RESEARCH ARTICLE

Ecological niche modelling and predicted geographic distribution of *Lutzomyia cruzi*, vector of *Leishmania infantum* in South America

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Abstract

In some transmission foci of *Leishmania infantum* in Brazil, *Lutzomyia cruzi* could be considered the main vector of this pathogen. In addition, *L. cruzi* is a permissive vector of *L. amazonensis*. Its geographical distribution seems to be restricted and limited to Cerrado and Pantanal biomes, which includes some areas in Brazil and Bolivia. Considering that predicting the distribution of the species involved in transmission cycles is an effective approach for assessing human disease risk, this study aims to predict the spatial distribution of *L. cruzi* using a multiscale ecological niche model based in both climate and habitat variables. Ecological niche modelling was used to identify areas in South America that are environmentally suitable for this particular vector species, but its presence is not recorded. Vector occurrence records were compiled from the literature, museum collections and Brazilian Health Departments. Bioclimatic variables, altitude, and land use and cover were used as predictors in five ecological niche model algorithms: BIOCLIM, generalised linear model (logistic regression), maximum entropy, random forests, and support vector machines. The vector occurs in areas where annual mean temperature values range from 21.76˚C to 26.58˚C, and annual total precipitation varies from 1005 mm and 2048 mm. Urban areas were most present around capture locations. The potential distribution area of *L. cruzi* according to the final ecological niche model spans Brazil and Bolivia in patches of suitable habitats inside a larger climatically favourable area. The bigger portion of this suitable area is located in Brazilian States of Mato Grosso do Sul and Mato Grosso. Our findings identified environmentally suitable areas for *L. cruzi* in regions without its known occurrence, so further field sampling of sand flies is recommended, especially in southern Goiás State, Mato Grosso do Sul (borders with Mato Grosso, São Paulo and Minas Gerais); and in Bolivian departments Santa Cruz and El Beni.
Leishmaniases are vector-borne diseases caused by *Leishmania* parasites which are transmitted to humans by the bites of infected female sand flies. The sand fly *Lutzomyia cruzi* is the vector of *Leishmania infantum*, the causative agent of visceral leishmaniasis (VL), in some specific areas of Brazil. The transmission of *Leishmania* species is climate-sensitive and involves complex ecological interactions between parasites, vectors and hosts. Considering that the vectors are strongly sensitive to climatic and environmental conditions, studies of their geographical distribution are important for understanding the eco-epidemiology of VL, as well as for the planning of disease control actions. The ecological niche of a species is a critical determinant of its distribution. Therefore, we conducted a study to evaluate and model the ecological niche of *L. cruzi* and predict susceptible areas to its occurrence in South America. The potential distribution area of *L. cruzi* according to the final ecological niche model spans Brazil and Bolivia in patches of suitable habitats inside climatically favourable areas. *Cerrado* and Pantanal biomes comprise the biggest portion of this suitable area which includes three Brazilians states, and some areas in Bolivia. Our findings reinforce the importance of conducting more ecological studies on sand fly fauna.

**Introduction**

World Health Organization data show that vector-borne diseases represent more than 17% of the global burden of all infectious diseases, causing more than 1 million deaths per year [1]. The dynamics and intensity of transmission of pathogens exhibit significant spatial and temporal heterogeneity, especially in vector-borne diseases [2,3]. Part of this lies in the fact that vector-borne diseases are climate-sensitive, because the species involved in their complex cycles of transmission are highly dependent on climatic variables [4–6]. In addition, there is evidence that ongoing climate change is affecting, and will continue to affect the distributions and burdens of these infections [4].

Predicting the distribution of the species involved in transmission cycles is an effective approach for assessing human disease risk. The spatial distribution of a species is a reflection of its ecology and evolutionary history, influenced by specific factors depending on the spatial scale [7–9]. Species distributions are hierarchically structured in space, with climatic variables limiting distributions at coarse scales, habitat variables gaining importance as the scale narrows, and biotic interactions affecting distributions at microscales [9,10].

Leishmaniases are climate-sensitive diseases transmitted to humans by the bites of female sand flies (Diptera: Psychodidae) infected with *Leishmania* parasites. The distribution and behaviour of the species involved in the transmission cycle, especially of the sand fly vectors, are strongly affected by climatic variables, such as precipitation, temperature and humidity [11,12]. In Latin America, *Lutzomyia longipalpis* is the main vector of *Leishmania infantum*, the causative agent of visceral leishmaniasis (VL) [13,14]. Due to its great epidemiological importance and wide distribution, *L. longipalpis* has been the object of different studies on the effects of environmental variables and anthropogenic environmental changes on its ecology [15–20]. Some of these studies have used ecological niche modelling to estimate the geographic distribution of this vector and predict its expansion or contraction under climate change scenarios [18–20].
However, in some transmission foci of *L. infantum* in Brazil, the sand fly *L. cruzi* may be acting as the main vector of this protozoan due to absence of *L. longipalpis* [21–25]. Although there were suspicions that *L. cruzi* was the vector responsible for the transmission of *L. infantum* since the 1980s [21,22], only recently this phlebotomine sand fly was confirmed as a proven vector of *L. infantum* [25], based on the Killick-Kendrick criteria [26], and as a permissive vector of *L. amazonensis* [25]. *Lutzomyia cruzi* can also act as an alternative vector in the location where both sand flies occur in sympatry [19]. In Brazil, the geographical distribution of *L. cruzi* seems to be restricted and limited to Cerrado and Pantanal biomes [23,24,27–29]. There are also reports of the presence of *L. cruzi* in Bolivia [30]. Recent evidences suggest introgressive hybridization between *L. cruzi* and *L. longipalpis* based on molecular analyses [31,32], reinforcing the idea that they are sibling species.

