

Chapter 3: Manuscript

Chagas Disease in the United States: The emerging threat and the role climate and awareness play in its spread

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Abstract

This study uses a geographic information system (GIS) and survey analysis to evaluate the interconnected role that temperature variability and disease awareness play in the potential emergence of Chagas disease (American trypanosomiasis) in the United States. Chagas disease is endemic in Central and South America, and primarily spreads to humans directly via the triatomine vector. Primary hosts for most triatomine species are rodents and occasionally dogs, tree toads, birds, and lizards. The disease itself is caused by a parasitic protozoan, *Trypanosoma cruzi* (*T. cruzi*) which is found in the triatomine's feces and is most often spread while the triatomine is consuming a blood meal. *T. cruzi* can enter the body through a minor abrasion on the skin, the mucous membranes, conjunctivae, or through oral consumption. *T. cruzi* can also be transmitted through a blood transfusion and organ transplantation, as well as congenitally. In the United States, reports that triatomines have been found in habitats that are in close proximity to humans indicates an opportunity for the emergence of Chagas disease.

To determine the risk of Chagas disease transmission, it is important to define characteristics of the triatomine that make it an effective disease vector as well as to depict the status of Chagas disease awareness among physicians and the general population. This study utilizes a GIS to spatially analyze individual samples from three triatomine species within the United States known to harbor *T. cruzi* naturally and that exhibit qualities of domesticity as well as to determine the population at high risk for disease transmission. The qualities of domesticity are based upon whether the species is known bite humans and domestic dogs as well as reports indicating that the species has been found in the domestic setting. An analysis of the 2000 and 2030 minimum temperature threshold for increased triatomine activity delineates the current and potential higher risk population and is followed by a vignette-based survey to gauge the level of physician awareness of Chagas disease within the delineated higher risk range.

Results reveal the current range at higher risk for Chagas disease extends throughout the southern United States and the higher risk range will expand into Utah, Nebraska, Iowa, and New Jersey based upon a predicted 1° C (2° F) increase in temperature by the year 2030. Survey results indicate a limited consideration of Chagas disease during differential diagnosis, illustrating that the low number of Chagas disease cases discovered in the United States may be attributable to a lack of disease awareness as opposed to a lack of disease threat.

Keywords: Chagas disease, physician survey, vector-borne disease, infectious disease, medical geography

Introduction

The potential for the emergence of Chagas disease (American trypanosomiasis) in the United States presents an example of the way in which climate conditions and physician awareness can affect disease dispersion. Chagas disease is endemic in Central and South America and primarily spreads to humans via the triatomine vector (also known as the “kissing bug”) (CDC 2006). The triatomine vector is present in the United States though there have only been five autochthonous (locally acquired) cases diagnosed in the U.S. since 1955 (Woody and Woody 1955; Anonymous 1956; Betz et al. 1984; Schiffler et al. 1984; Navin et al. 1985; Ochs et al. 1996; Herwaldt et al. 2000). However, reports indicate that additional cases may have gone undiagnosed (Kirchhoff et al. 1987; Kirchhoff 1993; Holbert et al. 1995; Leiby et al. 2000; Zayas et al. 2001; Leiby et al. 2002; Kirchhoff et al. 2006). Additionally, given the increasing domestic presence of the vector which places it in close proximity to humans, and changing human geographies within the vector’s range, the potential exists for the disease to become established in the United States. Consequently, through the use of a geographic information system (GIS) and survey analysis, this study examines the interconnected role that disease awareness and climate conditions play in the potential emergence of Chagas disease in the United States.

Increased globalization and human migration have contributed to the emergence of a number of infectious diseases in recent decades; specifically, global travel, and increased urbanization and suburbanization have played a role in the emergence of severe acute respiratory syndrome (SARS), dengue, and Lyme disease, respectively (Haggett 1994; Cooke and Shapiro 2003). Additionally, some researchers believe that climate variability (short-term variation) and change (long-term variation) have played a role in the spread of diseases as well. Consequences of climate variability and change are evident with diseases such as malaria, which has become established at higher elevations in recent years (Garrett 1994), and hantavirus pulmonary syndrome, which emerged in the Four Corners region of the United States as a result of changing precipitation patterns brought about by the El Niño-Southern Oscillation (Poveda et al. 2001; Meade and Earickson 2005). The dynamic nature of the relationship between environmental conditions and vector-borne diseases justifies the need to examine the spatial and temporal patterns of the triatomine through the use of a GIS as well as to monitor Chagas disease awareness in order to better understand the potential for Chagas to emerge in the United States.

Consequently, the objectives of this study are:

- To delineate the range that is at higher risk for Chagas disease transmission due to the temperature-induced increase in activity of three triatomine species in the United States that exhibit qualities of domesticity.
- To determine the level of Chagas disease awareness among physicians in regions defined as being at higher risk for disease transmission.

This study is built on the theoretical frameworks of landscape epidemiology and disease ecology within medical geography as it explores the range of the triatomine based on biogeography and how that relates to the three factors of disease ecology: environment, behavior, and population (Meade and Earickson 2005). Complimentary to all three factors of the disease ecology approach is landscape epidemiology, which defines a natural disease nidus as the locale where a disease maintains continued circulation (Meade and Earickson 2005). Accordingly, the research presented here will define the triatomine qualities that play a role in the transmission of *T. cruzi* to humans based upon whether or not the vector is in the domestic setting and if it is associated with dogs or people. When considering culture and the disease nidus within landscape epidemiology along with the three factors within disease ecology, we are able to bridge the gap between triatomine biogeography and disease awareness. Figure 1 serves as a template for the research presented here and is based upon the frameworks described above.

Background

Infectious disease eradication has seen both success and failure over the past fifty years. The development of antibiotics and the global eradication of smallpox are two examples of the massive strides made in the elimination of several infectious diseases. On the other hand, there has been an increase in vector-borne diseases due to the movement of populations into areas that were once heavily forested as well as through trade and commerce (Haggett 1994). For example, the *Aedes albopictus* mosquito was introduced to North America from Asia through shipping routes after being transported inside used tires that collected water resulting in a suitable breeding site for the mosquito (Hawley et al. 1987). Similarly, triatomines reportedly have been transported in luggage and with furniture (Lent and Wygodzinsky 1979). Examples such as these

demonstrate the need for ongoing infectious disease research and public health education in order to adapt to the dynamic nature of many diseases, such as Chagas disease.

