

Environmental suitability for *Lutzomyia (Nyssomyia) whitmani* (Diptera: Psychodidae: Phlebotominae) and the occurrence of American Cutaneous Leishmaniasis in Brazil

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Leishmaniasis represents an important public health problem in Brazil. The continuous process of urbanization and expansion of human activities in forest areas impacts natural habitats, modifying the ecology of some species of *Leishmania*, as well as its vectors and reservoirs and, consequently, changes the epidemiological pattern and contribute to the expansion of American Cutaneous Leishmaniasis (ACL) in Brazil. In epidemiology of ACL, we highlight *Lutzomyia (Nyssomyia) whitmani*, the main vector of ACL, transmitting two dermatropic *Leishmania* spp.: *Leishmania (Viannia) braziliensis* and *Leishmania (Viannia) shawi*. We used the maximum entropy niche modeling approach (MAXENT) to evaluate the environmental suitability of *L. (N.) whitmani* and the transmission of ACL in Brazil, in addition to designing models for a future scenario of climate change. MAXENT was used under the "auto-features" mode and the default settings, with 100-fold repetition (bootstrap). The logistic output was used with higher values in the Habitat Suitability Map, representing more favorable conditions for the occurrence of *L. (N.) whitmani* and human cases of ACL. Two models were developed: *Lutzomyia whitmani* model (LWM) and American Cutaneous Leishmaniasis model (ACLM). LWM identified that the species "prefers" (more appropriate habitat) regions with moderate Annual Precipitation (AP), between 1,000 - 1,600 mm, intermediate vegetation density (NDVI) values, Mean Temperature of The Coldest Quarter (MTCQ), between 15°C - 21°C, and Annual Mean Temperature (AMT), between 19°C - 24°C. ACLM indicates that ACL is strongly associated with areas of intermediate density vegetation, areas with Annual Precipitation (AP) between 800 and 1200 mm, MTCQ above 16 ° C and AMT below 23°C. The results obtained in this study are discussed in terms of epidemiology and surveillance of ACL in future scenarios in Brazil.

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2 **Phlebotominae) and the occurrence of American Cutaneous Leishmaniasis in Brazil**

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14

15 **ABSTRACT**

16 Leishmaniasis represents an important public health problem in Brazil. The continuous process
17 of urbanization and expansion of human activities in forest areas impacts natural habitats,
18 modifying the ecology of some species of *Leishmania*, as well as its vectors and reservoirs and,
19 consequently, changes the epidemiological pattern and contribute to the expansion of American
20 Cutaneous Leishmaniasis (ACL) in Brazil. In epidemiology of ACL, we highlight *Lutzomyia*
21 (*Nyssomyia*) *whitmani*, the main vector of ACL, transmitting two dermatropic *Leishmania* spp.:
22 *Leishmania (Viannia) braziliensis* and *Leishmania (Viannia) shawi*. We used the maximum
23 entropy niche modeling approach (MAXENT) to evaluate the environmental suitability of *L. (N.)*
24 *whitmani* and the transmission of ACL in Brazil, in addition to designing models for a future
25 scenario of climate change. MAXENT was used under the "auto-features" mode and the default
26 settings, with 100-fold repetition (bootstrap). The logistic output was used with higher values in
27 the Habitat Suitability Map, representing more favorable conditions for the occurrence of *L. (N.)*
28 *whitmani* and human cases of ACL. Two models were developed: *Lutzomyia whitmani* model
29 (LWM) and American Cutaneous Leishmaniasis model (ACLM). LWM identified that the
30 species "prefers" (more appropriate habitat) regions with moderate Annual Precipitation (AP),
31 between 1,000 - 1,600 mm, intermediate vegetation density (NDVI) values, Mean Temperature
32 of The Coldest Quarter (MTCQ), between 15°C - 21°C, and Annual Mean Temperature (AMT),
33 between 19°C - 24°C. ACLM indicates that ACL is strongly associated with areas of
34 intermediate density vegetation, areas with Annual Precipitation (AP) between 800 and 1200
35 mm, MTCQ above 16 ° C and AMT below 23°C. The results obtained in this study are discussed
36 in terms of epidemiology and surveillance of ACL in future scenarios in Brazil.

37

38 INTRODUCTION

39 The simplification of biological communities, the fragmentation and loss of habitats
40 resulting from human occupation modify the parasite/host interactions, which may lead to the
41 emergence and reemergence of several diseases in animal and human populations (Begon,
42 Harper & Townsend, 1990).

43 In the last decade, a growing number of studies have investigated the effects of
44 biodiversity on the risk of disease occurrence, mainly due to the interest in identifying and
45 evaluating the importance of biodiversity and the environmental services it provides (Loreau et
46 al., 2001). The influence of diversity on transmission cycles has been described for some
47 diseases (Van Buskirk & Ostfeld, 1995; Norman et al., 1999; Allan, Keesing & Ostfeld, 2003;
48 Allan et al., 2009; Telfer et. al., 2005; Vaz et al., 2007). However, little is known about the
49 ecological mechanisms related to these effects (Keesing, Holt & Ostfeld, 2006). Understanding
50 the structure and functioning of the ecological processes involved in the dynamics of the
51 interactions between parasites, hosts and the environment becomes critical in order to
52 comprehend the relationship between biodiversity and the emergence or reemergence of
53 zoonoses.

54 Due to the new and complex epidemiological scenarios, Leishmaniasis are considered
55 reemerging diseases (WHO, 2010) and important public health problems in Brazil. American
56 Cutaneous Leishmaniasis (ACL) represents an example of zoonosis related to land use and
57 biodiversity management, both by the severity of the disease and by the direct relationship of
58 elements and the environmental context (landscape) in its transmission cycle (Fonseca et al.,
59 2014).

