Land-use effects on infectious disease transmission: the case of Chagas disease in Colombia

Diana Erazo

Evolution and Ecology, International Institute for Applied System Analysis, Laxenburg, Austria

Universidad de Los Andes, Bogota, Colombia

Introduction

In 2012, the World Health Organization (WHO) defined the *2020 goals* program for controlling the burden of morbidity of neglected tropical diseases (NTDs). Chagas disease is a NTD in Latin America, with a burden of 10,000 deaths per year (Rassi et al., 2010). It is caused by the cell parasite *Trypanosoma cruzi* and it is transmitted to mammal hosts by various species of so-called kissing bugs. In Colombia, recent estimates suggest that 1% of the population is infected and 15% is at risk (Moncayo et al., 2009). Without treatment, Chagas disease can cause serious heart and digestive complications leading to death.

Control strategies, which include house spraying with insecticides, have reported successful outcomes in regions where the main vector is strictly domestic. This is, for example, the case of the vector *Triatoma infestans* in the Antiplano region in Bolivia (Salvatella et al., 2014). However, re-infestation after spraying occurs in the Orinoco region located in Colombia and Venezuela. *Rhodnius prolixus*, the main vector in this region, is found in both domestic and sylvatic habitats, where it is strongly associated with palm trees (Abad-Franch et al., 2015; Sanchez-Martin et al., 2006). Thus, it is suspected that an inflow of vectors from the sylvatic populations thwarts control efforts.

Land-use change has been suggested as a major driver of emerging infectious diseases (Patz et al., 2000). Deforestation, agriculture, urbanization, and resource exploiting could alter species diversity, abundance, and interactions including disease transmission. This could also be the case for Chagas disease in Colombia, where the annual deforestation rate between 1990 and 2005 was 0.62% (340,000 ha/year) (Armenteras et al., 2013). Additionally, *R. prolixus* is known for its resilience and ability of occupying human dwellings, natural and altered habitats. Concerning the latter, the insect has been found in oil-palm plantations (Guhl et al., 2005a), an expanding economy in Colombia.

Oil-palm plantations were established in Colombia during the 1960s. Currently, oil palm is the most relevant crop used for biodiesel production in the world. Colombia is the main producer in Latin America and policies have been established to ensure that Colombia contributes significantly to the future biodiesel markets (Castiblanco et al., 2013). One of the target regions is located in the Orinoco, known as an endemic area for several tropical diseases. This expansion of oil-palm plantations provides suitable habitats for the Chagas disease vector *R. prolixus* (Abad-Franch et al., 2015) and thus may have a significant impact on endemic levels and infection risks. More generally, land-use change may similarly interact with many vector-borne diseases (Gottdenker et al., 2014).

For Chagas, the WHO goal for 2020 is to reach regional elimination (WHO, 2012). Supporting policy development with quantitative research is one of the main approaches recommended by the WHO for achieving their 2020 goals (Hollingsworth et al., 2015).

Therefore, considering the expanding economy of oil-palm plantations in Latin America, the aim of this study is to analyze the effect of land use on Chagas-disease infection risk in Colombia using available data and a statistical model. In particular, I explore the bioclimatic factors and land-use characters that best predict Chagas incidence, focusing on the co-occurrence of plantations and other habitats. Finally using the model along with an expansion scenario of oil palm plantations in Colombia for 2020, I assess the expected disease incidence and an estimation of the possible health costs.

Methods

Here I implement a generalized linear model (GLM) for Chagas disease incidence prediction at the municipality level in Colombia. As explanatory variables, I consider social factors, bioclimatic factors, vector presence, control efforts and land cover. Using the statistical model and the projections of oil palm plantations in Colombia, I estimate the number of Chagas disease cases.

Data

The weekly number of cases of Chagas disease from January 2012 to August 2016 (week 35) is obtained from the National Institute of Health for the 1062 municipalities located in the continental territory of Colombia (INS, 2016) (see Fig. 1). The total number of cases during four and half years was 3485. A national land cover map at 100 m resolution with 98 land-cover types is available from the Institute of Hydrology, Meteorology and Environmental Studies (IDEAM, 2007). Altitude and bioclimatic variables derived from monthly temperature and rainfall values (19 biologically meaningful variables: bio1–bio19), are obtained as raster images from WorldClim (Hijmans et al., 2005). Population density, percentage of population located in rural areas, and unsatisfied basic needs at the municipality level are obtained from the National Administrative Department of Statistics (DANE, 2016). Data on seven species of kissing bugs, their distributions, and on fumigation are obtained from the database developed during the National Control Program of Chagas Disease in Colombia (1997–2001; Guhl et al., 2005b). Castiblanco et al. (2013) developed the projections for expansion of the oil palm in Colombia.

