

Phlebotominae of epidemiological importance in cutaneous leishmaniasis in northwestern Argentina: risk maps and ecological niche models

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Abstract. In Argentina, 58.2% out of the 8126 Cutaneous Leishmaniasis (CL) incident cases accumulated from 1954 to 2006 were reported in the provinces of Salta and Jujuy. The aim of this study was to develop an exploratory risk map and a potential distribution map of the vector, in order to offer recommendations for CL prevention. A total of 12 079 Phlebotominae (Diptera: Psychodidae) belonging to the species *Lutzomyia neivai* (Pinto), *Lu. migonei* (França), *Lu. cortelezzi* (Brèthes), *Lu. shannoni* (Dyar), *Lu. quinquefer* (Dyar) and *Brumptomyia* spp. (França & Parrot) were captured.

Potential distribution models were created for two species, *Lu. neivai* (incriminated vector of *Leishmania braziliensis*) and *Lu. migonei*, associated with domestic animals in Argentina and that in turn could be involved as a link between zoonotic transmission cycles and anthroozoonotic.

The Maximum Entropy Modeling System (MaxEnt) was used. The Jackknife test was performed, and the 'rainfall of the driest month' was the variable that best generalized the models. Accuracy was evaluated by the area under the curve (AUC) and validated by the Cohen's kappa index.

This approximation provides a new analytical resource of high potential for the prevention of the disease, in order to allocate resources properly and to develop the most suitable strategies for action.

Key words. Cutaneous leishmaniasis, ecological niche models, Phlebotominae, risk map, Argentina.

Introduction

The incidence of vector-borne diseases strongly associated with environmental modifications, such as leishmaniasis, has increased sharply in the world during the last decades. Deforestation and unplanned urbanization have been proposed as the main anthropic factors involved in the emergence/re-emergence of these diseases (Lainson, 1989;

Mott *et al.*, 1990; Walsh *et al.*, 1993; Dedet, 1999; Ashford, 2007; Shaw, 2007).

In Argentina, the re-emergence of Cutaneous Leishmaniasis (CL) has been recorded as epidemic with localized outbreaks, geographically restricted, associated with deforestation and the subsequent anthropic modifications in the deforested areas: conditions of safety/housing of the exposed workers, human settlements and urbanization (Sosa Estani *et al.*, 2001;

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Salomón *et al.*, 2001a, b, c, 2006a, 2008a, b; Sosa Estani & Salomón, 2002; Quintana *et al.*, 2010). The number of human cases of CL increased from 40 to 90 annual cases between 1954 and 1983 and from 90 to 400–1200 annual cases between 1984 and 2006. Out of the 8126 cases of CL recorded in the country from 1954 to 2006, 58.2% belonged to the provinces of Salta and Jujuy (Salomón, 2003; Salomón *et al.*, 2006b). *Lutzomyia neivai* and *Lu. migonei* are vectors of *Leishmania braziliensis*, a parasite associated with the outbreaks of CL in the region (Salomón, 2003; Córdoba-Lanús *et al.*, 2006).

Research on the mechanisms that operate from the environmental changes in modulating the incidence of vector-borne diseases, may have a strong impact on the development of control strategies (Walsh *et al.*, 1993; Beck *et al.*, 2000; Heymann & Rodier, 2001). This approach is even more appropriate in diseases such as CL as the distribution and abundance of vectors are the best indicators of the time and space of the transmission (potential risk). The space-time analyses based on human cases have many biases and do not allow accurate conclusions to be drawn for control, mainly because of the unknown asymptomatic incidence, the ambiguity of the information obtained from secondary sources and the individual differences in the anamnesis capability or physiological response (intrinsic period of incubation, microfocal transmission, etc.) (Peterson, 2006).

In the last decade, the use of algorithms to model ecological niches has grown steadily in different applications. Currently, there are about 16 models of ecological niche (Elith *et al.*, 2006) that differ between each other in the mathematical way used to estimate the potential niche of the modeled species. These models are applied to observe relations between the values of abiotic factors (temperature, rainfall etc.) and biotic factors (type of vegetation), with information of presence, presence-absence and/or known abundance of the species. As there is not a best method, the researcher should understand what each model does and choose which is the most suitable for the specific question he/she needs to address. The records of species of phlebotominae are still very scarce or non-existent in the study area, and in the short term it is difficult to obtain the geographical extension, therefore, the Maximum Entropy Modeling System (MaxEnt) method was chosen because of its use in estimating an unknown distribution, thus allowing more efficient sampling methods to be designed.

