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The impact of climate change on the geographical distribution of two vectors of Chagas disease: implications for the force of infection

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Chagas disease, caused by the parasite *Trypanosoma cruzi*, is the most important vector-borne disease in Latin America. The vectors are insects belonging to the Triatominae (Hemiptera, Reduviidae), and are widely distributed in the Americas. Here, we assess the implications of climatic projections for 2050 on the geographical footprint of two of the main Chagas disease vectors: *Rhodnius prolixus* (tropical species) and *Triatoma infestans* (temperate species). We estimated the epidemiological implications of current to future transitions in the climatic niche in terms of changes in the force of infection (FOI) on the rural population of two countries: Venezuela (tropical) and Argentina (temperate). The climatic projections for 2050 showed heterogeneous impact on the climatic niches of both vector species, with a decreasing trend of suitability of areas that are currently at high-to-moderate transmission risk. Consequently, climatic projections affected differently the FOI for Chagas disease in Venezuela and Argentina. Despite the heterogeneous results, our main conclusions point out a decreasing trend in the number of new cases of *Tr. cruzi* human infections per year between current and future conditions using a climatic niche approach.

1. Introduction

Understanding the link between climate and infectious diseases has become increasingly urgent given the predicted direct effects of climate change on vector-borne and zoonotic diseases [1]. Climate change affects not only interactions between pathogens and humans, but also those between pathogens and vectors (or other intermediate host species) [2,3]. The magnitude and direction of changes in climatic variables on host and vector populations are locally variable and depend upon interactions with physical (e.g. temperature and precipitation) and biological (e.g. competitors and predators) variables [4]. Vectorial transmission is one of the main routes of *Trypanosoma cruzi* (*Tr. cruzi*), the aetiological agent of Chagas disease, which affects six to eight million people in Latin America [5].

Chagas disease vectors belong to the Triatominae (Hemiptera, Reduviidae) that contains more than 140 species, grouped into 18 genera and five tribes [6,7]. With a few exceptions, triatomines have strict haematophagous feeding regime based primarily on the blood of birds and mammals, including rodents, edentates and carnivores as well as humans [8,9]. Triatomines inhabit a variety of environments (from wild to domestic and peridomestic habitats), and they are well adapted to a variety of climates. Although most triatomine species are distributed in inter-tropical areas, they also reach temperate regions with cold winters such as Patagonia (Argentina) and Indiana and Maryland (USA)

[10,11]. From an epidemiological perspective, *Rhodnius prolixus* (in Central America and northern South America) and *Triatoma infestans* (in the Southern Cone region of South America) are the most important vector species [12–14]; the former is adapted to tropical regions, whereas the latter is adapted to temperate regions.

The current geographical distributions of *R. prolixus* and *T. infestans* are coincident with high-risk areas of Chagas disease transmission that, in general, exhibit the highest human *Tr. cruzi* prevalence. The geographical ranges of these two species are well differentiated: *R. prolixus* is typically found from 18° to –3° latitude and –96° to –53° longitude, whereas *T. infestans* was originally found (before the Southern Cone Initiative) from –11° to –46° latitude and –76° to –51° longitude. *R. prolixus* inhabits from 0 to 2600 m.a.s.l. in regions with annual mean temperatures from 11°C to 29°C and annual mean precipitation from 250 to 2000 mm [15,16]. *T. infestans* inhabits from 0 to 4100 m.a.s.l. [11], in regions with annual mean temperature from –1.6°C to 27.1°C and annual mean precipitation from 0.5 to 2910 mm. Although *T. infestans* was considered an almost exclusively domiciliated species, sylvatic foci are increasingly found in endemic areas [17]. In the context of climate change, it is therefore likely that the geographical distributions of both species will be affected.

The effects of environmental variables, such as temperature and precipitation, on physiological and behavioural processes have been widely demonstrated for *R. prolixus* and *T. infestans*. In particular, temperature has been found to be related to thermal preference processes [18–20], as well as host finding, feeding, egg production, hatching rate, immature development time, cessation of moulting and metabolic rate processes [21–28]. Climate change could therefore have effects on vital processes and consequently on the potential geographical distribution of both species, affecting ultimately the areas of *Tr. cruzi* transmission. The study of the climatic niche of key vector species would provide insights not only for understanding the current geographical dimensions of disease transmission, but also to infer epidemiological changes under future conditions.

Ecological niche modelling (ENM) arises as a valuable tool in this respect by permitting exploration of geographical and ecological phenomena based on known species' occurrences [29,30]. ENMs attempt to predict the fundamental niche of a species (defined as the set of biotic and abiotic environmental conditions under which populations can be maintained without immigration) [31] and predict the *climatic niche* when they are based only on climatic variables [32]. Hereafter, the outcome of the niche models (i.e. the probability of finding a climatically suitable niche for each species) will be referred to as the *climatic niche* or simply *suitability*. In addition, ENMs are useful to test hypotheses regarding the role of different environmental variables in shaping species distribution patterns [33–36]. In the past decade, ENMs have been broadly applied to understand various aspects of Chagas disease transmission, including the characterization of vector species niches under current and future climate conditions [37,38], and the relationships between vector and reservoir distributions [39–41].

Since the 1950s and 1960s, chemical control campaigns have reduced domestic and peridomestic infestation by *R. prolixus* in Venezuela [42,43]. Similarly, a regional effort to eliminate *T. infestans* achieved interruption of vectorial transmission in many Southern Cone countries [44]. However, those areas where interrupted *Tr. cruzi* transmission has been certified are under a reactivation transmission risk owing to

either reinvasion of houses by relict sylvatic vector populations or through the replacement of the main vector species by other species (*Panstrongylus megistus*, *T. brasiliensis*, *T. pseudomaculata* and *T. sordida*) [43,44]. In Venezuela and Argentina, active *Tr. cruzi* transmission is mainly restricted to some states/provinces, whereas others have been certified as free of active transmission. Nevertheless, several authors have recently questioned this certification, pointing out that the current situation could be modified under future epidemiological scenarios [45].

Much of the research on the effects of global climate change on vector-borne diseases have focused on potential vector species' range shifts [46]. Some of these studies have presented the results of climate change impacts in terms of 'vulnerability', usually in the form of maps highlighting changing vector distributions [47]. Other studies, such as [48], have combined geographic information system (GIS) and survey analyses to evaluate the role that temperature variability and disease awareness among physicians play in the potential emergence of Chagas disease in the USA. In this paper, we use the most direct indicator of the rate at which susceptible individuals acquire the *Tr. cruzi* parasite, namely the force of infection (FOI). This concept is reflected by the rise in seropositivity with age in a given community, a relatively common epidemiological indicator in most public health statistics in most Latin American countries with respect to Chagas disease. Thus, the main goal of this study is to assess the impact of bioclimatic variables projected for 2050 on the climatic suitability of *R. prolixus* and *T. infestans*, and subsequently to estimate the epidemiological implications in terms of projected changes in the FOI of Chagas disease, and its corresponding incidence changes, in Venezuela and Argentina.