Chagas disease itself is caused by a parasitic protozoan, *Trypanosoma cruzi* (*T. cruzi*), and to cause an infection, the disease agent must enter the body either through a minor abrasion on the skin, the mucous membranes, conjunctivae, or through oral consumption; other potential transmission routes include blood donation, organ transplantation, and from mother to baby during pregnancy (CDC 2006). Chagas disease in its acute form lasts from four to six weeks and has mild symptoms of fever, depression, and facial edema. During this phase, the disease is treatable (Leiby et al. 2002); however, it is difficult to detect due to the presentation of unremarkable symptoms (Holbert et al. 1995; CDC 2006; Sánchez-Guillén et al. 2006). The second stage of infection is asymptomatic and is considered the indeterminate phase, which can last for decades (Prata 2001; Sánchez-Guillén et al. 2006). The final stage is chronic, and it is in this stage that the heart and the digestive tract can be damaged as a result of carrying *T. cruzi* in the blood (Holbert et al. 1995; CDC 2006; Sánchez-Guillén et al. 2006), resulting in 16-18 million human *T. cruzi* infections and 45,000 annual deaths (TDR 2003).

In the United States, the disease is considered to be sylvatic, which means the disease transmission cycle is zoonotic and is maintained between the triatomine vector and non-human reservoir hosts (Lent and Wygodzinsky 1979). The primary host for most triatomine species is rodents, and occasionally birds, dogs, lizards, and tree toads (Kagan et al. 1966; Lent and Wygodzinsky 1979; Ryckman 1984; Barr et al. 1995; Meurs et al. 1998; Bradley et al. 2000; Peterson et al. 2002; Beard et al. 2003).

Throughout South America, many triatomine species are considered domestic and maintain populations inside human dwellings (Lent and Wygodzinsky 1979). The transformation from a sylvatic habitat to a domestic habitat may be a byproduct of deforestation, which is partly occurring to accommodate population growth (Patz et al. 2004; Ramsey et al. 2005). Today in the United States, triatomine species that were once sylvatic are adapting to the peridomestic and domestic settings (Kagan et al. 1966; Ryckman 1984; Herwaldt et al. 2000; Beard et al. 2003).

Triatomine biogeography

A 1979 entomological cataloging of the triatomine describes nine species and numerous subspecies in the conterminous United States (Table 1) (Lent and Wygodzinsky 1979). Of the nine triatomine species listed, six are natural carriers of *T. cruzi*. The range of the triatomine in the United States covers twenty-six states and all of these states have at least one species which is found to be naturally infected with *T. cruzi* (Lent and Wygodzinsky 1979).

The triatomine is a parasitic arthropod; therefore, all species require a blood meal, and may feed on the blood of birds, mammals, and reptiles, depending on the species (Usinger 1944; Lent and Wygodzinsky 1979). The triatomine species with the largest range in the United States are *Triatoma sanguisuga*, *T. lecticularia*, and *T. protracta*, all of which have been found to harbor *T. cruzi* naturally (Usinger 1944; Lent and Wygodzinsky 1979). Over the past fifty years, numerous reports of these species in and around human habitations have been recorded (Sjogren and Ryckman 1966; Lent and Wygodzinsky 1979; Navin et al. 1985; Herwaldt et al. 2000; Beard et al. 2003). Furthermore, in cases where dogs test seropositive for *T. cruzi* and have triatomines living in their bedding, there is an increased risk of disease transmission to humans (Barr et al. 1995; Bradley et al. 2000; Beard et al. 2003; Enger et al. 2004; Crisante et al. 2006).

Depending on the disease, many factors can play a role in determining the potential risk for disease emergence. In the case of Chagas disease, one of the main determinants is the triatomine's efficiency for transmitting the disease agent. The primary factor considered is the rate of defecation, which is important given that the mode of transmission is via the feces. Therefore, when the triatomine defecates while consuming the blood meal or shortly thereafter, the chances of disease transmission via the bite wound are greater (Kagan et al. 1966). Reports of delayed defecation in triatomine species from the United States hinders the occurrence of disease transmission during the blood meal (Kagan et al. 1966; Lent and Wygodzinsky 1979). Additionally, the risk of disease transmission via the feces may be possible through contaminated food or the mucous membranes if hygienic practices are not followed (CDC 2006).

Another important component of disease transmission is the prevalence of infectivity in vector populations (Usinger 1944; Kagan et al. 1966). Studies of *T. protracta* and *T. sanguisuga* samples in the United States reveal a *T. cruzi* infection rate of 20% (Usinger 1944) and 6% (Kagan et al. 1966), respectively. Additionally, since the discovery of Chagas disease in the

United States, non-human reservoirs for *T. cruzi* have been identified. The geographic range of the reservoirs extends from California across the southeastern half of the United States and north into Maryland. Domestic dogs (primarily hunting dogs) are also found to be carriers of *T. cruzi* (Barr et al. 1995; Meurs et al. 1998; Bradley et al. 2000; Beard et al. 2003), and the triatomine's association with dogs is a defined quality of domesticity considered in the research presented here.

When a vector bites a human, it is considered an additional factor in triatomine domesticity. Despite the sylvatic nature of the triatomine species in the United States (Kagan et al. 1966; Ryckman 1984; Herwaldt et al. 2000; Beard et al. 2003), studies throughout the Americas report numerous cases of sylvatic species biting humans when an opportunity is present. Triatomines can enter a dwelling through an unscreened open window and events such as this may be exacerbated by a reported attraction to lights that increases the triatomine's lure to the domestic dwelling (Usinger 1944; Sjogren and Ryckman 1966; Wood and Wood 1967; Lent and Wygodzinsky 1979; Monroy et al. 2003; Vazquez-Prokopec et al. 2004; Vazquez-Prokopec et al. 2006).

Upon entering a home, triatomines often go undetected because they generally feed at night and are nocturnal by nature (Lent and Wygodzinsky 1979; Schofield 1979; Navin et al. 1985; Herwaldt et al. 2000). Furthermore, increased triatomine activity in warmer temperatures may result in triatomines entering the home and creating an opportunity for human contact with the disease vector. Consequently, modeling the potential triatomine range based on biogeography and climate is useful in predicting where disease emergence may occur.

