



**Texas Children's
Hospital®**

Baylor
College of
Medicine®

Chagas Disease Transmission Sources and Cardiac Outcomes among Texas Blood Donors

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Diseases in Nature Conference

26 June 2014

Pediatrics

Agenda

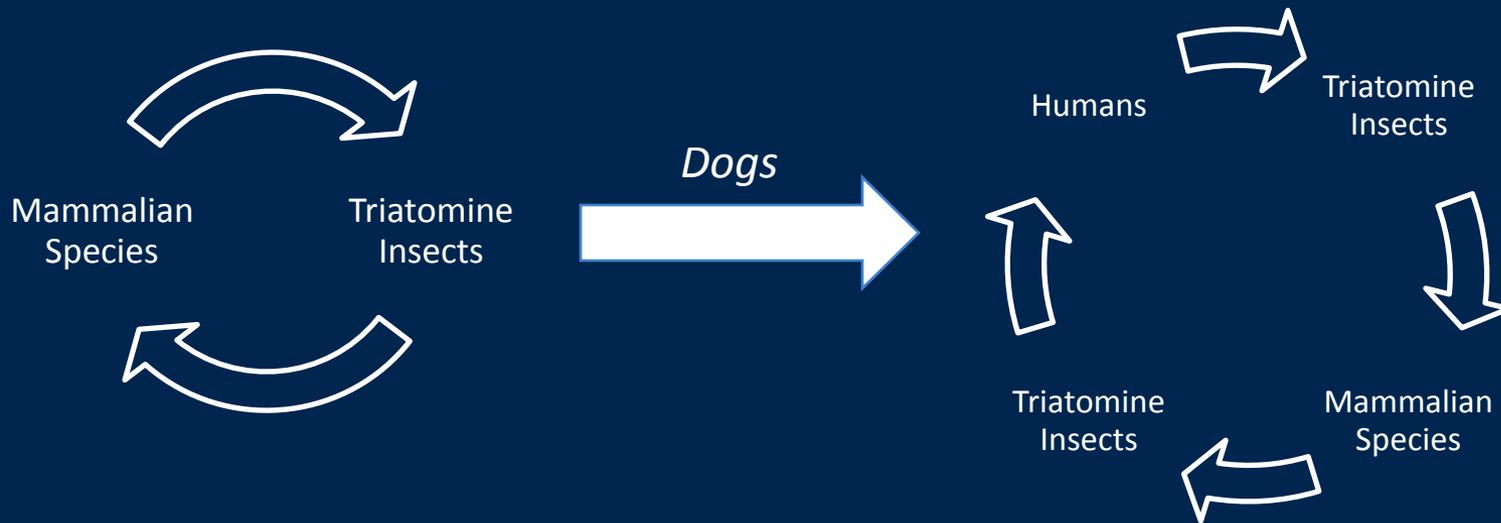
- History of Chagas disease in Texas & US
- Seroprevalence estimates of Texans
- Houston area human disease transmission sources
- Cardiac manifestations of Chagas in Texas residents



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YOU



Sylvatic vs Domestic Transmission Cycles



Triatomine Bug Stages

- 1** Triatomine bug takes a blood meal (passes metacyclic trypomastigotes in feces, trypomastigotes enter bite wound or mucosal membranes, such as the conjunctiva)

Metacyclic trypomastigotes in hindgut

8



Multiply in midgut

7



6 Epimastigotes in midgut



- 5** Triatomine bug takes a blood meal (trypomastigotes ingested)



i = Infective Stage
d = Diagnostic Stage

Human Stages

- 2** Metacyclic trypomastigotes penetrate various cells at bite wound site. Inside cells they transform into amastigotes.



- 3** Amastigotes multiply by binary fission in cells of infected tissues.

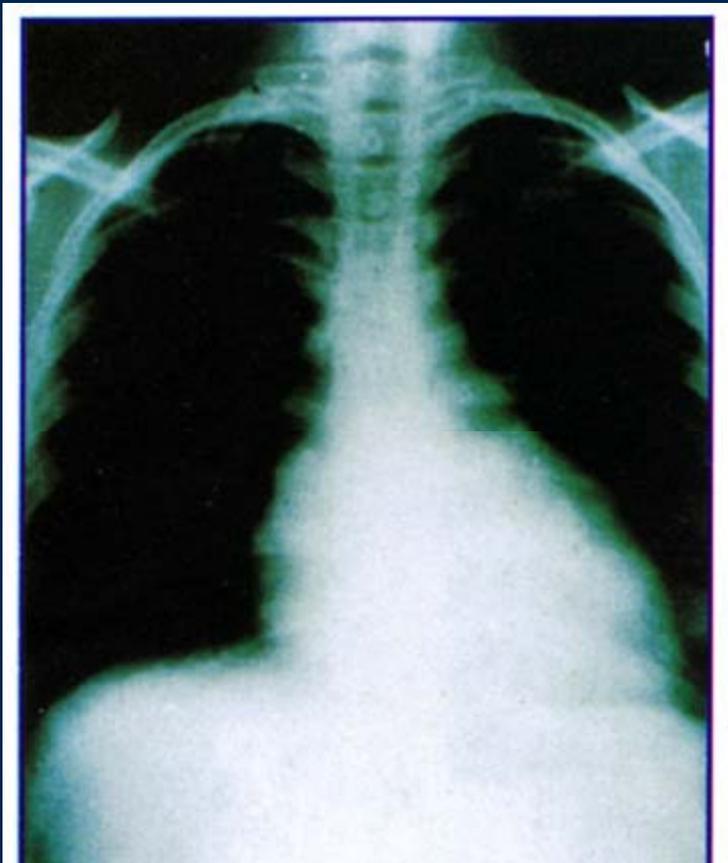
Trypomastigotes can infect other cells and transform into intracellular amastigotes in new infection sites. Clinical manifestations can result from this infective cycle.



