epidemiological data (Gutiérrez *et al.*, 2009).

Ecological niche modeling can be useful to predict regions of epidemiological importance, as it highlights regions of high suitability for a given species (i.e., venomous snakes), providing information on areas that are potentially occupied by such species but were not previously investigated (Needleman *et al.*, 2018). Consequently, these models can guide and support the distribution of antivenom, which is expensive and scarce (Gutiérrez *et al.*, 2009; Chippaux *et al.*, 2015). However, most studies about snakebites and their epidemiological importance have only focused on the description of the clinical aspects of the envenomation (Kasturiratne *et al.*, 2008).

Given the importance of the effective distribution of antivenom, our goal was to determine the potential distribution of a large venomous snake, *Lachesis muta* (Linnaeus, 1766) (Bushmaster) and its relation with the location of healthcare service for snakebite assistance in Brazil and the snakebite events caused by this species. Considering the areas of high suitability for this species, we also propose priority regions that should receive the *Lachesis* antivenom, the anti-botropic-laquetic serum (SABL). Despite the frequency of bushmaster's bites is lower than the others venomous snakes' (e.g., *Bothrops* spp.), from a clinical point of view, it is still an important snakebite, configuring a public health problem in Brazil. However, the available literature about the detailed distribution of this species and envenomation is scarce.

The present study is the first to propose actions to reduce the burden of *Lachesis muta* snakebites in Brazil through ecological niche modeling. It may also be a model for similar studies with other venomous species in other countries and regions worldwide.

Materials and methods

To identify if the regions with suitability for *Lachesis muta* have available healthcare services and if they correspond to the areas with snakebite records, we surveyed the occurrence of *L. muta* in South America, and used these dataset to select the least correlated bioclimatic variables. We used these variables to build a potential distribution model for *L. muta* using the Maxent algorithm, and then we identify and mapped the municipalities that counted on healthcare services. We also surveyed the number of snakebites and calculated their incidence rates by municipality between 2006 and 2017.

Study species

The genus *Lachesis* (Bushmaster) comprises the largest venomous snakes in the Americas, reaching up to 3.5 m of total length (Campbell and Lamar, 2004). All bushmaster's snakebites are considered critical, posing a high risk of death (Haad, 1981; Jorge *et al.*, 1997; Souza *et al.*, 2007) or causing irreversible sequelae, such as necrosis (e.g., Rosenthal *et al.*, 2002).

In Brazil, there is only one species of the genus, *Lachesis muta* (see Fernandes *et al.*, 2004). It has been recorded from Panama to southeastern Brazil, in tropical rainforests such as the Amazonia and the Atlantic Forest (Campbell and Lamar, 2004; Fernandes *et al.*, 2004; Almeida *et al.*, 2007). It inhabits well-preserved forests, with high humidity levels and temperature usually ranging from 24-28° C (Melgarejo, 2002).

Lachesis muta is sensitive to handling, because it has little resistance to injuries and rarely tolerates the stress caused by capture and transportation (Melgarejo, 2002). Due to these sensitivity, captive breeding is quite complex, and consequently, the production of its antivenom is expensive and scarce. Therefore, there is a need to send medication serum to strategic locations to avoid wastes. Since the clinical symptomatology of the bushmaster's snakebites can be mistaken with the ones caused by another snake of the same family, *Bothrops*, a pentavalent antivenom is used in Brazil (Ministry of Health, personal communication) to cope with accidents caused by either of these two snakes: the anti-botropic-laquetic serum (SABL).

Lachesis muta occurrences

The identification and mapping of museum specimens can be used to produce ecological niche mo-