Chagas disease awareness in the United States

While an understanding of the vector's biogeography is important for the control of vector-borne diseases, ultimately it is physicians' awareness of a disease and its symptoms that is crucial for detecting a disease's emergence. The diagnosis of only five human autochthonous Chagas disease cases in the United States corresponds to decades in which there was a considerable increase in Chagas disease research and publication and serves as a working hypothesis within the context of disease ecology for the purpose of this research (Woody and Woody 1955; Anonymous 1956; Betz et al. 1984; Schiffler et al. 1984; Navin et al. 1985; Ochs

et al. 1996; Herwaldt et al. 2000). This study defines the risk for Chagas disease based upon reported increases in the proximity of the disease vector to humans as well as limited disease awareness.

As shown in Figure 2, there has been an increase in the number of publications on Chagas disease between 1910 and 1980 (Coutinho 1999 Figures, Reproduced with permission by Sage Publications), and the diagnosis of four out of the five Chagas disease cases in the United States is loosely correlated with peaks in the number of articles published. The fifth case (not shown in Figure 2) was diagnosed in 1998 after a mother recognized a *T. sanguisuga* in her son's crib and realized the disease threat after watching a television program about parasitic insects (Herwaldt et al. 2000). This relationship supports the notion that the perceived low risk currently associated with Chagas disease in the United States is more a lack of awareness than it is a lack of actual threat. The 1983 case in the United States was diagnosed by chance nearly a year after the patient's death (Betz et al. 1984; Ochs et al. 1996), supporting the notion that Chagas disease is not always considered as a diagnosis. Additionally, a Hispanic immigrant in the chronic phase of Chagas disease diagnosed in Mississippi had previously been mis-diagnosed and treated for acute depression prior to the appearance of a heart problem, which prompted a test for *T. cruzi* given the patient's history and origin (Holbert et al. 1995). Physicians state that the symptoms presented in the acute stage are often misdiagnosed, and that the differential diagnosis does not consider Chagas disease unless there is a strong indication (Holbert et al. 1995).

Diagnosis can be further complicated if the vector's bite is not recognized as a triatomine bite; the bite is reportedly painless and often misdiagnosed as a bite from another arthropod or a spider (Vetter 2001). Reports such as these illustrate a gap in Chagas disease research and indicate a need to investigate awareness of the disease among physicians. In the context of disease ecology, if physicians and the public are not aware of the potential disease threat due to the bite or presence of a disease vector, the potential for misdiagnosis is greater.

Additionally, physician awareness of the various transmission routes is an important component in diagnosis. A study of blood banks in Mexico reveals a *T. cruzi* prevalence rate of 0.75%, which yields approximately 1,800 new cases each year in Mexico (Kirchhoff et al. 2006), supporting the potential for Chagas disease to be transmitted through the blood supply (CDC 2006). In particular, Kirchhoff et al. (2006) found that four recipients of infected blood demonstrated acute symptoms of Chagas disease, but physicians failed to make the diagnosis.

Consequently, the oversight was attributed to mild symptoms and the physicians' lack of awareness with respect to Chagas disease transmission through blood transfusion (Kirchhoff et al. 2006).

It is estimated that 50,000 to 100,000 Latin American immigrants in the United States are infected with *T. cruzi* (Kirchhoff et al. 1987). These estimates reveal the risk of disease transmission through blood transfusion and organ transplantation in the United States, as well as indicate a need for increased physician awareness (Leiby et al. 2000; Leiby et al. 2002; CDC 2006). Studies of blood donors who tested seropositive for *T. cruzi*, reveal that 63% do in fact have *T. cruzi* parasites circulating in their blood, which may result in a recipient acquiring the disease agent (Leiby et al. 2002). Recent reports state that blood screening for Chagas disease will begin soon in the United States (CDC 2006; Lee 2006), but concerns about the past and current condition of the blood supply should not be discounted.

Data and Methods

Delineating triatomine range

In the context of disease ecology, investigating changes in a disease vector's range and habitat is important in order to gauge the vector's proximity to humans and quantify disease risk. Wood (1938) described the northward expansion of *T. protracta*'s range in California, but since that time, research on the triatomine's range has been limited in the United States with the exception of the modeling of the species' range in parts of Texas using the genetic algorithm for rule-set prediction (GARP) model (Peterson et al. 2002; Beard et al. 2003). A number of modeling efforts have mapped the triatomine range in much of Latin America (Abad-Franch et al. 2001; Costa et al. 2002; Peterson et al. 2002; Guzman-Tapia et al. 2005; López-Cárdenas et al. 2005). In particular, Peterson et al. (2002) apply the GARP model to the *T. gerstaeckeri* species' range in Mexico in order to uncover the environmental characteristics under which the disease agent and its vector thrive. The broad-scale study presented here uses a GIS to analyze the current and potential triatomine range in the United States and intends to fill a gap in the research of Chagas disease emergence from a spatial perspective.

The data used to delineate the range of increased triatomine activity and the area at highest risk for disease emergence includes: information regarding triatomine activity threshold levels

from the literature; minimum temperature data; and census data for the United States. The Sjogren and Ryckman (1966) outlined thresholds for increased triatomine activity are utilized in this study to delineate the range where the triatomine is most active, with the purpose of defining areas within the United States that are at a higher risk for the emergence of Chagas disease. The threshold for increased triatomine activity occurs between 19° C (67° F) to 29° C (84° F) with more activity exhibited at the higher end of the range (Sjogren and Ryckman 1966). The triatomine species highlighted in this portion of the study are *T. protracta*, *T. sanguisuga*, and the *T. lecticularia*, all of which demonstrate the defined qualities of domesticity illustrated in Figure 1. The qualities of domesticity are based upon whether the species bites humans and domestic dogs as well as reports indicating the species is in the peridomestic setting. These three species comprise the largest range in the United States and are found to be natural carriers of *T. cruzi* (Lent and Wygodzinsky 1979). In addition, samples from all three species have been discovered inside human dwellings (Sjogren and Ryckman 1966; Lent and Wygodzinsky 1979; Navin et al. 1985; Herwaldt et al. 2000).

Gridded average (1971-2000) minimum temperature data, based on the parameter-elevation regressions on independent slopes model (PRISM) (2006), were acquired from the Spatial Climate Analysis Service. Data were acquired for the months of June, July, and August based upon accounts of increased triatomine activity in warmer temperatures and their tendency to be the hottest months of the year in the United States (Sjogren and Ryckman 1966; Wood and Wood 1967). The 800-meter resolution temperature dataset is at an appropriate scale given the broad, country-wide scope of the project. Other climate variables, specifically humidity, wind speed, and precipitation, were considered but not included in the study given that Sjogren and Ryckman (1966) found that they had no relationship on the flight of *T. protracta*. In addition, to analyze the population at risk under current and warmer climate conditions based on the predicted 2030 temperature increase of 1° C (2° F) (IPCC 2001), we acquired 1-kilometer raster grids depicting census data for the continental United States from the Socioeconomic Data and Applications Center (SEDAC) (2007). To depict the proximity of the reported triatomine samples and the five autochthonous cases to the densely populated areas within the United States, a gridded nightlights layer was obtained from NOAA's Defense Meteorological Satellite Program (NOAA-NGDC 2007).

