PREDICTIONS OF FUTURE GEOGRAPHICAL DISTRIBUTION OF TWO VECTORS OF AMERICAN TRYPANOSOMIASIS: IMPLICATIONS FOR ENDEMIC CHAGAS DISEASE IN TEXAS, USA

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ABSTRACT

It is known that climate has a direct effect on vector-borne and zoonotic diseases, and in the face of climate change, understanding this link has become more urgent. Many such vector-borne diseases primarily afflict impoverished populations and have therefore been previously understudied. One major focus of our research is to understand the influence that climate has on the distribution of disease causing microorganisms and their vectors, especially those in relation to American trypanosomiasis (Chagas disease). Chagas disease is caused by the hemoflagellate protozoan parasite, *Trypanosoma cruzi*. For this study, we hypothesized that the increasing prevalence Chagas in the state of Texas is due to expanding distributions of vectors. To test this hypothesis, historical data on vector distribution and climate was used to determine the probable locations of prevalent vectors in Texas. Predictions for the future distributions were made using environmental niche models for bioclimatic variables with a maximum entropy algorithm. Of the two Triatominae species studied, the range and concentration of both decreased under a global warming scenario, a finding that is consistent with the current research of risk of Chagas disease in Venezuela. In future, this same procedure will be used on more Chagas vectors to better understand if there is a northward shift for vectors, or if Texas is becoming more inhospitable to all vectors of Chagas.

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- *T. cruzi*
- Chagas disease
- Triatomine
- Climate Change
- Vector

INTRODUCTION

It has long been understood that the Earth's climate has wide ranging impacts on human health (9). One such impact that has been previously understudied is the effect climate has on microbial diseases. Changes in temperature and rainfall, as we are currently seeing in anthropogenic climate change, may affect the distribution and abundance of disease vectors (9).

These vectors may carry microbial agents of disease, such as viruses (causative agents of diseases such as Chikungunya, Dengue, and West Nile Virus), bacteria (causative agents of diseases such as Lyme Disease), and protozoans (causative agents of diseases such as Leishmaniasis) (7). The focus of this study is the vector-borne disease American trypanosomiasis, or Chagas disease.

Chagas disease is a tropical infectious disease that is estimated to have affected as many as 18 million people worldwide, with more conservative estimates placing the number in the 8-10 million range (18, 12, 13, 7, 20). The majority of human infections occur in Mexico and Central and South America (1, 18). The variable estimates of disease prevalence are caused by underreporting of infection, often due to the fact that many people do not know they are infected and do not seek treatment (12, 5). This is, in part, due to the dual phased nature of the disease (1). The acute and the chronic phase are often separated by several decades (18). The first phase (the acute phase) may last anywhere from a few weeks to several months after initial infection (12, 18). The acute phase is asymptomatic or characterized by mild flu-like symptoms not unique to Chagas, including fever, fatigue, body aches, headache, rash, loss of appetite, diarrhea, and vomiting (12, 18). The chronic phase, which develops in 30% of all people infected, may exhibit cardiac or gastrointestinal (GI) complications and can be life threatening (12, 18). Common cardiac signs include cardiomyopathy, heart failure, altered heart rhythm, and cardiac arrest/sudden death (12, 18). Less commonly, chronic GI symptoms include enlarged esophagus (megaesophagus) and enlarged colon (megacolon), both of which can lead to difficulties with eating or passing food (18). While there are cures for Chagas, they are most effective in the acute phase (18). Symptom management and treatments in the chronic phase may inhibit the progression of cardiomyopathy and lower the fatality rate, but the evidence for their efficacy is weak (18).