- 4** Intracellular amastigotes transform into trypomastigotes, then burst out of the cell and enter the bloodstream.



<http://www.dpd.cdc.gov/dpdx>

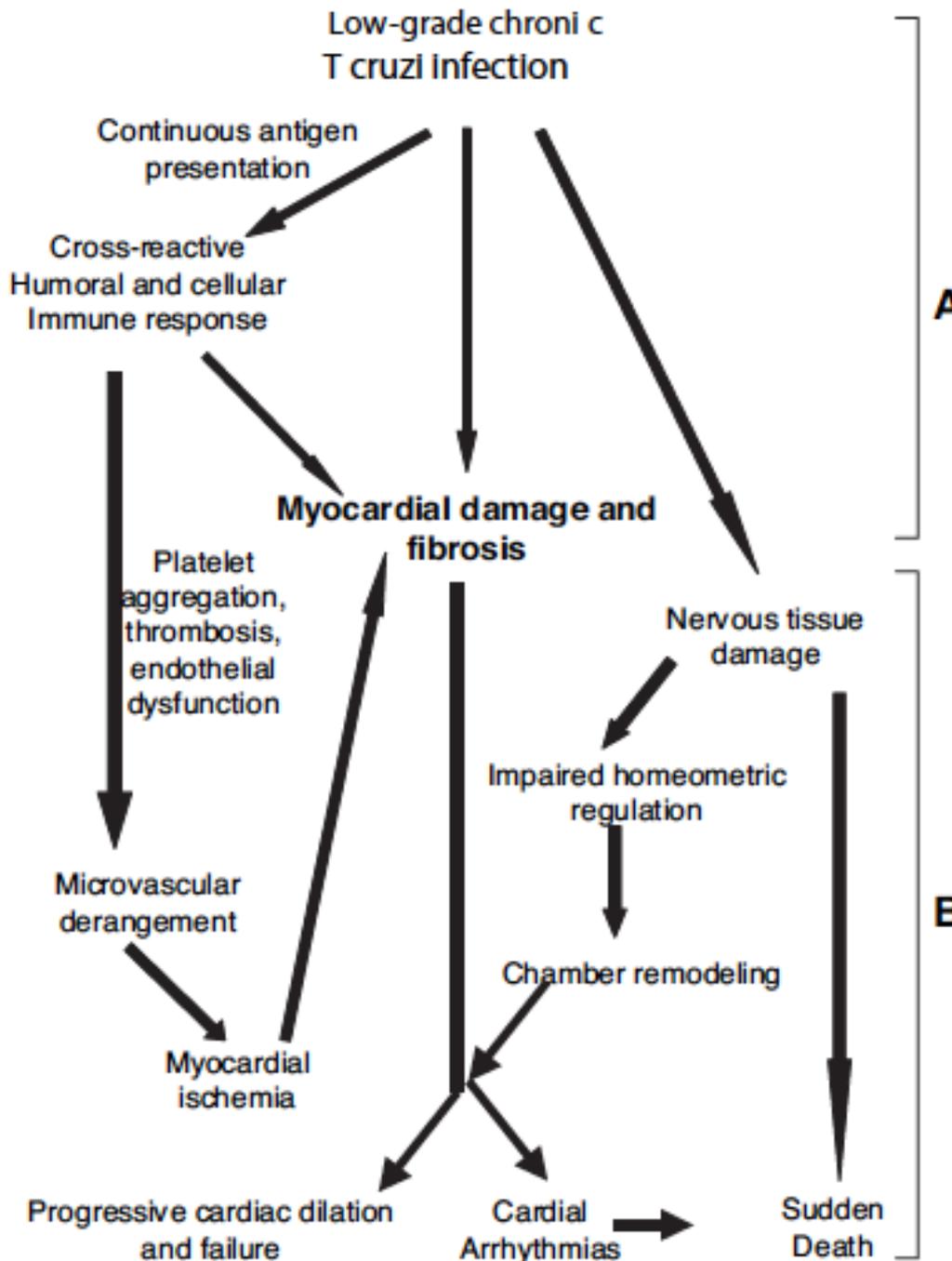


>30% develop cardiac outcomes

Marin-Neto J A et al.
Circulation 2007;115:1109-1123

[ftp://ftp.cdc.gov/pub/infectious_diseases/iceid, 2002/pdf/schmunis.pdf](ftp://ftp.cdc.gov/pub/infectious_diseases/iceid/2002/pdf/schmunis.pdf)