2. Material and methods

(a) Study areas

Venezuela and Argentina were selected based on the criterion that both are characterized by well-differentiated climatic conditions as well as by the presence of one dominant Chagas disease vector species. Our analyses were restricted to country level to avoid the use of heterogeneous epidemiological data provided by different health sources, to reduce uncertainties and to improve our epidemiological inference. In Venezuela, we analysed 12 states considered as high-risk areas with active vectorial transmission [42]. These states (Barinas, Carabobo, Anzoátegui, Portuguesa, Guárico, Lara, Yaracuy, Aragua, Trujillo, Falcón, Mérida and Cojedes) are located mainly along the Venezuelan 'llanos', which are tropical grassland plains characterized by piedmont features [49]. In Argentina, we analysed 13 provinces considered to be at high-to-moderate risk of vectorial transmission, located mainly along central and northern areas of the country [50]. These provinces (Córdoba, Formosa, Santiago del Estero, Mendoza, Tucumán, Misiones, Corrientes, Chaco, Salta, San Luis, San Juan, Catamarca, and La Rioja) are placed across three biogeographic provinces: Chaco, Espinal and Monte [51].

(b) Triatomine species and epidemiological data

Geographical distribution data of *R. prolixus* and *T. infestans* were obtained from the atlas of Carcavallo *et al.* [11] that consists of maps depicting the geographical range of 115 triatomine species at a resolution of 1:3 700 000. This information was digitized and a database built, at a resolution of 0.1° (approx. 10 km), by assigning to each species a presence value for all the geographical space occupied by the species in the range maps, resulting in 47 000 and 24 819 presence points that were available for

analysis for *T. infestans* and *R. prolixus*, respectively. We are aware that not all these points are actual presence points, for a certain fraction of them may be ‘pseudo-presences’; in §4, we consider the possible prediction errors that may result, and how they compare with prediction errors resulting from the use of confirmed presence occurrences that may involve pseudo-absences. To deal with the potential over-fitting of the niche models, we randomly selected 5% of our data, resulting in 1240 presence points for *R. prolixus* and 2350 presence points for *T. infestans* (available at http://figshare.com/articles/Original_data_points_for_MaxEnt_5_of_total_coordinates_/1009053). Both subsamples included presence points of the complete distribution range (central and marginal areas) of each species [52].

To gather the required entomo-epidemiological information, we searched all relevant bibliographic sources (national and international journals, congress proceedings, university graduate theses, workshop summaries, and national and international reports on Chagas disease). Additionally, in the case of Venezuela, we used entomo-epidemiological information available from the database of the Ministry of Public Health of Venezuela (made available by staff members of the Directorate of Environmental Health, who participated in a preliminary analysis of this database [42,53]) covering a 16-year period (1990–2005). In the case of Argentina, because there is currently no centralized database equivalent to that of Venezuela, and data from various data sources in publications and reports were insufficient for model fitting, we additionally included some publications from neighbouring countries (Bolivia, Brazil, Chile and Paraguay).

(c) Environmental data

Bioclimatic data layers [54] downloaded from WorldClim (<http://www.worldclim.org/>) were used as predictor variables to apply the climatic niche models to *R. prolixus* and *T. infestans* for current (average for 1950–2000) and 2050 (average for 2041–2060) conditions. For future climate conditions, we considered the representative concentration pathways (RCPs) 4.5, 6.0 and 8.5 [55] (hereafter scenarios), and we used the bioclimatic projections of the HadGEM2-ES model [56] for 2050. These projections are the result of downscaling and calibration of the most recent global circulation model used in the last report of the IPCC [55]. All bioclimatic variables were applied at 30 arc-second (approx. 1 km²) resolution. Despite the scale of our analysis being regional (national coverage), we decided to use a fine grain of 30'' spatial resolution because of the importance for the triatomines of local climatic conditions; de la Vega *et al.* [57] have linked geographical distribution to physiological traits in the same two species analysed here, and WorldClim generated the climatic data through interpolation of average monthly climate data from weather stations also on a 30 arc-second resolution grid.

(d) Multi-collinearity analysis

We performed a principal component analysis (PCA) among the 19 bioclimatic variables that could be potentially associated with the occurrence of each species [58]. This PCA summarized the complete set of variables into a smaller number of components and selected only the first two components that accounts for at least 65% of the explained variance. All analyses were carried out using Statgraphics CENTURION XVI (v. 16.1.18) [59].

(e) Ecological niche modelling for current and future climate conditions

We used MAXENT (v. 3.3.3k) [60] to predict the climatic niche for *R. prolixus* and *T. infestans* under current and future conditions. MAXENT uses a maximum entropy algorithm that has been shown to be robust for ENM construction from presence-only data [34], and this also allowed us to fit models using future

climatic projections based on current distribution [61,62]. Because there was at most one sample per pixel, MAXENT was run with auto features and the most relevant settings, including 10 000 background points, were kept at default values. We used 10-fold cross-validation run type, selecting the average response of these 10 replicates. This replication allows taking data uncertainty into account, especially considering that range maps tend to have larger commission errors. Additionally, we selected the Jackknife procedure to quantify the contribution of each bioclimatic variable to each model. The goodness-of-fit of the model's predictions was evaluated using the partial area under the curve (pAUC) procedure as described by Peterson *et al.* [63], because the use of the whole AUC of the receiver operating characteristic curve has been criticized [64]. To estimate the pAUC (calculated as the ratio between the AUC of the restricted receiver operating characteristic (ROC) curve and the AUC of the restricted null model), we used the same number of data points as used for testing in MAXENT but with a set of points independent of the one used for training, and we counted the absolute frequency of predicted suitability. Then, pAUC ratios were estimated by bootstrapping a 50% of presence points, based on 1000 iterations, with an omission threshold (*E*) of 5%, using a program developed by Barve [65], and kindly provided by Abdallah M. Samy.

We also tested the accuracy of MAXENT's results using an independent dataset for each species. For *R. prolixus*, the independent dataset consisted of 777 points extracted from the database of the Venezuelan Ministry of Public Health (see §2b). For *T. infestans*, the independent dataset consisted of 104 field collected points from different sources between 2002 and 2012 (Gerardo Marti, Universidad Nacional de La Plata, personal communication, 2014) as well as 19 records we collected from La Plata Museum, National University of La Plata, Argentina (data available at http://figshare.com/articles/Independent_data_set_of_occurrence_points_T_in_festans_and_R_prolixus/1152725). We used the 10th percentile training presence logistic threshold of MAXENT's average model to classify ‘presence’ and ‘absence’ points; thus, a coordinate where suitability was higher than the threshold was classified as ‘presence point’, whereas a coordinate where suitability was lower than the threshold was classified as ‘absence point’. For each coordinate of the independent dataset used to test accuracy, we extracted the suitability produced by the MAXENT model and then estimated the sensitivity by assessing the relative frequency of suitability values higher than the threshold value.