In order to delineate the areas at highest risk for Chagas disease emergence, the raster minimum temperature data values for the defined months were entered into a GIS and reclassified based on the triatomine activity threshold information. All values $>19^{\circ}\text{C}$ (67°F) were assigned a value of 1, and all other values were assigned a value of 0. Next, we employed a raster to polygon conversion for each reclassified layer representing the months of June, July, and August. The same process of reclassification and conversion was then applied using the predicted approximate 1°C (2°F) increase in temperature so as to illustrate the potential triatomine range for each month under warmer climate conditions.

Finally, we incorporated the SEDAC population density data into the GIS using an overlay analysis. The spatial analyst zonal statistics tool in ArcGIS (ESRI 2005) was utilized to establish the population at higher risk due to increased triatomine activity. By incorporating the 2000 and 2030 June, July, and August polygons into spatial analyst as individual datasets, we established the population at higher risk of Chagas disease transmission. To analyze the area contained within the higher risk range for 2000, we performed a field calculation for area within the June, July, and August polygons.

The second portion of the study gauges the level of Chagas disease awareness in areas delineated as geographically at higher risk for disease transmission through a review of diagnosed cases and other relevant literature as well as through a physician survey.

Evaluating disease awareness

After delineating the geographic areas at higher risk for Chagas transmission, we evaluated the level of Chagas disease awareness among physicians working in the higher risk areas using an online survey; it is through physician diagnosis that a disease's emergence will be recognized. The survey was tested using a pilot study with three physician participants, and an invitation to participate in the final survey was sent to 300 physicians. We recruited physician participants using information gathered from online searches of hospitals within the following cities/county, all of which have a population over 50,000 and are within the potential range of the vector: Corpus Christi, Texas; Modesto, California; Rutherford County, Tennessee; Jackson, Mississippi; and Santa Fe, New Mexico. These areas are selected because three of the cases of

Chagas disease in the United States were discovered in or around them, and/or represent locations within the area at higher risk for disease transmission.

In preparation for the survey, we consulted two medical professionals along with past physician surveys for procedural and content advice (Tambor et al. 1993; Bowen et al. 2005). The survey included a vignette depicting a patient with typical symptoms of Chagas disease as well as questions to help categorize the canvassed physicians. The vignette was identical in every way except for the ethnicity of the patient (African American, Caucasian, and Hispanic). After creating 100 vignettes per ethnicity, we then sent 20 surveys per ethnicity to physicians in each of the five participating cities, which totaled 60 physician surveys per city. Each physician was asked to rank ten of eleven diseases/health problems listed according to their likelihood for diagnosis, along with the lab studies/tests they would order to further evaluate the patient. The physicians' personal information, such as: ethnicity and gender; commonly read journals; specialty and geographic location of the practice; patient base; and when/where they received their professional education was also requested. Follow-up reminders were sent to those physicians who did not initially complete the survey.

In order to perform the preferred *chi-square test*, 80% of the cell values must be greater than or equal to 5; therefore, due to our small sample size, we utilized the VassarStats website to run a one-tailed *Fisher's exact test*, which is found to be useful for this type of analysis (Lowry 2007). Under the null hypothesis, the proportion of physicians that considered Chagas disease based upon both the Hispanic and non-Hispanic patient vignette is equal to the proportion of physicians who considered Chagas disease based up the Hispanic patient only. Under the alternative hypothesis, the proportion of physicians ranking Chagas disease in differential diagnosis is not identical in the two populations.

Results

Areas of Increased Risk of Chagas disease transmission

Triatomine samples have been catalogued from the west coast to the east coast throughout the southern United States and as far north as northern California to Maryland. As depicted in Figure 3, reported triatomine samples are used as point data to illustrate the vector's range and the five autochthonous cases of Chagas disease are depicted for the purpose of model validation.

The gridded nightlights layer delineates populated areas within the United States and illustrates the vector's proximity to these areas. For example, samples are depicted in the largely populated areas of southern California, northern Utah, Missouri, central Tennessee, and northern Georgia.

Despite the sizeable triatomine range, only certain areas within the United States are considered at higher risk for Chagas disease transmission. The areas at highest risk for Chagas disease transmission are based on warmer temperatures and both the current and predicted risk ranges are shown in Figure 4. In Figure 4A, the current June range considered at higher risk covers a small portion of southern California and Nevada and extends through the southern half of Arizona, most of Texas (except the extreme western portion and the panhandle), and the southern half of Oklahoma. The current June range shifts from the south in central Arkansas and expands northward in the eastern portion of the state, crossing into Tennessee and the western portion of Mississippi. All of Florida and the southern portions of Alabama, Georgia, and South Carolina are included.

Between the months of June and July, the current northern range considered at higher risk for Chagas disease expands into southern Utah (Figure 4B). In the Midwestern and eastern regions of the United States, given the predicted 1° C (2° F) temperature increase (IPCC 2001), the current higher risk range increases considerably in July, expanding into northern Kansas and Delaware. The current higher risk range contracts between July and August affecting primarily the central United States, which by August only covers a small portion of Kansas and excludes Missouri and Illinois. The areas of higher elevation across the southern United States, including the southern Rocky Mountains and the southern Appalachians, are excluded from the higher risk areas.

The 2000 data suggest that the population considered at higher risk increases considerably between June and July and only decreases a fraction of that in August (Figure 5). This is the result of a large temperature increase between the months of June and July that is to some extent sustained into the month of August. Between July and August, the eastern coast does not experience as much of a decrease in higher risk range as does the central United States. Consequently, the larger population found on the eastern coast may explain why Figure 5 depicts only a slight decrease in affected population for the month of August.

The month of July continues to have the largest defined higher risk range based on the predicted 1° C (2° F) temperature increase (IPCC 2001). The area affected by the climate change

illustrated in Figure 4 increases between 2000 and 2030 by 23% for the month of June (Figure 6). As depicted in Figure 6, the June increase between 2000 and 2030 is noticeably higher than the increase for July and August, which is 15% and 16%, respectively. As is evident from Figure 4B, the range at higher risk due to a temperature-induced increase in triatomine activity will expand northward in the Midwest and north along the Atlantic coast, placing a considerably larger population in the higher risk range for disease transmission. The area affected by increasing temperatures between 2000 and 2030, illustrates the impact of predicted climate change on vector-borne disease transmission and reveals a need for ongoing studies to prevent disease emergence.