Pediatrics



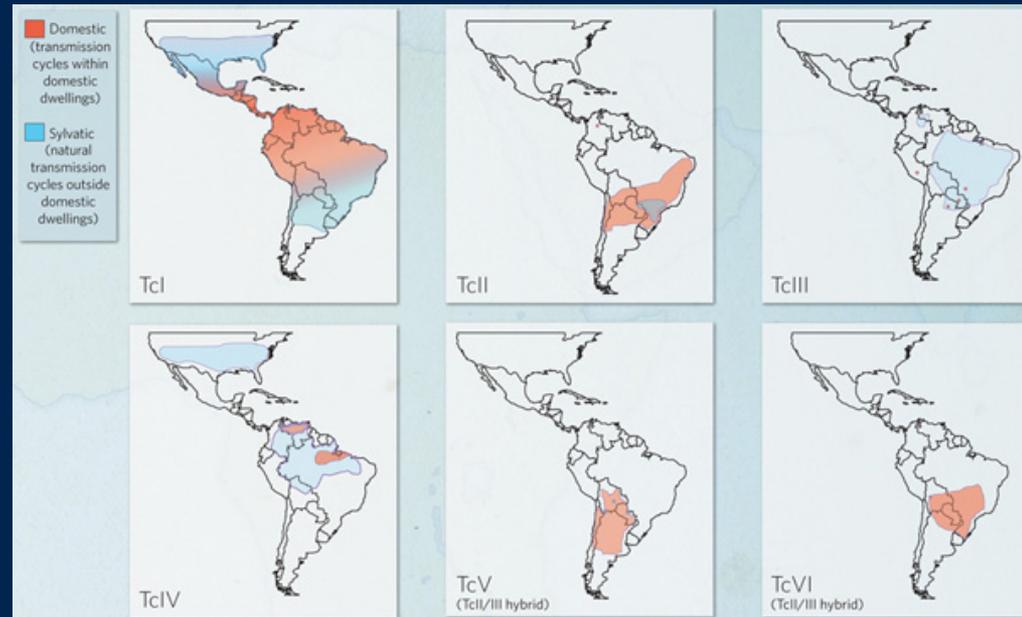
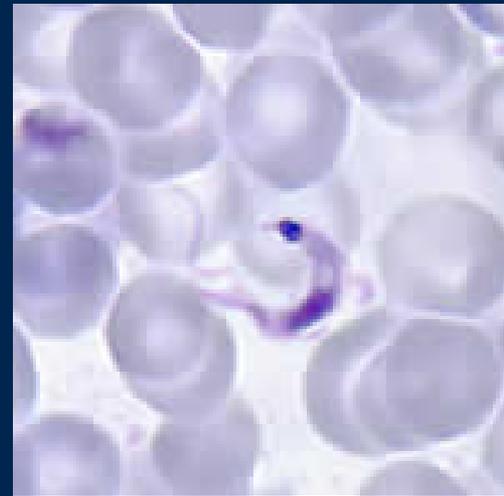
Diagnosis

-Acute Phase

- Microscopic examination
- PCR

-Chronic Phase:

- Two positive test results
 - ELISA (multiple), IB, IFA
- Clinical history & exposure
- Locally acquired cases*



Treatment

- Investigative Drug Protocol under CDC regulation
 - Approved by CDC for distribution
 - Treatment Failure in 19-97% of patients

Drug	Age group	Dosage and duration
Benznidazole	< 12 years	10 mg/kg per day orally in 2 divided doses for 60 days
	12 years or older	5-7 mg/kg per day orally in 2 divided doses for 60 days
Nifurtimox	≤ 10 years	15-20 mg/kg per day orally in 3 or 4 divided doses for 90 days
	11-16 years	12.5-15 mg/kg per day orally in 3 or 4 divided doses for 90 days
	17 years or older	8-10 mg/kg per day orally in 3 or 4 divided doses for 90 days

Jackson et al. 2013. *BMC Infect Dis.*

Pinazo MJ et al. 2010. *Antimicrobial Agents and Chemotherapy*

History of Chagas Disease in Texas and the United States

Chagas Disease in a Domestic Transmission Cycle in Southern Texas, USA

Charles B. Beard,* Greg Pye,† Frank J. Steurer,*
Ray Rodriguez,‡ Richard Campman,†
A. Townsend Peterson,§ Janine Ramsey,¶
Robert A. Wirtz,* and Laura E. Robinson†

After three dogs died from acute Chagas cardiomyopathy at one location, an investigation was conducted of the home, garage, and grounds of the owner. A serologic study was conducted on stray dogs, and an ecologic niche model was developed to predict areas where the vector *Triatoma gerstaeckeri* might be expected.

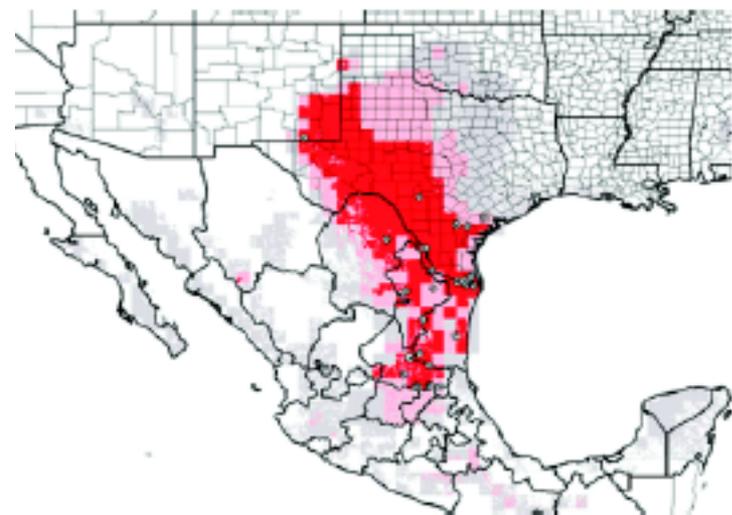


Figure 5. Genetic Algorithm for Rule-set Prediction-generated ecologic niche model, predicting distribution of *Triatoma gerstaeckeri*. Small circles show actual collection sites. Area in dark red is where high certainty exists for the specific niche of the species. The area in light red is the zone of moderate certainty, and the area in gray is for low certainty.