deling maps to indicate potential areas of occurrence in Brazil. We obtained data on *Lachesis muta* occurrence records from the following herpetological collections: Museu Nacional, Universidade Federal do Rio de Janeiro (MNRJ), Coleção Científica do Instituto Vital Brazil (CCIVB) and Museu de Zoologia da Universidade de São Paulo (MUZUSP). In addition, we included available records from the online databases: Specieslink (splink.org.br) and GBIF (<https://www.gbif.org/>): Brazil: Amazonas: Coleção Herpetológica do Instituto Nacional de Pesquisas Amazônicas (INPA-HERPETO); Bahia: Coleção de Serpentes do Museu de História Natural da Bahia (CRMZUFBA); Mato Grosso: Herpetologia-Répteis Coleção Científica de Serpentes da Universidade Federal do Mato Grosso (UFMT-R); Minas Gerais: Coleção Científica de Serpentes da Fundação Ezequiel Dias (FUNED-SERP); Coleção de Répteis do Centro de Taxonomia da Universidade Federal do Rio de Janeiro (UFMG-REP); Pará: Coleção Herpetológica do Museu Paraense Emílio Goeldi (MPEG.HOP); Rio Grande do Sul: Coleção de Répteis do Museu de Ciências e Tecnologia da Pontifícia Universidade Católica do Rio Grande do Sul (MCT-PUCRS); São Paulo: Coleção de Répteis do Museu de Zoologia da Universidade de Campinas (ZUEC-REP); Coleção Herpetológica Alphonse Richard Hoge (Instituto Butantan - IBSP); Colombia: Bogota: Museo de La Salle – Universidad de La Salle (MLS-of); Fundación Puerto Rastrojo (FPR - Colombia) and United States of America: Washington: Smithsonian National Museum of Natural History (NMNH-Animalia_BR). To minimize possible misidentification of specimens, all occurrences referred as "observations", without a voucher specimen held by a scientific collection, were excluded. To build accurate maps, we only considered the specific geographical coordinates informed by the collectors, and excluded unspecified coordinates of municipal headquarters.

Climate Variables

We used nineteen bioclimatic variables from World-Clim – Global Climate Data (www.worldclim.org) version 2.0, restricted to the period between 1970-2000, with a resolution of 2.5 arc minutes (ca., 5 km) (Fick and Hijmans, 2017) for South America. We performed a principal component analysis (PCA) in the R environment (version 3.4.1; R Core Team, 2017) using *vegan* (Oksanen *et al.*, 2017), *dismo* (Hijmans *et al.*, 2017) and *rgdal* packages (Bivand *et al.*, 2017) to identify a subset of available biocli-

matic variables that were not strongly correlated ($R^2 < 0.7$). Variables were chosen according to *Lachesis muta*'s ecological characteristics (see *Lachesis muta* section; Cunha and Nascimento, 1978; Melgarejo, 2002; Campbell and Lamar, 2004). Thus, we selected seven variables for the model: mean temperature diurnal range, isothermality, maximum temperature of warmest month, minimum temperature of coldest month, precipitation of wettest month, precipitation of driest month, and precipitation of warmest quarter.

Healthcare services

The distribution process of the antivenom is decentralized and based on the needs of each region along the country. To determine which regions of suitability for *Lachesis muta* have medical assistance for snakebites, we identified municipalities with healthcare services by requesting this information to each federative unit (total = 26). We used online protocols related to the Brazilian Law of Access to Public Information (Law No. 12,527, November 18, 2011; Brasil, 2011). The geographic coordinates were obtained from the Brazilian Institute of Geography and Statistics (IBGE), datum Sirgas 2000.

Ecological Niche Models

We used the Maximum Entropy algorithm - MaxEnt (Phillips *et al.*, 2006) for modeling the potential areas of occurrence of *Lachesis muta*, one of the most popular and high-performance algorithms for ecological niche modeling (Hijmans and Graham, 2006; Fourcade *et al.*, 2014). This algorithm has a high performance and less sensitivity to possible geographical positioning errors (Hijmans and Graham, 2006; Fourcade *et al.*, 2014). Occurrences were randomly separated into 70% for training and 30% for validating the model, with 1000 bootstrap pseudoreplicates. We used the area under the ROC curve (AUC) for accessing the model performance, where values closer to 1 indicate a better agreement between model outputs and the test occurrences.

A less conservative threshold (minimum training presence) was applied to MaxEnt's outputs to build the final binary map at Quantum GIS 2.18.1 (QGIS Development Team, 2016). To validate the final map, we considered the literature about *Lachesis muta* that suggests the Atlantic Forest of Rio de Janeiro state (Brazilian coast) and the Amazon region of Mato Grosso state (central-western Brazil) are the south and southwest limit regions for the species' distribution, respectively (e.g., Cunha

and Nascimento, 1978; Campbell and Lamar, 2004; Fernandes *et al.*, 2004; Melgarejo, 2009). A recent biogeographic analysis showed *L. muta* does not occur in the southern Atlantic Forest (Moura *et al.*, 2016). Therefore, these regions were removed from the analyses performed here.