There is a large number of mathematical methods, these are an incentive to use new mathematical procedures to model the ecological niche of species, to allowing an integrated result obtained by different algorithms (Araújo & New, 2007). The objectives of this study were (a) to elaborate a qualitative risk map mainly based on the abundance of Phlebotominae, and (b) to develop the potential geographical distributions of the species incriminated as vectors of CL in northwestern Argentina by modeling their ecological niche. These models could be used to improve the allocation of resources, to develop strategies and generate recommendations about prevention and control of CL, according to the endemic or epidemic risk.

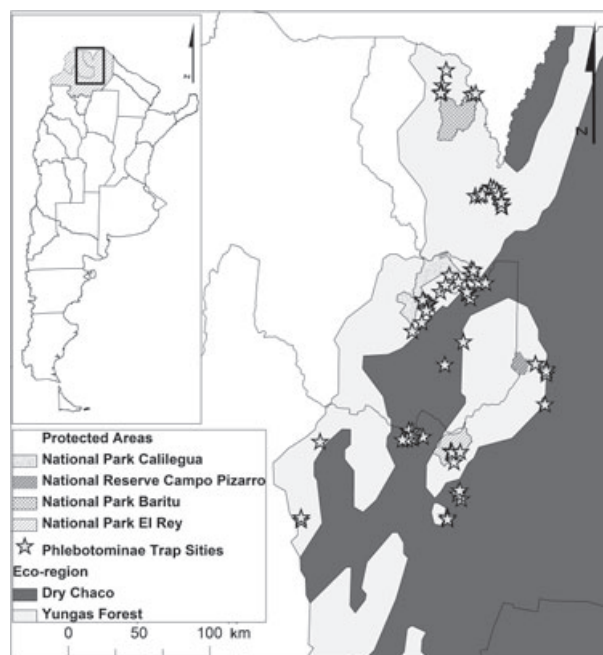


Fig. 1. Capture sites of phlebotomine adults in Jujuy and Salta provinces, Argentina, between 1 and 16 November 2006.

Material and methods

Study area. The study area included the provinces of Jujuy and Salta (Fig. 1, upper left corner: 66°16'24.08"W, 22°04'50.21" S; upper right corner: 63°34'44.6"W, 22°02'36.64" S; lower left corner: 66°17'17.51"W, 25°41'33.55" S; lower right corner: 63°31'39.18"W, 25°32'33.43" S), in areas that belong to two phytogeographical provinces, the Yungas or Tucumano-oranense forest, with a mean temperature between 14 and 26 °C and annual rainfall between 900 and 2500 mm, and the Chaco, which presents temperatures between 20 and 23 °C and rainfall between 500 and 1200 mm (Cabrera, 1971). The sites were localized in protected areas representing virgin zones of Yungas and Chaco and also in their areas of mitigation and outskirts (National Parks Baritú, Calilegua, and El Rey, in the National Reserve General Pizarro).

Phlebotominae sampling. Phlebotomines were captured between 1 and 16 November 2006. The sites were selected in order to cover different altitudinal gradients, latitudes, water basins and degrees of anthropic interventions, and to include known areas of CL transmission. The captures were made with CDC-like light mini-traps (M&G similar to Collection Bottle Traps) (Sudia & Chamberlain, 1962). To try to reduce the differences in the days and at the sites, two traps were placed in each georeferenced site between the 1 and 16 November 2006. In addition, samples were considered as adequate catch-night without rain, otherwise repeated the next night. The captures days were homogeneous, during the same period, and without the presence of precipitation. The traps operated overnight in 97 georeferenced sites.

Phlebotominae identification. The clarification's techniques (KOH, acid fuchsin and alcohols batteries) used were followed according to E.A.B Galati (personal communication, 2004). The sandfly species were identified according to Young & Duncan (1994). In the microscopic analysis, *Lutzomyia neivai*'s male and female genitalia were compared to the drawings of Andrade Filho *et al.* (2003), in order to distinguish this sandfly from other species, *Lu. intermedia*.

Data analyses: predefined risk categories with statistical support

Based on hypotheses in previous studies in the area (Salomón *et al.*, 2008b, 2011), three categories of risk of CL transmission were defined (Fig. 2): (a) no/unknown risk: sites without phlebotomines or sites with ≤ 10 individuals/trap associated with the presence of *Brumptomyia* spp, a zoophilic species not associated with *Leishmania* transmission (Rangel & Lainson, 2009). (b) Sporadic risk of transmission: sites with *Lu. cortelezzii*, *Lu. migonei* and/or *Lu. quinquefer*, species with vectorial competence that are neither incriminated as the primary vectors nor associated with outbreaks (Rangel & Lainson, 2003), forested environments or sites with current reports of sparse human CL cases. (c) Potential risk/epidemic transmission: sites with *Lu. neivai* (≤ 30 individuals/trap) in contiguous sites modified by man, with constant supplies of food for insects (humans and pets), or sites with current reports of scattered human CL cases/sites with *Lu. neivai* (30–3 781 individuals/trap) + *Lu. migonei*, sites with current reports of clustered human CL cases, zoonotic vector as a link to the domestic cycle + an anthropophilic and abundant peridomestic vector (Chávez & Añez, 2004).