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An Estimate of the Burden of Chagas Disease in the United States

Caryn Bern and Susan P. Montgomery

Division of Parasitic Diseases, National Center for Zoonotic, Vector-Borne and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

Chagas disease causes the highest burden of any parasitic disease in the Western hemisphere. By applying published seroprevalence figures to immigrant populations, we estimate that 300,167 individuals with *Trypanosoma cruzi* infection live in the United States, with 30,000–45,000 cardiomyopathy cases and 63–315 congenital infections annually. *T. cruzi* causes a substantial disease burden in the United States.

Table 1. Calculated Prevalence of *Trypanosoma cruzi* Infections in Latin American-Born Persons living in the United States in 2005

Country of origin	Immigrant population living in the United States	<i>T. cruzi</i> prevalence in country of origin, %	Estimated no. of immigrants with <i>T. cruzi</i> infection in the United States
Mexico	16,963,851	1.03	174,388
El Salvador	1,458,014	3.37	49,164
Guatemala	1,014,669	1.98	20,131
Honduras	567,002	3.05	17,311
Argentina	223,931	4.13	9246
Ecuador	345,204	1.74	6003
Colombia	554,821	0.96	5304
Brazil	501,036	1.02	5106
Bolivia	61,453	6.75	4149
Nicaragua	223,931	1.14	2553
Peru	371,980	0.69	2552
Venezuela	151,350	1.16	1754
Chile	92,761	0.99	914
Costa Rica	95,761	0.53	509
Paraguay	16,707	2.54	425
Uruguay	51,737	0.66	339
Belize	42,130	0.74	312
Panama	107,601	0.01	6
Total	22,843,939	1.31	300,167

DONOR INFECTIOUS DISEASE TESTING

The United States *Trypanosoma cruzi* Infection Study: evidence for vector-borne transmission of the parasite that causes Chagas disease among United States blood donors

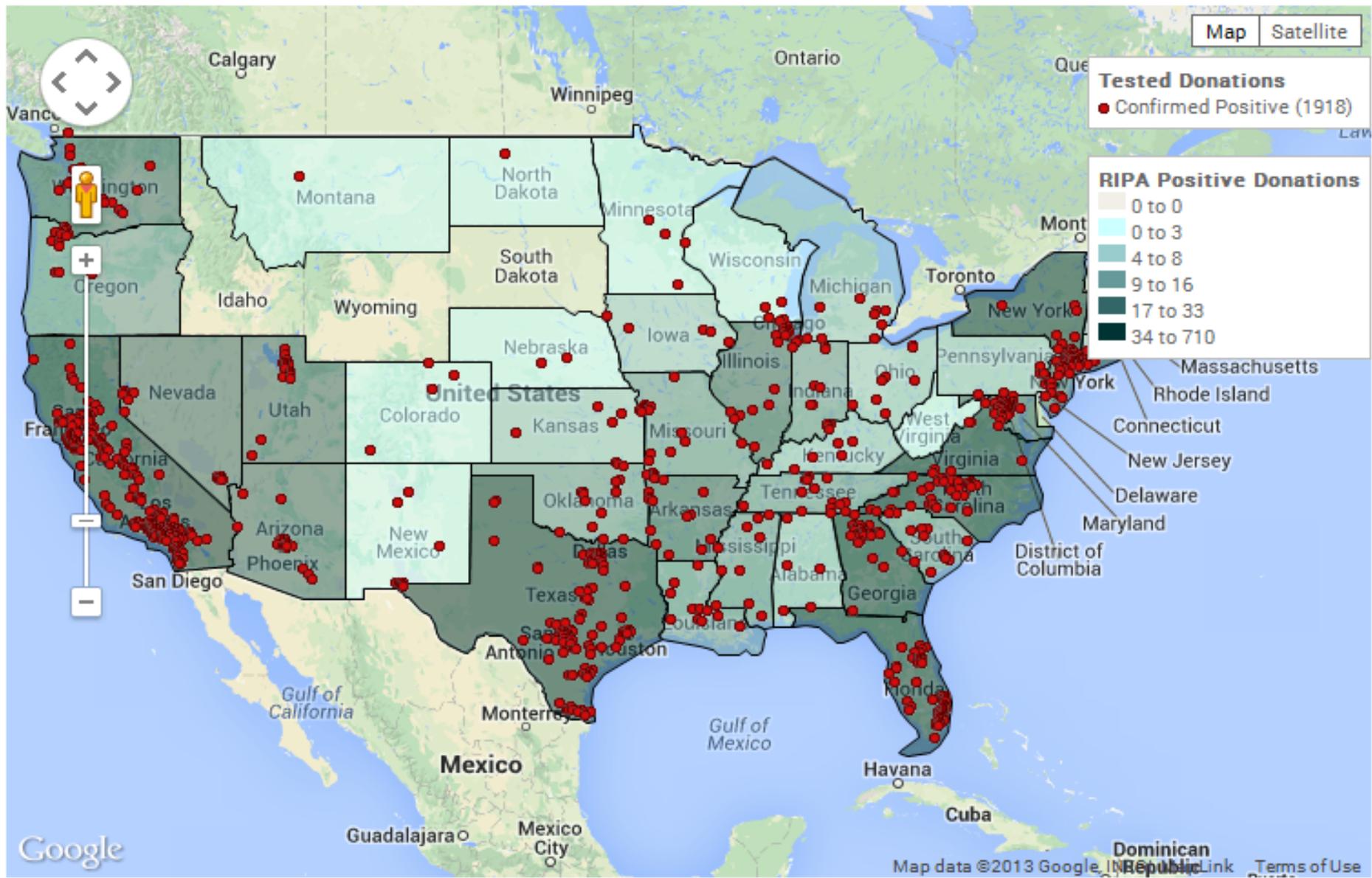
Paul T. Cantey, Susan L. Stramer, Rebecca L. Townsend, Hany Kamel, Karen Ofafa, Charles W. Todd, Mary Currier, Sheryl Hand, Wendy Varnado, Ellen Dotson, Chris Hall, Pamela L. Jett, and Susan P. Montgomery