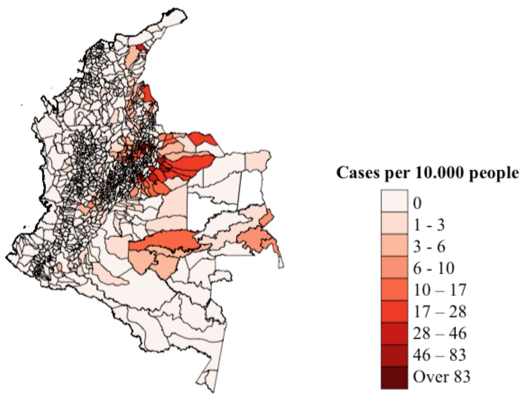

Figure 1. Chagas disease incidence in Colombia (2012–2016). Administrative map of Colombia at the municipality level. The color coding indicates the number of cases per 10.000 people reported from 2012 to August 2016 (white: zero cases, dark red: max. number of cases). Most highly populated areas have the most reports in the country.

Spatial-structure analysis

In a first step, I rasterize and reduce the national land-cover map from 98 to four land-cover types of interest, namely, forests, oil palm plantations, urban areas. and other habitats (grasslands, other crops and mining) (see Fig. 2). The rationale behind this procedure is that forests are the natural habitats for kissing bugs, while human settlements and oil palm plantations are potential habitats. Grasslands, others crops and mining areas are considered bug-unsuitable environments.

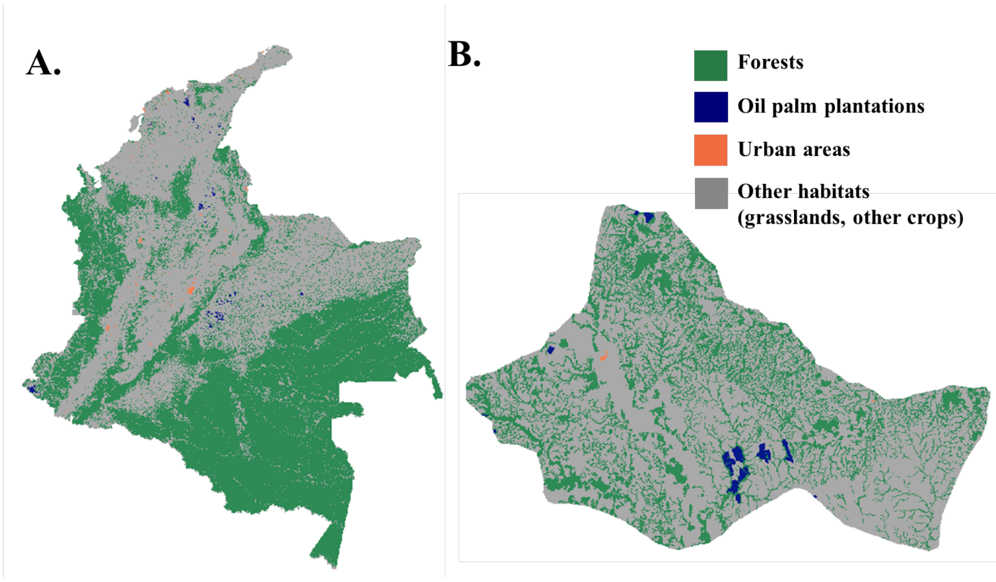

Figure 2. Land-cover maps of A. Colombia, B. Municipality example: Puerto Lleras located in the department of Meta, showing four land-cover types of interest: forests (green), palm plantations (blue), urban areas/human settlements (orange), other habitats (grasslands, scrublands, other crops, and mining; grey). The first three are considered bug-suitable habitat and the latter bug-unsuitable habitat. Resolution: 100 m.

Using these four land-cover types, I obtain for each municipality: percentage of protected areas, percentage of area covered by each land-cover type and a measure of characteristic extents/distances between patches of a certain land cover. The values of the former two measures are computed as the number of cells in the municipality corresponding to the land-cover type of interest, divided by the total number of cells. The computation of the latter measures is described below.

The inputs for determining the characteristic extent of land-cover patches for a given land-cover type or auto-correlation are two images: the masked/inside and the unmasked municipality, both displaying the land-cover type of interest. For computing the characteristic distance or cross-correlation, the input images are the masked municipality showing the focal patches and the unmasked municipality presenting the target patches. In both cases, the correlation functions are computed as the convolution of the image of the masked municipality with the image of the unmasked municipality. The measure is therefore directional. I compute this convolution efficiently through Fourier transforms.

The correlation function, or correlogram, shows the pairwise densities as a function of distance. I fit an exponential function to the auto-correlation functions to obtain the characteristic extent of land-cover patches for a given land-cover type. I fit an exponential function to the the cross-correlation functions to obtain the characteristic distances between patches of certain land covers (see Fig. 3). In this manner, I assemble for each municipality a matrix of characteristic lengths of the following form:

$$\begin{pmatrix} \xi_{\text{forest}} & \xi_{\text{forest}\rightarrow\text{plantation}} & \xi_{\text{forest}\rightarrow\text{urban}} & \xi_{\text{forest}\rightarrow\text{others}} \\ \xi_{\text{plantation}\rightarrow\text{forest}} & \xi_{\text{plantation}} & \xi_{\text{plantation}\rightarrow\text{urban}} & \xi_{\text{plantation}\rightarrow\text{others}} \\ \xi_{\text{urban}\rightarrow\text{forest}} & \xi_{\text{urban}\rightarrow\text{plantation}} & \xi_{\text{urban}} & \xi_{\text{urban}\rightarrow\text{others}} \\ \xi_{\text{others}\rightarrow\text{forest}} & \xi_{\text{others}\rightarrow\text{plantation}} & \xi_{\text{others}\rightarrow\text{urban}} & \xi_{\text{others}} \end{pmatrix} \tag{1}$$

where $\xi_{i\rightarrow j}$ is the characteristic distance between focal patches of land-cover types i and surrounding patches of land-cover type j when $i \neq j$, and the characteristic extent of patches of land-cover type i when $i = j$.

Finally the distances are transformed into proximity measures, by using a modified version of the dimensionless Proximity Index (PX) suggested by Gustafson and Parker (1992). The proximity P_{ij} from patches of land-cover type i to patches of land-cover j measure is defined by:

$$P_{ij} = \frac{A_i}{{\xi_{i\rightarrow j}}^2} \tag{2}$$

where A_i is the area of land-cover type i. Note that if $i \neq j$, i represents the focal type and j the surrounding type and $P_{ij} \neq P_{ji}$.

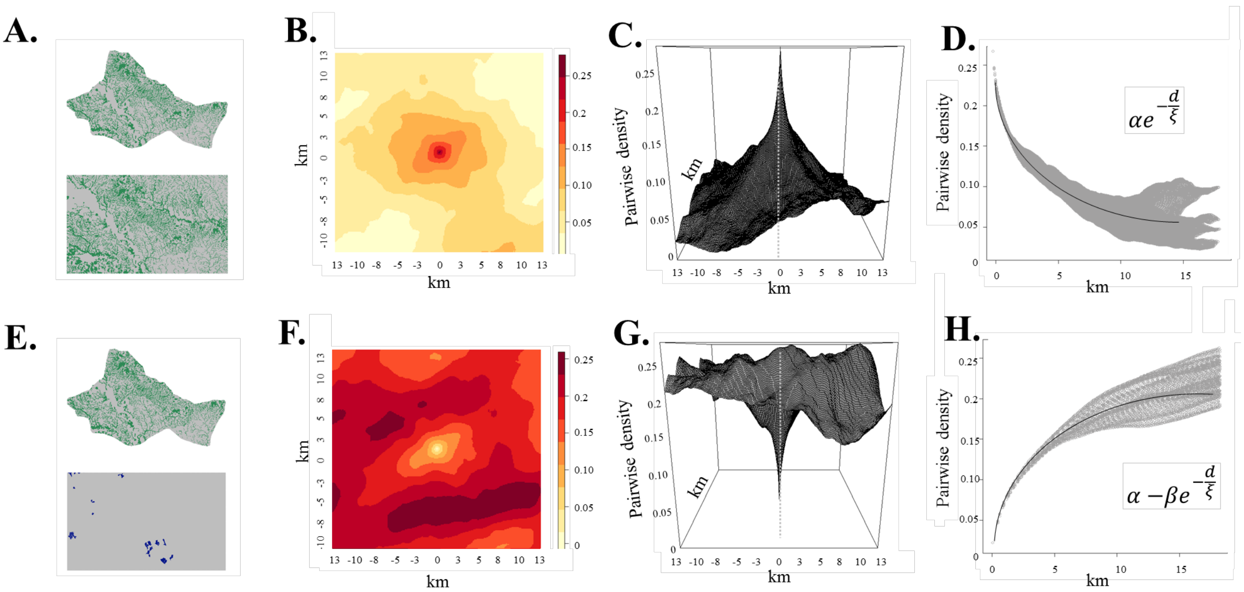

Figure 3. Correlation distances. Rows illustrate the computation of auto-correlation (upper) and cross-correlation (lower) distances on a typical example. Left panels illustrate the input images: masked and unmasked municipality displaying the land-cover patches of interest. Middle panels show the correlogram (pair density as a function of distance) as B., F. level plots, C., G. surface plots, while right panels demonstrate the fitting of exponential functions, whence the corresponding correlation distance is obtained as ξ.

Statistical model

I construct a Generalized Linear Model (GLM) with Chagas disease incidence at the municipality level as the response variable. GLMs are commonly used to model binary and count data, appropriate for the type of data that I consider here. I use a Poisson error distribution for the response variable and a logarithmic link function, resulting in a linear model of the form:

$$Y \backsim \text{Poisson}\ (\bar{Y}) \tag{4}$$

$$\log \bar{Y} = X_1 + \dots + X_n \tag{5}$$

where Y and $\bar{Y}$ are, respectively, the actual and the expected number of cases of Chagas disease in a municipality. The Poisson distribution represents the stochasticity of Y around $\bar{Y}$. The X_k are the explanatory variables. Additionally, I consider the interactions between the proximities P_{ij} between patches of land-cover types i and j, and the percentage a_j of area covered by land-cover type j in a municipality. The model considering the interactions follows the form:

$$\log \bar{Y} = X_1 + \dots + X_n \dots + P_{ij} * a_j + \dots \tag{6}$$

where $a_j = A_j / A_{\text{total}}$ and A_{total} is the total municipality area. See Table 1 for all variables used in the statistical model.