Spatial Pattern Validation

Validation through the use of field data and results from other studies is necessary in order to illustrate the usefulness of a model (Rykiel 1996). This study utilized two forms of model validation in order to support the value of our outcomes. The first validation describes results from an ecological niche model and the second validation incorporates the five autochthonous cases of Chagas disease in the United States. Our first example of model validation uses results from a GARP model published after the discovery that triatomines from the species *T. gerstaeckeri* had colonized a peri-domestic location in Texas (Beard et al. 2003). The illustration depicts the *T. gerstaeckeri* range as covering the southwestern portion of Texas, extending into the panhandle and the southeastern corner of New Mexico. The range depicted in the GARP model overlaps our results through the southeastern tip of New Mexico and southwestern Texas; however, the maps differ where the GARP model's range extends further north through the Texas panhandle and southeastern New Mexico.

Additionally, the five autochthonous cases in the United States, while a small sample, serve as the second form of validation of our model. This model validation reveals that four of the five autochthonous cases in the United States occurred within the area currently delineated as higher risk for disease transmission. The use of these data help to validate our model and delineate the current higher risk range for Chagas disease in order to assist regional health departments in preventing the emergence of Chagas disease. All point data representing the five diagnosed cases

are within the 2000 range for both July and August except for the case from Lake Don Pedro, California, which is not depicted in the defined higher risk range for June, July, or August.

Physician awareness of Chagas disease in the United States

Of the 300 physicians canvassed for this study there was only a 7% response rate. This lackluster response limits quantitative analysis; however, through the use of a contingency table and the *Fisher's exact test*, we were able to establish a measure of statistical significance based upon the patient's race/ethnicity as described in the vignette (Table 2). As illustrated in the contingency table, of the 22 physicians that responded to the survey, 8 ranked Chagas disease in differential diagnosis and 14 did not. Among those who ranked Chagas disease, 4 were based upon the Hispanic vignette, whereas, 4 were not. Among the 14 physicians not ranking Chagas disease, one was based upon the Hispanic patient and 13 were not. Based upon the contingency table, the *Fisher's exact test* reveals a *p value* of 0.039. This is significant in that it indicates that physicians within the range at higher risk for Chagas disease in the United States do consider Chagas disease in differential diagnosis of Hispanic patients but not for the rest of the population.

Qualitative analysis reveals that fourteen percent of participating physicians requested information on the patients' travel history alone, indicating recognition that travelers can be responsible for the importation of disease agents. In one case, Chagas disease is specifically written next to the statement indicating the need for travel history and another states "must know geography or travel history to prioritize infectious etiologies." These data lack statistical significance yet are valuable to further illustrate that Chagas disease is not always considered in the higher risk areas of the United States. Physician ethnicity or education information did not appear to be a factor in the survey results.

Discussion

This study has identified areas of increased triatomine activity within the United States and has defined the areas at higher risk for Chagas disease emergence. While the sylvatic nature and delayed defecation exhibited in triatomine species within the United States indicates a relatively

low risk of Chagas disease transmission, there is evidence of increased triatomine domesticity (Beard et al. 2003). Additional concerns pertain to the growing population from Latin America that may serve as disease carriers and reports of misdiagnosis, both of which reveal a potential for the emergence of Chagas disease (Kirchhoff et al. 2006).

The blood supply in the United States is vulnerable to *T. cruzi* contamination due to an increasing Latin American population which is emigrating from countries where Chagas disease is endemic (Kirchhoff et al. 1987; Kirchhoff 1993; Leiby et al. 2002; Beard et al. 2003; Kirchhoff et al. 2006). In addition, as the *T. cruzi* infected population grows and the close proximity of triatomines to people becomes greater, it is necessary to study the risk of direct disease transmission via the vector. For example, an in-depth study of similarities among the five autochthonous cases in the United States as well as their proximity to farms employing Latin American workers may be useful.

The concepts presented in this study offer a different perspective with which to investigate broad-scale disease potential. In the case of Chagas disease, reports of climate variability affecting increased triatomine activity that results in a larger human population in close proximity to the vector, illustrates a need for fine-scale studies as well as follow-up studies measuring the population at higher risk in these areas. Consideration of the optimum temperature thresholds for both *T. cruzi* and the triatomine is necessary in order to adequately measure transmission risk. For example, the minimum threshold for *T. cruzi* transmission is estimated to be 18° C (64° F) and higher temperatures reportedly increase pathogen development in the triatomine; however, temperatures greater than 38° C (100° F) become lethal to the pathogen (IPCC 2001). Other important considerations that may be useful in future studies is the minimum triatomine threshold for biological activity which is 2-6° C (36-37° F) as well as reports that insufficient humidity may increase feeding rates at higher temperature (IPCC 2001).

The use of the predicted 1° C (2° F) temperature increase by 2030 is based upon an IPCC (2001) report that is derived from expert collaborations and the assimilation of numerous climate models. For example, both the Hadley model (DEFRA 2005) and the Canadian model (Hengeveld 2000) state that the projected increase in temperatures will vary between land and water surfaces due to the nature of land surfaces to warm faster than water. Therefore, predicted temperature increases for North America may be higher than the global average (Hengeveld

2000). Nonetheless, for the purpose of this broad-scale study, the predicted global mean average is used.

Reports that triatomine contact with domestic dogs presents an increased risk of Chagas disease transmission to humans and points toward the need for increased collaboration between epidemiologists, entomologists, and veterinarians in future disease risk predictions (Barr et al. 1995; Bradley et al. 2000; Beard et al. 2003; Enger et al. 2004; Crisante et al. 2006). The results presented here are to serve as insight for comprehensive fine-scale studies of areas that are in the margins of the defined higher risk ranges through a GIS model that utilizes weighted variables acquired from landscape, ecological and environmental data. For example, fine-scale studies may explain why the case of Chagas disease discovered in Lake Don Pedro, California is not included in the higher risk range defined in this research.