Even though *L. cruzi* has medical and epidemiological relevance, until now there are few published reports focused on the ecology and effects of environmental variables on the distribution and abundance of this sand fly [19,21,27,28,33,34]. A recent study applied ecological niche models to predict the distributions of *L. longipalpis* and *L. cruzi* in Brazil, but models were based on both species together, thus making it impossible to evaluate their distributions separately [19]. A further assessment of the potential distribution of *L. cruzi* is needed, especially for those areas where *L. longipalpis* does not occur.

Considering that ecological niche modelling represents a tool for monitoring disease trends in natural ecosystems and identify opportunities to mitigate the impacts of climate-driven disease emergence [35], this report aims to predict the spatial distribution of *L. cruzi* using a multiscale ecological niche model based in both climate and habitat variables. Besides contributing to the study of the ecological niche of *L. cruzi*, our goal includes the identification of specific areas in Brazil and neighbour countries that are environmentally suitable for this particular vector species, but its presence is not recorded.

**Methods**

**Occurrence records**

We conducted a literature review to compile records of the presence of *L. cruzi*. On July 2016, the online databases PubMed, ISI, Scopus and SciElo were searched for relevant studies using the terms ‘Psychodidae’ and ‘Lutzomyia’. After removal of duplicate references, the papers were scanned for mention of *L. cruzi* captures, and all records compiled in a Microsoft Excel database with the available description of the capture sites (country, state/province/department, district/municipality, and locality). Additionally, the sand fly distribution lists compiled by Martins et al. [36], Young & Duncan [37], Aguiar & Medeiros [38] and Galati [39] were also consulted to ensure known presence records were not missed. As females of *L. cruzi* and *L. longipalpis* are morphologically indistinguishable [37,39], only the records with species identification based on captured males were considered as valid.

The main sand fly collections in Brazil were physically visited to search for additional unpublished records of the species. These included Centro de Pesquisas René Rachou (FIOCRUZ, Belo Horizonte, assisted by Dr J. D. Andrade-Filho), Instituto Butantan (IBUT, São Paulo, assisted by Dr R. Moraes), Instituto Evandro Chagas (IEC, Belém, assisted by Dr T. Vasconcelos dos Santos), Instituto Oswaldo Cruz (FIOCRUZ, Rio de Janeiro, assisted by Dr J. M. Costa), Instituto de Pesquisas da Amazônia (INPA, Manaus, assisted by Dr R. Freitas and Dr M. L. Oliveira), Universidade de São Paulo/Faculdade de Saúde Pública (USP, São Paulo, assisted by Prof. M. A. Sallum), and Universidade de São Paulo/Museu de Zoologia (USP, São Paulo, data provided by Dr A. J. Andrade). The online databases SpeciesLink (http://splink.
cria.org.br/) and GBIF (https://www.gbif.org/) were also searched for presence records on February 2018.

All presence records were associated with geographical coordinates (latitude and longitude) and classified in three levels according to their spatial precision: High level: coordinates of the capture site were available in the original source of the record; Medium level: coordinates were obtained at Google Earth (https://earth.google.com/) by visually searching for the capture site when its description was available in the source of the record; Low level: coordinates of the municipality/district centre were obtained at Google Earth when the source of the record had no information on the capture locality, but only at this administrative level. We excluded from the database those records with information only at state/province/department or country levels.

The occurrence database thus contained the following information for each record: country, state/province/department, municipality/district, locality, year of capture, longitude, latitude, spatial precision, reference (S1 Table). The year of capture and spatial precision were used to split the records in separate sets for model training and validation, in accordance with the spatial and temporal precision of the variables used in the ecological niche models.

**Pseudo-absence records**

As some modelling algorithms require presence/absence data, we randomly sampled pseudo-absences in the space outside the environmental domain favourable for the species [40] but restricted to a maximum distance of 1000 km from the presence records. This environmental domain was estimated using the bioclimatic envelope model BIOCLIM [41]. The number of pseudo-absences was 10 times the number of presence records for each model run. We ran the pseudo-absence sampling procedure once for each modelling step (climate and habitat models). These procedures were performed in R platform [42], using the packages raster [43] and dismo [44].

**Climate and habitat variables**

We obtained historical (1970–2000) climate data for South America at WorldClim (version 2), an online database of 19 bioclimatic variables derived from monthly averages of temperature and precipitation [45]. For the climate model, we obtained the variables at the spatial resolution of 2.5 minutes (approximately 5x5km per pixel), which is an adequate coarse resolution where climate influences species distributions [9]. We selected a subset of the original 19 variables by running a Pearson correlation matrix and retaining only the six less correlated ones ($r < 0.6$). The final set of climate variables used to run the climate model consisted of annual mean temperature (BIO1), mean diurnal range of temperature (BIO2), temperature seasonality (BIO4), annual precipitation (BIO12), precipitation seasonality (BIO15) and precipitation of warmest quarter (BIO18) [45].

Remote sensing variables representing vegetation and topography were used as potential habitat indicators of *L. cruzi*. The Enhanced Vegetation Index (EVI), a product of the MODIS (Moderate Resolution Imaging Spectroradiometer) sensor was obtained at NASA’s EarthExplorer website (https://earthexplorer.usgs.gov/) and processed with the MODIS Reproject Tool (https://lpdaac.usgs.gov). Monthly EVI data for 2000–2015 was obtained for the study area at the spatial resolution of 1 km. A Principal Component Analysis (PCA) was performed in order to reduce collinearity in the dataset. We retained the first five components, because they represented 99% of the cumulative variance in the monthly EVI dataset. Altitude, aspect and slope variables were derived from a digital elevation model from SRTM (Shuttle Radar Topographic Mission) and obtained at AMBDATA, an online database of environmental
layers maintained by INPE (Instituto Nacional de Pesquisas Espaciais, http://www.dpi.inpe.br/Ambdata/). The eight habitat variables were resampled to 1 km² resolution by bilinear interpolation and cropped at the extension of the study area, which was determined by the results of the climate model. All variable processing was done using the R packages raster and RSToolbox [46].