Multicollinearity test

Before fitting the statistical models, I remove multi-collinearities from the set of explanatory variables (see Table 1). To do so, I discard explanatory variables based on their Variance Inflation Factor (VIF). Fitting a linear model for each explanatory variable as a function of the remaining explanatory variables, its VIF is obtained as

$$\text{VIF} = 1/(1 - R^2), \tag{3}$$

where R^2 is the coefficient of determination of the respective regression. Only variables with a VIF smaller than or equal to 10 are included in the statistical models (Zuur et al., 2009).

Palm expansion scenario

Castiblanco et al. (2013) provide projections for the expansion of oil palm plantations in Colombia until 2020, based on biofuel blending goals (930,000 ha). The government plans to replace 20% of diesel with biofuel by 2020. To predict the effect of this expansion on Chagas disease incidence (see *Statistical Model* above), I modify the current land-cover map by converting non-plantation land-cover types to plantations accordingly, and recompute the characteristic lengths matrices and related proximity measures for the expansion scenario. The values of the remaining explanatory variables for each municipality remain unchanged.

Software

Modeling was done using R version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria) and the RStudio Integrated Development Environment (IDE).

Symbol/ Short name	Long name	Source
	Response variable	
Y	Chagas disease incidence in Colombia (2012–2016)	National Health Institute Colombia (INS, 2016)
	Explanatory variables	
P_{ij}	Proximity between land-cover types i and j (Eq. 1)	Developed from (IDEAM, 2007)
A_i	Area of land-cover type i (Eq. 2)	
SPAR	Percentage of special protected areas	
Minalt	Min altitude	WorldClim (Hijman et al., 2005)
Malt	Mean altitude	
RPOP	Percentage of population in rural areas	National Administrative Department of Statistics (DANE, 2016)
DENS	Population density	
UBAS	Unsatisfied basic needs	
bio1	Annual mean temperature	Worldclim (Hijmans et al., 2005)
bio2	Mean diurnal temperature range	
bio3	Isothermality (bio2/bio7) (×100)	
bio4	Temperature seasonality (standard deviation ×100)	
bio5	Max temperature of warmest month	
bio6	Min temperature of coldest month	
bio7	Temperature annual range (bio5– bio6)	
bio8	Mean temperature of wettest quarter	
bio9	Mean temperature of driest quarter	
bio10	Mean temperature of warmest quarter	
bio11	Mean temperature of coldest quarter	
bio12	Annual precipitation	
bio13	Precipitation of wettest month	
bio14	Precipitation of driest month	
bio15	Precipitation seasonality (coefficient of variation)	
bio16	Precipitation of wettest quarter	
bio17	Precipitation of driest quarter	
bio18	Precipitation of warmest quarter	
bio19	Precipitation of coldest quarter	
VPRES	Vector presence	Chagas disease national control program (Guhl et al., 2005b)
FUM	Previous fumigation	

Table 1. Variables considered for the statistical model. Discarded variables (see *Multicollinearity test*) are shown with gray background. Variables used in the model are shown with white background.

Results

Removing multi-collinearities

The 47 explanatory variables initially considered are reduced to 31 variables by discarding the variables with a variance inflation factor > 10 (see Table 1, *Methods: Multicollinearity* *test*). The bioclimatic variables that are excluded are: max temperature of the warmest month (bio5), mean temperature of the coldest quarter (bio11), annual mean temperature (bio1), mean temperature of the warmest quarter (bio10), min temperature of the coldest month (bio6), mean temperature of the driest quarter (bio9), temperature annual range (bio7), precipitation of the wettest quarter (bio16), annual precipitation (bio12) and precipitation of driest quarter (bio17). Regarding proximity variables, the test eliminates: proximity from plantations to other habitats $P_{\text{plantations}\rightarrow\text{others}}$, the characteristic extent of other habitats P_{others} and the characteristic extent of urban areas P_{urban}. Finally, the percentages of area covered by natural habitat, the minimum altitude, and the mean altitude are also excluded.

Fitting the statistical model

The GLM considering interactions has a lower Akaike Information Criterion (AIC) compared to the simple model, meaning it better fits the data ($\text{AIC}_{\text{interactions}}: 8989.4 < \text{AIC}_{\text{simple}}: 9130$) Among the 31 variables considered, 24 are statistically significant (p-value < 0.05) and two of the eight interactions.