Snakebites by bushmaster

To identify the incidence rate and evaluate the distribution of accidents caused by *Lachesis* in Brazil and its relation with suitability regions, we obtained epidemiological data from the DATASUS platform, from the Ministry of Health (www.datasus.com). We used all the available period for the analyses (between 2007-2016); and selected the type of snakebite by "*Lachesis muta*". All Brazilian states were considered for the analyses.

Analyses

We identified the states with the largest area of potential occurrence of *Lachesis muta* and most suitable municipalities according to the ecological niche modeling. For this, we calculated the proportion

of suitable areas in each state. To identify the most suitable municipalities, we calculated the median values of suitability of each municipality. We selected priority areas for receiving the SABL according to the municipalities and states that showed the highest suitability rates. Both analyses were done at Quantum GIS 2.18.4 (QGIS Development Team, 2016).

To identify the current number of accidents caused by *Lachesis muta*, we calculated the incidence rates of accidents by municipality (number of new cases over a defined period in a population at risk of begin affected). This rate was calculated by dividing the sum of all accidents occurred between 2007 and 2016, by the estimated population in the same period. Finally, we identify if the regions with accident records correspond to the areas with potential occurrence of *L. muta*.

Results

Suitability for *Lachesis muta* and Snakebites

We obtained 226 occurrences of *Lachesis muta* distributed in South and Central America, 56 of which