To analyse suitability changes between current and 2050 conditions, we classified habitat suitability into three equally sized classes (0–0.33 = low, 0.33–0.66 = medium and 0.66–1 = high). The transitions between these classes from current to future conditions express climate-related suitability changes, and these were mapped to help facilitate the visualization (QGIS Desktop, v. 2.0.1 software) [66]. We also estimated the relative frequency of each categorical transition to quantify the impact of climate change on the potential suitability of each species. For both species, we compared the relative frequency of each categorical transition among the three different scenarios [67].

(f) Entomo-epidemiological analysis

Conversion from climatic suitability to the transmission risk of *Tr. cruzi* was through the FOI, which was undertaken via two methods: (i) a one-step approach directly relating suitability and FOI, and (ii) a two-step approach, which first relates suitability with household vector density, and then vector density with FOI.

(i) The one-step method

To directly estimate FOI, we used the Grenfell & Anderson [68] model that requires data on human prevalence by age class. This model is derived from the simple catalytic model of

Muench [69], which originally assumed that the FOI $\lambda(a)$ (defined per susceptible individual per unit time) is constant and independent of age a ; Grenfell & Anderson [68] generalized this model to a polynomial function (of degree k) of the form

$$\lambda(a) = \sum_{i=0}^k b_i a^i \left. \begin{array}{l} (L < a \leq U) \\ \text{and } \lambda(a) = 0 (a \leq L), \end{array} \right\} \quad (2.1)$$

where U is the upper age limit of human life expectancy (i.e. the oldest age class for which data are available), the lower age threshold L accounts for maternally derived antibodies in children born from mothers who have experienced infection and the b_i s are parameters to be estimated; $\lambda(a)$ is set to zero below L . This model was used to assess whether the FOI estimated from field prevalence data demonstrates a direct relationship with suitability.

We obtained relevant prevalence data from the database of the Ministry of Health of Venezuela, whereas for Argentina we examined appropriate publications and reports (as described in §2b.e). Inclusion criteria for selection were based on, wherever possible: (i) a minimum of six individuals per age class for the calculation of age-class-specific prevalence, (ii) rejecting data with two or more successive age classes with 0% prevalence (particularly in the older age classes), (iii) pooling different years of the same locality (where available), (iv) deleting all houses with any record of recent spraying with insecticide and (v) an available association with a system of geographical coordinates. This data selection process aimed to provide a more homogeneous prevalence dataset (available at http://figshare.com/articles/T_infestans_and_R_prolixus_data/1024617). Once $\lambda(a)$ was estimated, and as each $\lambda(a)$ was associated with a given geographical coordinate, we looked for a relationship between suitability and FOI. In most cases, because the data were extremely variable (e.g. from different periods and various social, environmental and control activity situations), we first divided suitability values into equal length classes (between zero and one) and calculated the mean FOI for each class. Preliminary analyses showed a tendency for FOI to flatten out at high suitability values, so we fitted a more flexible sigmoidal-shaped curve, namely the generalized logistic model of the form

$$y = A + \frac{C}{(1 + Te^{-B(x-M)})^{1/T}}, \quad (2.2)$$

where y is the dependent variable (FOI here), x the independent variable (climatic niche here), A the lower asymptote, C the upper asymptote, M the point of maximum rate of change, B the rate of change and T the point near which asymptotic maximum rate of change occurs. Because we expect FOI = 0 for zero suitability, we *a priori* set $A = 0$ and used the Solver tool within Microsoft EXCEL (with the GRG nonlinear solving algorithm) to calculate the sum of squares (SSQs) as the goodness-of-fit criterion.

(ii) The two-step method

Step 1. Relationship between suitability and vector density

We proceeded in two phases: (i) relating climatic suitability and entomological household infestation, and (ii) relating household infestation to vector density per house. For the former relationship, we could not find any previous analyses relating these two variables, either for Chagas disease vectors or any other disease vectors. As climatic suitability reflects the potential niche of a vector species, we decided to use climatic suitability as a surrogate for the proportion of infested houses.

The second relationship (house infestation to vector density) is motivated on the basis that population size and the extent of regional occupancy by a species are correlated such that a positive occupancy–abundance relationship generally exists [70]. Additionally, it has been established that total population size

typically rises faster than occupancy, so that more widely distributed species have higher local densities at sites where they occur than those more restricted in their distribution [71–75]. This pattern has been documented in a large and rapidly growing number of empirical ecological studies [70], providing patterns with a high level of generality, and several mechanisms have been proposed to explain this relationship [76,77].

For Venezuela, we also checked whether other factors (such as house construction material and domestic animal presence) affected the density of bugs per house. In addition, we scaled the bug household density estimated from the infestation per house values in the database of the Ministry of Health of Venezuela; because the number of bugs collected was the result of one man-hour effort, we converted these numbers into actual bug densities per house. It was shown in Rabinovich *et al.* [78] that for *R. prolixus* (and in similar rural houses to those referred to in the database used here), this proportion was, on average (pooling different instars and places within a house), approximately 10:1 (actual density per house: collected bugs per house with one man-hour effort), and we therefore adjusted accordingly.

Step 2. Relationship between vector density and transmission risk of Trypanosoma cruzi. To convert from bug density per house to FOI, we adopted the model of *Tr. cruzi* transmission in Rabinovich *et al.* [79], a binomial transmission model in which neither the vector nor host population dynamics are explicitly considered. Model output is captured by the transmission risk R (the daily probability of seropositive conversion of a susceptible individual per unit time; equivalent to the FOI) as a function of the daily probability P that a susceptible individual suffers an infection if bitten by an infected bug, as

$$R = 1 - (1 - P)^n, \quad (2.3)$$

where n is the number of daily bites by an infected bug on a susceptible individual (and we consider the household as the unit of transmission). Here, n depends on several factors: (i) the average number of bugs per house V , (ii) the average proportion of bugs that are infected I , (iii) the number of bites an average bug makes per day f , (iv) the average proportion of bites that are made on humans F and (v) the average number of susceptible people in the household H . We used the estimate of P for *T. infestans* in Argentina from Rabinovich *et al.* [79] as 0.00198 (95% CI: 0.00029–0.00367) and because there are currently no estimates of P for *R. prolixus*, we assumed close similarity between the species and adopted a rounded value of $P = 0.002$. The value of n was calculated using the formula proposed by Rabinovich *et al.* [79]:

$$n = \frac{VI f F}{H}. \quad (2.4)$$

Although, in reality, factors influencing n are likely to vary spatially and temporally, we assume for this analysis (for projections over many decades) that these values remain approximately constant (except for V , which is calculated in Step 1 as a function of suitability); we assume standard literature values for Venezuela and Argentina as $I = 0.2$, $F = 0.5$, $f = 0.143$ (equivalent to bugs feeding once every 7 days), and $H = 4.6$ (which is multiplied by 0.9, the average proportion of susceptible individuals per household). Because the contact rate was defined per day, n was multiplied by 365 to convert R to an annual value. We calculated the FOI for states/provinces at high-to-moderate risk of vectorial Chagas disease transmission in Venezuela and Argentina. To estimate the expected number of new cases in 2050, we first linearly projected the current rural population (considered to be the more vulnerable population owing to the higher relative vector exposure compared with urban populations) by a demographic factor of 0.61 in Argentina [80] and 0.74 [80] in Venezuela. We then estimated the average FOI for those states/provinces at high *Tr. cruzi* transmission risk using QGIS Desktop (v. 2.0.1) [66]. Finally, we estimated the total number of new cases of *Tr. cruzi* as the product of the rural

population size for each state/province and the corresponding average localized FOI, repeating for both the current and 2050 conditions. We also estimated the ‘relative contribution’ (%) of each state/province to the overall predicted incidence, as the ratio of the predicted number of new cases per state/province and the total number of new cases across all states/provinces at high *Tr. cruzi* transmission risk, for current and 2050 conditions.

3. Results

(a) Changes in climatic suitability for *Rhodnius prolixus* and *Triatoma infestans*, from current to 2050 conditions

PCA indicated that 15 of 19 bioclimatic variables on the first two principal components account for 68.8% and 73.8% of the explained variance for *R. prolixus* and *T. infestans*, respectively. For both species, the ENMs were based on the following 15 variables: bio01, bio03, bio05, bio06, bio08, bio09, bio10, bio11, bio12, bio13, bio14, bio16, bio17, bio18, bio19 (see §1 in the electronic supplementary material). For both species, comparison of suitability changes between the RCP4.5, RCP6.0 and RCP8.5 scenarios revealed no significant differences using a non-parametric test (see §2 in the electronic supplementary material; table S1 shows suitability statistics per scenario and per species, and electronic supplementary material, table S2 shows confidence intervals of the suitability differences between pairs of scenarios). Therefore, we restricted our analysis only to the intermediate scenario (RCP6.0), which considerably reduced the amount of data handling, processing and storage. Despite full analysis being restricted to scenario RCP6.0, tables S3 and S4 in §3 of the electronic supplementary material summarize the relative frequency of each class of suitability transitions from current to 2050 for *T. infestans* and *R. prolixus*, under the three climatic scenarios.

The average MAXENT model fitted for current climate conditions showed a pAUC ratio of 1.001 and 1.055 for *R. prolixus* and *T. infestans*, respectively (table 1). The accuracy of the model’s predictions tested by the independent dataset showed that for *R. prolixus*, 84.2% of coordinates with confirmed presence were predicted as ‘presence points’ (i.e. suitability values were higher than the 10th percentile training presence logistic threshold), whereas for *T. infestans*, 93.5% of the coordinates with confirmed presence were predicted as ‘presence points’ (electronic supplementary material, see §4).

The most important bioclimatic factors for both species (after application of the Jackknife procedure) were mainly related to temperature and, to a lesser extent, precipitation. For *R. prolixus*, the most important variable was the minimum temperature of the coldest month, followed by isothermality, mean temperature of the driest quarter, mean temperature of the coldest quarter, precipitation of the wettest month, precipitation of the wettest quarter and annual precipitation. For *T. infestans*, the most important predictor variable was the mean temperature of the coldest quarter, followed by isothermality, and the minimum temperature of the coldest month.

For Venezuela, estimates of suitability ranged from 0.029 to 0.75 (mean 0.50, standard deviation (s.d.) 0.099, coefficient of variation (COV) 19% and $N = 10\,745$) for the current conditions, and between 0.023 and 0.83 (mean 0.59, s.d. 0.16, COV 26%, and $N = 10\,745$) for 2050. For Argentina,

Table 1. Summary of statistics describing the pAUC ratios from omission threshold of 5% and 1000 bootstrap replicates, for *R. prolixus* and *T. infestans*.

	<i>R. prolixus</i>	<i>T. infestans</i>
minimum	0.9674	1.0292
maximum	1.0169	1.0923
mean	1.0014	1.0551
standard deviation	0.0132	0.009

suitability ranged from 0.0047 to 0.67 (mean 0.49, s.d. 0.14, COV 29%, $N = 24\,957$) for the current conditions, and between 0.0058 and 0.84 (mean 0.41, s.d. 0.16 COV 30%, $N = 24\,957$) for 2050.

Both species show unchanged medium suitability transition class as the dominant one between current and 2050 conditions (figure 1). The relative frequency of this transition class was 46% for *R. prolixus* and 71% for *T. infestans*.

For *R. prolixus*, current states at high-risk transmission (located along the ‘llanos’ on the northwest of Venezuela) show a 6% decrease from medium-to-low suitability in future climatic conditions (figure 1a), whereas current states at low risk (i.e. Amazonas, Bolivar and Apure located in the centre and southeast of Venezuela) show a 40% increase from medium-to-high suitability under future climatic changes. For *T. infestans*, a considerable area of the provinces at high-to-moderate risk (located across the Chaco biogeographic province) show a 20% decrease from medium-to-low future climatic suitability (figure 1b). This suitability decrease includes north-eastern (Formosa, Chaco, Santiago del Estero) and western areas (Catamarca, La Rioja and San Juan) of Argentina. Additionally, both species show unchanged low suitability areas along the Andes mountain range in South America, where the northeastern extreme corresponds to Venezuela and the southeastern extreme to Argentina.

(b) Impact of climate change on the vectorial transmission of Chagas disease

Conversion from suitability to FOI worked considerably better with the one-step method in Argentina and the two-step method in Venezuela.

(i) The one-step method applied to Argentina

We retrieved 56 localities from five countries (28 from Argentina, two from Bolivia, three from Brazil, 21 from Chile and two from Paraguay). However, many were not subsequently included in our analysis, either because the data were pooled for large areas, too few age classes were recorded, or the data were subjected to strong vector control interventions. Applying our inclusion criteria left 15 localities, and once these 15 coordinates with suitability and FOI values had been extracted, the results showed a significant fit to the generalized logistic model (equation (2.2)). The best-fit parameter values (and *t*-test statistics) were $B = 38.653$ (1.03×10^{-6}), $C = 12.092$ (1.24×10^{-7}), $M = 0.979$ (2.33×10^{-6}) and $T = 1.978$ (1.033×10^{-6}); figure 2 shows the expected FOI values with their 95% confidence intervals.