Ecological niche description

To describe the ecological niche of *L. cruzi*, the values of the main bioclimatic variables and altitude in the location of each presence record were extracted. We also assessed the types of land use and cover where the vector occurs using data from MapBiomas (http://mapbiomas.org/), a high-resolution database of annual land use and cover for Brazil. Each presence record was associated with the land use and cover data of the same year of capture. We excluded the records with low spatial precision at this step, because they do not match the native resolution of the MapBiomas data layers (30x30m). The percentage of each land cover type was extracted in a 500 m buffer created on each presence record. Analyses were performed in R package raster.

Ecological niche modelling

There are several algorithms available for developing ecological niche models, which produce different results and predictive maps even when running with the exact same input data [47–49]. There is not a consensus on the literature about one single best algorithm, thus researchers are encouraged to apply different methods to overcome this methodological uncertainty in their model predictions [50,51]. Therefore, we applied the same five modelling algorithms as McIntyre et al. [52], which had satisfactory results in niche models of Brazilian sand flies: BIOCLIM, Generalised Linear Models (GLM, logistic regression), Maximum Entropy (MaxEnt), Random Forests (RANFOR), and Support Vector Machines (SVM). For a short description of the five algorithms, see McIntyre et al. [52].

To reduce spatial auto-correlation, we randomly selected a subset of species occurrences which were at least 10 km apart from the nearest record. We ran all models with their default settings on the dismo package of R platform. In order to use the whole set of unique presence/pseudo-absence records in model training, we used 10-fold cross-validation, with 10% of the records retained for internal model testing. For internal evaluation, we used the True Skill Statistic (TSS), which ranges from -1 to +1, with +1 indicating complete agreement between predicted and observed records, and values close to and below 0 representing models no better than random predictions [53]. Model outputs with TSS scores lower than 0.6 were discarded. Outputs with the highest TSS scores from each algorithm were overlaid and consensus areas extracted by the majority ensemble rule [54]. Final maps were produced based on the consensus between the five modelling algorithms. Uncertainty was mapped by calculating the standard deviation of pixel values from model outputs produced by each of the five algorithms.

Because of the great difference in spatial precision of the species records, we ran two models with adequate settings for each spatial scale (Table 1). On a first step, we ran a climatic suitability model at the coarse spatial resolution of the climatic variables (2.5 minutes). For this model we used the set of *L. cruzi* records captured between 1970 and 2000 with the six bioclimatic variables. Model calibration area was restricted to a hypothesised accessible area of 1000 km around all known species records [55]. As we were aiming for a more conservative output for this first model, we chose the “zero omission” threshold rule [56] to convert model outputs into binary predictions. With this threshold rule, all presence records are retained inside the
predicted area of occurrence, thus maximizing sensitivity (the proportion of correctly predicted presences), but sacrificing specificity (the proportion of correctly predicted absences).

The resulting binary map of climatic suitability was then used to limit the calibration area of the habitat suitability model, which was based on the vegetation and topography variables at higher scale (Table 1). As we narrowed the spatial resolution, at this second stage we only used the presence records classified as precision levels high and medium, with capture years matching the variables (2004–2013). The same model settings were applied, except for the threshold rule to produce binary predictions. For the final models, we chose threshold values that maximised both sensitivity and specificity [56]. With this, the final outputs become more objective, minimising both false positives and false negatives.

External validation of both models was done with independent records, separated from model training (Table 1). Model significance was evaluated by binomial probabilities calculated over binary outputs, and model performance was evaluated by sensitivity (number of correctly predicted presences divided by total number of records). Resulting model outputs were exported to QGIS software version 3.0.1 [57] for preparation of final maps.

### Results

The compiled database included 116 presence records of *L. cruzi* with associated geographical coordinates (S1 Table). Most records of the vector are in Mato Grosso and Mato Grosso do Sul Brazilian states, with a single record in State of Goiás and one in Bolivia, in Santa Cruz Department (Fig 1). Most of the records have low spatial precision (68%), followed by records with medium (25%) and high (7%) precision levels (Fig 1).

The vector occurs in areas where annual mean temperature values range from 21.76°C to 26.58°C, and annual total precipitation varies from 1005 mm and 2048 mm (Table 2). In these areas, temperatures in the coldest month of the year reach 11.3°C and the warmest month can reach as high as 34.3°C (Table 2). Extremes of monthly precipitation range from 1 mm to 157 mm (Table 2). In terms of elevation, most records of *L. cruzi* occur around 270 m above sea level, with a minimum of 86 m and up to 741 m (Table 2).
Nine different types of land use and cover were detected around records of *L. cruzi* (Fig 2). Urban areas were most present around capture locations (64%), followed by open forests (10%), dense forests (5%), pasture areas (4%), and open fields (3%). The remaining land use and cover types were identified only eventually and are presented in Fig 2.