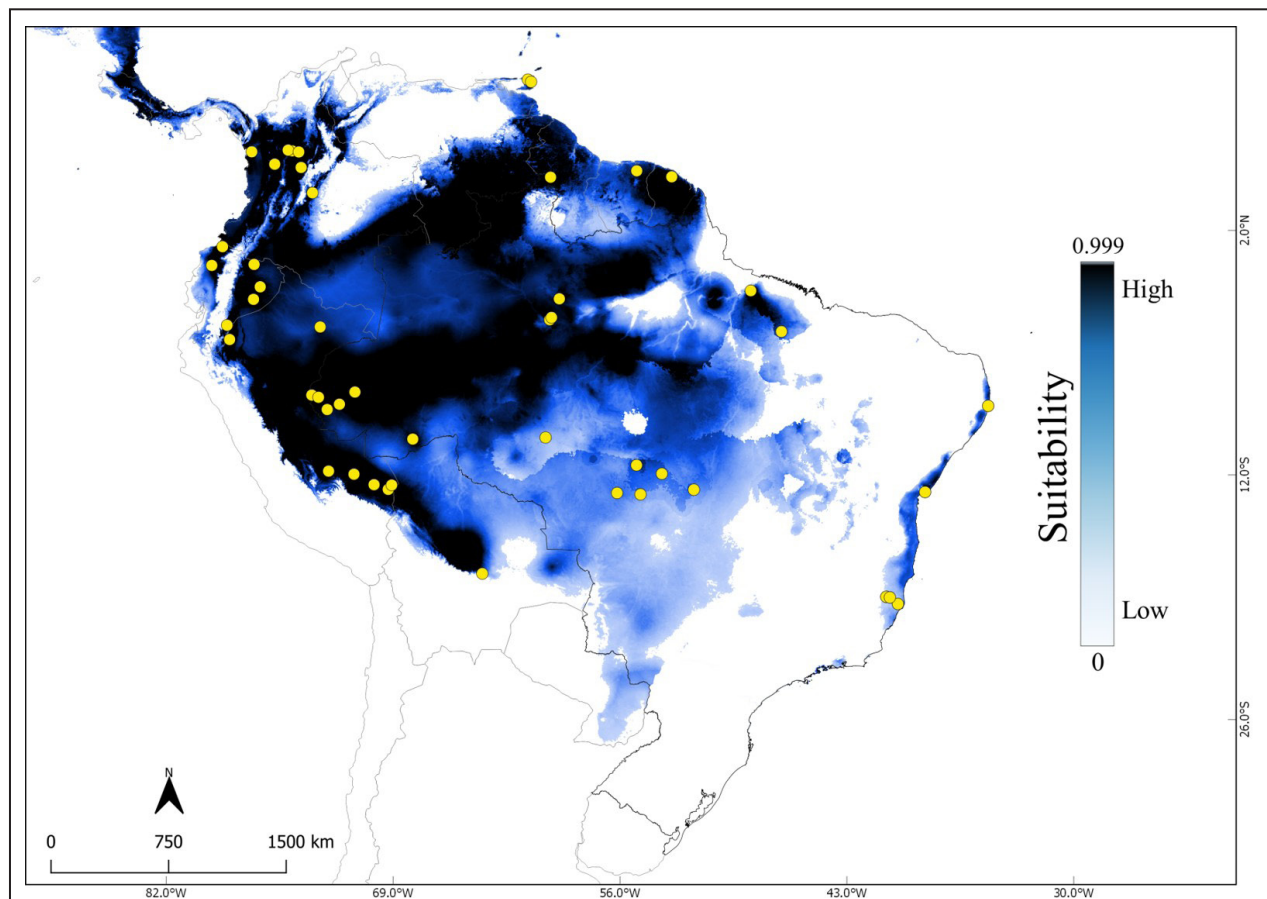


Figure 1. Potential distribution of *Lachesis muta* in South America. Yellow dots are the occurrences. There is high suitability for *L. muta* at the North region, which should be a priority for receive Anti-biotropic-laquetic Serum – SABL.

were specific geographical coordinate occurrences. The model performance was high (AUC = 0.98). The final map showed two large regions of high climatic suitability, one in the Amazonia with enclaves in the Cerrado and another in the Atlantic Forest, distributed along the Brazilian coast (Fig. 1). After applying the threshold (0.130), the total territorial extent with suitability was 5.2 million km². In Brazil, the area with suitability occupy 60% of the country. The states that covered the greatest extensions of suitability were Amazonas with 30% of total suitability, Pará with 21.9%, and Mato Grosso with 18.43% (Table 1). One thousand three hundred and six municipalities (23% of the total Brazilian municipalities) showed suitability for *L. Muta* occurrence. The highest suitability values were in the Amazonia, for the municipalities of Mâncio Lima (0.97) in the state of Acre, and Eirunepé (0.97), Ipixuna (0.96), Envira (0.96) and Guajará (0.95) in the Amazonas State.

In Brazil, approximately 41.5% (n = 788) of the

municipalities with hospital assistance for snakebites have climatic suitability for *Lachesis muta*. Among the 3,663 municipalities that do not have medical assistance for snakebites, 15.5% (n = 518) presented climatic suitability for the occurrence of *L. muta*. The highest values were found in Bujari (0.68) and Porto Acre (0.67), both in the states of Acre; Careiro da Várzea (0.66) in Amazonas State; Cujubim (0.65) in Rondônia State and Capixaba (0.64) also in Acre State.

In Brazil, 8,500 accidents were reported as caused by *Lachesis muta* between 2007 and 2017. The highest incidence rates (in 100,000 inhabitants) were for the states of Acre (10.73), followed by Amazonas (10.09) and Roraima (6.34). The municipalities with the highest incidence rates were Uiramutã (166) in Roraima, Uarini (64.2), Nova Olinda do Norte (60.9) and Alvarães (57.4) in Amazonas state, as well as Rodrigues Alves (57.3) in Acre state (Fig. 2). The municipalities with the lowest incidence rates included Rio de Janeiro (0.005), in the state of Rio de Janeiro, Salvador (0.003) in Bahia State and São Paulo (0.001), in São Paulo State. About 69% (472) of the municipalities that reported accidents with *L. muta* presented suitability for the species' occurrence, and 31% (n = 214) did not presented any suitability. We found low correlation with climatic suitability and incidence rate (Spearman Correlation: 0.36, p < 0.001).

Discussion

The present study is the first to suggest an effective distribution of *Lachesis muta* antivenom (Anti-biotropic-laquetic Serum - SABL) based on areas of high suitability for the species in Brazil. First, we discuss the regions that have more incidence rates of accidents and suitability for the occurrence of the species. We point the municipalities that should be prioritized to receive antivenom. We point out regions that have records of *Lachesis* bites, but do not have suitability for its occurrence. We also show the importance of studies that recognize areas of occurrence of venomous animals for supporting the efficient distribution of the antivenom.

The highest values of suitability and incidence rates of snakebites were in northern Brazil showing the importance of distributing SABL to this region as a priority. This region also has shown the highest incidence of other snakebites (Rebouças Santos *et al.*, 2019), and can be treated as a priority for health

Table 1. Brazilian states and the percentage of total suitability found for *Lachesis muta* after the threshold. There are high values for North region.