Chagas disease is caused by the hemoflagellate protozoan parasite *Trypanosoma cruzi* (12, 20). Infection may occur *via* organ transplants and blood transfusions from infected donors, and the consumption of uncooked food contaminated with feces from infected bugs and congenital transmission (12, 22). However, the most common route is vector transmission (12). *T. cruzi* lives in the gut of a variety of insects in the trypomastigote form, and is shed in the feces of the insect vector (4, 2, 4, 23). The parasite is then able to enter the bloodstream of a host *via* the wound left by the insect vector's bite. Once in the host cells, *T. cruzi* transforms from a trypomastigote, a mature flagellate form of the trypanosome, to an amastigote, when no external cilia or flagella are present, and multiplies within the tissue (4). Progeny are released as trypomastigotes into the blood, to spread the infection to other tissues within the current host (4). While trypomastigotes are in the blood the host can serve as a reservoir, and any uninfected insect vectors that take a blood meal from this host may become infected, thus perpetuating infection to other organisms (4). The insect vectors, all from the Triatominae family, are commonly called kissing bugs, due to their tendency to bite around the lips and eyes (1, 22, 7). In the endemic areas of the disease range, approximately 50% of permissive vectors (vectors capable of transmitting disease to humans) carry detectable burdens of *T. cruzi* (5, 20). The most common species that transmit Chagas are *Triatoma sanguisuga*, *Triatoma gerstaeckeri*, *Triatoma protracta*, and *Rhodinus prolixus* (5, 7, 20). *T. gerstaeckeri* and *T. sanguisuga* were chosen to be the focus of the study as they are among the most common Chagas vectors in Texas, and are commonly linked with human

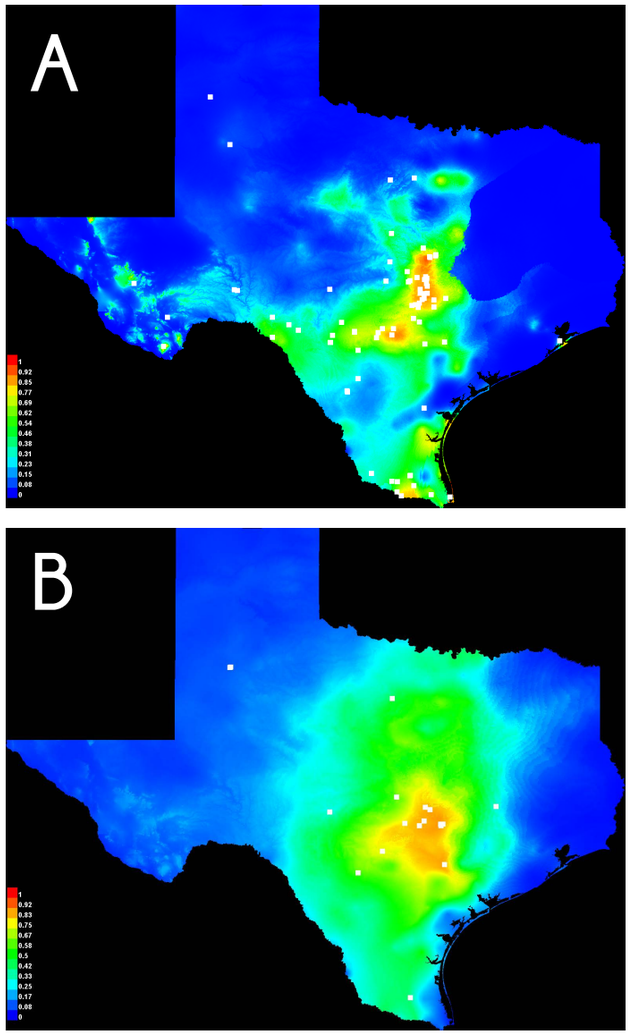

Figure 1. Maxent model for distribution under current conditions (average of 1960 to present). White dots are training locations, warmer colors indicate higher risk of vectors being present for A) *Triatoma gerstaeckeri* and B) *Triatoma sanguisuga*

and canine *T. cruzi* infection. *T. gerstaeckeri* has the highest *T. cruzi* infection rate in Texas, with 58% of all *T. gerstaeckei* individuals testing positive, making it a clinically relevant vector (5, 7).