60 The circulation of phlebotomine vectors (sandfly) in environments outside the
61 geographical limits of natural foci is increasing, and leads to modifications in the classic
62 epidemiological patterns (wild, occupational/leisure, and rural/periurban. For more detail, see
63 (Brasil, 2013). Such modifications are related to changes in the determinant factors for the
64 exposure of man to transmission, demographic expansion and the process of urbanization on the
65 limits of natural foci, as well as the occurrence of forest remnants adjacent to urban areas
66 (Lainson & Rangel, 2005; WHO, 2010; Brazil, 2013).

67 In this context, we highlight *Lutzomyia (Nyssomyia) whitmani*, sandfly species registered
68 in 25, of the 27 Brazilian federative units (Costa et al., 2007) and incriminate it as transmitter of

69 two dermatropic leishmaniasis: *Leishmania (Viannia) shawi*, in the Amazon, and *Leishmania*
70 (*Viannia*) *braziliensis*, in the North, Northeast, Midwest, Southeast and South Regions (Lainson
71 & Shaw, 2005; Rangel & Lainson, 2009). The species presents different behavior in different
72 regions, has a wide geographical distribution, and is adapted to several climates and types of
73 vegetation cover (Costa et al., 2007; Rangel & Lainson, 2003; Rangel & Lainson, 2009). This
74 ecological plasticity reflects the occurrence of this species in all epidemiological patterns
75 described for ACL (Brasil, 2013). Throughout Brazilian territory, according to qualitative
76 changes related to anthrophilia and domesticity, Lainson (1988) suggested that *L. (N.) whitmani*
77 represented a complex of cryptic species.

78 The characterization of factors influencing the spatial distribution of the species, in
79 general, has been an efficient tool for a better understanding of ecological processes. The
80 Ecological Niche Models (ENM) has been widely used as a tool to describe conditioning factors
81 and to identify patterns related to environmental suitability for species occurrence (Guisan &
82 Zimmerman, 2000; Franklin, 2010; Peterson et al., 2011). In recent years, many techniques for
83 modeling niches and species distributions have been developed and applied extensively in
84 biogeography, ecology and conservation studies (Guisan & Zimmerman, 2000; Guisan &
85 Thuiller, 2005; Elith & Leathwick, 2009). The maximum entropy model (Maxent), (Elith et al.,
86 2006) is consistently competitive with the highest performing methods, and is one of the most
87 common approaches used to determine geographic distribution and ecological features of species
88 (Elith et. al., 2011; Renner & Warton, 2013; Václavík & Meentemeyer, 2009; Braunisch &
89 Suchant, 2010; Rebelo & Jones, 2010; Rodríguez-Soto et. al., 2011).

90 Peterson and Shaw (2003) modeled three sandfly vector species (*L. (N.) whitmani*, *L.*
91 (*Nyssomyia*) *intermedia* and *L. migonei*) for South America, and identified an increase in areas of
92 climate suitability for the year 2050. According to the models, *L. (N.) whitmani* presented the
93 greatest areas of dispersion. The purpose of the present; study was to evaluate the environmental
94 suitability and project future scenarios (via ENM), for *L. (N.) whitmani* and for the ACL in
95 Brazil, in face of global climate change.

96 MATERIALS AND METHODS

97 Occurrence data

98 For data related to the occurrence of the disease, we used municipalities with records of
99 endemic areas for ACL (N = 1882, of which 1506 were used for modeling and 376 for additional
100 accuracy test). For *L. (N.) whitmani* occurrence, the municipalities with confirmed record of
101 vector (N = 992, of which 794 were used for modeling and 198 for additional accuracy test) were
102 considered in *L. (N.) whitmani* model.

103 This set of occurrence data was extracted from previously published data (online
104 databases, PubMed, <http://www.ncbi.nlm.nih.gov/pubmed>; ISI Web of Knowledge,
105 <http://apps.webofknowledge.com> and SCOPUS, <Http://www.scopus.com>, CAPES). We also
106 collected unpublished records from the Health Departments of Brazil and from major Brazilian
107 sandfly collections (Centro de Pesquisas Rene Rachou - FIOCRUZ, Instituto Evandro Chagas -
108 IEC and Faculdade de Saude Publica—USP).

109 **Environmental descriptors**

110 Ten environmental variables (0.04° of spatial resolution, ~ 5 km) were used, eight of
111 which were WorldClim (Hijmans et al., 2005) climatic variables, as well as data on altitude and
112 vegetation indices, all displayed in Table 1. The adopted variables are commonly used in species
113 distribution predictions, and consist of easily usable ecological information.

114 For the projection to the environmental conditions of the future (2050), we used two
115 Representative Concentration Pathways (RCPs) of HadGEM2-ES General Circulation Model:
116 RCP 4.5 and RCP 8.5 greenhouse gas concentration trajectories adopted by the IPCC for its fifth
117 Assessment Report (AR5) in 2014 (IPCC, 2013). These were selected to represent contrasting
118 scenarios in projections for climate change. RCP 4.5 represents a relatively optimistic scenario
119 and assumes that the radiative forcing of greenhouse gas stabilizes shortly after 2100, and RCP
120 8.5, more pessimistic, radiative forcing keeps rising after 2100.

