INTRODUCTION

In 2002, the World Health Organization estimated that more than 120 million (25 percent) of the inhabitants of Latin America were at risk for contracting infection with *Trypanosoma cruzi* – the protozoan parasite that is responsible for causing American trypanosomiasis, or Chagas disease (WHO, 2002). As of 2004, it was estimated that 16 to 18 million of the inhabitants of Latin America were already infected (WHO, 2002).

In the countries throughout which the disease is endemic, it is estimated that Chagas disease caused 45,000 deaths during the 1980s, 23,000 deaths throughout the 1990s, and 11,000 deaths from 2000 to 2007 alone (Schmunis, 2007). From a global perspective, infection with *T. cruzi* represents the third largest tropical disease burden after malaria and schistosomiasis, primarily from the heavy rates of morbidity and mortality caused by both the acute and chronic phases of the disease (Figure1; Appendix 1).
There are two phases of the human disease: the acute, which occurs immediately after infection, lasts from a few weeks to months, and is usually asymptomatic; and the chronic, which occurs in approximately 30 percent of cases. The thickness of arrows indicates the relative probability of a depicted pathway.

Source: Rassi et al. 2007

Morbidity from Chagas disease has large effects on the Latin American economy. In 1997, while the average annual per-capita gross domestic product in Latin America was US$2,966, the economic loss for the continent due to early mortality and disability caused by Chagas disease was US$8,156 million – meaning that the economic loss in productivity caused by the disease was equivalent that year to 2.5 percent of the continent’s entire external debt in 1995 (Moncayo, 1997).

While anti-parasitic drugs are available to treat Chagas disease, they tend to be most efficacious during the acute phase of the disease. However, the acute form of Chagas disease
often has a mild and non-specific presentation, meaning that the majority of those who are infected are not aware until chronic stages occur years to decades later (Figure 1). During chronic stages of the disease, treatment is mainly focused on supportive care and addressing specific symptomatic complaints (CDC, 2007).

Because Chagas’ elusive disease presentation presents difficulties in terms of treatment, over the last four decades the focus for combating Chagas disease has been mainly through preventative intervention (Dias et al., 2002). In 1991, the six countries of Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay began an international program to control Chagas disease through vector elimination and blood donation screening, entitled the Southern Cone Initiative (Schofield and Dias, 1999). By the end of the 1990s, the Southern Cone Initiative had set a global precedent that combating Chagas Disease through vector control was highly efficacious. Through the Initiative, the countries of Uruguay and Chile, along with large parts of Brazil and Argentina, were declared free of Chagas disease in less than a decade, through intervention methods such as repetitive spraying and diligent disease surveillance (Dias et al., 2002). Additionally, cost-benefit analyses done in Brazil revealed that for every dollar spent on the prevention of Chagas disease, US$17 was saved in medical care and disabilities (Moncayo, 2003). The success of the Southern Cone Initiative led to the formation of similar intervention programs in both the Andean region and Central America (Dias et al., 2002).

In 1997, Peru joined the Southern Cone Initiative in order to decrease infection rates of Chagas disease in southern Peru. Growing evidence suggests that Chagas disease in the northern region of the country is increasing as well (Aguilar et al., 2007; Vargas et al., 2007). In the near future, these growing rates of infection in the northern region will need to be combated through efficacious vector-focused interventions (Aguilar et al., 2007; Vargas et al., 2007). However, *T. cruzi* is carried by more than 13 different vector species in this region, meaning that the transmission rates of the most prevalent species need to be analyzed in order to maximize the efficacy of future vector-related interventions (Cuba Cuba et al., 2002).

**SPECIFIC AIMS**

**BECAUSE CHAGAS DISEASE CONTROL MEASURES** have only been implemented in the southwestern departments of Peru in Tacna, Moquegua, Arequipa, and Ica, due to the habitat range of *Triatoma infestans*, the primary vector in the Southern Cone Initiative, in-depth information on
the epidemiology of Chagas disease in northern Peru is insufficient, although there is growing evidence that the disease is a national problem (Dias et al., 2002; Moncayo, 2003; Aguilar et al., 2007; Vargas et al., 2007). The primary objective of this research is to assess the correlation between the infection rate of the main triatomine vectors of *T. cruzi* and the prevalence of the disease in the human populations in northwestern Peru. The Peruvian Ministry of Health, in association with the Pan American Health Organization (PAHO) and the World Health Organization (WHO), may then add this data to the present database to use as a baseline for the implementation of future control programs.