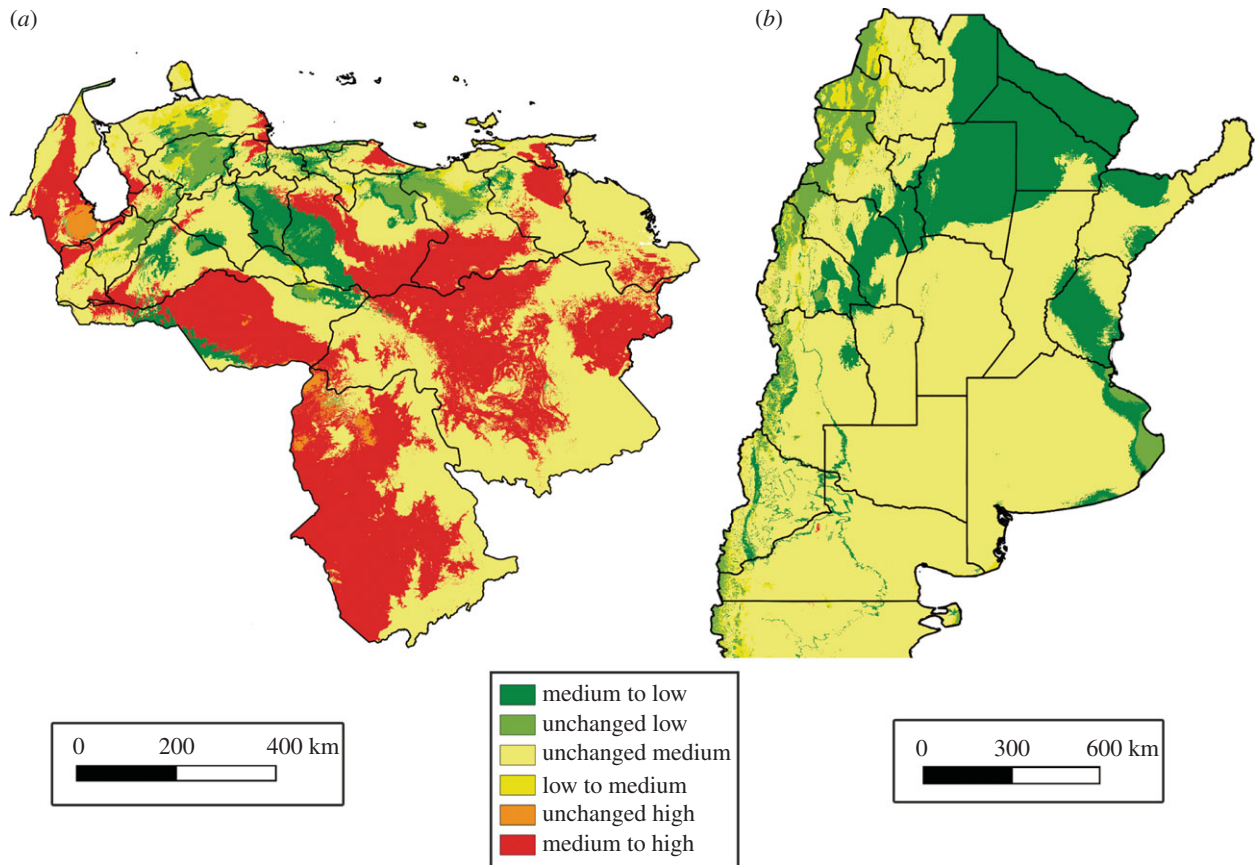


Figure 1. Climatic suitability changes from current to 2050 conditions for (a) *R. prolixus* and (b) *T. infestans*. Colours indicate climatic suitability transitions between the three main suitability categories (low, medium and high). (Online version in colour.)

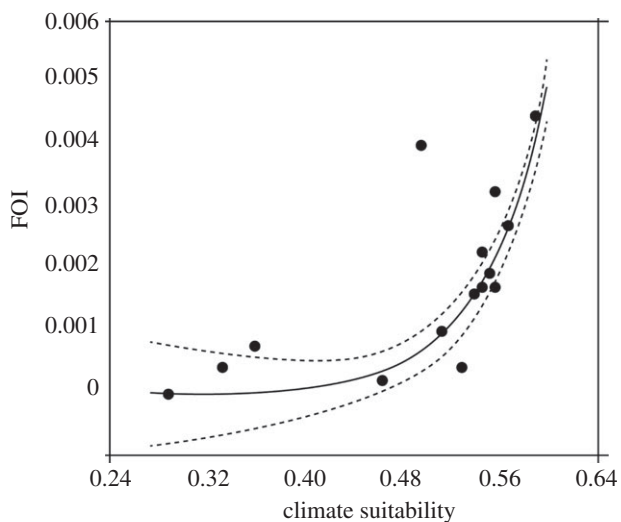


Figure 2. Fit of FOI as a function of climatic suitability of *T. infestans*.

For *T. infestans*, the current climatic conditions indicate medium suitability values along the majority of provinces at high-to-moderate transmission risk (figure 3), excluding the western side of the country which instead demonstrated low suitability values. The 4751 new cases of *Tr. cruzi* human infection per year predicted for all provinces at high-to-moderate transmission risk (black bar, figure 3) under current conditions are considerably greater than the 1581 cases predicted for the same provinces in 2050 (blue/grey bar, figure 3). Currently, four provinces (Córdoba, Santiago del Estero, Tucumán and Mendoza) captured more than 56% of the

relative contribution to the total number of predicted new cases. The most significant decrease in incidence is observed in three provinces in the northeast of Argentina: Formosa, Chaco and Santiago del Estero. These provinces, currently at high risk, show not only a decrease in the predicted number of new cases in 2050, but also a decrease from medium-to-low climatic suitability. The pie charts (figure 3) provide us with an overall picture of the degree of change from the present to 2050 in terms of the 'relative contribution' (%) of each province at high risk to the total number of predicted new cases. The mean FOI and total number of new cases for each province are summarized in tables S5 and S6 in §5 of the electronic supplementary material.

(ii) The two-step method applied to Venezuela

The density of bugs per house in the 73 selected localities from the database of the Ministry of Public Health of Venezuela was fitted significantly to suitability using the Gaston & He model [81]. However, the predicted densities showed an exponential increase at high climatic suitability values, a pattern different from our observed data, which showed a flattening out of vector density for high values of climatic suitability. To reduce the heterogeneity in the observed density of bugs per house, we estimated its average according to six equal-sized classes of climatic suitability. Because the flattening out of vector density for high house infestation values was still evident, we again fitted the generalized logistic function (equation (2.2)) in order to capture the sigmoidal shape of this relationship. The parameters of the logistic model (equation (2.2)) were $C = 0.371$, $M = 0.401$, $B = 294.13$ and $T = 21.22$. (SSQ = 0.0014, with one-degree of freedom, and $p = 0.030$; figure 4).