121 **Ecological Niche Models**

122 We used the maximum entropy niche modelling approach, as implemented in the
123 MAXENT software (version 3.3.3k), to evaluate the environmental suitability for *L. (N.)*
124 *whitmani* and occurrence of ACL in Brazil, as well as to model projections for future climate
125 change scenarios. The method considers the requirement of the species based on presence and on
126 the set of environmental variables (Phillips, Anderson & Schapire, 2006), providing
127 environmental variable response curves which indicate how each variable affects the predicted

128 distribution (Phillips & Dudík, 2008). MAXENT has been shown to be robust for ENM
129 construction from presence-only data (Elith et. al., 2006), and to describe of the ecological and
130 spatial relationships between species and environmental conditions.

131 MAXENT was applied under the ‘auto-features’ mode and the default settings, with 100-
132 fold replicates generated by bootstrap (Phillips & Dudík, 2008). The logistic output was used
133 (habitat suitability on a scale of 0–1), with higher values in the Habitat Suitability Map (HSM)
134 representing more favorable conditions for the occurrence of the *L. (N.) whitmani* or ACL. Two
135 models were developed: i) the *Lutzomyia whitmani* model (LWM), and ii) American Cutaneous
136 Leishmaniasis model (ACLM). Both models were developed using 10 environmental variables
137 and 80% of occurrence data for training and 20% for test.

138 In order to infer the effect of climate change on the distribution of *L. (N.) whitmani* and
139 ACL, each model was projected using both scenarios, RCP 4.5 and RCP8.5. For these
140 projections, the NDVI environmental variable was removed.

141 We assessed the accuracy of each model using the AUC (area under the receiver
142 operating characteristic [ROC] curve). Additionally, we used an independent set of 127 and 376
143 actual occurrence records, for *L. (N.) whitmani* and ACL human cases, respectively (randomly
144 selected from total points and not used in the generation of models), to evaluate the predictive
145 capacity of the models. The predicted suitability of the models was extracted for each test point,
146 and the average suitability was used to evaluate model accuracy.

147 For *L. (N.) whitmani* and ACL potential distribution binary maps (suitable/unsuitable)
148 were applied the Minimum Training Presence (MTP) as a threshold value for models, because it
149 is the most conservative threshold, identifying the minimum predicted area possible while still
150 maintaining a zero omission rate for both training and test data.

151 For comparative purposes, the images resulting from each model (with continuous values
152 from 0 to 1) were reclassified into five environmental suitability zones: (1) Unsuitable Zone
153 (UNSZ; value pixel suitability < Minimum Training Presence, MTP), (2) Low Suitability Zone
154 (LSZ, value pixel suitability between MTP value and 0.25), (3) Intermediate Suitability Zone
155 (ISZ, value pixel suitability between 0.25 and 0.50), (4) High Suitability Zone (HSZ, value pixel
156 suitability 0.50 and 0.75), and (5) a Very High Suitability Zone (VHSZ, value pixel suitability
157 >0.75).

158 **Model Comparison**

159 The generated models ACLM and LWM were compared using Fuzzy for continuous
160 maps, and Kappa index for categorical maps (suitable/unsuitable) using Map Comparison Kit
161 v.3.2, software developed by the Netherlands Environmental Assessment Agency (Visser & Nijs,
162 2006; Hagen, 2002; Hagen-Zanker, Straatman & Uljee, 2005). Both indices express the pixel
163 similarity for a value between 0 (fully distinct) and 1 (fully identical).

164 Additionally we used Olson et al.'s (2001) delineation of the terrestrial "Ecoregions of the
165 World" and the Brazilian biomes (IBGE) as base map to better demonstrate the comparison
166 between generated.

167

168 **RESULTS**

169 With an average AUC of 0.77 (SD = 0.004; 100-fold replicates), the ACLM achieved a
170 satisfactory model fit and the modeled distribution performed better than random. The predictive
171 capacity of ACLM, evaluated by the average suitability test of 0.53 (SD = 0.12) in each test
172 point, indicates that the model achieved high accuracy. This average value corresponds to the
173 High Suitability Zone for ACL. Based on the Minimum Training Presence (MTP = 0.07) cutoff
174 criteria (MTP = 0.07), the ACLM identified many of the regions of Brazil appropriate for the
175 occurrence of ACLM (Figure 1), covering 82.3% of the Brazilian territory. The LWM model
176 showed similar performance, mean AUC of 0.82 (SD = 0.006; 100-fold replicates) and average
177 suitability test of 0.54 (SD = 0.15), indicating satisfactory predictive capacity of both models
178 (Figure 1), covering 83.4% of the Brazilian territory.

179 The vegetation density index (NDVI) was the variable with the highest gain in the model,
180 when it was omitted or used alone, the significance of the ACLM model decreased. The response
181 curves for EV of this model indicate that ACL are strongly associated with intermediate density
182 vegetation areas, zones with Annual Precipitation (AP) between 800 to 1200 mm, Mean
183 Temperature of Coldest Quarter (MTCQ) above 16°C, and Annual Mean Temperature (AMT)
184 lower than 23°C (suitability of occurrence > 0.5) (Figure 2A; 3A).

185 *Lutzomyia (Nyssomyia) whitmani* was identified by the LWM model as a species that
186 occurs "prefers" (more suitable habitat) in regions with relative moderate rainfall (AP between
187 1000 - 1600 mm), intermediate density vegetation values (NDVI), and regions with MTCQ
188 between 15° - 22°C and AMT between 19° - 24°C (Figure 2B; 3A). These characteristics are in
189 accordance with previous analysis discussing the distribution of this sandfly vector in Brazilian
190 biomes, occurring in high frequency in Southern Brazil, Amazonian region, Caatinga and
191 Pantanal biomes showing low suitability and unsuitable areas (based on MTP = 0.06) in the
192 LWM.