This study will use data reported in Cuba Cuba et al. (2002) to identify rates of Chagas disease in the Department of La Libertad, located along the coast of northwestern Peru (Figure 2).

![Image of Peru map with arrow pointing to La Libertad](http://www.silvanatours.com.pe/aboutperu/images/map.jpg)

**FIGURE 2.** The geographical and political regions of Peru, with an arrow pointing to La Libertad, the proposed study region.


Cuba Cuba et al.’s 2002 research summarizes information on the distribution and synanthropic behavior of triatomines in northern Peru in order to provide further evidence for Chagas disease.
vector control. Additionally, the current research will serve as a follow-up study of Vargas et al.’s 2007 research, whose main objective was to update epidemiological data of the main vectors of *T. cruzi* in northern and northeastern Peru.

Using Cuba Cuba et al.’s 2002 data supplemented by information from Vargas et al. (2007), the current study will gather epidemiological data on the current prevalence of Chagas disease infection in humans in 21 rural localities in the Cascas district of La Libertad. Prevalence will be assessed on-site using a Chagas Stat-Pak rapid immunochromatographic test for Chagas disease (Ponce et al., 2005). This test has several advantages over standard serological tests (such as ELISA and IIF) because of its simplicity, short execution time, no need for special equipment or expertise, and consequently, its reduced cost (Ponce et al., 2005). Surveys, interviews with the study population, and investigation of hospital records dating back to 2000 will also be utilized.

The prevalence rates of human subjects presenting with either acute or chronic Chagas disease at the time of surveying will then be analyzed for possible correlations between the infection rate of *T. cruzi* in humans and in the main vector species in La Libertad. Ultimately, this data may be used to determine which vector species should be targeted in vector-based intervention programs.

Because of the high biodiversity of vector species in the region, populations of different species of insect vectors overlap, leading to the possibility of vector transmission overlap, with several species acting as possible disease vectors in one region. Because numerous studies cite more than one vector species as harboring *T. cruzi*, it is highly likely that vector transmission overlap is occurring in the La Libertad region (Cuba Cuba et al., 2002; Aguilar et al., 2007; Vargas et al., 2007). Furthermore, while purely sylvatic populations of these species may exist in the study region, some species such as *R. ecuadoriensis* appear to have become purely domestic, making them feasible candidates for eradication (Cuba Cuba et al., 2002; Dias et al., 2002). Therefore, domestic vectors with high transmission rates of *T. cruzi* should be labeled as primary targets for vector control.

**BACKGROUND**

**POVERTY IN NORTHERN PERU** puts this region of the country at high risk for Chagas disease transmission. As a developing country, the average per capita income in 2006 was just above
US$6,000 (Watkins, 2007). A 2007 study in northern Peru found a low prevalence of urban structures; less than ten percent of houses were made with brick and/or concrete walls, while over 90 percent of structures were made of a mixture of adobe, moist soil, and thatched roofing (Vargas et al., 2007). Rural houses such as these harbor higher rates of triatomines in thatched roofing and wall cracks, which provide excellent protection for the vectors during daylight hours (Vargas et al., 2007).

The country of Peru is geographically divided into three main parts – the Pacific west coastal area, the Amazonian east, and the central mountain range of the Andes (Vargas et al., 2007) (Figure 1). Currently, the Southern Cone Initiative targets *T. infestans* in southern Peru, while the Andean Countries’ Initiative covers the remainder of the country (Guhl, 2007) (Figure 3).