Vector presence ($\beta = 1.975$) and previous fumigation ($\beta = 2.184$) show a positive effect on disease incidence. Both variables could be interpreted as indicators of disease presence in a municipality. Mean diurnal range (bio2, $\beta = 1.631$) and precipitation in the wettest month (bio13, $\beta = 4.948$), are also positively associated with disease incidence. On the other hand precipitation: in the driest month (bio14, $\beta = 0.743$), seasonality (bio15, $\beta = 0.292$) and in the warmest quarter (bio18, $\beta = 0.505$) are negatively associated. Results regarding the bioclimatic variables suggest two main points: high precipitation along with weak seasonality, and high temperature variation during the day; predict higher incidence.

Variable	**β**
Negatively associated	
RPOP	0.314
UBAS	0.343
SPAR	0.344
bio8	0.918
bio14	0.743
bio15	0.292
bio18	0.505
$P_{\text{forest}\rightarrow\text{plantation}}$	1.000
$a_{\text{plantation}}$	0.000
$P_{\text{forest}\rightarrow\text{urban}}$	0.999
a_{others}	0.506
$a_{\text{plantation}} * P_{\text{urban}\rightarrow\text{plantation}}$	0.000
a_{urban}	0.150

Variable	**β**
Positively associated	
FUM	2.184
VPRES	1.975
bio2	1.631
bio4	1.014
bio13	4.948
P_{forest}	1.000
$P_{\text{plantation}}$	1.023
$P_{\text{plantation}\rightarrow\text{urban}}$	1.058
$P_{\text{urban}\rightarrow\text{plantation}}$	1.000
$P_{\text{others}\rightarrow\text{forest}}$	1.000
$P_{\text{others}\rightarrow\text{plantation}}$	1.000
$a_{\text{urban}} * P_{\text{plantation}\rightarrow\text{urban}}$	472.26
$P_{\text{urban}\rightarrow\text{others}}$	1.000

Table 2. Statistical significant variables (p-value < 0.05). β-values substantially different from 1 (white background) indicate a contribution to disease incidence**.**

Percentage of area covered by plantations in a municipality ($a_{\text{plantation}}$) has a negative effect in disease incidence ($\beta = 7\times10^{-18}$). However, the interaction term between the percentage of urban area and proximity from the plantation to urban area ($a_{\text{urban}} * P_{\text{plantation}\rightarrow\text{urban}}$) is strongly associated with disease incidence ($\beta = 472.26$). The latter suggests that the proximity between plantations and the human habitable areas plays a role in increasing the number of cases of Chagas disease in a municipality, however, the percentage of area occupied by palm plantations in a municipality does not. Furthermore, the higher the percentage of area covered by special protected areas (national parks), the lower number of cases ($\beta = 0.344$). For more information about the explanatory variables elasticities see Fig. 4. For coefficients see Table 2.