193 Figure 1 shows the future predicted distributions for ACL and *L. (N.) whitmani* in 2050,
194 under both the RCP 4.5 and RCP 8.5 (HadGEM2-ES model) for future climate scenarios. For
195 ACL model these two projections differ moderately from current scenario (Fuzzy of 0.58 and
196 0.59, for RCP 4.5 and RCP 8.5 respectively) and are very similar to each other (Fuzzy of 0.75).
197 Similar results were found in the projections for *L. (N.) whitmani* (Figure 1), but with greater

198 similarity (Fuzzy of 0.74 and 0.64, for current model versus RCP 4.5 and RCP 8.5 respectively,
199 and Fuzzy of 0.77 between future climate scenarios).

200 Comparisons between the models for ACL and *L. (N.) whitmani* indicate high similarity.
201 Fuzzy of 0.77, between current models, and 0.77 and 0.78, for RCP 4.5 and RCP 8.5 scenarios,
202 respectively.

203 All the projections presented gain in area in the coverage of the Brazilian territory. *L. (N.)*
204 *whitmani* increases by 5% in the RCP 4.5 scenario and in 7.6% in the RCP 8.5 scenario. For
205 ACL the area gain values were relatively higher (12.3% and 15.5% area gain, RCP 4.5 and RCP
206 8.5 respectively).

207 Suitable areas (above MTP cutoff values) for *L. (N.) whitmani* are more extensive than
208 those suitable for ACL. Suitability areas for *L. (N.) whitmani* covers 7,113,644.7 km² of
209 Brazilian territory, 1.2% more than the suitability for ACL (7,025,688.6 km²). In future
210 projections, this behavior is repeated, but with higher gain values in the suitable area for this
211 vector (8.8% and 9.1%, RCP 4.5 and RCP 8.5 respectively).

212 Figure 4 shows the Most Dissimilar variables (MoD) between current and future climate
213 scenarios. The MoD for a point *P* is the variable with respect to which *P* has the smallest value
214 of similarity - i.e., the variable driving the dissimilarity result (Elith et al., 2010). For ACL and *L.*
215 *(N.) whitmani* the Mean Temperature of Warmest Quarter (MTWAQ), Mean Temperature of
216 Coldest Quarter (MTCQ) and Annual Mean Temperature (AMT) were the drivers of
217 current/future dissimilarity.

218 DISCUSSION

219 *Lutzomyia (Nyssomyia) whitmani* has the ability to "adapt" to environmental changes,
220 new ecological niches, tolerating and overcoming the effects of changes that constantly occur in
221 natural environments (Peterson & Shaw, 2003; Rebelo et. al., 2009). According to Peterson &
222 Shaw (2003), *L. (N.) whitmani*, *L. (N.) intermedia* and *L. migonei*, phlebotomines vectors of
223 ACL widely distributed in South America, in the year 2050 will have their climatic suitability
224 areas increased. These species are expanding to different areas of the continent, and Peterson &
225 Shaw, (2003) identified the southern direction as the most evident for *L. (N.) whitmani*. Our
226 results corroborate this study. However, when using data from the most recent occurrence of *L.*
227 *(N.) whitmani*, we show that it is predicted to expand even in the current model.

228 Therefore, the future projections of the LWM model indicate a larger area of expansion
229 of climatic suitability for *L. (N.) whitmani* for the northern region of Brazil, and reinforces the
230 trend of expansion towards the South, as described by Peterson & Shaw (2003). Other vectors of
231 ACL e present projections of future displacements towards higher latitudes, as observed in
232 sandflies from Central and North America (González et al., 2010; Moo-Llanes et al., 2013).
233 *Phlebotomus ariasi* showed increased abundance at higher latitudes in Central Spain. According
234 to the authors, the species would be migrating to these areas in order to compensate for the
235 increase in temperatures in the region (Gálvez et al., 2010). Carvalho et al., (2015) describes an
236 expansion of *Lutzomyia (Nyssomyia) flaviscutellata* to the south and southeast of Brazil in the
237 face of future climatic scenarios. Therefore, one can infer that the area of overlap between these
238 vectors (*L. (Nyssomyia) flaviscutellata* and *L. (N.) whitmani*) will be larger and more evident in
239 the future. Similarly, greater overlap between *L. (N.) whitmani* and *L. neivai* is expected for the
240 southern region, compared to future climate projections.

241 The results point to the predicted expansion of *L. (N.) whitmani* in the northern region,
242 especially the State of Amazonas: although future projections show that the Amazon region will
243 become drier, as a consequence of the increase in intensity and duration of the dry season
244 (Joetzjer et al., 2013), *L. (N.) whitmani* remains present in the region and will have a more
245 extensive climatic suitability area in the future. Considering the extensive latitudinal range of
246 Brazil, regional climates play an important role in the definition of species distribution.
247 According to Carvalho, Rangel & Vale (2016), most projections of climate change endorse that
248 vectors of diseases will find good climatic conditions for their geographic expansion in the
249 higher latitudes during the coming decades.

250 In relation to the epidemiology of ACL in Brazil, the disease expansion process is related
251 to environmental changes with new human cases being registered in areas of recent
252 deforestation, mining, hydroelectric plant construction and population settlements (Brazil, 2013;
253 Rangel & Lainson, 2009). These changes in the transmission pattern favor the dispersion of wild
254 animals and sandflies mainly to the peridomestic environment, where new transmission cycles
255 can be established close to houses (Brazil, 2013). In this case, *L. (N.) whitmani* and *L. (N.)*
256 *flaviscutellata* would be particularly good examples of species, in different epidemiological
257 situations (Rangel et al., 2014). This relationship is identified in the ACLM model by the strong

258 relation of the most suitable areas for ACL with areas of intermediate vegetation cover density.
259 Therefore, the most conserved Amazonian areas are identified as unsuitable.