![Figure 3](image-url)  
**FIGURE 3.** Intervention programs in Latin America for controlling the main vectors of Chagas disease associated with human habitat. Source: Guhl, 2007

While the Southern Cone Initiative has been successful at intervening with vector transmission in southern Peru, installing successful interventions in the northern region of the country has been slow in part due to the complicated nature through which Chagas disease transmits as well uncertainty about the most efficacious ways to combat the disease (Guhl, 2007; Vargas et al., 2007).
Chagas disease is transmitted via fecal contamination of a bite wound initially caused by a triatomine vector (Figure 4).

FIGURE 4. The vector-human transmission cycle of *Trypanosoma cruzi* in Latin America. Triatomines become infected with *T. cruzi* after ingestion of an infected blood meal. The ingested trypomastigotes transform into epimastigotes in the vector’s midgut, where they multiply and differentiate. The parasites then travel to the hindgut of the vector where they further differentiate into metacyclic trypomastigotes that are infective to a new host if bitten.

Source: Franco-Paredes et al., 2007

In South America alone, 25 species in nine genera of wild *T. cruzi* reservoir hosts and vectors are present, with 19 triatomine species reported in the country to date (Aguilar et al., 2007; Guhl, 2007). Because the majority of research on Chagas disease vectors has been on *T. infestans*, much less is known about the regions in which *T. infestans* is absent, such as northern Peru (Vargas et al., 2007). The main disease vectors that are all naturally infected with *T. cruzi* in northern Peru along the Pacific north coast include *Triatoma dimidiata, Rhodnius ecuadoriensis, Triatoma carrioni, Panstrongylus herreri,* and *Panstrongylus chinai* (Guhl, 2007) (Figure 5).
**FIGURE 5.** Geographic distribution of triatomine vectors with *T. infestans* in southern Peru and *R. ecuadoriensis* in northern Peru. Source: Guhl, 2007

*T. dimidiata, P. herreri,* and *R. ecuadoriensis* are strongly synanthropic and are considered significant disease vectors, while *T. carrioni,* and *P. chinai* come from peri-domestic settings (Cuba Cuba *et al.*, 2002; Vargas *et al.*, 2007). It should be noted that targeting only the primary domestic vectors such as *R. ecuadoriensis* might allow other competent peri-domestic vectors such as *P. chinai* to fill in newly opened domestic niches, thus continuing the transmission of the disease (Vargas *et al.*, 2007). These autochthonous triatomine species that might act as secondary vectors can also be targeted for elimination, but would require more surveillance to prevent re-infestation of the domestic populations (Dias *et al.*, 2002; Cuba Cuba *et al.*, 2002).

While some records of disease incidence in the northern region do exist, the literature currently lacks strong epidemiological records regarding overall prevalence of Chagas disease in northern Peru (Cáceres *et al.*, 2002; Cuba Cuba *et al.*, 2002). Available records are limited to acute presentation of the disease as well as blood donor seropositivity, and lack mention of chronic infection, which comprises the majority of infections (Anon., 2004 in Vargas *et al.*, 2007). In order to design future interventions, epidemiological data needs to be collected to
determine which vectors are most frequently transmitting Chagas disease to northern Peruvian populations and which targeted vectors will lead to the most significant reductions in disease transmission (Aguilar et al., 2007; Vargas et al., 2007).

EXPERIMENTAL DESIGN

This research will focus on the same 21 rural localities studied in Cuba Cuba et al.’s 2002 research, to determine the prevalence of Chagas disease in the study population in comparison to T. cruzi infection rates in the local vector species.

The proposed research plan will include an assessment of prevalence using:

• An immunochromatographic assay (Chagas Stat-Pak) performed according to methods in Ponce et al.’s 2005 study (Appendix 2)
• Interviews and surveys given to the study population at the time of assessment
• Hospital records dating back to 2000

The immunochromatographic assay will be used to determine study subjects presenting with the acute phase of the disease. Interviews and hospital records will be used to estimate those who are infected, but either not presenting with symptoms, or who are in between the acute phase and the chronic phase of the disease. Consequently, data collected within this study might be an underestimate of the actual prevalence within the region, due to the number of people who are infected but not presenting with the acute or chronic phases. However, the use of the two extremes (acute and chronic) as surrogate markers for all subjects infected in the region is not a severe limitation when estimating where to implement vector-based interventions, since precise disease numbers are not needed to begin a control campaign.