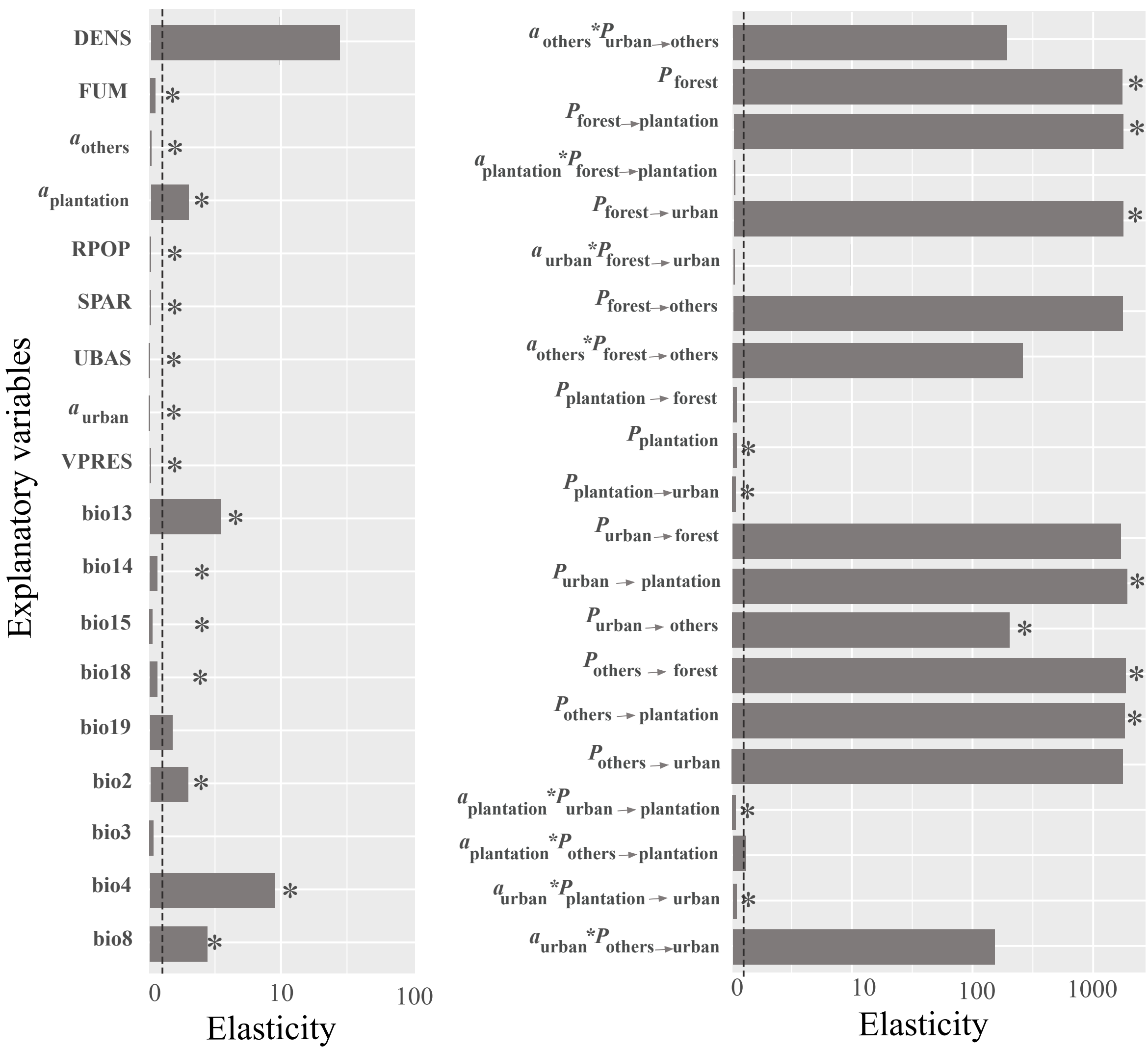

Figure 4. Elasticity: explanatory variables. Bars show the degree of responsiveness in disease incidence in relation to changes in an explanatory variable. Dashed lines represent elasticities equal to 1. Asterisks indicate statistically significant variables. Note that RPOP, UBAS, SPAR, a_{others}, $a_{\text{plantation}}$, and a_{urban} variables are expressed in percentages; and VPRES and FUM are binary variables (0: absence, 1:presence).

Model predictions: oil palm expansion – biofuel blend goals scenario 2020

Currently in Colombia there are more than 400,000 ha cultivated with oil palms. To meet the biofuel blend goals, other 530,000 ha need to be established in the national territory for 2020 (Castiblanco et al., 2013). Based on this scenario and using the statistical model, the results show that 686 cases is the estimated incidence due to oil palm plantations expansion in Colombia for the next four years. The treatment of a chronic Chagas disease patient for lifetime averaged to 11,619 USD in 2008 (Castillo-Riquelme et al., 2008). Therefore, the total treatment costs for the predicted infections with Chagas disease due to oil palm plantation expansions in Colombia would be 8 million USD or 2 million USD per year.

Discussion

Vector biology: bioclimatic variables

Chagas disease occurrence is certainly predicted by vector presence, therefore environmental conditions that have an influence on vector biology and ecology may play a significant role in disease emergence. De la Vega et al. (2014) explored the impacts of climate change for the vectors *Rhodnius prolixus* and *Triatoma infestans*. Authors emphasized the latitude difference between both species, where *T. infestans* has a larger geographical range than *R. prolixus,* which inhabits Colombia and Venezuela. The current study suggests that abiotic factors such as mean diurnal range and precipitation seasonality play a significant role in disease emergence. De la Vega et al. (2014) indicated that both variables significantly affect the distribution of *R. prolixus*.

It has been reported that the El Niño-Southern Oscillation (ENSO), the warming phase of the Southern Oscillation, has an influence on vector-borne diseases (Poveda et al., 2000). The association was shown for malaria and dengue fever (Poveda et al., 2000), however, for Chagas disease in Colombia it remains unknown, although one study conducted in Brazil shows that ENSO could have an impact on the annual incidence of Chagas disease by affecting the reproductive cycle of the vectors and/or host behavior (Benchimol-Barbosa, 2010). Another study in the semiarid region of Chile showed that during El Niño events, sylvatic host outbreaks were observed and could be related to the high availability of hosts for Chagas disease vectors (Botto-Mahan et al., 2010). The current study highlights the role of high precipitation during the wettest month in Chagas disease incidence. Given that El Niño is associated with warm wet-weather months in April–October (Trenberth et al., 1996), future research on this association could contribute to understanding the possible ENSO effects in Chagas disease dynamics in Colombia.

Health system in rural areas

Percentages of rural population within a municipality and unsatisfied basic needs were negatively correlated with Chagas disease incidence, both decreasing the number of cases by nearly 30%. Santos et al. (2015) reported a similar phenomenon in the state of Pernambuco in Brazil. Authors suggested that the lack of access to specialized services in rural municipalities could induce the movement of people from their places to close major centers, increasing the number of reports in these municipalities (Santos et al., 2015).

Underreporting of Chagas disease and other neglected tropical diseases (NTDs) is a common concern in Colombia and Latin America. NTDs are characterized by affecting rural populations, involving at least three main problems: i) human settlements location in remote rural areas, ii) typically associated with low income, and iii) disease unawareness. Additionally, Chagas disease has a tendency to lie dormant in infected persons for decades, until heart or digestive failures occur (Reed, 1998). All these factors interact, leading to reports in health centers located in different areas than where the person acquired the disease, or in the worst case, to no report at all.