The TSS scores of the climatic suitability models ranged from 0.48 to 1 (8% were discarded with TSS < 0.6); and in the final models, from 0 to 1 (22% with TSS < 0.6). Outputs produced

![Compiled occurrence records of *Lutzomyia cruzi* classified in different spatial precision levels (green: high; yellow: medium; red: low). The blue line delimits the model calibration area. Map produced in QGIS.](https://doi.org/10.1371/journal.pntd.0006684.g001)

Table 2. Minimum, median, mean and maximum values of climatic variables and altitude recorded at capture locations of *Lutzomyia cruzi*.

| Variable name                                    | Min. | Median | Mean  | Max.  |
|--------------------------------------------------|------|--------|-------|-------|
| Annual Mean Temperature (°C)                     | 21.76| 24.91  | 24.71 | 26.58 |
| Max Temperature of Warmest Month (°C)            | 30.3 | 33.3   | 33.1  | 34.3  |
| Min Temperature of Coldest Month (°C)            | 11.3 | 15.3   | 15.13 | 17.9  |
| Temperature Seasonality (standard deviation *100)| 46.77| 171.68 | 164.91| 240.74|
| Annual Precipitation (mm)                        | 1005 | 1445   | 1457  | 2048  |
| Precipitation of Wettest Month (mm)              | 157  | 226    | 242.9 | 349   |
| Precipitation of Driest Month (mm)               | 1    | 17     | 16.17 | 41    |
| Precipitation Seasonality (Coefficient of Variation) | 51.77| 67.54  | 68.91 | 83.86 |
| Altitude (m)                                     | 86.45| 270.84 | 305.7 | 741.41|

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by different algorithms varied considerably (S1 Fig), but consensus areas showed less uncertainty (S2 Fig). The climatic suitability model performed significantly better than random predictions (binary probabilities, $p = 0.00498$) and had sensitivity of 0.92; while the final ecological niche model was also significant (binary probabilities, $p < 0.001$) with a sensitivity of 0.72.

The coarse resolution model predicted an area of climatic suitability for *L. cruzi* that occupies the Central-West region of Brazil, extending westwards into Bolivia (blue and green areas in Fig 3). However, when considering the habitat variables at high resolution, the results of the final ecological niche model show that the area with suitable climate and habitat conditions for *L. cruzi* is much smaller, occupying 38.7% of the climatically suitable regions (only green areas in Fig 3).

The potential distribution area of *L. cruzi* according to the final ecological niche model spans Brazil and Bolivia in patches of suitable habitats inside climatically favourable areas. The bigger portion of this suitable area is located at Brazilian States of Mato Grosso do Sul and Mato Grosso, where most known records of the species are located (Fig 4). Four known records of the vector fell out of the predicted area: one in Bolivia (El Carmen), and three in Mato
Grosso State (Nova Canã do Norte, Colider and Rondolândia) (see arrows in Fig 4). Suitable areas without known occurrence of the vector are located in Bolivian departments Santa Cruz and El Bení; southern State of Goiás in Brazil, as well as northern Mato Grosso do Sul and in border areas with São Paulo and Minas Gerais States (see circles in Fig 4).

Discussion

This study represents the first report of the predicted spatial distribution of *L. cruzi* using a multiscale ecological niche model based on both climate and habitat variables, applying different algorithms for the same data. The final ecological niche model comprises mainly areas of the Central-West region of Brazil and some parts of East Bolivia.

The low number of occurrence records and their low spatial precision were limitations of the modelling process, being the most probable reason for the low TSS scores of a minority of model outputs. We reduced these limitations by discarding outputs with TSS < 0.6 in the final models and subsampling the records by spatial precision, thus running models at appropriate spatial scales. Models produced by different algorithms had great spatial variability, as expected [47–51]. Uncertainty mapping provided more confidence to the areas predicted as environmentally suitable by most algorithms.

Our results describe the ecological niche of *L. cruzi* in terms of climate, altitude and vegetation/land cover where the species occurs. The climatic values recorded at capture locations of *L. cruzi* are in accordance with the Köppen’s climate classification for most parts of the Central-West region of Brazil: tropical zone with monsoon period (Am) and with dry winter (Aw) [58]. Ecological studies that evaluated the linear relationship between *L. cruzi* abundance and climatic variables showed no significant statistical association [24,27,59]. However, it was
observed that the species occurs throughout the year, with population peaks in the months with high temperature [21,24,27,59]. These previous studies considered both male and female specimens of \textit{L. cruzi} and reported data from regions where \textit{L. longipalpis} has not been detected, except in Corumbá city [60]. However, \textit{L. longipalpis} was reported in Corumbá only once [60]. Successive sand fly surveys performed by different research groups were unable to confirm the presence of \textit{L. longipalpis} in this area [21,27,28,61,62]. It should be noted that the occurrence sites of this vector have annual mean temperature relatively constant and annual precipitation ranging from moderate to high (Table 1).

Altitude data show that most records of \textit{L. cruzi} occur in the Central and Southern plateau and in the Pantanal plains of Brazil. This observation allows us to hypothesize that the distribution of \textit{L. cruzi} may be limited, among other factors, by altitude, since there is no record of the species in coastal regions. \textit{Cerrado} and Pantanal are the biomes where \textit{L. cruzi} mostly occurs, with few observations in southern Amazon. Our results of the percentage of land use and cover types demonstrate that \textit{L. cruzi} is present predominantly in urban areas. However, this does not necessarily mean that \textit{L. cruzi} prefers urban areas, because most of the sand fly samplings where performed in these areas or in peri-urban localities. Nevertheless, considering that \textit{L. cruzi} and \textit{L. longipalpis} are sibling species [31,32], the probable preference of \textit{L. cruzi} for urbanized environments would not be surprising. As an example, data from the city of Corumbá, State of Mato Grosso do Sul, showed that in the 1980s the greatest abundance of \textit{L. cruzi} was in native forest areas with low human interference [21]. Almost 30 years later a lower abundance was observed in the city’s peripheral forests, while in the urban area, the vector

![Fig 4. Potential distribution of \textit{Lutzomyia cruzi} based on ecological niche modelling predictions and known presence records. Circles represent areas of environmental suitability that need further field studies to assess vector occurrence. Arrows indicate records that were not predicted by the models. Map produced in QGIS.](https://doi.org/10.1371/journal.pntd.0006684.g004)
increased its abundance [27,28]. Similar situation was found in the city of Camapuã (Fernandes et al., 2017), also located in Mato Grosso do Sul State. No significant association was found between the absolute frequencies of *L. cruzi* and percentage of vegetal coverage and three spectral indices (normalized difference vegetation index, NDVI; normalized difference water index, NDWI; impervious surface areas, ISA) [27].