The broad-scale geographic perspective utilized in this study is helpful to public health officials who are concerned about the emergence of Chagas disease in the United States. The framework presented here is a culmination of disease ecology and landscape epidemiology that can be utilized in future studies of vector-borne disease as well as in comprehensive fine-scale studies of Chagas disease. In order to eradicate established diseases and prevent disease emergence in new locations, there must be ongoing epidemiological research as well as continued dialogue among public health professionals and the general population. Consequently, health officials and the public must recognize that a disease exists before control or eradication efforts can begin. Furthermore, the general population should be aware of the routes of disease transmission in order to control or eradicate a disease. Moreover, these results illustrate a need to measure awareness of Chagas disease among the general population as well as to study whether triatomine bites have increased over the years.

Limitations of Study

Limitations of the study presented here are related to differing opinions in the classification of triatomine species, selection of the utilized threshold data, and the use of 2000 census data in predictive mapping. Due to the broad-scale approach used in this study, we believe the general argument is adequately represented in spite of these limitations. Nevertheless, future fine-scale studies of Chagas disease in the United States should factor in these limitations as well as

additional variables that pertain to the specific region of study as well as the triatomine species present.

Ryckman (1984) indicates that the lack of taxonomic information on the triatomine has led to conflicting scientific conclusions about the species' distribution. Threshold data is frequently difficult to obtain and oftentimes reports vary. Uncertainty may arise due to application of the 19° C (67° F) minimum threshold to the three highlighted species when, in fact, it is based upon a study of simply the *T. protracta*, given the lack of information on other species (Sjogren and Ryckman 1966). Finally, the gridded population data are based on the 2000 census, and when considering the population at risk under warmer temperatures, population growth and the movement of people is not taken into account.

Conclusion

While Chagas disease is endemic in Central and South America, the potential exists for the emergence of Chagas disease in the United States. At present, the disease transmission cycle is considered to be sylvatic and therefore is less of a threat, but a Texas outbreak in 2003 in which infected triatomine colonized a peridomestic dwelling illustrates the potential for direct transmission of the protozoan to humans via an infected vector in the United States (Beard et al. 2003). Further investigation into reports such as these is necessary in order to prevent the emergence of Chagas disease in the United States. By using the frameworks of disease ecology and landscape epidemiology in a geographic approach, we are able to delineate areas at higher risk for disease emergence.

This 2003 occurrence serves as an example of a zoonotic disease threat to domestic dogs which is a focal point in landscape epidemiology (Patz et al. 2004). When human encroachment into a vector's habitat causes domestic animals to become seropositive for a normally sylvatic disease agent, a potential disease reservoir is created that is inherently linked to humans (Bradley et al. 2000; Beard et al. 2003; Patz et al. 2004). The factors related to vector-borne disease emergence among people include the ecology of the disease and its evolution, the regional culture of the people, and the disease nidus (Meade and Earickson 2005). The discovery of *T. cruzi* infected dogs is an example of how changes in the disease nidus can lead to disease emergence in the human population.

Previous research suggests that the northern limit of the triatomine range in the United States currently extends beyond 40 degrees latitude based on collection data; however, the study presented here indicates that the risk of Chagas disease transmission is highest in the lower latitudes in the southern portion of the country. Chagas disease is potentially an emerging threat in the United States based upon the effects of current and predicted temperature patterns on the triatomine range as well reports indicating a lack of disease awareness in areas defined as being at a higher risk for transmission.

In order to maintain an able-bodied society, it is necessary to direct public health resources toward present health threats as well as toward emerging diseases such as Chagas disease. The factors of triatomine biogeography and Chagas disease awareness characterize the regions at higher risk for Chagas disease emergence in the United States and justify a need for in-depth investigation so as to alleviate the potential for disease emergence. In order to prevent or control vector-borne disease epidemics, it is first necessary to delineate areas at highest risk for transmission followed by implementation of a plan of action that includes educating both the general population and public health officials about the disease risk and methods for eradication of the vector.

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Table 3.1 United States Summary of Lent and Wygodzinsky's (1979) *Triatoma* species.

| <i>Triatoma</i> species in the United States | | | |
|---|-------------------------|---|--|
| State | Species | Naturally Infected with <i>T. cruzi</i> | |
| New Mexico, Texas | <i>T. gerstaeckeri</i> | X | |
| Arizona | <i>T. incrassata</i> | | |
| Arizona, New Mexico, Texas | <i>T. indictiva</i> | | |
| Arizona, California, Florida, Georgia, Illinois, Kansas, Louisiana, Maryland, Missouri, New Mexico, North Carolina, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas | <i>T. lecticularia</i> | X | |
| Arizona, California, Colorado, Nevada, New Mexico, Texas, Utah | <i>T. protracta</i> | X | |
| Arizona | <i>T. recurva</i> | X | |
| Arizona, California, New Mexico, Texas | <i>T. rubida</i> | X | |
| Florida | <i>T. rubrofasciata</i> | | |
| Alabama, Arizona, Arkansas, Florida, Georgia, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maryland, Mississippi, Missouri, North Carolina, Ohio, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Virginia | <i>T. sanguisuga</i> | X | |

Table 3.2 Contingency table depicting the outcome of a physician survey based on a ranking of Chagas disease in differential diagnosis where vignettes representing Hispanic and non-Hispanic patients are presented.

| Hispanic | Chagas disease ranked | | Total |
|----------|-----------------------|----|-------|
| | Yes | No | |
| Yes | 4 | 1 | 5 |
| No | 4 | 13 | 17 |
| Total | 8 | 14 | 22 |

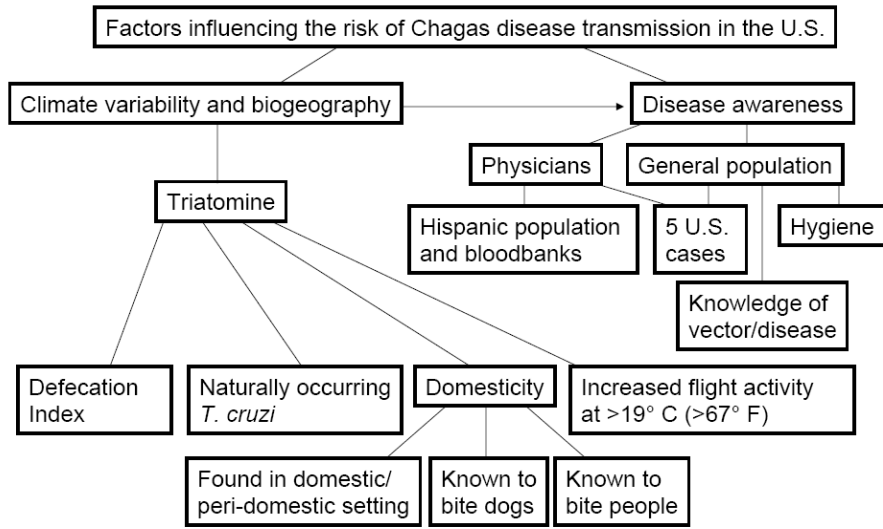


Figure 3.1 Schematic defining variables for Chagas disease risk in the United States. Topics of focus in this study are domesticity and its components, naturally occurring *T. cruzi*, increased flight activity, and physician awareness.