State	Percentage of Climatic Suitability
Amazonas	30,1
Pará	21,9
Mato Grosso	18,3
Rondônia	4,8
Tocantins	4,5
Roraima	3,9
Goiás	3,8
Bahia	3,2
Acre	3,0
Amapá	2,1
Maranhão	1,6
Espirito Santo	0,6
Piauí	0,5
Minas Gerais	0,4
Pernambuco	0,1
Alagoas	0,1
Sergipe	0,1
Paraíba	0,1
Rio de Janeiro	0,1
Rio Grande do Norte	0,01
Ceará	0,01
Distrito Federal	0,00

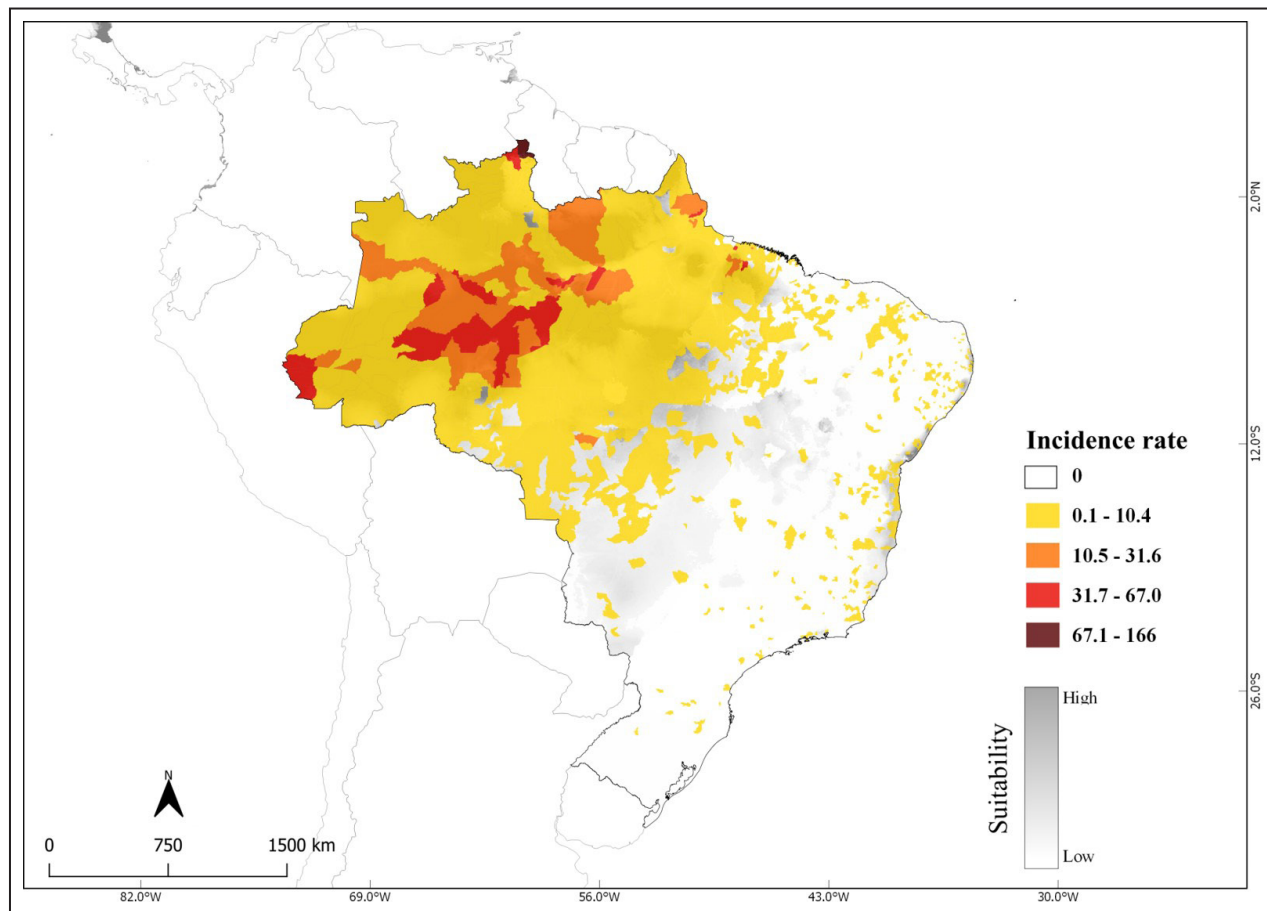


Figure 2. Incidence rates of accidents by *Lachesis muta* in Brazilian municipalities. The highest incidence rates were at Amazon region.