The predicted area of occurrence from our models corroborates a previously published distribution model of *L. cruzi* that was restricted to the Central-West region of Brazil [34]. The predicted area of occurrence of *L. cruzi* cannot be determined in Andrade-Filho et al. [19], but the general distribution of the species records used in the models is similar. Neither of the two studies give information on the spatial precision of the presence records. Positional uncertainty in species occurrence records have direct effects on ecological niche model predictions [63] and must be considered especially when developing models from secondary data. The vast majority of information available on species occurrence databases from Brazil is restricted to the municipal level. This can lead to serious bias in model predictions, as municipalities in Brazil have widely different areas, ranging from approximately 3 km² to 160,000 km² [64]. It is crucial that the spatial precision of species records match the spatial resolution of the models [65]. With our multiscale approach, we were able to develop models that incorporated the records with low spatial precision, thus reducing positional bias in our predictions. In addition, the spatial thinning process reduced the spatial auto-correlation bias. The four records that were not successfully predicted by the final models had low spatial precision, so it is not possible to determine the exact location of the species occurrence.

Our models predict occurrence areas of *L. cruzi* in Bolivia, where the vector was found in chicken coops and pigsties in the town of El Carmen, Santa Cruz District [30]. This is the only published record from the country, and according to our predictions, *L. cruzi* is probably present, but so far undetected in many Bolivian regions. Both visceral and cutaneous leishmaniasis are endemic in Bolivia with occurrence of *L. infantum*, *L. braziliensis* and *L. amazonensis* [66–69]. However, there are few reports of ecological studies of phlebotomine fauna in this country, so further field sampling of sand flies is recommended.

According to the Brazilian Ministry of Health [70], except for the southwest Minas Gerais State, in the confluence region between the Grande river and the Paranaiba river (boundary with the states of São Paulo, Goiás and Mato Grosso do Sul), there are autochthonous human cases of VL reported in almost all the predicted suitable areas for *L. cruzi*. However, in many regions there are also the presence of *L. longipalpis* and/or *L. cruzi* [19]. A particular region, predicted as favorable to the vector, deserves to be highlighted due to the presence of autochthonous VL cases [70] and absence of *L. longipalpis* records according to Andrade et al. [19]: Brazil-Bolivia border in the extreme southwest Rondônia State, in the area adjacent to the municipality of Pimenteiras do Oeste. In Bolivia, few VL human cases have been reported and the disease appears to be restricted to Yungas region in the Bení department [71].

In Brazil, although the vector’s occurrence is widely known in State of Mato Grosso, some municipalities in Mato Grosso do Sul and the southern region of Goiás remain to be investigated. The border region between the states of Minas Gerais, São Paulo and Mato Grosso do Sul is also a predicted area of occurrence according to our models, but without known records of *L. cruzi*. This region, where the Paraná river basin divides the states, has many records of *L. longipalpis*, especially on the east side of the river [19]. To our knowledge, there is not a published study on the ecological interactions between *L. cruzi* and *L. longipalpis* that could justify their separation in space. Further studies on the phylogeography of both species might investigate if the Paraná river basin could have been a relevant dispersion barrier for their speciation.

In conclusion, our results contribute to the study of the ecology and distribution of an important vector of VL. The disease is being increasingly reported in urban and peri-urban
areas of Brazil, especially because of the geographical expansion of its main vector, *L. longipalpis* [72]. Given the genetic proximity of this vector with *L. cruzi* [31,32] and its absence in specific VL foci, our predictive maps also indicate potential risk areas of this disease associated with *L. cruzi*. It is crucial that entomological surveillance activities are performed in these areas, especially where the vector has not been detected so far.

**Supporting information**

S1 Table. Compiled presence records of *Lutzomyia cruzi*. (XLSX)

S1 Fig. Ecological niche models of *Lutzomyia cruzi* produced by different algorithms. Maps produced in QGIS. (TIF)

S2 Fig. Model uncertainty for climate and habitat models of *Lutzomyia cruzi*. Maps produced in QGIS. (TIF)

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References

1. World Health Organization. Global vector control response 2017–2030. Geneva, Switzerland: WHO. 2017. Available from: http://www.who.int/vector-control/publications/global-control-response/en/

2. Brooker S, Utzinger J. Integrated disease mapping in a polyparasitic world. Geospat Health. 2007; 1(2):141–146. https://doi.org/10.1081/gh.200068639

3. Hay SI, Snow RW. The Malaria Atlas Project: developing global maps of malaria risk. PLoS Med. 2006; 3(12):e473. https://doi.org/10.1371/journal.pmed.0030473 PMID: 17147615

4. Campbell-Lendrum D, Manga L, Bagayoko M, Sommerfeld J. Climate change and vector-borne diseases: what are the implications for public health research and policy?. Philos Trans R Soc Lond B Biol Sci. 2015; 370(1665):20130552. https://doi.org/10.1098/rstb.2013.0552 PMID: 25688013

5. Parham PE, Waldock J, Christophides GK, Hemming D, Agusto F, Evans KJ, et al. Climate, environmental and socio-economic change: weighing up the balance in vector-borne disease transmission. Philos Trans R Soc Lond B Biol Sci. 2015; 370(1665):20130551. https://doi.org/10.1098/rstb.2013.0551 PMID: 25688012

6. Altizer S, Ostfeld RS, Johnson PT, Kutz S, Harvell CD. Climate change and infectious diseases: from evidence to a predictive framework. Science. 2013; 341(6145):514–519. https://doi.org/10.1126/science.1239401 PMID: 23908230