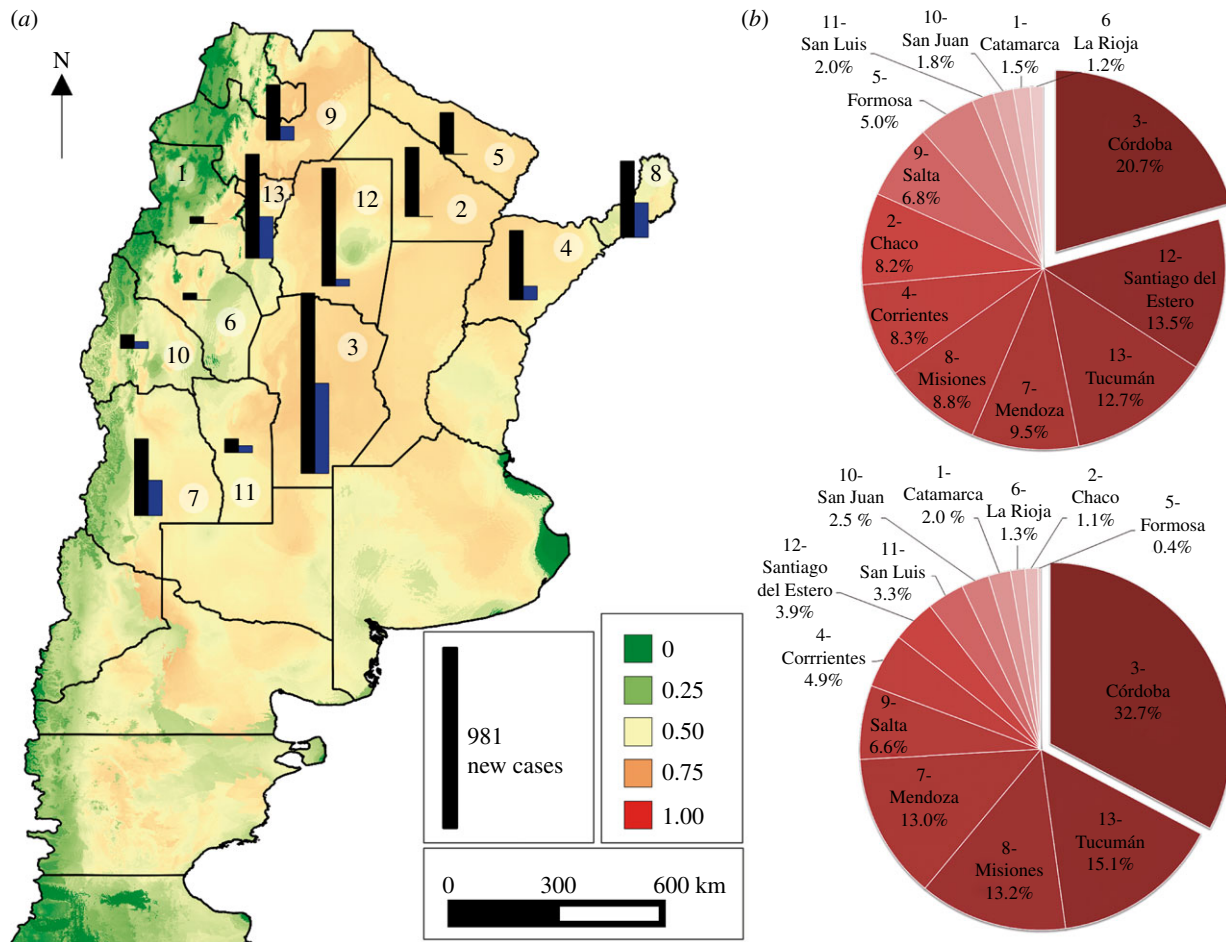


Figure 3. Current climatic suitability (base map green to red/grey to black colours) and predicted number of new human cases of *Tr. cruzi* infection (current: black bar, 2050: blue/grey bar) in Argentina. Provinces were numerated (white circle on the map) to facilitate the identification on the pie charts (number preceding name). Pie charts indicate the ‘relative contribution’ (%) of each province to the total number of new predicted cases over all high transmission risk provinces. Upper pie chart: current conditions; lower pie chart: 2050 conditions. (Online version in colour.)

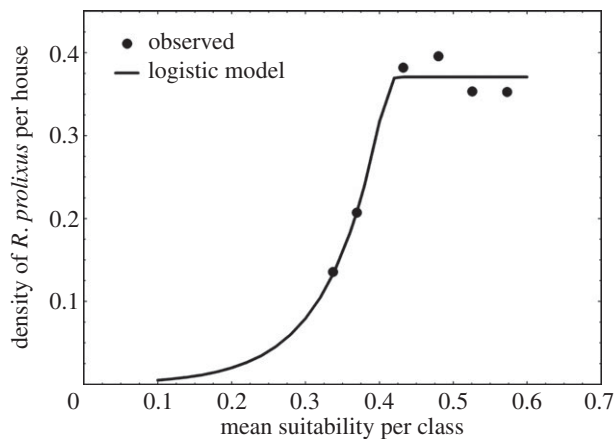


Figure 4. Density of *R. prolixus* bugs per explored house and mean current climatic suitability per class. Vector densities are in the original one man-hour collection units averaged for each suitability class and not corrected by the ‘catchability’ factor.

The generalized logistic function predicts an asymptotic vector density of about 30 bugs per explored house after applying the ‘catchability’ correction factor. While this appears to be a fairly low density, it is expressed as bugs per explored house and the density distribution is extremely clumped (80% or more of the houses do not harbour any vectors), so this average implies a small, but significant, proportion of houses with several hundred insects. We tried to further improve our

predictions of vector densities by additionally accounting for the number of animals in the house and the house construction material, but despite frequent reporting that triatomine densities are related to these factors, we were unable to significantly improve the generalized logistic model fit. Once the vector density (per explored house) was estimated, this was used within the binomial transmission model (equations (2.3) and (2.4)) using average parameter values from the Venezuelan database ($I = 0.2$, $f = 0.5$, $F = 0.143$, $H = 4.6$, and an assumed proportion of susceptible people within a household of 0.9). The results of these combined steps are shown in figure 5.

Table S7 in §5 of the electronic supplementary material gives the mean FOI values estimated by the two-step method for each high transmission risk state in Venezuela; these are compared with those estimated by the one-step method in figure 6. In general, and in agreement with the climatic suitability values and figure 1a, there is an overall tendency towards a decrease in incidence in most states at high risk of vectorial transmission in Venezuela from present to 2050 conditions (figure 7). The current annual total of 4677 new human cases of *Tr. cruzi* infection predicted for all states at high risk of vectorial transmission (black bar, figure 7) is greater than the 3690 predicted new cases in 2050 (blue/grey bar, figure 7). All states, at high risk, contribute a similar relative percentage to both current and future new cases. The most significant decrease in incidence from current to 2050 is observed in Cojedes (from 303 to 116 new cases), whereas the

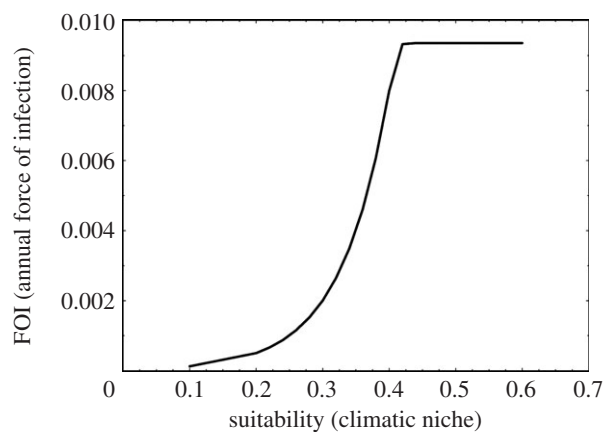


Figure 5. Results of the two-step procedure to estimate FOI from climatic suitability for *R. prolixus* in Venezuela.

most significant increase (and indeed the only state demonstrating an increase at all) is in Falcón (from 317 to 374 new cases); for more details, see table S8 in §5 of the electronic supplementary material.