Gibbons et al. (2014) suggested an approach to refine the incidence data and solve the underestimation concern for salmonellosis and campylobacteriosis in the European Union. The authors developed a measure of the magnitude of underestimation by using Multiplication Factors (MF) taken directly from the literature. The MFs considered: asymptomatic population, people that does not attend to the healthcare and under-diagnosed/under-notified individuals. Therefore, this approach considers different levels: communities, healthcare institutions, regional and national public health agencies. MFs could be derived from a morbidity surveillance pyramid. Future work could consider this type of approach to improve the collected data on Chagas disease and other NTDs.

Land-use effects and Chagas disease incidence

Landscape structure has been suggested as an important factor in influencing disease dynamics, through impacts on both abiotic conditions and species interactions (Ostfeld et al., 2005). For instance, malaria and onchocerciasis have been linked to land use and forest cover (Thompson et al., 1999 and 2000). Furthermore, the role of distance between patches of different land covers has been studied for leishmaniasis, where urban proximity to forests and pastures has been identified as a major risk factor (Werneck et al., 2002).

Here, I have explored the effects of habitat proximity as a means of investigating the role of land use in Chagas disease incidence in Colombia. In particular, I focused on the role of oil palm plantations. Evidence suggests that oil palms can sustain *R. prolixus* populations (Guhl et al., 2005a). Therefore, palm plantations close to forests located in regions with optimal environmental conditions for kissing bugs are susceptible to being infested. A study conducted in Colombia’s eastern plains showed a 47% palm infestation index and 41% vector infection in oil palm plantations (Guhl et al., 2005a). This phenomenon could be studied in the field at small geographical scales such as villages, however, at bigger scales the complexity of the analysis increases, requiring computational approaches.

Regarding policy recommendations, it appears important to avoid establishing guidelines based on short-term effects of land-use change. Long-term studies could guide policies in a more effective way, although this represents a financial and logistic challenge (Gottdenker et al., 2014). The present study results suggest that proximity between urban areas and oil palm plantations, and in particular, the combined effect of proximity and urban area size, rather than area covered by plantations, has a positive effect on Chagas disease infection risk. Considering the expanding economy of oil palms in Colombia based on the biofuel blend goals for 2020, the results suggest establishing the forthcoming plantations distant from human settlements and reducing the interface area as much as possible. Additionally, accounting for the flying ability of kissing bugs when developing control strategies is strongly encouraged (Lazzari & Lorenzo, 2009).

Finally, this study could also pave the way to a wider understanding of land-use change effects on vector-borne diseases in general and thus potentially support many other WHO vector-control initiatives.

Acknowledgments

I thank the staff at the Evolution and Ecology Program (EEP) for their insightful comments, my supervisors Dr Rupert Mazzuco and Dr Ulf Dieckmann for their significant contribution, and Dr Andrés Etter for sharing the spatial expansion map of oil palm in Colombia.

References

Abad-Franch F *et al.,* (2015). On palms, bugs, and Chagas disease in the Americas. *Acta Tropica* 151: 126–141

Benchimol-Barbosa PR (2010). Trends on acute Chagas' disease transmitted by oral route in Brazil: Steady increase in new cases and a concealed residual fluctuation. *International Journal of Cardiology* 145: 494–496

Botto-Mahan C, Campos R, Acuna-Retamar M, Coronado X, Cattan PE & Solari A (2010). Temporal variation of *Trypanosoma cruzi* infection in native mammals in Chile. *Vector-borne and Zoonotic Diseases* 10: 317–319

Castiblanco C, Etter A, & Aide TM (2013). Oil palm plantations in Colombia: a model of future expansion. *Environmental Science & Policy* 27: 172–183

Castillo-Riquelme M, Guhl F, Turriago B, Pinto N, Rosas F, Martínez MF & Campbell-Lendrum D (2008). The costs of preventing and treating chagas disease in Colombia. *PLoS Neglected Tropical Diseases* 2: e336

DANE - Colombia (1999). National Administrative Department of Statistics. Proyecciones municipales de población por sexo y edad, 1990–2015. Estudios censales.

de la Vega GJ, Medone P, Ceccarelli S, Rabinovich J & Schilman PE. (2015). Geographical distribution, climatic variability and thermo–tolerance of Chagas disease vectors. *Ecography* 38: 851–860

GADM (2012). GADM database of global administrative areas.

Garrigues S, Allard D, Baret F & Weiss M (2006). Quantifying spatial heterogeneity at the landscape scale using variogram models. *Remote Sensing of Environment* 103: 81–96

Gibbons CL, Mangen MJJ, Plass D, Havelaar AH, Brooke RJ, Kramarz P, Peterson KL, Stuurman AL, Cassini A, Fèvre EM & Kretzschmar ME (2014). Measuring underreporting and under-ascertainment in infectious disease datasets: a comparison of methods. *BMC Public Health* 14:1.