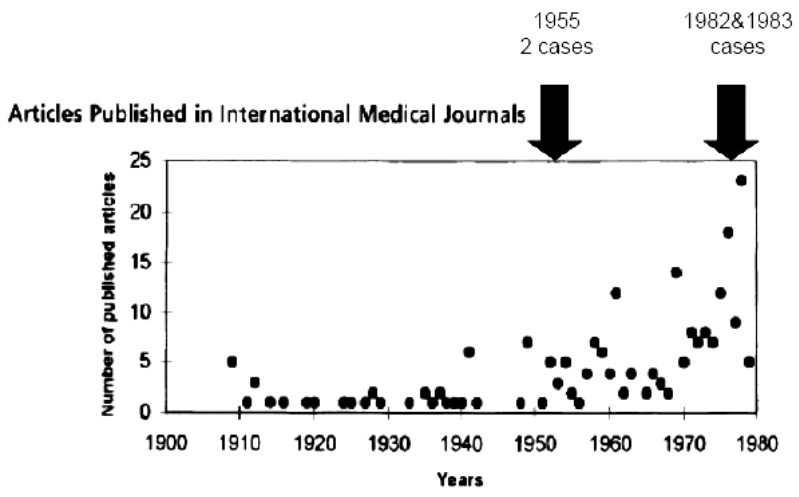


Figure 3.2 International articles published on Chagas disease (Coutinho 1999 Figures, Reproduced with permission by Sage Publications). An increase in the publication of articles related to Chagas disease is loosely correlated with four of the five autochthonous cases in the United States.

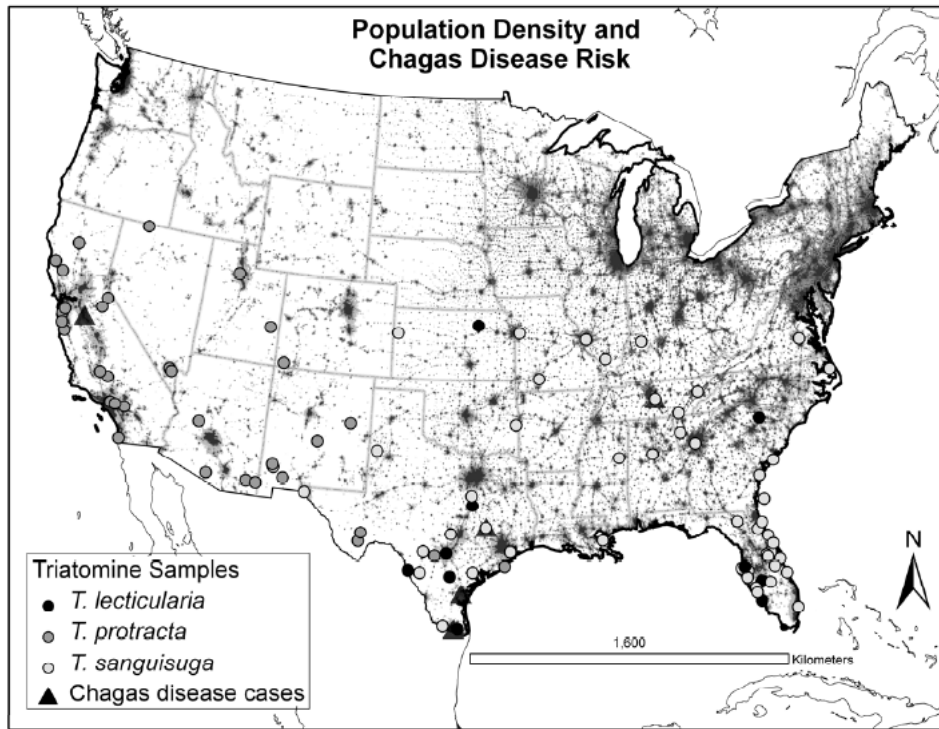


Figure 3.3 Triatomine samples and autochthonous Chagas disease and their proximity to populated areas in the United States (Usinger 1944; Woody and Woody 1955; Anonymous 1956; Sjogren and Ryckman 1966; Ryckman and Ryckman 1967; Lent and Wygodzinsky 1979; Betz et al. 1984; Ryckman 1984; Schiffler et al. 1984; Navin et al. 1985; Ochs et al. 1996; Bradley et al. 2000; Herwaldt et al. 2000; Yabsley and Noblet 2002). [Data sources: (ESRI 2005); (NOAA-NGDC 2007)]