To evaluate if there were differences in the association and abundance of the captured species, percentages of gravid females (chorionated eggs by transparency) and the sexes

ratio were counted as a surrogate of risk of transmission (Salomón *et al.*, 2004, 2008b) and bivariate analyses were used (chi-square tests, χ^2), whereas to quantify the degree of association, Cramer's V coefficient, which ranges from 0 (weak association) to 1 (strong association), was used. All the tests were considered statistically significant with $P < 0.05$. The analyses were performed from applets programmed in JAVA (<http://e-stadistica.bio.ucm.es/>).

Data processing: maps of potential distributions

The maps were developed with ecological niche modeling analysis and the distribution algorithm of maximum entropy was chosen, using the program MaxEnt, Version 3.2.19 (Phillips *et al.*, 2006).

The model was run from the geographical coordinates of the records of *Lu. neivai*, a species incriminated as a CL vector in the area (Córdoba Lanús *et al.*, 2006), and of *Lu. migonei*, a species associated with domestic animals Rangel & Lainson (2003) that could be the link between the zoonotic cycle and the anthroponotic cycle of CL (Chávez & Añez, 2004). Bioclimatic variables and a Digital Elevation Model (DEM) were included (USGS, 2004), based on variables related to the risk and vector biology reported in the literature in the study area (Salomón *et al.*, 2008b, 2011) and other regions (Piscopo & Mallia Azzopardi, 2007; Morillas-Márquez *et al.*, 2010; Brazil *et al.*, 2011; Gálvez *et al.*, 2011). Human cases were not used because, as explained in the introduction, they introduce biases.

The 19 bioclimatic variables were taken from the database WorldClim (<http://www.worldclim.org>), with a spatial resolution of 30 s ($0.93 \times 0.93 = 0.86 \text{ km}^2$) (Hijmans *et al.*, 2005); the same resolution was used for the DEM [Shuttle Radar Topographic Mission (SRTM) <http://www2.jpl.nasa.gov/srtm/>].

The value of the parameters was appropriate to warrant the convergence of the algorithm (Phillips *et al.*, 2006), and the Jackknife test was used.

Evaluation of the model. In order to evaluate the model, the records of *Lu. neivai* were divided in two groups. The same was done for the records of *Lu. migonei*. The first group of points (training, 75%) was used to run the models and the second group (test, 25%) to perform the test of evaluation, to look for statistical significance of the test.

The results of the evaluation are visualized as a ROC curve (receiver-operating characteristic) or 'AUC' (area under the curve), which indicates the global accuracy of the test (Deleo, 1993).

Validation of models. The records of captures made in the area of transmission of CL in northwestern Argentina from our own unpublished collections were used: eight records of presence and eight of absence by each species used, *Lu. neivai* and *Lu. migonei*. Cohen's kappa was applied to the

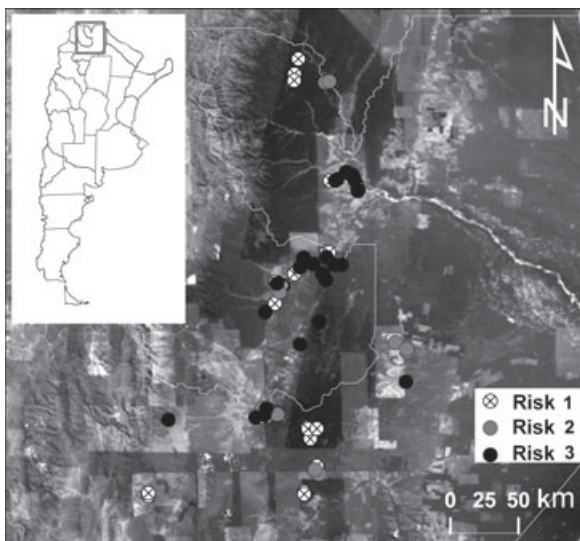


Fig. 2. Risk categories according to the diversity and abundance of phlebotomine species captured in northwestern Argentina, 2006.

results of the validation in the field in order to determine the concordance of the model obtained with the reality, therefore, if it is higher than the distribution it could be expected to be obtained randomly. The Kappa's scale of valuation is <0.20 = poor, $0.21-0.40$ = weak, $0.41-0.60$ = moderate, $0.61-0.80$ = good and $0.81-1.00$ = very good concordance (Altman, 1991).