Historically, endemic Chagas disease has been limited to rural areas of Mexico, Central America, and South America (1, 18). This range has been maintained due to the suitable environment for the reservoirs, Triatominae vectors, and the *T. cruzi* parasite (12, 20). Relevant reservoirs in Texas include dogs, feral swine, woodrats, and armadillos (12). Ideal climate parameters for the transmission of the parasite are tropical conditions, with mild winters, high humidity, and warm nights (1). With changing climates and global warming, there has been a recent shift in the distribution of vectors, including those transmitting diseases such as malaria, lyme disease, leishmaniasis, as well as Chagas disease

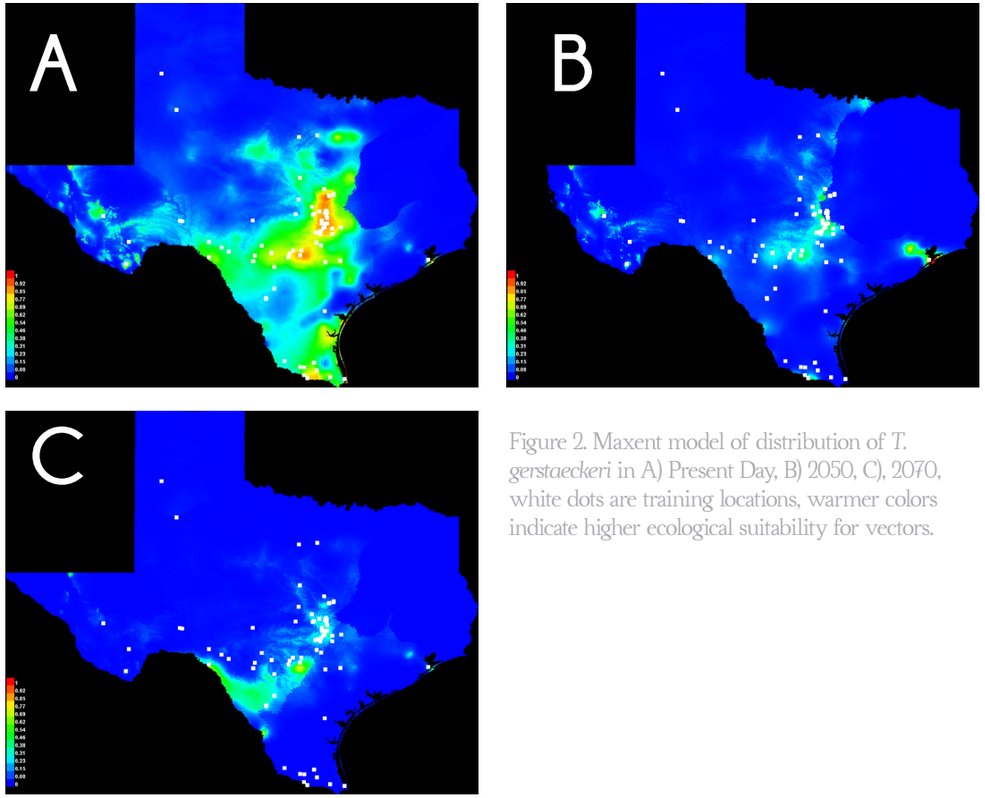

Figure 2. Maxent model of distribution of *T. gerstaeckeri* in A) Present Day, B) 2050, C), 2070, white dots are training locations, warmer colors indicate higher ecological suitability for vectors.

(1, 6, 20).