7. Wiens JA. Spatial scaling in ecology. Funct Ecol. 1989; 3(4):385–397. https://doi.org/10.2307/2389612

8. Levin SA. The problem of pattern and scale in ecology. Ecology. 1992; 73(6):1943–1967. https://doi.org/10.2307/1941447

9. Pearson RG, Dawson TP. Predicting the impacts of climate change on the distribution of species: are bioclimatic envelope models useful? Glob Ecol Biogeogr. 2003; 12(5):361–371. https://doi.org/10.1046/j.1466-822X.2003.00042.x

10. Mackey BG, Lindenmayer DB. Towards a hierarchical framework for modelling the spatial distribution of animals. J Biogeogr. 2001; 28(9):1147–1166. https://doi.org/10.1046/j.1365-2699.2001.00626.x

11. Chaves LF, Calzada JE, Valderrama A, Saldaña A. Cutaneous leishmaniasis and sand fly fluctuations are associated with El Niño in Panama. PLoS Negl Trop Dis. 2014; 8(10):e3210. https://doi.org/10.1371/journal.pntd.0003210

12. Ready PD. Leishmaniasis emergence and climate change. Rev Sci Tech. 2008; 27(2):399–412. PMID: 18819668

13. Deane LM, Grimaldi G. Leishmaniasis in Brazil. In: Chang KP, Bray RS, editors. Leishmaniasis. Amsterdam: Elsevier; 1985. pp. 247–281.

14. Lainson R, Shaw JJ. New World leishmaniasis. In: Cox FEG, Wakelin D, Gillespie SH, Despommier DD, editors. Topley & Wilson's Microbiology and Microbial Infections: parasitology. London: Hodder Arnold ASM Press; 2005. pp. 313–349.

15. Oliveira EF, Silva EA, Fernandes CE, Paranhos Filho AC, Gamarra RM, Ribeiro AA, et al. Biotic factors and occurrence of Lutzomyia longipalpis in endemic area of visceral leishmaniasis, Mato Grosso do Sul, Brazil. Mem Inst Oswaldo Cruz. 2012; 107(3):396–401. https://doi.org/10.1590/S0074-027620120000300015 PMID: 22510836

16. Ximenes MDM, Castelão EG, de Souza MD, Menezes AA, Queiroz JW, Macedo e Silva VP, et al. Effect of abiotic factors on seasonal population dynamics of Lutzomyia longipalpis (Diptera: Psychodidae) in Northeastern Brazil. J Med Entomol. 2006; 43(5):990–995. https://doi.org/10.1093/jmedent/43.5.990 PMID: 17017238

17. Fernández MS, Salomón OD, Cavia R, Perez AA, Acardi SA, Guccione JD. Lutzomyia longipalpis spatial distribution and association with environmental variables in an urban focus of visceral leishmaniasis, Misiones, Argentina. Acta Trop. 2010; 114(2):81–87. https://doi.org/10.1016/j.actatropica.2010.01.008 PMID: 20096256

18. Almeida PS, Sciamarelli A, Batista PM, Ferreira AD, Nascimento J, Raizer J, et al. Predicting the geographic distribution of Lutzomyia longipalpis (Diptera: Psychodidae) and visceral leishmaniasis in the state of Mato Grosso do Sul, Brazil. Mem Inst Oswaldo Cruz. 2013; 108(8):992–996. https://doi.org/10.1590/0074-0276201300300015 PMID: 24402151

19. Andrade-Filho JD, Scholte RG, Amaral AL, Shimabukuro PH, Carvalho OD, Caldeira RL. Occurrence and Probability Maps of Lutzomyia longipalpis and Lutzomyia cruzi (Diptera: Psychodidae: Phlebotominae) in Brazil. J Med Entomol. 2017; 54(5):1430–1434. https://doi.org/10.1093/jme/tjx094 PMID: 28472338

20. Peterson AT, Campbell LP, Moo-Llana DA, Travi B, González C, Ferro MC, et al. Influences of climate change on the potential distribution of Lutzomyia longipalpis sensu lato (Psychodidae: Phlebotominae). Int J Parasitol. 2017; 47(10–11):667–674. https://doi.org/10.1016/j.ijpara.2017.04.007 PMID: 28668326
21. Galati EA, Nunes VL, Rego FD Jr, Oshiro ET, Chang MR. Estudo de flebotomíneos (Diptera: Psychodidae) em foco de leishmaniose visceral no Estado de Mato Grosso do Sul, Brasil. Rev Saude Publica. 1997 Aug; 31(4):378–390. https://doi.org/10.1590/S0034-89101997000400007 PMID: 9595767

22. Santos SO, Arias J, Ribeiro AA, Hoffmann MD, Freitas RA, Malacoo MA. Incriminação de Lutzomyia cruzi como a vector de American Visceral Leishmaniasis. Med Vet Entomol. 1998; 12(3):315–317. https://doi.org/10.1046/j.1365-2915.1998.00104.x PMID: 9737605

23. Missawa NA, Veloso MA, Maciel GB, Michalsky EM, Dias ES. Evidência de transmissão de leishmaniose visceral por Lutzomyia cruzi no município de Jaciara, Estado de Mato Grosso. Rev Soc Bras Med Trop. 2011; 44(1):76–78. https://doi.org/10.1590/S0037-868220110001000017 PMID: 21340413

24. Brito VN, Almeida AD, Nakazato L, Duarte R, Souza CD, Sousa VR. Phlebotomine fauna, natural infection rate and feeding habits of Lutzomyia cruzi in Jaciara, state of Mato Grosso, Brazil. Mem Inst Oswaldo Cruz. 2014; 109(4):899–904. https://doi.org/10.1590/0074-0276140112 PMID: 25410993