Results

Phlebotomines collected in pre-defined areas of risk of CL transmission

A total of 12 079 phlebotomines belonging to the species *Lu. neivai* 85.7%, *Lu. migonei* 11.5%, *Lu. cortelezzii* 2.6% and in *Lu. shannoni*, *Lu. quinquefer* and *Brumptomyia* spp. less than 0.1% were captured (Table 1). *Lutzomyia neivai* is a confirmed vector of *Leishmania braziliensis*, the parasite associated with the outbreaks of CL in the area (Córdoba Lanús *et al.*, 2006).

Maxent analysis

The maps of potential distributions for both species are shown in Fig. 3A and B. The intensity of the colour towards the darkest one indicates a higher probability of the proper conditions for the species according to the model. The pixel meets the conditions of the restrictions imposed by the values of environmental variables known localities of the species. These conditions for both species involve the north and central areas of the provinces of Salta (departments of Orán, San Martín, and departments of Güemes and Anta respectively), the east areas of Jujuy (departments of Ledesma, San Pedro, El Carmen and northern Santa Bárbara), northwestern Tucumán (departments of Trancas and Burruyacu), and northwestern Santiago del Estero (department of Pellegrini).

Prediction of the influence of the variables. The variables that contributed most to the training of the model and their percentage values can be seen in Table 2, the variables with greatest percentage value: the 'Precipitation of Warmest Quarter' and 'Precipitation Seasonality' for both species. As these variables were estimated heuristically, the Jackknife test was applied, indicating the most important variable in the model and the one that more effectively forecasted the distribution of the data for *Lu. neivai* was the 'Precipitation of Driest Month' (BIO14), whereas those for *Lu. migonei* were BIO14 and the 'Precipitation of Warmest Quarter' (BIO18). The performance of DEM, BIO15, BIO17 and BIO4 showed that the prediction improved when these are not in use.

Evaluation of models. The algorithm converged after 360 iterations and the test AUC was of 0.966, with a standard deviation (SD) of 0.029 for *Lu. neivai*. The algorithm for *Lu. migonei* converged after 280 iterations and the test AUC was of 0.995, with a SD of 0.002.

Table 1. Relative abundance of Phlebotominae species by categories of risk (CR), Jujuy and Salta provinces, Argentina.

CR	<i>Lu. neivai</i>		<i>Lu. migonei</i>		<i>Lu. cortelezzii</i>		<i>Lu. shannoni</i>		<i>Lu. quinquefer</i>		<i>Brumptomyia</i>		Total	F:M	% GF Ln	% GF Lm	% GF Lc
	F	M	F	M	F	M	F	M	F	M	F	M					
1*	9	0	0	0	0	0	0	0	0	0	45	0	22	4.5	1	0	0
2*	1	8	59	15	0	0	0	2	1	0	0	0	205	2	0	0	23
3*	38	49	4	8	1	0	0	0	0	0	0	0	11 851	0.8	200*	20*	7*
Total%	85.7	11.5	2.6	0.03	0.07	0.1	0.8	0.8	0.8	0.8	0.8	0.1	12 079	0.8	201	20	30

* $P < 0.05$.

CR, 1 (no/unknown risk), 2 (sporadic risk of transmission), 3 (potential risk/epidemic transmission); % GF, gravid females percentage (15 individuals); F:M, *Lu. neivai* female/male ratio; Lc, *Lu. cortelezzii*; Lm, *Lu. migonei*; Ln, *Lu. neivai*.