4. Discussion

All temperature-related variables were important in determining the climatic suitability of both species, with a dominant contribution from the minimum temperatures of coldest months. However, for *R. prolixus*, precipitation variables were also related to climatic suitability. This is consistent with the biology [25] and ecology of this species [82], which inhabits predominantly tropical savannahs and foothills (500–1500 m.a.s.l.) with climatic conditions typically consisting of highly variable rains and temperatures. For *T. infestans*, the same thermal variables, except the minimum temperature of the driest quarter, were also the most important factors determining the climatic suitability; this is also consistent with the biology of this temperate species that is well adapted to areas characterized by cold temperatures and a broad thermal-tolerance range [83].

The wide areas in Venezuela (mostly in central and south-eastern regions) where *R. prolixus* shows transitions from medium to high suitability suggest a potential shift in its geographical distribution. Because these areas are currently considered at low transmission risk, new vectorial transmission seems a distinct possibility for Venezuela in the climatic change scenario considered here (RCP6.0). On the other hand, the predicted decrease from medium-to-low suitability in high-risk *Tr. cruzi* transmission states in Venezuela suggests a decrease in the geographical distribution of this species, mainly at the foothills of the Andean and coastal mountain ranges, thus suggesting less serious epidemiological implications in a climate change context. In contrast, no changes from medium-to-high climatic suitability were observed for *T. infestans* in Argentina, but instead a marked change from medium-to-low suitability (mainly in northeast and western provinces of Argentina) may occur, thus suggesting a decrease in the geographical distribution of this species. This result agrees with both empirical field data and ecogeographical models [84], which suggest that *T. infestans* has a limited ability to thrive in a warm and humid climate.

Many studies to date addressing the question of climate change impacts on vector-borne diseases have suggested

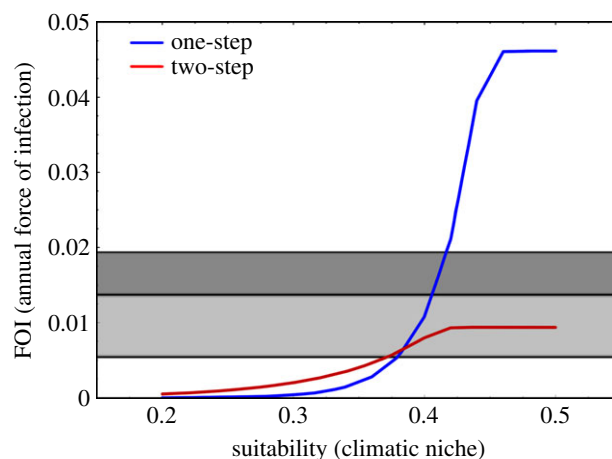


Figure 6. FOI predicted values by both the one-step (blue/black line) and two-step (red/grey line) methods for *R. prolixus* in Venezuela. Horizontal bands are FOI estimates used as reference values (white lower band = 0–0.005; light grey band = 0.005–0.015; dark grey band = 0.015–0.019). (Online version in colour.)

that environmental change is likely to strengthen transmission potential and expand the geographical range of disease vectors into, for example, higher latitudes [85]. However, recent studies suggest a shift (rather than expansion) in the geographical distribution of species and vector-borne diseases in a global warming context [85–87], which is consistent with our results for both *R. prolixus* and *T. infestans* as well as other triatomine studies [37,38]. In accounting for the fact that insects adapted to higher latitudes may present a broader thermal-tolerance range than those adapted to lower latitudes, some authors have proposed that tropical organisms will be more sensitive to temperature changes [88] and consequently, the impact of climate change will be different across latitudes and species [89]. In agreement with these considerations, we observed a differential impact of climate change on the two vector species analysed here: *R. prolixus* shows a future expansion to new areas, whereas *T. infestans* shows a future decrease in its geographical range compared with current conditions.

Several authors, based on simple theory models, have proposed a link between presence (or occupancy) of species and their population abundance [70,72,81,90]. Despite the fact that the house infestation–vector density relationship used here is beginning to become recognized in certain other vector species such as phlebotomine sandflies associated with the transmission of leishmaniasis [85], *R. prolixus* and *T. infestans* do not seem to show such a direct relationship, and this could be due to the existence of other variables (socio-environmental or economic among others) that were not included in our ecological niche models. Because the climatic suitability estimated by the ENMs does not take into account socio-environmental variables such as vector control strategies, the relationship between occupancy and population abundance becomes difficult to verify. Socio-environmental variables, as well as many other factors such as the adequate criterion of spatial and temporal scale selection, remain to be addressed for full application of ENMs to disease systems [29], and this may affect the precision and accuracy of predictions about the likely future behaviour of disease transmission under climate change [91]. Similarly, Roura-Pascual *et al.* [92] claim that proper choice of environmental