The southern United States are already suitable habitats for the kissing bug vectors, as seen in recent autochthonous cases (cases acquired within the United States) of Chagas disease (12). As the disease is underdiagnosed and unreported, estimates of the true prevalence of Chagas in the southern United States vary wildly. In Texas alone, estimates of infection range from 4 to 267,000 total locally acquired cases (1,15). The large range of suspected cases exists because Chagas is often underdiagnosed and untreated. The two phase course of the disease, nonspecific symptoms, and possibility of totally asymptomatic infection makes diagnosis difficult (12). Surveillance of donated blood supply in Texas has highlighted that there are a number of Chagas disease cases that were never treated. In Texas, 0.01% of donated blood tested positive for *T. cruzi*. Texas leads the United States in autochthonous cases, reported mainly in the southern regions of the state (12). The first autochthonous case of Chagas disease in the United States was in southern Texas in 1955, and since then the number of locally acquired cases have continued to grow. However, most studies use seroprevalence, which does not differentiate between locally acquired cases and those that were contracted in traditionally endemic countries. No recent publications specifically assessed locally acquired infection in a larger setting than individual case reports. While human data is far from complete, the use of sentinel species, including dogs, also shows an increasing number of cases over time since the mid 20th century. This

trend is expected to continue, with more and more cases occurring in the U.S. with the highest risk in Texas (14). The main goal of this project is to assess the impact climate change is projected to have on bioclimatic variables in the years 2050 and 2070, and if this will change the ecological suitability of Texas for *T. gerstaeckeri* and *T. sanguisuga*. To explain the increase in locally acquired Chagas disease cases, we predicted that the ranges and concentrations of our species of interest would increase. However, our results do not agree with this prediction, indicating that the future Chagas cases in Texas are more likely to be caused by species that are coming to Texas from Latin and South America in response to a changing climate worldwide.

METHODS

DATA

Data of the occurrence and distribution of specific triatomine vectors was assembled from previous collections dating from present day to 1960. Records of previously collected, identified, and *T. cruzi* tested specimens were obtained from museum collections (Texas A&M University, College Station; and University of Texas Brackenridge Field Laboratory, Austin), and published peer-review journal articles (2, 5, 6, 7, 10, 11, 17, 20, 23, 14). Only collections post-1960 were used because the WorldClim (Version 1.4, http://www.worldclim.org/) data used to in the environmental layers of analysis was an average of information since that year.

MODEL CONSTRUCTION

A maximum entropy algorithm was used to construct distribution models for each of the species of interest. The collected Triatominae occurrence points and bioclimatic environmental layers were used with Maxent software (version 3.3.3k) for a historical average of species distributions across Texas. Maxent was used as it is standard in the literature for use in constructing species distributions from a large number of collected specimens, a presence-only record (10). Bioclimatic parameters were obtained for the state of Texas from WorldClim and are as follows: annual mean temperature, mean diurnal range, isothermality, maximum temperature of the warmest month, minimum temperature of the coldest month, temperature annual range, annual precipitation, precipitation of the wettest month, precipitation of the driest month, precipitation of the wettest quarter, precipitation of the driest quarter, precipitation of the warmest quarter, precipitation of the coldest quarter. The technical specifications of the Maxent run include, a convergence threshold of 1.0 x 10-5, and use of the threshold and hinge features, without duplicates.

FUTURE MODELS

Bioclimatic predictions under the AIM 6.0 pathway, RCP6.0, from the version 1.1 of the Beijing Climate Center Climate System Model (BCC_CSM1.1) GCM were retrieved in a 30 second spatial resolution from WorldClim.

RESULTS

Principle component analysis indicated that of 19 bioclimatic variables, the first two principal components (minimum temperature of the coldest month, and annual mean diurnal temperature for *T. gerstaeckeri*, and precipitation seasonality, followed by precipitation of the coldest quarter for *T. sanguisuga*) account for 44.9% and 47.2% of