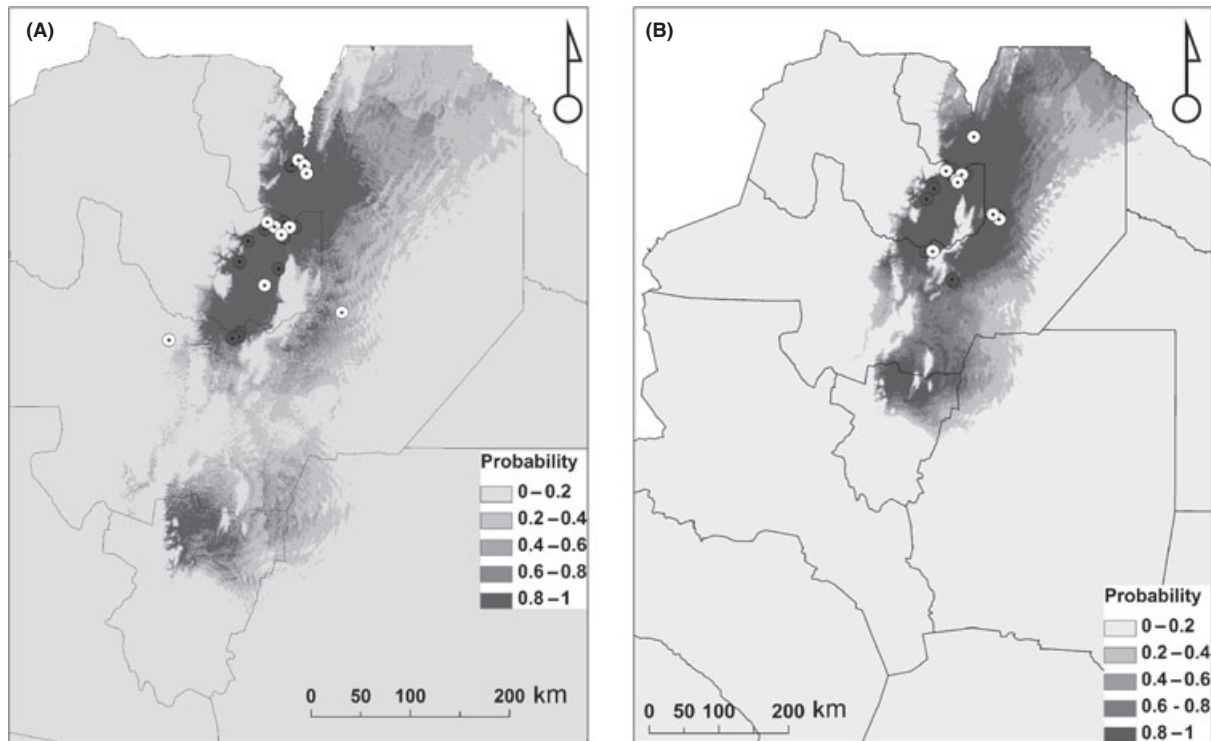


Fig. 3. Map of potential distribution of *Lutzomyia neivai* (A) and *Lutzomyia migonei* (B) in northwestern Argentina, by Maxent. The black dots (A and B) were used in training and white dots (A and B) were used for the test.

Validation of models

The value of probability on the maps (Figs 3 and 4) is reflected in the intensity of colour, from zero (light colour, low probability) to 1 (dark colour, high probability).

Lutzomyia neivai. From the 16 new records taken in the field to validate (eight of presence/eight of absence), the model correctly predicted 81%, the 8/8 presence records, and 5/8 absence records. Four of the eight sites for the presence of *Lu. neivai* were located in the province of Salta, three in Jujuy and one in

Table 2. Relative contributions of the variables to the Maxent model of *Lutzomyia neivai* and *Lutzomyia migonei*.

Code	Variables	<i>Lutzomyia neivai</i>		<i>Lutzomyia migonei</i>	
			(%)		(%)
BIO1	Annual mean temperature	BIO18	28.4	BIO15	35.6
BIO2	Mean diurnal range	BIO15	27.8	BIO18	23.6
BIO3	Isothermality	BIO11	9.9	BIO11	14.3
BIO4	Temperature seasonality	BIO2	6.6	DEM	5.9
BIO5	Max temperature of warmest month	BIO14	6.4	BIO17	5.1
BIO6	Min temperature of coldest month	DEM	4.9	BIO16	4.5
BIO7	Temperature annual range (BIO5-BIO6)	BIO4	4.5	BIO4	2.4
BIO8	Mean temperature of wettest quarter	BIO16	2.4	BIO19	2.1
BIO9	Mean temperature of driest quarter	BIO19	2.4	BIO8	1.5
BIO10	Mean temperature of warmest quarter	BIO13	1.8	BIO2	1.4
BIO11	Mean temperature of coldest quarter	BIO7	1.7	BIO7	1.3
BIO12	Annual precipitation	BIO3	1.2	BIO14	1.2
BIO13	Precipitation of wettest month	BIO9	0.6	BIO1	0.7
BIO14	Precipitation of driest month	BIO1	0.6	BIO3	0.4
BIO15	Precipitation seasonality	BIO17	0.5	BIO9	0
BIO16	Precipitation of wettest quarter	BIO8	0.3	BIO10	0
BIO17	Precipitation of driest quarter	BIO10	0	BIO5	0
BIO18	Precipitation of warmest quarter	BIO6	0	BIO6	0
BIO19	Precipitation of coldest quarter	BIO5	0	BIO13	0
DEM	Digital elevation model	BIO12	0	BIO12	0

Tucumán (Fig. 4A). In addition, 4/8 sites of confirmed presences, had probability values from 0.4 to 0.6, and the other four sites with probability values of 0.8 to 1. The value of Kappa's index was of 0.63, showing good accuracy, which demonstrates a high consistency of the model with the reality.