TRANSFUSION Volume 52, September 2012

- 23 autochthonous cases
- 28 states have vector
- 17 states have infected reservoir

TABLE 6. US states with documented presence of the vector for *T. cruzi* or infected reservoir mammalian species²¹

State	Vector	Infected reservoir
Alabama	Yes	Yes
Arizona	Yes	Yes
Arkansas	Yes	
California	Yes	Yes
Colorado	Yes	
Florida	Yes	Yes
Georgia	Yes	Yes
Hawaii	Yes	
Illinois	Yes	
Indiana	Yes	
Kansas	Yes	
Kentucky	Yes	Yes
Louisiana	Yes	Yes
Maryland	Yes	Yes
Mississippi	Yes	Yes
Missouri	Yes	Yes
Nevada	Yes	
New Jersey	Yes	
New Mexico	Yes	Yes
North Carolina	Yes	Yes
Ohio	Yes	
Oklahoma	Yes	Yes
Pennsylvania	Yes	
South Carolina	Yes	Yes
Tennessee	Yes	Yes
Texas	Yes	Yes
Utah	Yes	
Virginia	Yes	Yes



AABB Chagas Biovigilance Network

How many people have *T. cruzi*
infection in Texas now?

And who are they?

Methods

- Blood center *T. cruzi* testing