260 Future projections for ACL indicate an expansion to northwestern Brazil. This is more
261 evident in the RCP 8.5 scenario, which is more pessimistic in relation to policies to control the
262 emission of greenhouse gases, adding 15.5% to the total area of occurrence of the disease. The
263 lack of future scenarios of the change in density and/or vegetation cover, in the way of those that
264 exist for climatic data, made it impossible to quantify the role of changes in forest cover in future
265 forecasts. However, the known and progressive environmental degradation, associated with
266 future climate predictions that indicate that the Amazon region will tend to become more suitable
267 climatically for both ACL and *L. (N.) whitmani*, design a scenario of higher risk of cases of
268 disease.

269 The larger distribution predicted in the models for *L. (N.) whitmani* in regard to ACL
270 epidemiology, is possibly related to the sole presence of the vector not being deterministic for the
271 disease. Other factors influence pathogen transmission as well as the development of the disease.
272 However, the little difference between the areas identified as adequate for *L. (N.) whitmani* and
273 ACL, associated with the high similarities between the models reinforce the geographical
274 importance of this vector in the transmission of ACL.

275 CONCLUSION

276 Regardless of whether it is a complex of cryptic species or not (Lainson, 1988), it is a fact
277 that *L. (N.) whitmani* has a wide geographic distribution, occurs in all five Brazilian regions, and
278 is an important ACL vector in Brazil. In this context, and in view of the geographic expansion
279 projected for the future, the models reinforce the importance of *L. (N.) whitmani* spatialization in
280 the transmission of ACL in Brazil, and confirm that this ACL vector is well established in the
281 Brazilian territory and will most likely maintain this behavior in the expected climate change.

282 Although climate change scenarios show that Amazon region will become gradually drier
283 (Joetzjer et al., 2013), the presented results indicate that *L. (N.) whitmani* will remain present in
284 the region and should expand its area of climate suitability in the future.

285 The models were able to identify that continuous process of environmental degradation
286 favors the establishment of *L. (N.) whitmani* and the occurrence of ACL. Future projections of
287 ACL models indicate the ongoing process of disease expansion in the face of the predicted
288 climatic changes and reinforce the broad geographical expanse of the disease. In this view and

289 associated with the new epidemiological patterns resulting from the drastic environmental
290 changes (coupled with the presence of highly adapted vectors, reservoirs, and parasites) the
291 epidemiological scenario for ACL indicates a continuous increasing of human cases.

292 Several evidences have suggested that epidemiology of vector-borne diseases are
293 dependent on global climate changes (Gálvez et al., 2010; Gálvez et al., 2011; González et al.,
294 2010). Policies for monitoring / controlling neglected diseases, such as leishmaniasis, should be
295 aligned with agendas committed to assessing climate, besides environmental changes (WHO,
296 2011)

297 Considering that changes in the climate can impact the ecoepidemiology of leishmaniasis
298 (WHO, 2010), the results discussed here should be assessed in vector surveillance actions,
299 contributing to the promotion of health in risk areas for ACL associated to *L. (N.) whitmani* ,
300 projected for future scenarios in Brazil.

301

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306

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453 health.
- 454

Table 1 (on next page)

Environmental Variables (EV)

Environmental Variables (EV) used to model the potential distribution of *Lutzomyia (N.) whitmani* and American Cutaneous Leishmaniasis in Brazil. All variables were resampled from original resolution to 0.04° (~5km), using the average value of all involved pixels, where the source pixels are covered by the target pixel.

1

Environmental Variable (EV)	Acronym	WorldClim Acronym	Source
Annual Mean Temperature	AMT	BIO1	WorldClim (Hijmans et al.,2005)
Mean Temperature of Wettest Quarter	MTWEQ	BIO8	
Mean Temperature of Driest Quarter	MTDQ	BIO9	
Mean Temperature of Warmest Quarter	MTWAQ	BIO10	
Mean Temperature of Coldest Quarter	MTCQ	BIO11	
Annual Precipitation	AP	BIO12	
Precipitation of Wettest Quarter	PWQ	BIO16	
Precipitation of Driest Quarter	PDQ	BIO17	
Altitude - Digital Elevation Model	ALT	--	
MODIS Normalized Difference Vegetation Index (NDVI)-32 day composites-Oct/15 - Nov/15/2004. Date of the composite represents well the contrast between forest and open formations.	NDVI	--	Global Land Cover Facility (GLCF) (http://www.landcover.org/data/modis/)

2

Figure 1

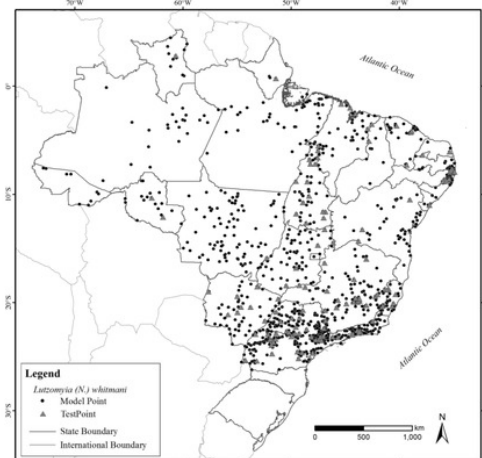
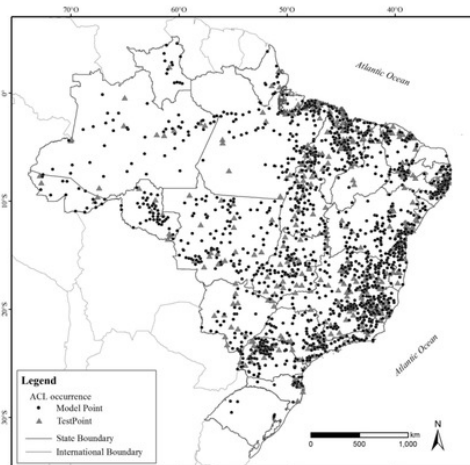
American Cutaneous Leishmaniasis (ACL) and *Lutzomyia (N.) whitmani* (LW) Models