Lutzomyia migonei. The presence-absence was predicted correctly in 69% of the predetermined sites. Kappa's index presented a value of 0.4, a value between weak and moderate accuracy, with a poor consistency of the model with the reality. The eight presence records were correctly predicted, and in this case, three out of five absence records were correctly predicted. Two of the eight records of presence were confirmed with values of probability of 0–0.2, two sites with 0.4–0.6, one between 0.6 and 0.8 and three with values of 0.8–1 (Fig. 4B).

Bivariate analyses: risk categories

The risk categories differed significantly from each other in the composition and abundance of species ($\chi^2 = 53.11$, d.f. = 10, Cramer's V = 0.36) (Table 1). As the difference in the percentage of gravid females was statistically significant between the categories with a strong association ($\chi^2 = 1688$, d.f. = 4, Cramer's V = 0.60), category 3 had the highest number of gravid females indicating a high relative risk.

Although statistically significant ($\chi^2 = 78.68$, d.f. = 2), the sexes ratio (F : M) had a Cramer's V coefficient of 0.03, so it could be concluded that the association between the variables category/sex is low or that there is no association at all (Table 1).

The percentage of trap-nights positives in category 1 was 38.5%; 20% correspond to *Lu. neivai*, 20% to *Lu. migonei*, 20% to other species of *Lutzomyia* and 40% to non-*Lutzomyia* (*Brumptomyia spp*). In category 2, the percentage of trap-nights positives was 100%, of which the 20% was for *Lu. neivai*, and the 80% for *Lu. migonei*. In category 3, the percentage of trap-nights positives was of 100%, *Lu. neivai* was present in 100% of them, *Lu. migonei* in the 66.6% and other species of *Lutzomyia* in the 55.5%.

Regarding the percentage of trap-locations positives, in category 1 was of the 11%; the 40% with *Lu. neivai*, the 20% for *Lu. migonei*, the 20% for other species of *Lutzomyia*, and the 80% of non-*Lutzomyia*. In Category 2, the percentage of trap-locations positives was of the 100%, in which the 7% had *Lu. neivai*, the 71.4% presented *Lu. migonei*, and the 78.5% had other species of *Lutzomyia*. In category 3, the percentage of trap-locations positives was of 100%, *Lu. neivai* was present in 100% of them, *Lu. migonei* in the 54% and other species of *Lutzomyia* in the 57%.

Discussion

These categories were consistent with previous data of captures in 14 provinces (>100 000 phlebotomine) (Salomón *et al.*, 2008b).

The sites of category 1 showed low or no risk of transmission of CL, and are restricted to the area of influence of the National Park Baritú, in the northern border of the province of Salta with Bolivia, with the presence of *Brumptomyia*, zoophilic species and lack a proven association with CL transmission (Zuleta & Bolkovic, 1994; Salomón *et al.*, 2008c); whereas in

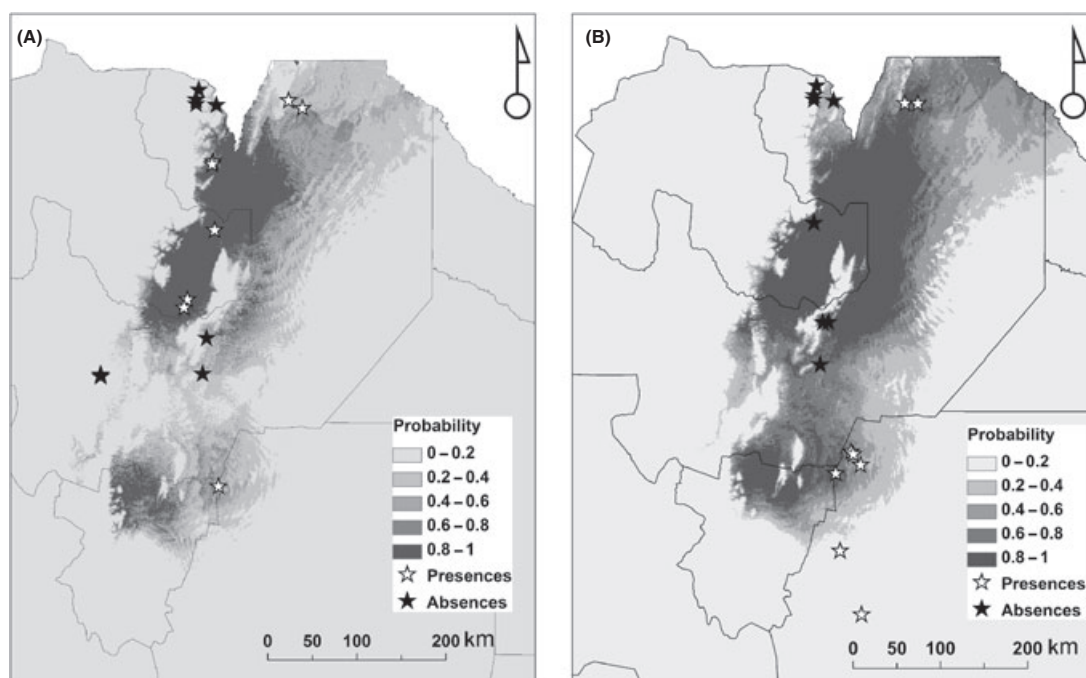


Fig. 4. Validated maps of *Lutzomyia neivai* (A) and *Lutzomyia migonei* (B). The white stars are the records of presences of phlebotomines, and the black stars are the records of absences.

the southern areas the sites presented very low abundance of other species or no individuals captured.