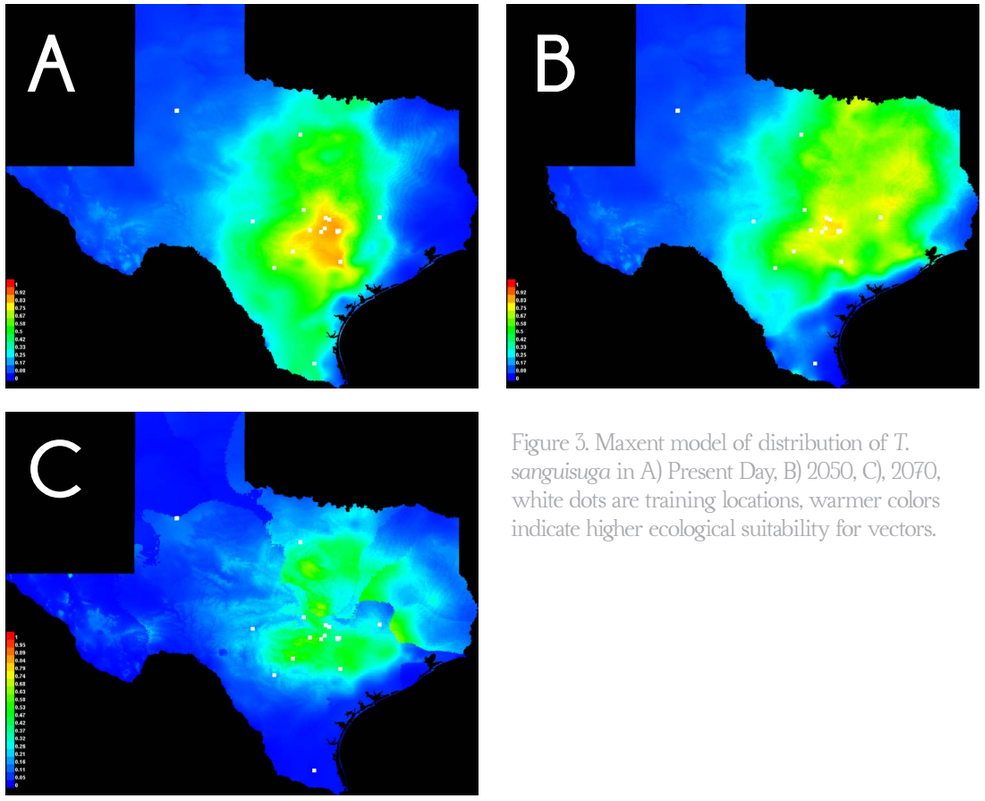

Figure 3. Maxent model of distribution of *T. sanguisuga* in A) Present Day, B) 2050, C), 2070, white dots are training locations, warmer colors indicate higher ecological suitability for vectors.

the explained variance for *T. gerstaeckeri* and *T. sanguisuga*, respectively.

The most important bioclimatic factors for each species (after application of the Jackknife procedure) differed between the two at all time points. For *T. gerstaeckeri*, the most important variable was the minimum temperature of the coldest month, followed by annual mean diurnal temperature, annual precipitation, and precipitation seasonality. For *T. sanguisuga*, the most important predictor variable was the precipitation seasonality, followed by precipitation of the coldest quarter, and minimum temperature of the coldest month. In 2050, the most important variable for *T. gerstaeckeri* changed to annual temperature range. Annual temperature range remained as the most important variable for *T. gerstaeckeri* in 2070.

For *T. gerstaeckeri*, estimates of suitability across the state ranged from 0.00 to 0.92 for the current conditions, between 0.00 and 1.00 for 2050, and between 0.00 and 0.77 for 2070. For *T. sanguisuga*, suitability ranged from 0.00 to 0.85 for the current conditions, between 0.00 and 0.75 for 2050 and between 0.00 and 0.68 for 2070. These both show an overall decrease in suitability. Areas of current high suitability for *T. gerstaeckeri*, such as in South Texas along the USA-Mexico border, saw a decrease in suitability by 85% by 2070. Whereas current areas at medium risk saw a dramatically localized increase of suitability, such as the 46% increase in the Houston and Galveston area, near Trinity bay along the

Gulf coast. Areas of current high suitability for *T. sanguisuga* decreased by 33% by 2070 in central Texas where the highest suitability is currently. No areas saw an increase in suitability for *T. sanguisuga*. Additionally, both species show unchanged low suitability in the Texas panhandle in the northwest part of the state.