- 2008-2012

- Ortho or Abbott Repeat Reactive

- RIPA confirmation

- Demographic info

- Zip code data from US Census

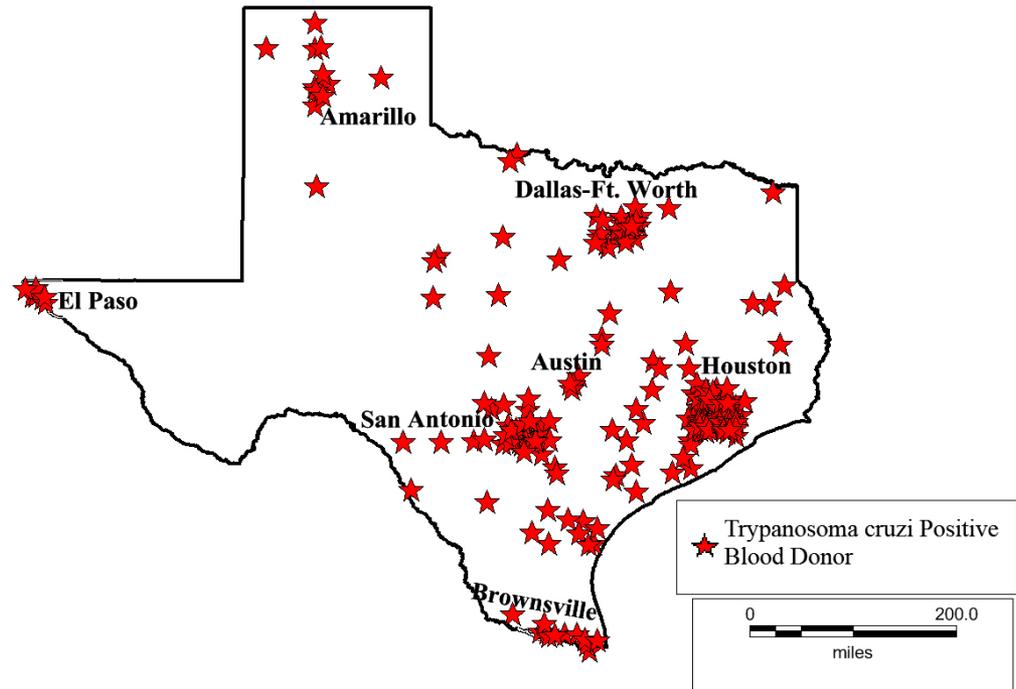
- Percent Poverty & Rural Land Use



907,398
tested

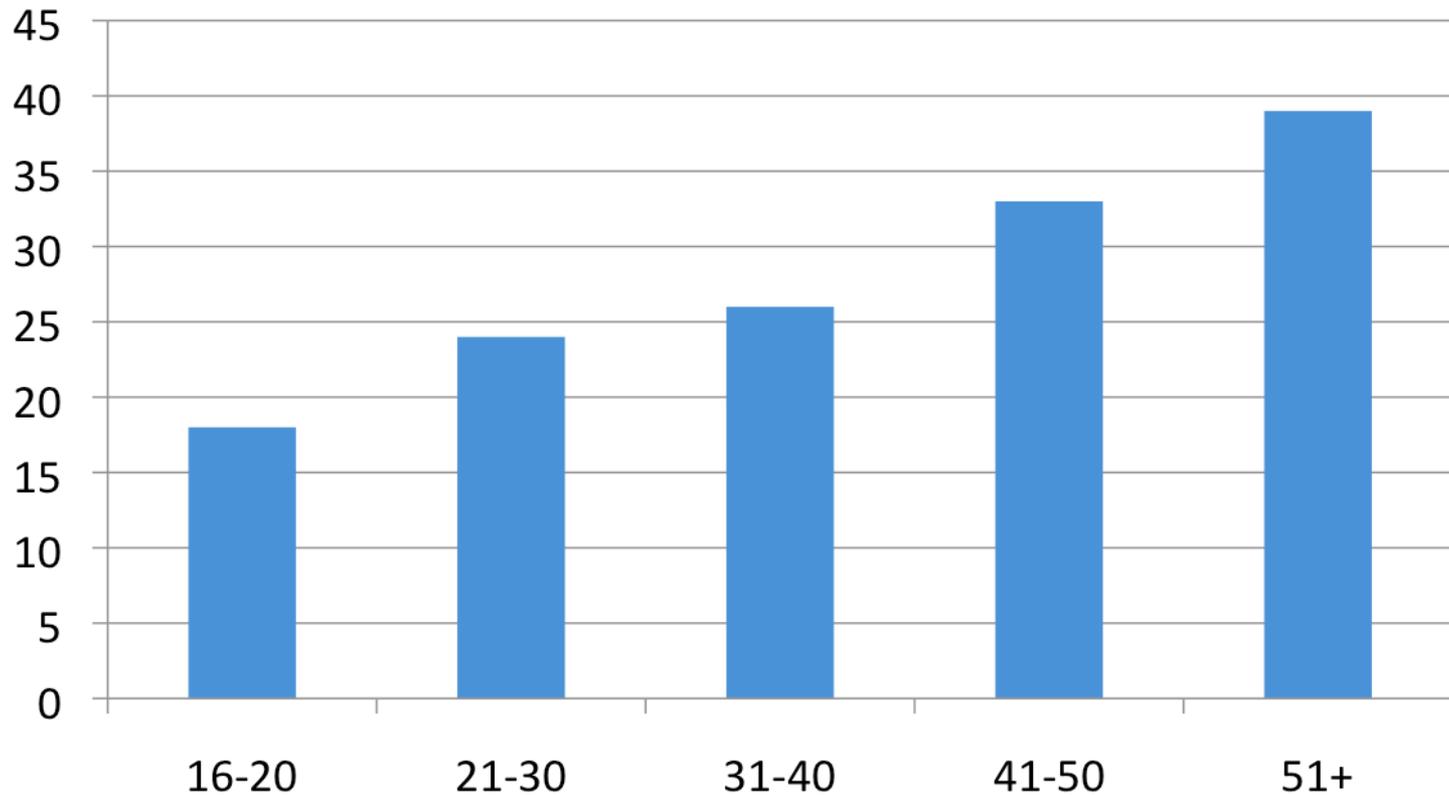
261 repeat
reactive

140 RIPA
confirmation

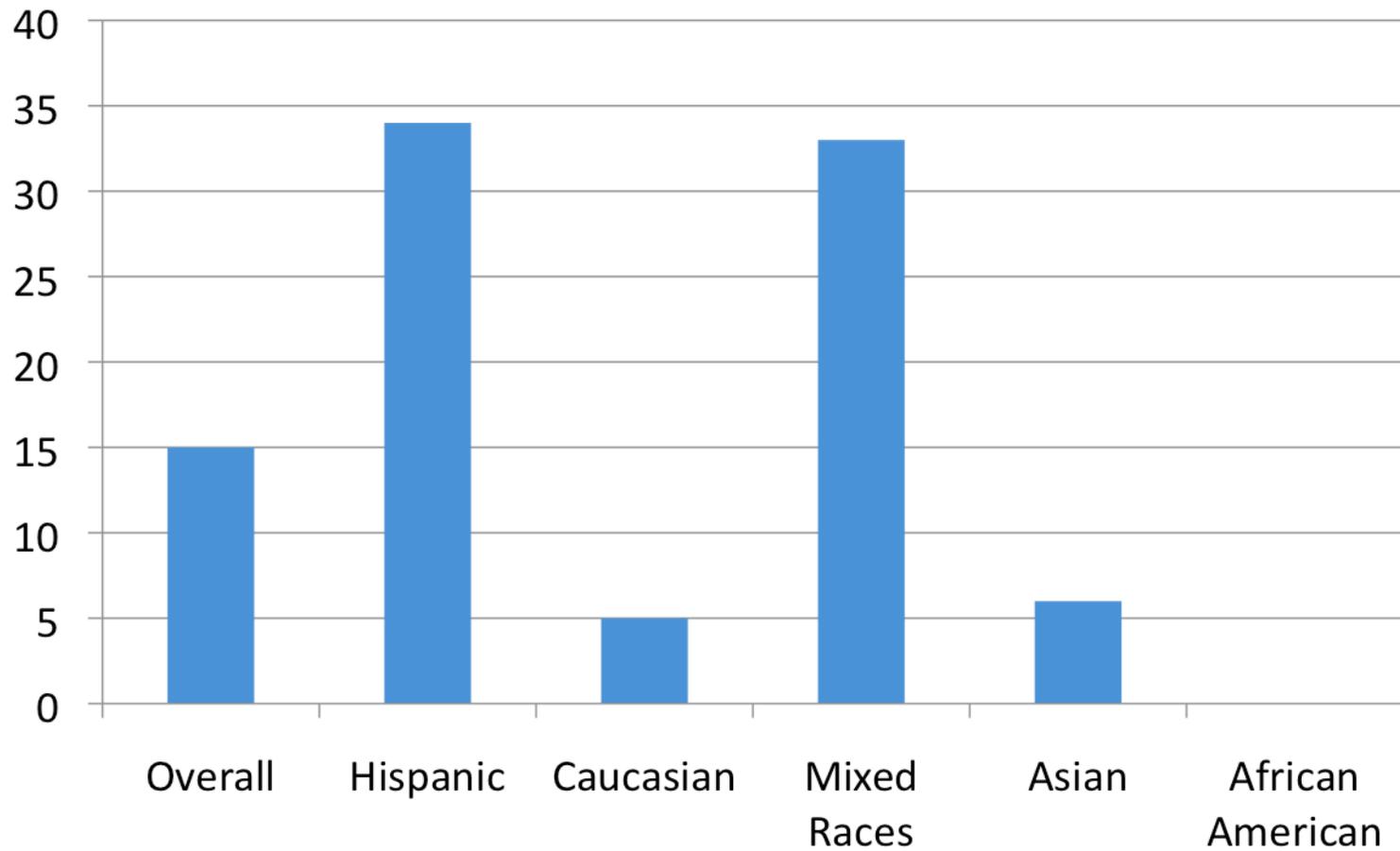


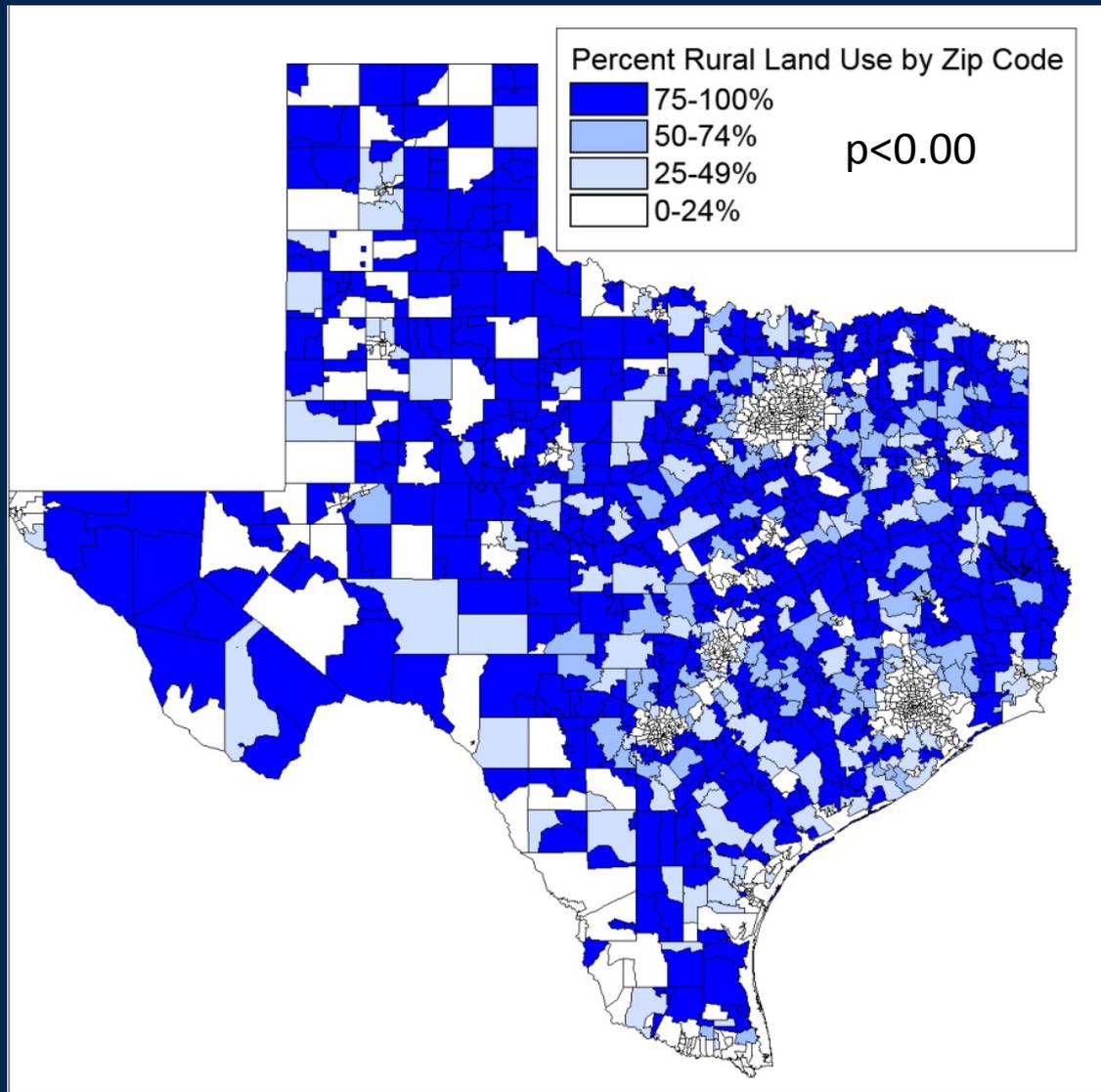
1 per 6,500 confirmed positive for *T. cruzi* infection