25. Oliveira EF, Oshiro ET, Fernandes WS, Murat PG, de Medeiros MJ, Souza AI, et al. Experimental infection and transmission of Leishmania by Lutzomyia cruzi (Diptera: Psychodidae): Aspects of the ecology of parasite-vector interactions. PLoS Negl Trop Dis. 2017; 11(2):e0005401. https://doi.org/10.1371/journal.pntd.0005401 PMID: 28234913

26. Killick-Kendrick R. Phlebotomine vectors of the leishmaniases: a review. Med Vet Entomol. 1990; 4(1):1–24. https://doi.org/10.1111/j.1365-2915.1990.tb00255.x PMID: 2132963

27. Oliveira EF, Casaril AE, Fernandes WS, Ravanelli MS, de Medeiros MJ, Gamarra RM, et al. Monthly distribution of phlebotomine sand fly species, and biotic and abiotic factors related to their abundance, in an urban area to which visceral leishmaniasis is endemic in Corumbá, Brazil. PloS One 2016; 11(10): e0165155. https://doi.org/10.1371/journal.pone.0165155 PMID: 27783667

28. Casaril AE, Monaco NZN, Oliveira EF, Eguchi GU, Paranhos Filho AC, Pereira LE, et al. Spatiotemporal analysis of sandfly fauna (Diptera: Psychodidae) in an endemic area of visceral leishmaniasis at Pantanal, Central South America. Parasit Vectors. 2014; 7:364. https://doi.org/10.1186/1756-3305-7-364 PMID: 25128480

29. Martins AV, Falcão AL, Silva JE, Dias ES. Nota sobre Lutzomyia (Lutzomyia) cruzi (Mangabeira, 1938), com a descrição da fêmea (Diptera, Psychodidae, Phlebotominae). Mem Inst Oswaldo Cruz. 1984; 79(4):439–442. https://doi.org/10.1590/S0037-86821984000400007

30. Brazil RP, Passos WL, Brazil BG, Temeljkovic M, Andrade Filho JD. Diptera, Psychodidae, Phlebotominae Rondani, 1840: range extension and new records from lowland Bolivia. Check List. 2010; 6(4):587–588. https://doi.org/10.15560/6.4.587

31. Ribolla PE, Gushi LT, Pires e Cruz MD, Costa CH, Costa DL, Lima Junior MS, et al. Leishmania infantum genetic diversity and Lutzomyia longipalpis mitochondrial haplotypes in Brazil. Biomed Res Int. 2016; ID 9249217. https://doi.org/10.1155/2016/9249217 PMID: 27119085

32. Santos MF, Ribolla PE, Alonso DP, Andrade-Filho JD, Casaril AE, Ferreira AM, Fernandes CE, Brazil RP, Oliveira AG. Genetic structure of Lutzomyia longipalpis populations in Mato Grosso do Sul, Brazil, based on microsatellite markers. PLoS One. 2013; 8(9):e74268. https://doi.org/10.1371/journal.pone.0074268 PMID: 24066129

33. Missawa NA, Lima GBM. Distribuição espacial de Lutzomyia longipalpis (Lutz & Neiva, 1912) e Lutzomyia cruzi (Mangabeira, 1938) no Estado de Mato Grosso. Rev Soc Bras Med Trop. 2008; 39(4):337–340. https://doi.org/10.1590/S0037-86822008000400004 PMID: 17119747

34. Almeida PS, Andrade AJ, Sciamarelli A, Raizer J, Menegatti JA, Hermes SC, et al. Geographic distribution of phlebotomine sandfly species (Diptera: Psychodidae) in Central-West Brazil. Mem Inst Oswaldo Cruz. 2015; 110(4):551–559. https://doi.org/10.1590/0074-02760140462 PMID: 26018450

35. Peterson A.T., Martínez-Campos C., Nakazawa Y., & Martínez-Meyer E. Time-specific ecological niche modeling predicts spatial dynamics of vector insects and human dengue cases. Trans R Soc Trop Med Hyg. 2005; 99(9), 647–655. https://doi.org/10.1016/j.trstmh.2005.02.004 PMID: 15979656

36. Martins AV, Falcão AL, Williams P. American sand flies (Diptera: Psychodidae, Phlebotominae). Rio de Janeiro: Academia Brasileira de Ciências; 1978.

37. Young DG, Duncan MA. Guide to the identification and geographic distribution of Lutzomyia sand flies in Mexico, the West Indies, Central and South America (Diptera: Psychodidae). Gainesville: American Entomological Institute; 1984.

38. Aguiar GM, Medeiros WM. Distribuição regional e habitats das espécies de flebotomíneos do Brasil. In: Rangel EF, Lainson R, editors. Flebotomíneos do Brasil. Rio de Janeiro: Fiocruz; 2003. pp. 207–255.

39. Galati EAB. Classificação de Phlebotomíneos. In: Rangel EF, Lainson R, editors. Flebotomíneos do Brasil. Rio de Janeiro: Fiocruz; 2003. pp. 23–51.
40. Lobo JM, Tognelli MF. Exploring the effects of quantity and location of pseudo-absences and sampling biases on the performance of distribution models with limited point occurrence data. J Nat Conserv. 2011; 19(1):1–7. https://doi.org/10.1016/j.jnc.2010.03.002

41. Booth TH, Nix HA, Busby JR, Hutchinson MF. BIOCLIM: the first species distribution modelling package, its early applications and relevance to most current MaxEnt studies. Divers Distrib. 2013; 20(1):1–9. https://doi.org/10.1111/ddi.12144

42. R Core Team. 2018. R: A language and environment for statistical computing. R Foundation for Statistical Computing. Vienna, https://www.R-project.org/.