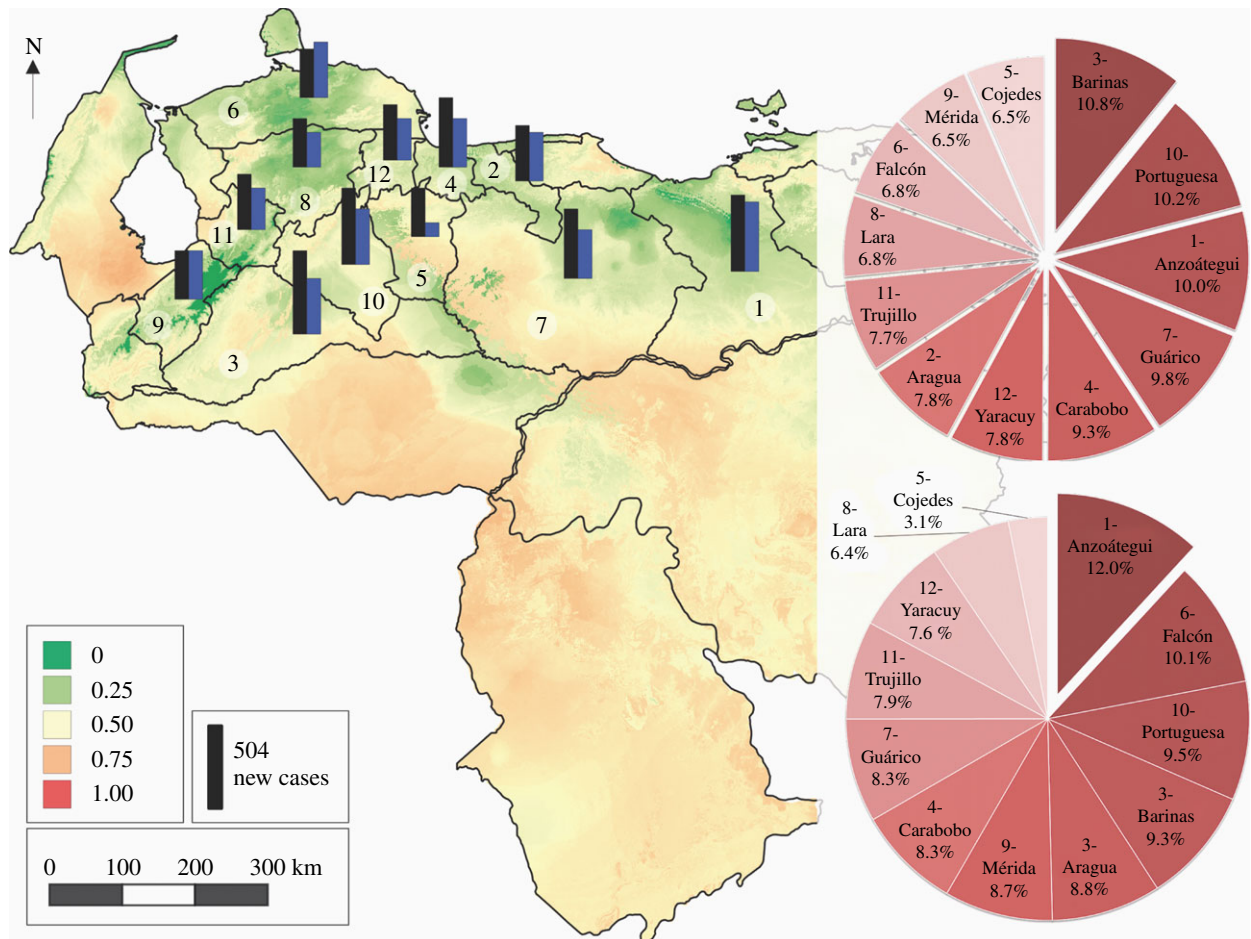


Figure 7. Current climatic suitability (base map green to red/grey to black colours) and predicted number of new cases of *Tr. cruzi* human infection (current: black bar, 2050: blue/grey bar) in Venezuela. States were numerated (white circle on the map) to facilitate the identification on the pie charts (number preceding name). Pie charts indicate the 'relative contribution' (%) of each province to the total number of new predicted cases over all high transmission risk states. Upper pie chart, current conditions; lower pie chart, 2050 conditions. (Online version in colour.)

datasets is important, because climatic data provide longer temporal applicability. Although remotely sensed data can provide finer spatial resolution, by measuring aspects of ecologic landscapes that climate parameters alone may not capture, we used variables provided by weather stations (interpolated data) because these represent the only available datasets for future conditions. Additionally, comparison between predictions for current and future conditions could be problematic, because the current bioclimatic variables could be far from reality (observed climatic data).

Our use of climatic variables to predict species suitability as a surrogate for population densities has been the subject of few ecological studies to study the epidemiology of vector-borne diseases. Given that the entomological database was reduced to decrease the high heterogeneity observed, we note that our results should be cautiously interpreted in the context of the large uncertainties present in epidemiological and climatic data, and thus unavoidably inherent in the integrated modelling approach developed here. Potential changes in the transmission risk of *Tr. cruzi* should also not be used as indicators of short-term vectorial control decisions, but rather cautiously interpreted as indicators of a potential longer-term trend given the best available current entomological and epidemiological data.

Despite these heterogeneous results, our main conclusions point to a decreasing trend in the number of new human cases of *Tr. cruzi* infection per year between current and future

conditions. However, it is important to be aware of recent (and ongoing) decreases in the size of the rural population; future demographic projections for rural populations in 2050 predict a decrease in size of 26% and 49% for Venezuela and Argentina [80], respectively. This implies that even if an FOI value remains constant between current and future scenarios, a decrease in incidence suggests a decreasing risk; however, this would lead to a false conclusion in the event of a decrease in the rural population size. For *R. prolixus*, our FOI estimates were of a similar order of magnitude as those previously estimated for Venezuela by Feliciangeli *et al.* [42] for the period prior to the initiation of the National Campaign for Chagas Disease Control. Our conversion from FOI to incidence could have been improved further by considering only susceptible individuals from the rural population. Additionally, we could also have separated 'marginally dispersed' and plain 'rural' populations as undertaken by Chuit [93] in relation to Chagas disease. However, these additional details would have taken us beyond the main purpose of this manuscript and are unlikely to have substantially affected the key qualitative conclusions drawn.

In relation to the use of occurrence points from geographical range maps, it is well known that range maps are not able to capture environmental areas where the species is actually absent within its distribution. Although this is not the usual approach to model species distributions since it may overestimate the geographical distribution of a species introducing a

great number of false positives, the presence points derived from geographical distribution atlas allow us to understand large-scale distribution patterns of species [94,95]. Nevertheless, the use of data based upon individual occurrences from surveys would not necessarily produce more accurate suitability predictions, because this kind of data may itself introduce uncertainties related to different sampling efforts, both in space and time, introducing cases of false negatives. Particularly for *T. infestans* and *R. prolixus*, even if several occurrence points could be compiled from the literature, these points would not represent the geographical distribution of these species because they do not respond to a specific ecological sampling design and are, generally, biased to certain study areas. In our case, because the main goal was to analyse the effect of climate change on Chagas disease transmission, it was decided that it was preferable to overestimate the potential transmission risk (owing to false positives) than to underestimate it (owing to false negatives).

In addition to the caveats identified above, we have analysed only one of the various possible downscaled prediction models (HadGEM2-ES), and only one of the future projection periods (2050). Limitations arising from the spatial resolution and interpolation process associated with the WorldClim dataset should also be noted, in particular, because there are fewer

weather stations in Latin America compared with those in other parts of the world (forcing interpolation between larger distances). Because of the uncertainties associated with the climatic variables, the inference of the *Tr. cruzi* transmission risk based on climatic suitability of vector species, require the incorporation of other environmental variables and/or socio-economic factors, which likely affect the estimation of disease incidence. Further research is therefore needed to more thoroughly assess the robustness and generality of our conclusions about future *Tr. cruzi* transmission risk, which are affected here by the range of uncertainties that unavoidably arise from an integrated modelling approach based on ecological, epidemiological and climatic factors.

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