Gottdenker NL, Streicker DG, Faust CL & Carroll CR (2014). Anthropogenic land use change and infectious diseases: A review of the evidence. *Ecohealth* 11: 619–32

Gustafson EJ & Parker GR (1992). Relationships between landcover proportion and indices of landscape spatial pattern. *Landscape ecology* 7: 101–110

Guhl F, Pinto N, Marín D, Herrera C, Aguilera G, Naranjo JM & Vallejo, G. (2005a). Primer reporte de Rhodnius prolixus Stal, en Elaeis guineensis variedad Papúa, en plantaciones agroindustriales de Villanueva, Casanare. *Biomedica* 25: 158–159

Guhl F, Restrepo M, Angulo VM, Antunes CM, Campbell-Lendrum D & Davies CR (2005b). Lessons from a national survey of Chagas disease transmission risk in Colombia. *TRENDS in Parasitology* 21: 259–62

Hijmans RJ, Cameron SE, Parra JL, Jones PG & Jarvis A (2005). Very high resolution interpolated climate surfaces for global land areas. *International Journal of Climatology* 25: 1965–1978

Hollingsworth TD, Adams ER, Anderson RM, Atkins K, Bartsch S, Basáñez MG, Behrend M, Blok DJ, Chapman LA, Coffeng L & Courtenay O (2015). Quantitative analyses and modelling to support achievement of the 2020 goals for nine neglected tropical diseases. *Parasites & Vectors* 8: 1

IDEAM & Sinchi (2007). Ecosistemas continentales, costeros y marinos de Colombia. Bogotá: Imprenta Nacional de Colombia

INS (2006-2016). Instituto Nacional de Salud de Colombia Bogota, Colombia. http://www.ins.gov.co/boletin-epidemiologico/Paginas/default.aspx

Lazzari CR & Lorenzo MG (2009). Exploiting triatomine behaviour: alternative perspectives for their control. *Memórias do Instituto Oswaldo Cruz* 104:65–70.

Moncayo A & Silveira AC (2009). Current epidemiological trends for Chagas disease in Latin America and future challenges in epidemiology, surveillance and health policy. *Memórias do Instituto Oswaldo Cruz* 104: 17–30

Ostfeld RS, Glass GE & Keesing F (2005). Spatial epidemiology: an emerging (or re-emerging) discipline. *Trends in Ecology & Evolution* 20: 328–336

Patz JA, Graczyk TK, Geller N & Vittor AY (2000). Effects of environmental change on emerging parasitic diseases. *International Journal for Parasitology* 30: 1395–1405

Poveda G, Graham NE, Epstein PR, Rojas W, Quiñones ML, Velez ID & Martens WJ (2000). Climate and ENSO variability associated with vector-borne diseases in Colombia. El Niño and the southern oscillation, Multiscale variability and global and regional impacts. 1: 183–204

Rassi A & Marin-Neto JA (2010). Chagas disease. *The Lancet* 375: 1388–1402

Reed SG, (1998). Immunology of Trypanosoma cruzi infections. *Immunology of intracellular parasitism* 70: 124–143

Salvatella R, Irabedra P & Castellanos LG (2014). Interruption of vector transmission by native vectors and “the art of the possible”. *Memórias do Instituto Oswaldo Cruz* 109: 122–130

Sanchez-Martin MJ, Feliciangeli MD, Campbell-Lendrum D & Davies CR (2006). Could the Chagas disease elimination programme in Venezuela be compromised by reinvasion of houses by sylvatic *Rhodnius prolixus* bug populations? *Tropical Medicine & International Health* 11: 1585–1593

Santos, FLN, Lorena VMBD, Souza WVD & Gomes YDM (2015). Spatiotemporal analysis of reported cases of acute Chagas disease in the State of Pernambuco, Brazil, from 2002 to 2013. *Revista da Sociedade Brasileira de Medicina Tropical* 48: 181–187

Thomson MC, Connor SJ, D'Alessandro U, Rowlingson B, Diggle P, Cresswell M & Greenwood, B (1999). Predicting malaria infection in Gambian children from satellite data and bed net use surveys: the importance of spatial correlation in the interpretation of results. *The American Journal of Tropical Medicine and Hygiene* 61: 2–8

Thomson MC, Obsomer V, Dunne M, Connor SJ & Molyneux DH (2000). Satellite mapping of Loa loa prevalence in relation to ivermectin use in west and central Africa. *The Lancet* 356: 1077–1078

Trenberth KE & Hoar TJ (1996). The 1990–1995 El Niño‐Southern Oscillation event: Longest on record. *Geophysical Research Letters* 23: 57–60

Werneck GL, Costa CH, Walker AM, David JR, Wand M & Maguire JH (2002). The urban spread of visceral leishmaniasis: clues from spatial analysis. *Epidemiology* 13: 364–367

World Health Organization (2012). Accelerating work to overcome the global impact of neglected tropical diseases: a roadmap for implementation: executive summary

Zuur AF, Ieno EN, Walker NJ, Saveliev AA & Smith GM (2009). Mixed effects models and extensions in ecology with R. New York: Springer. 574 p.