43. Hijmans RJ, van Etten J, Cheng J, Maugetti M, Sumner M, Jonathan A. raster: Geographic Data Analysis and Modeling. R package version 2.6–7. 2017. https://CRAN.R-project.org/package=raster

44. Huiams RJ, Phillips S, Leathwick J, Elith J. dismo: Species distribution modeling. R package version 1.0–15. 2016. https://CRAN.R-project.org/package=dismo

45. Fick SE, Hijmans RJ. WorldClim 2: new 1-km spatial resolution climate surfaces for global land areas. Int J Climatol. 2017; 37(12):4302–4315. https://doi.org/10.1002/joc.5086

46. Leutner B, Horning N. RStoolbox: Tools for Remote Sensing Data Analysis. R package version 0.1.10. 2017. https://CRAN.R-project.org/package=RStoolbox

47. Buisson L, Thullier W, Casajus N, Lek S, Grenouillet G. Uncertainty in ensemble forecasting of species distribution. Glob Change Biol. 2009; 16, 1145–1157. https://doi.org/10.1111/j.1365-2486.2009.02000.x

48. Araujo M, New M. Ensemble forecasting of species distributions. Trends Ecol Evol. 2007; 22(1):42–7. https://doi.org/10.1016/j.tree.2006.09.010 PMID: 17011070

49. Liu C, Berry PM, Dawson TP, Pearson RG. Selecting thresholds of occurrence in the prediction of species distributions. Ecography. 2005; 28(3):385–93.

50. QGIS Development Team 2018. QGIS Geographic Information System, version 3.0.1. Available from: http://www.qgis.org

51. McIntrye S, Rangel EF, Vale MM. Evaluation of the impacts of climate change on disease vectors through ecological niche modelling. Bull Entomol Res. 2017; 107(4):419–430. https://doi.org/10.1017/S0007485316001097 PMID: 27974065

52. Santos SO, Arias JR, Hoffmann MD, Furlan MB, Ferreira WF, Pereira C, et al. The presence of Lutzomyia longipalpis in a focus of American visceral leishmaniasis where the only proven vector is Lutzomyia cruzi. Corumbá, Mato Grosso do Sul State. Rev Soc Bras Med Trop. 2003; 36(5):633–634. https://doi.org/10.1590/S0037-96822003000500017 PMID: 14576882

53. Almeida PS, Nascimento JC, Ferreira AD, Minzão LD, Portes F, Miranda AM, et al. Species of phlebotomines (Diptera, Psychodidae) collected in urban municipalities with transmission of visceral leishmaniasis in Brazil. PLOS Neglected Tropical Diseases | https://doi.org/10.1371/journal.pntd.0006684 July 30, 2018 15 / 16
62. de Pita-Pereira D, Cardoso MA, Alves CR, Brazil RP, Britto C. Detection of natural infection in Lutzomyia cruzi and Lutzomyia forattini (Diptera: Psychodidae: Phlebotominae) by Leishmania infantum chagasi in an endemic area of visceral leishmaniasis in Brazil using a PCR multiplex assay. Acta Trop. 2008 Jan 1; 107(1):66–9. https://doi.org/10.1016/j.actatropica.2008.04.015 PMID: 18502392

63. Naimi B, Hamm NA, Groen TA, Toxopeus AG. Where is positional uncertainty a problem for species distribution modelling?. Ecography. 2014; 37(2):191–203. https://doi.org/10.1111/j.1600-0587.2013.00205.x

64. Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística-IBGE). IBGE Cidades. 2017. Available from: https://cidades.ibge.gov.br/

65. Peterson AT, Soberón J, Pearson RG, Anderson RP, Martínez-Meyer E, Nakamura M, et al. Ecological Niches and Geographic Distributions. Monographs in Population Biology 49. New Jersey, Princeton University Press. 2011.

66. Martínez E, Mollinedo S, Torrez M, Munoz M, Bañuls AL, Le Pont F. Co-infection by Leishmania amazonensis and L. infantum/L. chagasi in a case of diffuse cutaneous leishmaniasis in Bolivia. Trans R Soc Trop Med Hyg. 2002; 96(5):529–532. https://doi.org/10.1016/S0035-9203(02)90428-1 PMID: 12474481

67. Martínez E, Le Pont F, Torrez M, Tellera J, Vargas F, Muñoz M, et al. A new focus of cutaneous leishmaniasis due to Leishmania amazonensis in a Sub Andean region of Bolivia. Acta Trop. 1998; 71 (2):97–106. https://doi.org/10.1016/S0001-706X(98)00049-7 PMID: 9821459

68. Alvar J, Yactayo S, Bern C. Leishmaniasis and poverty. Trends in parasitology. 2006; 22(12):552–557. https://doi.org/10.1016/j.pt.2006.09.004 PMID: 17023215

69. Le Pont F, Desjeux P. Leishmaniasis in Bolivia. I. Lutzomyia longipalpis (Lutz & Neiva, 1912) as the vector of visceral leishmaniasis in Los Yungas. Trans R Soc Trop Med Hyg. 1985; 79(2):227–231. https://doi.org/10.1016/0035-9203(85)90341-4 PMID: 4002292

70. Brazilian Ministry of Health (Ministério da Saúde do Brasil). Sistema de Informação de Agravos de Notificação. Available from: http://www2.datasus.gov.br/DATASUS

71. García AL, Parrado R, Rojas E, Delgado R, Dujardin JC, Reithinger R. Leishmaniases in Bolivia: comprehensive review and current status. Am J Trop Med Hyg. 2009; 80(5):704–711. https://doi.org/10.4269/ajtmh.2009.80.704 PMID: 19407110

72. Salomón OD, Feliciangeli MD, Quintana MG, Afonso MMS, Rangel EF. Lutzomyia longipalpis urbanisation and control. Mem Inst Oswaldo Cruz. 2015; 110(7):831–846. https://doi.org/10.1590/0074-02760150207 PMID: 26517497