The sites of category 2, of sporadic transmission, were located mainly in the Chaco region characterized with xerophytic vegetation and the main species are *Lu. cortelezzii*, *Lu. migonei* and *Lu. quinquefer*, all considered vectors and associated with outbreaks (Rangel & Lainson, 2003, 2009; Salomón *et al.*, 2006b, 2008c), but the first found with natural infection of *L. braziliensis* (Rosa *et al.*, 2011). *Lutzomyia quinquefer* was known to be restricted to the Paranaense region in Argentina before 1960 (northeast) with unknown risk until 2009. In 2007, a new report of its presence in the Dry Chaco region was recorded, associated with peridomicile and forest (Salomón *et al.*, 2008c). This study is the first to report *Lu. quinquefer* in the northwest Argentina.

The sites of category 3, with epidemic potential or effective risk, are principally in the Yungas's foothills, basins of the river San Francisco, Bermejo. This category presented two kinds of sites: areas of the foothills of the Yungas, which are little disturbed, and where usually the abundance of *Lu. neivai* was low, and contiguous sites, where the landscape was anthropically modified, and a constant source of food for the phlebotomines was consequently provided (human and domestic animals) (Chávez & Añez, 2004; Salomón *et al.*, 2008a, 2011; Quintana *et al.*, 2010). Hereby any environmental modification in the area of risk defined in this study, and close to the sites with current cases of CL, can generate epidemic transmission of CL. Therefore, on the basis of these results, before any environmental modification in the area is carried out, it is necessary to assume this potential risk and, if the intervention is allowed, the following should be recommended:

1. Active surveillance of human CL cases and vector control in the sites with high density of *Lu. neivai* and clustering of CL cases.
2. Vectorial monitoring before, during and after any extensive environment modification is carried out in the Bermejo-San Francisco river basin area.

In the Chaco region, the sporadic condition of the transmission (Salomón *et al.*, 2008c; Rosa *et al.*, 2010) is probably related more to behaviours of risk associated with environmental management and focal deforestations. It was proposed to develop a strategy of specific prevention for the region as soon as the total records for Argentina are analysed.

The two most abundant species on the analysis of the risk categories were modeled, *Lu. neivai*, specie incriminated as vector of *L. braziliensis* in the study area (Córdoba-Lanús *et al.*, 2006), and *Lu. migonei*, specie incriminated as secondary vector (Salomón *et al.*, 2008a; Rangel & Lainson, 2009). The analyses of ecological niche modeling for *Lu. neivai* and *Lu. migonei* resulted in a very good prediction of their geographical distributions.

The potential distribution of *Lu. neivai*–*Lu. migonei* forecasted by the model from bioclimatic variables fitted very well at the northern and central region of the Yungas, involving mainly the provinces of Jujuy and Salta, whereas in the southern Yungas (centre—south of the province of Tucumán's and

north of the province of Catamarca) the potential distribution was unbalanced owing to a lack of records. The biases could be introduced by the fact that there are no records from these areas in the model, and one disadvantage of this algorithm is that it tends to over-fit the distribution according to the introduced points (Phillips *et al.*, 2006). The model will thus be improved including all the available records of the whole area.

The test and training data for both species were not autocorrelated spatially, they were independent, therefore, indicating a good adjustment of the test to the data of training. Therefore, the models fit better than a random distribution and so they could forecast the presence of the modeled species in the sample test.

The three variables that contributed more to the models in both species were the same: 'Precipitation of Warmest Quarter' (BIO18), 'Precipitation Seasonality' (BIO15) and 'Mean Temperature of Coldest Quarter' (BIO11).

For *Lu. neivai*, 'Max Temperature of Warmest Month' (BIO5), 'Min Temperature of Coldest Month' (BIO6), 'Mean Temperature of Warmest Quarter' (BIO10) and 'Annual Precipitation' (BIO12) and, for *Lu. migonei* the above-mentioned ones plus 'Mean Temperature of Driest Quarter' (BIO9); 'Precipitation of Wettest Month' (BIO13) did not contribute to the model.