With the permission of Cuba Cuba et al., this study will test the subjects living in the same houses as those tested in Cuba Cuba et al.’s 2002 study (M. Miles, personal communication, 20 May 2008). Alternatively, because of foreseen complications and limitations including, but not limited to: not being able to locate the same houses as were used in the previous study; families no longer living in the same house; and differing prevalence rates due to the study occurring in 2002, the study subjects will be chosen randomly from the same 21 rural localities in the Cascas District in the Department of La Libertad, Peru. The results will not be biased based on this randomization, because the localities for Cuba Cuba et al.’s 2002 research were also chosen randomly.
The study will be carried out in the summer of 2009, and all data will be analyzed in the United States after fieldwork is completed.

SIGNIFICANCE

Although international attention has been focused on Chagas disease in the past decades and many control programs such as the Southern Cone Initiative has cut transmission by as much as 70 percent in some regions, Chagas disease still accounts for almost 700,000 DALYs in Latin America (Moncayo, 2003; WHO, 2004). There are estimates of prevalence of the disease being as high as 15 million existing cases, with between 50,000-200,000 new infections occurring each year, yet funding for research, prevention, and control continues to be limited (Tarleton et al., 2007).

Chagas disease has a significant economic impact on afflicted regions and countries, where affects such as decreased worker productivity help to explain why it is both a disease of poverty as well as poverty-inducing. Currently, vector control methods and strategies have significant limitations, diagnostic tools are variable and have unknown reliability, drugs for treatment are inadequate, and there are no vaccines on the horizon (Tarleton et al., 2007). Additionally, programs such as the Southern Cone Initiative that rely heavily on insecticide use to control vector populations have been experiencing problems with vector resistance to insecticides (Tarleton et al., 2007). Consequently, a multi-pronged approach to vector control intervention is imperative for successful regional elimination of Chagas disease.

Multiple studies cite the need for a comprehensive research and control program in northern Peru, including the need for prevalence surveys and the characterization of transmission dynamics in affected regions (Aguilar et al., 2007; Vargas et al., 2007). As such, this study recognizes the urgent need for further research, and seeks to help fill the knowledge gap concerning transmission rates, prevalence, and relative importance of the main vectors of T. cruzi in northern Peru, so that future control programs may succeed in being highly efficacious.

LITERATURE CITED


**APPENDIX**

**APPENDIX 1.** Clinical signs and symptoms of the acute and chronic form of Chagas disease. The acute form of Chagas disease occurs immediately after infection and can last from a few weeks to months presenting as an acute flu-like illness (CDC, 2007). Primary presentation of acute disease consists of an erythematous indurated area where the parasite entered the human host’s skin known as a chagoma (John and Petri, 2006). Generally, swelling of the chagoma will subside over a period of two to three months (John and Petri, 2006). The acute phase of Chagas disease can also cause inflammation of the heart, brain, or lining of the brain, resulting in mortality, particularly in infants (CDC, 2007).
The chronic form of the disease tend occurs in approximately 30 percent of those who are infected (CDC, 2007). The disease’s chronic form can present as heart rhythm abnormalities and/or swelling of different parts of the gastrointestinal tract. Heart rhythm abnormalities most often lead to sudden death through congestive cardiac failure and/or syncope, and are caused by actual infestation of parasites within the heart tissue (John and Petri, 2006). Megaeosophagus and megacolon can cause prolonged constipation and/or fecal impaction in the host years after initial infection (John and Petri, 2006).

“A drop of serum (5µl) is placed in the sample well at the holder, and buffer provided with the kit is added. After 5 to 15 min, the mixture of serum plus buffer migrates to the top of the device. The end of the reaction is indicated by a colored line on the top (positive control). The presence of anti-*T. cruzi* antibodies in the sample produces a pink/purple line (positive), whereas in its absence no line appears in the reaction zone (negative). A second pink/purple line in the control zone confirms that the reaction was completed and that the test is, hence, validated. Reading of the results on the appropriate region of the device is performed by recording the absence of any line as negative and a strong or weak line as positive.”