Environmental suitability for American Cutaneous Leishmaniasis (ACL) and *Lutzomyia (N.) whitmani* (LW) in Brazil. Current conditions and future climate projections

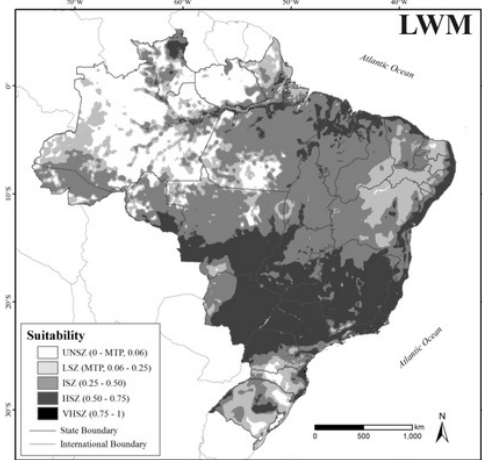
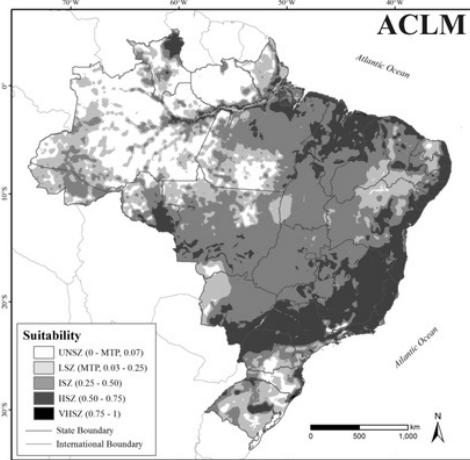
American Cutaneous Leishmaniasis (ACL)

Lutzomyia (N.) whitmani (LW)

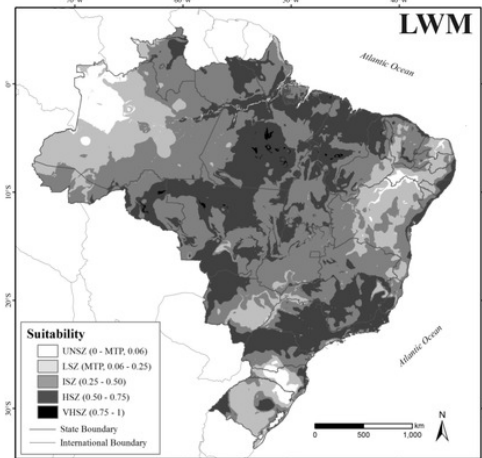
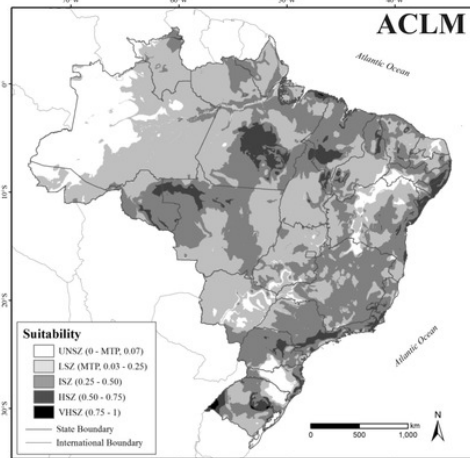
Occurrence data



Current Model



RCP 4.5 future climate projection



RCP 8.5 future climate projection

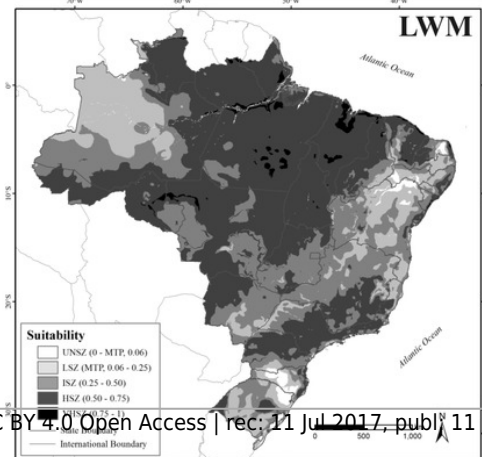
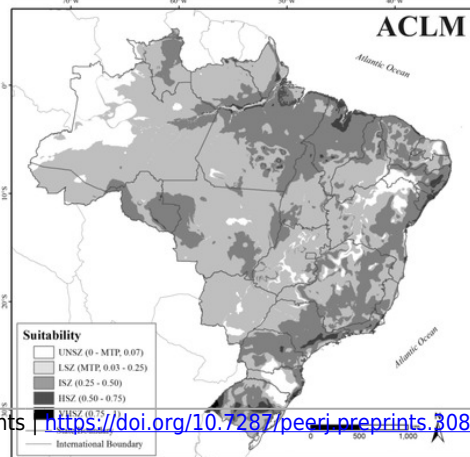