As for the importance of the variables, the Digital Elevation Model (DEM), 'Precipitation Seasonality' (BIO15), 'Precipitation of Driest Quarter' (BIO17) and 'Temperature Seasonality' (BIO4), for both *Lu. neivai* and *Lu. migonei*, suggesting a low forecasting capability. Therefore, to improve the predictive power of the model, these variables were not included in its construction. The DEM for *Lu. neivai* had a negative gain, indicating that it worsens the model if it is used, thus reinforcing the decision to avoid these variables in the final model.

Although the variable of 'Precipitation of Warmest Quarter' (BIO18) contributes to the fitting of the model to the training data, the variable 'Precipitation of Driest Month' (BIO14) better generalizes the model, so that the results are comparatively better on the data of the sample test. This allows that the model constructed with this variable could be transferable. This information is important if the final aim is to transfer a model able to estimate a future distribution under changes that take place in the variables.

The variable 'Precipitation of Driest Month' (BIO14) indicates that the presence or absence of rainfall could be the triggering or limiting factor in the potential new distributions of these species. The rainfall also influences the dynamics, reproduction and breeding, as already observed in previous works with different time-space scales of analyses (Peterson & Shaw, 2003; Salomón *et al.*, 2004, 2006a, b; Quintana *et al.*, 2010).

Although the evaluation of the model for *Lu. neivai* and *Lu. migonei* showed an 'almost perfect' accuracy, in the validation the prediction was more precise for *Lu. neivai*, with 81% of the sites predicted correctly and Kappa's index with a great conformity with the reality. This could be partly because of the fact that there are fewer records of *Lu. migonei*, and although the number of records used is statistically significant, the validation would be better by increasing the records, both in quantity such as in homogeneity when choosing sites. It is true that the ideal would be to take more checkpoints, but taking

into account the extent of the study area, we gave greater value to the field validation, especially given the high concordance in the records of presences and absences confirmed. As mentioned above, it is proposed that in a future study to improve the model, records of the rest of the country's endemic area and new records should be added.

Some of the areas predicted with the presence of vectors by the model are currently under increasing anthropic environmental modifications; for example, the north of the province of Salta is having a large expansion of the agricultural lands used (Salomón *et al.*, 2004, 2008a, 2008b; Quintana *et al.*, 2010). According to the results of this study these changes should trigger the abundance and distribution range of these insects, mainly *Lu. neivai*, the main species incriminated as an epidemic vector (Córdoba Lanús *et al.*, 2006). This is an example of the strong impact that human activities could have on the current distribution of these species. Therefore, it is recommended for future predictive models, to also add representative variables of land use.

In the construction of the models, we only used climatic variables and records of presence that summarize the conditions of the sites analysed (Stockwell & Noble, 1992; Phillips *et al.*, 2006). The number of variables is not negligible, especially as it was wanted to use variables that could be related to the biology of vector and based on variables related to works performed in the study area (Salomón *et al.*, 2008b, 2011) and other regions (Piscopo & Mallia Azzopardi, 2007; Morillas-Márquez *et al.*, 2010; Brazil *et al.*, 2011; Gálvez *et al.*, 2011).

The use of models is just the first steps in this biological group, the search for articles on climate change and leishmaniasis recorded 25 papers, 14 of them reviews (MEDLINE). Those defined geographically to Europe are 16, 3 to Latin America, 2 to Asia and 1 to North America.

The use of predictive models of distribution of vectors of *L. braziliensis* was of great value to extrapolate localities with known records to other areas where the environmental conditions are adequate for this species. The technologies of modelling allowed us to obtain the distribution of the entity modelled with a high degree of accuracy. One of the criticisms of this analytical tool is the over-fitting to data entry. Still, in this algorithm advantages were found working with only a few records, with continuous and categorical environmental data. In addition, the software show a continuous outcome, fast and with the possibility of ecological interpretations from the response curves of the variables.

This study tried to contribute to a preliminary exploration of the variables, so we can extrapolate the results, adjusted for scales of work, but we believe that the resolution chosen was the proper one for the current stage of development of the issue. In a future study new variables will be included in the model, such as changes of use and land cover.

The evaluation of our model with MaxEnt's algorithm showed an approximation that provides a new resource for the early-prevention warning systems for CL, in order to design more efficient strategies of action, and to be able to offer recommendations for geographically defined areas according to their potential risk: besides, by better understanding the

climatic modulation of the density of vectors you may define better operational variables for the surveillance.

In conclusion, with macro-scale records, the potential distributions of *Lu. neivai* and *Lu. migonei* were predicted based on bioclimatic variables. The maps obtained as final products are an indispensable input in predictive models to design control and surveillance strategies with a rational allocation of resources based on risk.

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