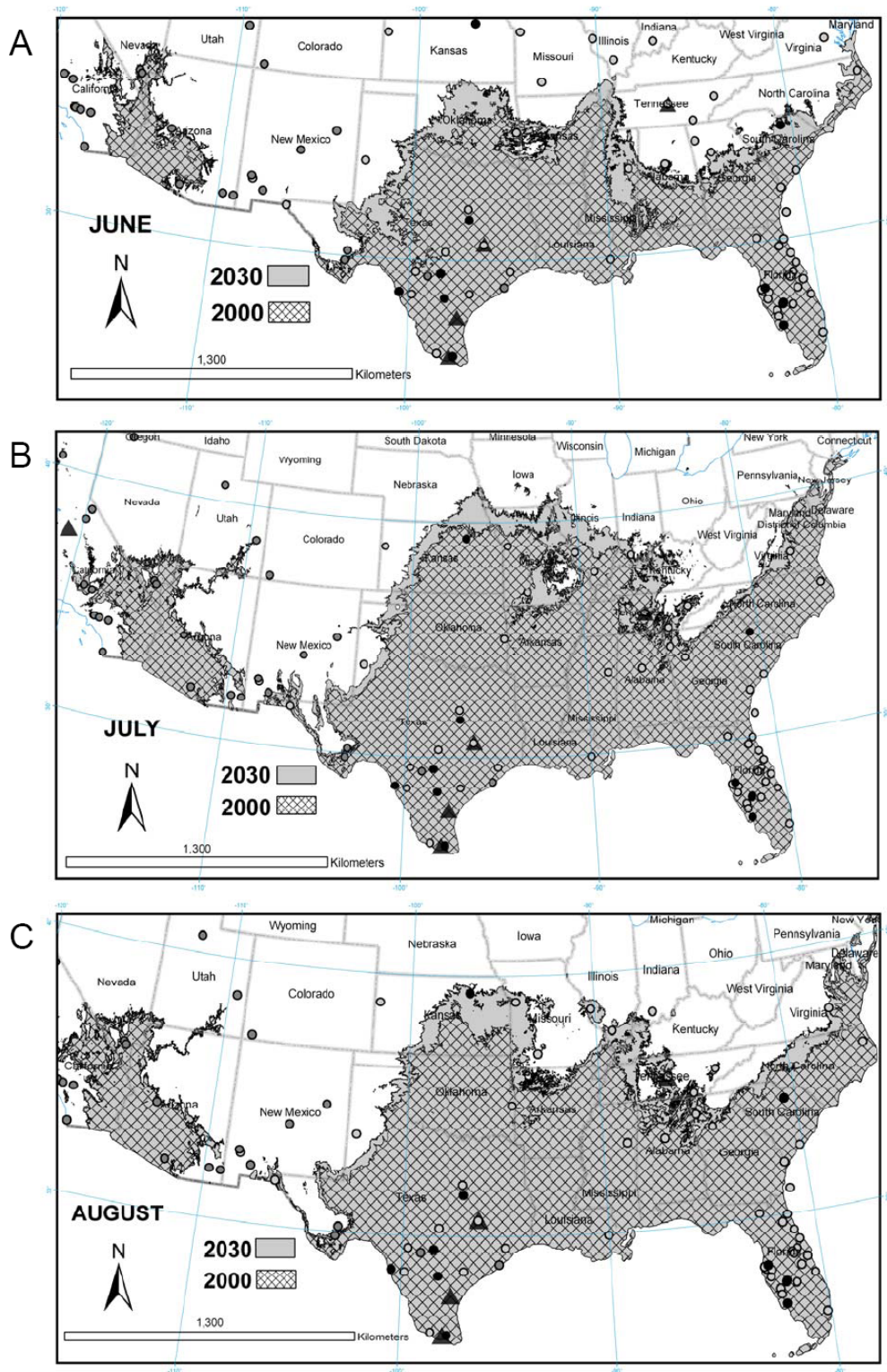


Figure 3.4 Areas of Increased Risk of Chagas disease transmission [Data sources: (ESRI 2005); (PRISM 2006)].

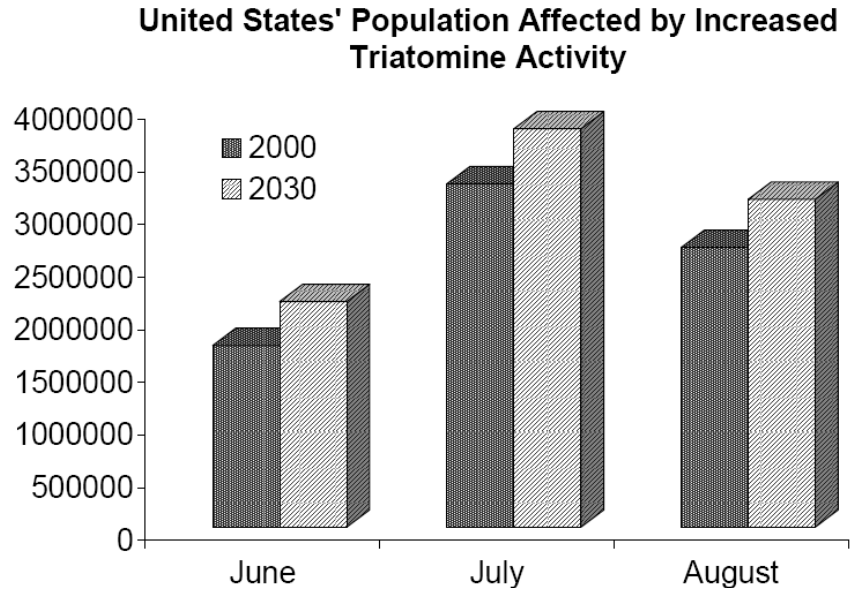


Figure 3.5 Population at higher risk for Chagas disease transmission due to climate change (SEDAC 2007).

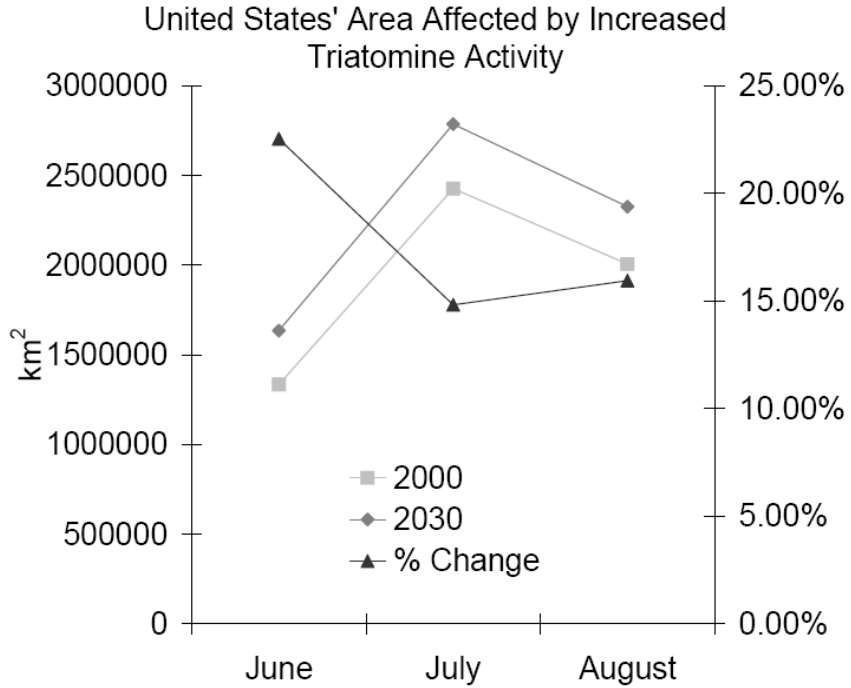


Figure 3.6 Area affected by increased triatomine activity and the percent change between the 2000 and 2030 calculations.