Figure 2

Response-curves of the variables in the American Cutaneous Leishmaniasis Model (ACLM), and *Lutzomyia (N.) whitmani* Model (LWM)

Response-curves of the variables in the (A) American Cutaneous Leishmaniasis Model (ACLM), and (B) *Lutzomyia (N.) whitmani* Model (LWM). Normalized Difference Vegetation Index (NDVI), Annual Precipitation (AP - BIO12), Mean Temperature of Coldest Quarter (MTCQ - BIO11), Annual Mean Temperature (AMT - BIO1). These curves show how each environmental variable affects the MAXENT prediction when all environmental variables are used to build the model

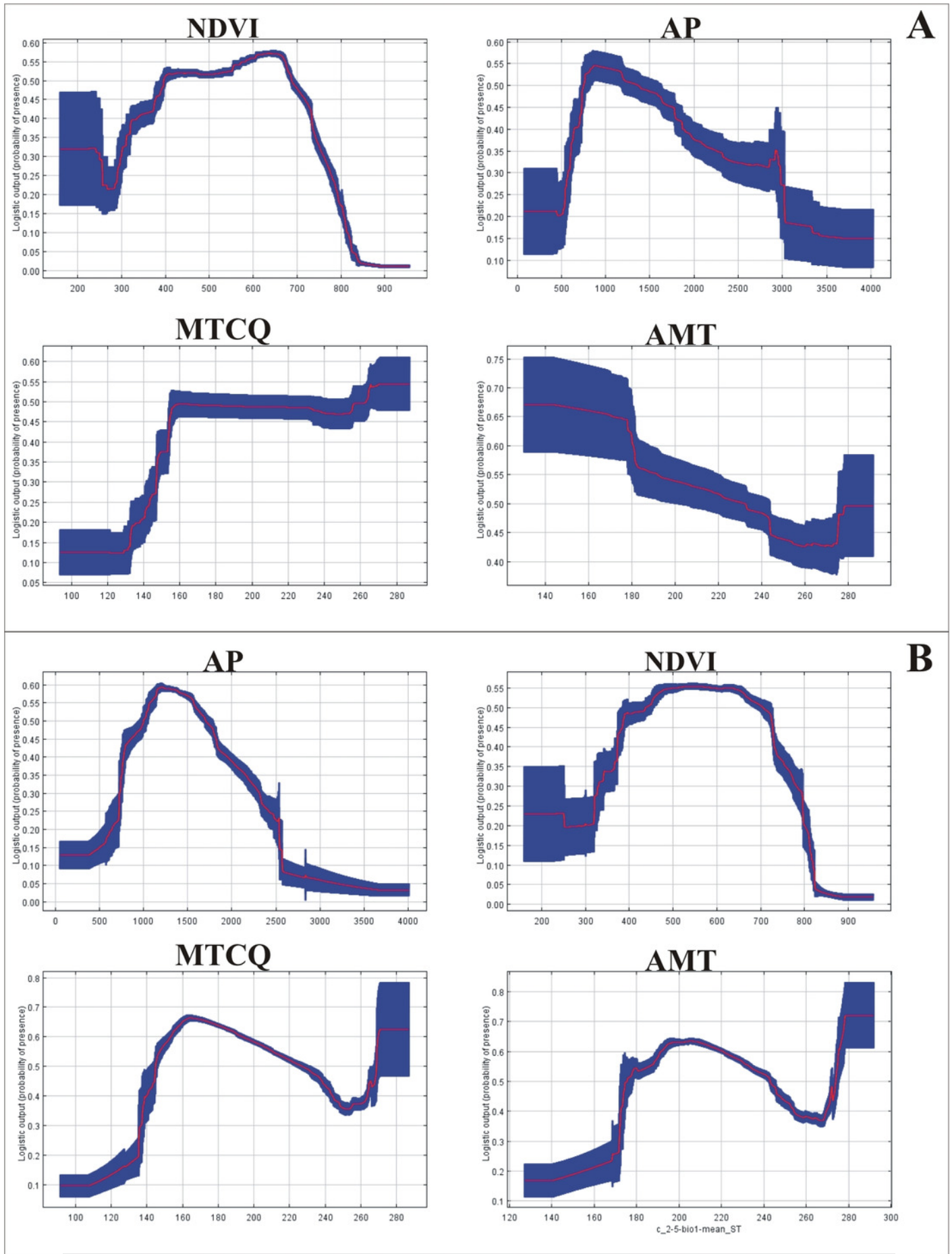
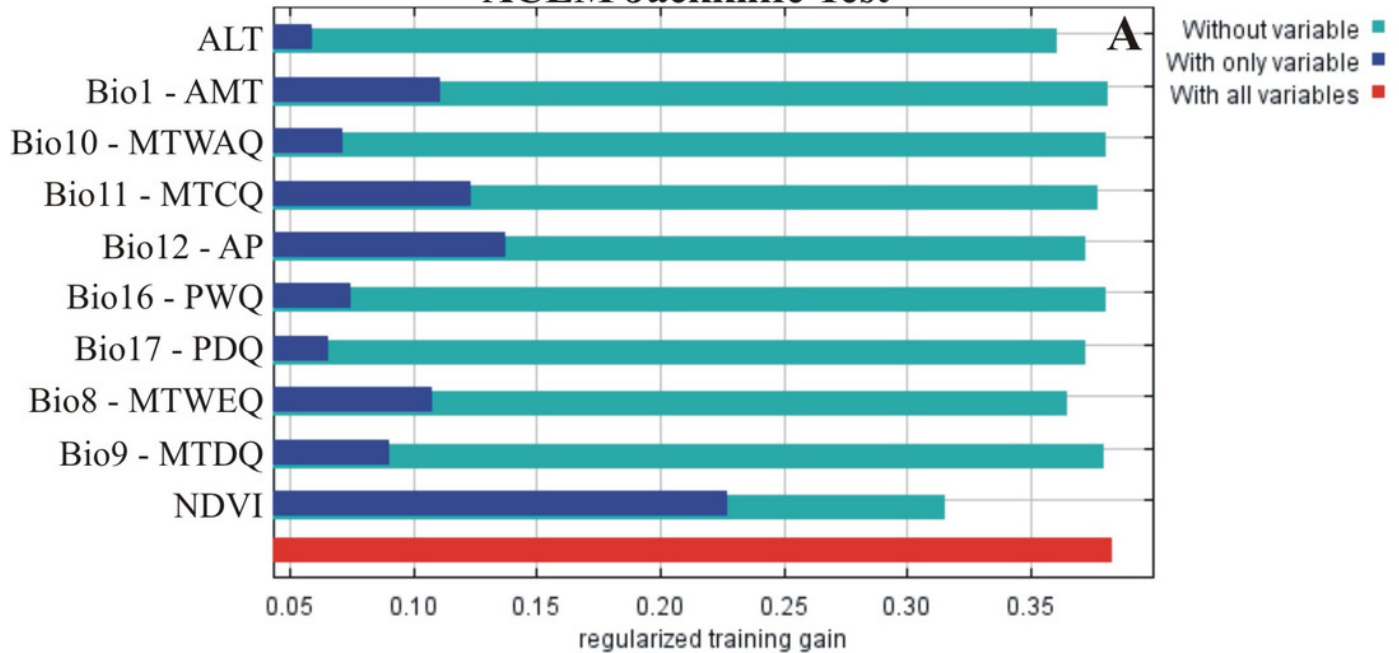