DISCUSSION

The current distribution of vectors of Chagas disease is based on bioclimatic variables.

Of the bioclimatic variables studied to determine vector distribution, as listed above, different variables were more important to some species of vector than to others. *Triatoma gerstaeckeri*'s niche was most heavily influenced by the minimum temperature of the coldest month, indicating a threshold temperature, below which the vectors die, most likely while in egg or nymphal stages. The niche of *Triatoma sanguisuga* was determined by the precipitation variation throughout the year, favoring areas with constant and dependable rainfall. This requirement results in a distribution more toward the gulf coast region of Texas and the east of the state, which tend to have more stable precipitation levels than the west and immediately along the coast. (Figure 1A and 1B).

Presence of *T. gerstaeckeri* and *T. sanguisuga* will decrease and shift in response to climate change across the state of Texas.

Under the RCP6.0 climate pathway, "Aim 6.0", the densities of both studied vectors will decrease and the distribution will shift towards the east. By 2050, *T. gerstaeckeri* will have a highly restricted range with an epicenter in central Texas, as well as a large density on the gulf coast near Houston. Both trends are continued in 2070 (Figure 2). In 2070, distribution of *T. gerstaeckeri* is restricted further, with the exception of a large increase of ecological suitability in the southern region, which may be caused by the presence of microclimates along rivers in the area or that the rural area is suited for the vectors than further north in more populous areas (Figure 2). The trends observed for *T. gerstaeckeri* contrasts somewhat with *T. sanguisuga* which will have a much broader range in 2050 and 2070, comparable to its present day range, but with a much lower concentration (Figure 3). The distribution for *T. sanguisuga* will be centered in central and east Texas (Figure 3). The presence of both vectors decreases along the Texas–Mexico border and southernmost regions of the state. This indicates that there is also a maximum suitable temperature being exceeded in these climatic scenarios. The consensus in the field is that Chagas disease rates will increase in America, with Texas being the first state affected. The finding of decreased vector range and density was thus very surprising and did not agree with our hypothesis that vector ranges will increase. However, the vectors studied do not represent all Chagas competent vectors. And while the species studied have been major sources of concern in Texas in the past, they may not be major vectors for disease in the future (14, 20). Both of these species have been endemic to Texas for many years, and are thus likely highly adapted to its current climate (10.1). Future Chagas infections may be caused more by invading species coming from Latin America as the climate warms and becomes too hot to be suitable, and find refuge in Texas with a warmer climate to match that of the previously inhabited endemic areas. Therefore, for a better understanding of risk of infection, further research would open up this study to newer triatomine species to Texas, including: *T. indictiva, T. lecticularia, T. protracta, and T. rubida*. This future direction would look to see if these species show the same northward trend over time. Anthropogenic effects on the environment increase the risk of Chagas transmission.

The risk of Chagas infection increases in cities, specifically in the largest cities of Texas: Houston, Dallas, and Austin due to the high human population in each of the cities. A high human population favors the establishment of a local infection cycle because the triatomine bugs are attracted to areas of human activity and the presence of infected reservoirs increases the risk of transmission to humans (20). While bugs are often found in rural areas, they are attracted to gaseous CO2 which is emitted at higher levels in urban areas than rural ones (23). Larger cities also tend to have high immigration rates; people raised where Chagas is already endemic often are chronically infected without knowing it and can serve as a reservoir to infect naive vectors and perpetuate infection into their new area (4). Larger cities also exhibit an urban heat island, where the inner city is warmer, specifically overnight than the outlying rural or suburban areas (9). This affects the mean diurnal temperature (the average temperature range for each day in any given month), which, as seen with *T. gerstaeckeri*, can have a strong effect on vector distribution (17). Because of this a strong urban heat island, yields a stable overnight temperature, making cities more suitable than other areas for some vectors (20).

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