surveillance and control. Although northern Brazil has low values of land use (high values is related to the most common epidemiological profile in snakebites; e.g., men at productive age working at agriculture), remotes communities are present in such places (Bochner and Struchiner, 2003; IBGE 2010). Fifty per cent of the Brazilian indigenous populations live in the northern region (IBGE, 2010; 2016). These populations already suffer from many other health problems and the available systematized information on the subject is scarce (Montenegro and Stephens, 2006; Leite *et al.*, 2013). Most part of these health problems would be easy to control (e.g., Tuberculosis - Coimbra and Basta, 2007), but they still prevail due to the lack of investment and the difficulty of accessing adequate healthcare services (Stephens *et al.*, 2006; Gracey and King, 2009). Our results also indicate the importance of hospitals with SABL closer to indigenous populations. The states with high suitability, such as Acre, Amazonas and Pará (northern Brazil) should always be prioritized for receiving SABL, especially the municipalities of Mâncio Lima, Eirunepé, Ipixuna, Envira, and

Guajará. All these municipalities must receive antivenom and hospital assistance to treat the bitten patients and reduce their chances of dying or having permanent sequelae.

Even though the coastal Atlantic Forest presented lower values of climatic suitability, not being a priority when compared to the northern region (maximum of 0.66 and 0.97, respectively), it should not be neglected. Therefore, we recommend regular shipments of SABL to this region. However, we find no need to distribute antivenom for *Lachesis* snakebites to certain municipalities such as Salvador (Bahia State), Rio de Janeiro (Rio de Janeiro State) and São Paulo (São Paulo State). *Lachesis muta* is considered locally extinct in Salvador (Lira-da-Silva *et al.*, 2011), its last record for Rio de Janeiro State was more than 30 years ago (IVB 01, in 1986), and do not have current or historical records in São Paulo State.

Approximately 70% of the municipalities that have reported snakebites showed high suitability for *Lachesis muta*. However, the remaining municipalities with reported accidents (30%) do not show any suitability, supporting low correlation. For example,

accidents reported for Distrito Federal, Paraná, Rio Grande do Sul, Santa Catarina and São Paulo were not congruent with our modeling results and neither with the results of other studies (see Moura *et al.*, 2016), since these localities were not suitable areas for the species occurrence. Therefore, we suggest these accidents may have been caused by captive animals, such as Zoos and vivaria or even misidentified. Inaccurate completion of accident report sheets might also have caused this incongruence between the modeling results and the states with snakebite notifications.

Lachesis muta can be mistaken by health professionals with species from a high diversity and abundant genus in Brazil, the genus *Bothrops* (Silva *et al.*, 2019). Studies that prioritize environmental education about medically important animals, associated with professional training and the dissemination of correct information are indispensable (Gutiérrez *et al.*, 2009; Chippaux, 2017). We recommend all municipalities with reported accidents must invest in environmental education for population and training health agents. Since it is not easy to distinguish between *Bothrops* and *Lachesis* envenomation, another strategy for treatment is the administration of polyspecific antivenom (e.g., Madrigal *et al.*, 2017). Thus, the current use of SABL by the Ministry of Health, which is a conjugated antivenom made from the venoms of *Bothrops* and *Lachesis* is the most appropriate.

In the period from 2007 to 2017 alone, 260,000 snakebites were reported in Brazil, 100,000 of which were considered as moderate and severe. There are regions in Brazil where the access to antivenom is still limited and where patients have to travel long distances to receive antivenom treatment (Gutiérrez *et al.*, 2009). Adequately guiding the distribution of antivenom is crucial, because it would not only improve the treatment of snakebites, but it would also improve the logistics of antivenom production, and even the policies of snakebite prevention. We also encourage mapping the medically important species, because such technique can reveal subsampled areas of occurrence and guide the efficient distribution of antivenom. Ecological modeling can complement and even point out problems on snakebite mapping. It can also be applied to any region of the world, showing results that can help to create policies to minimize public health issues.

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