Figure 3

Jackknife test results of individual environmental variable importance in the development of the MAXENT models

Jackknife test results of individual environmental variable importance in the development of the MAXENT models relative to all environmental variables (red bar), for each predictor variable alone (blue bars), and the drop in training gain when the variable is removed from the full model (lighter blue bars). A) American Cutaneous Leishmaniasis Model (ACLM) and B) *Lutzomyia (N.) whitmani* Model (LWM) jackknife test results

ACLM Jackknife Test



LWM Jackknife Test

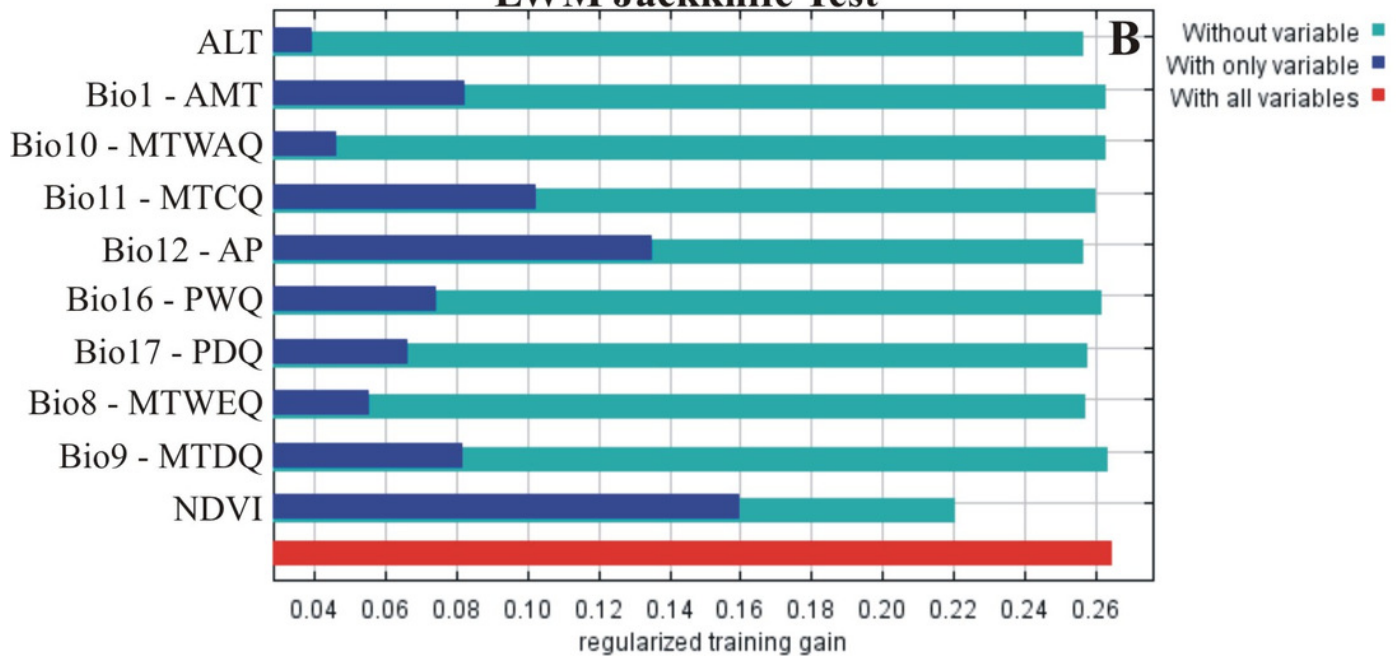


Figure 4

The most dissimilar variables (MoD) between current and future climate scenarios

The most dissimilar variables (MoD) between current and future climate scenarios - i.e., the variable driving the dissimilarity result