T. cruzi RIPA positive per 100,000 blood donors by age

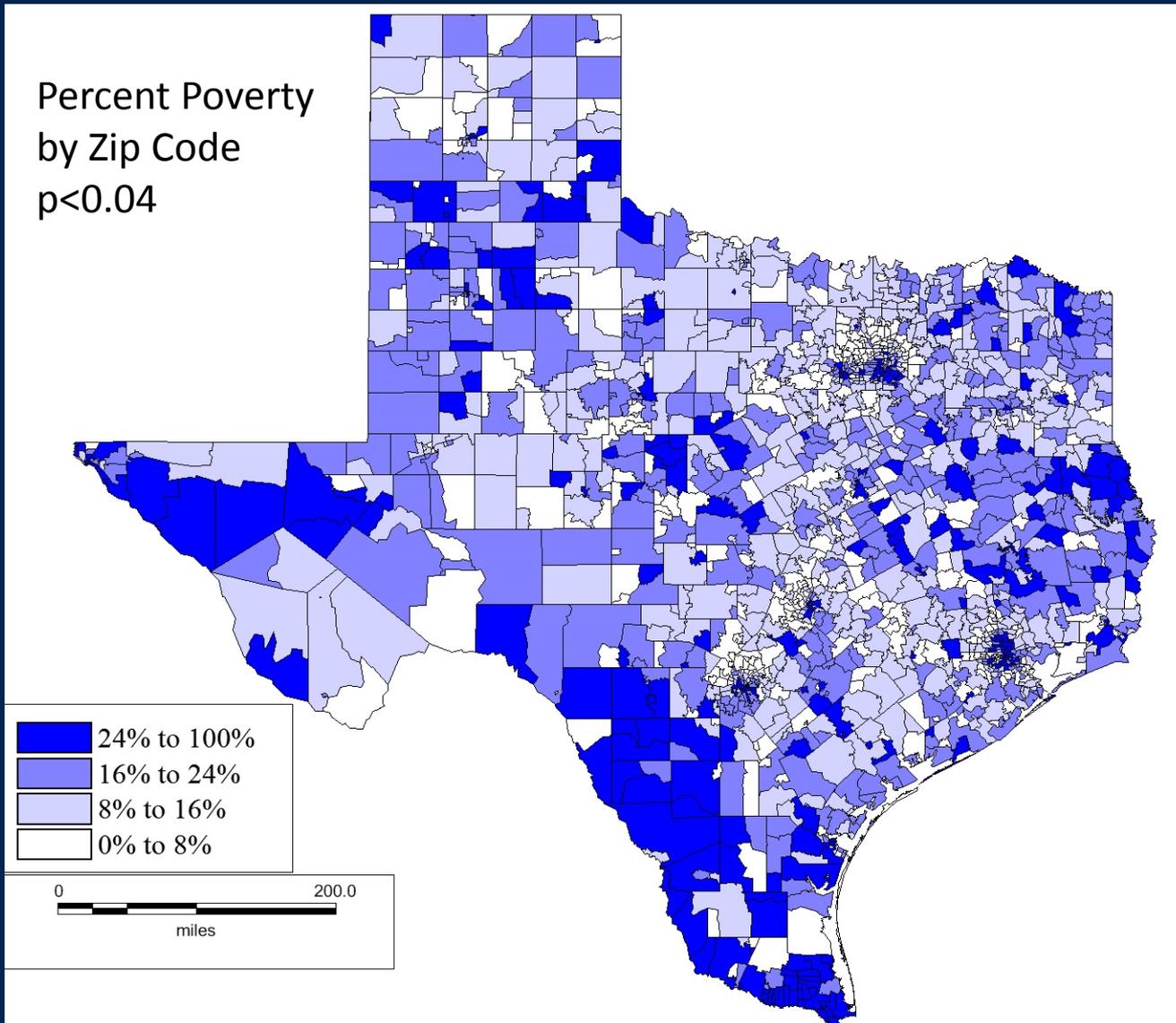


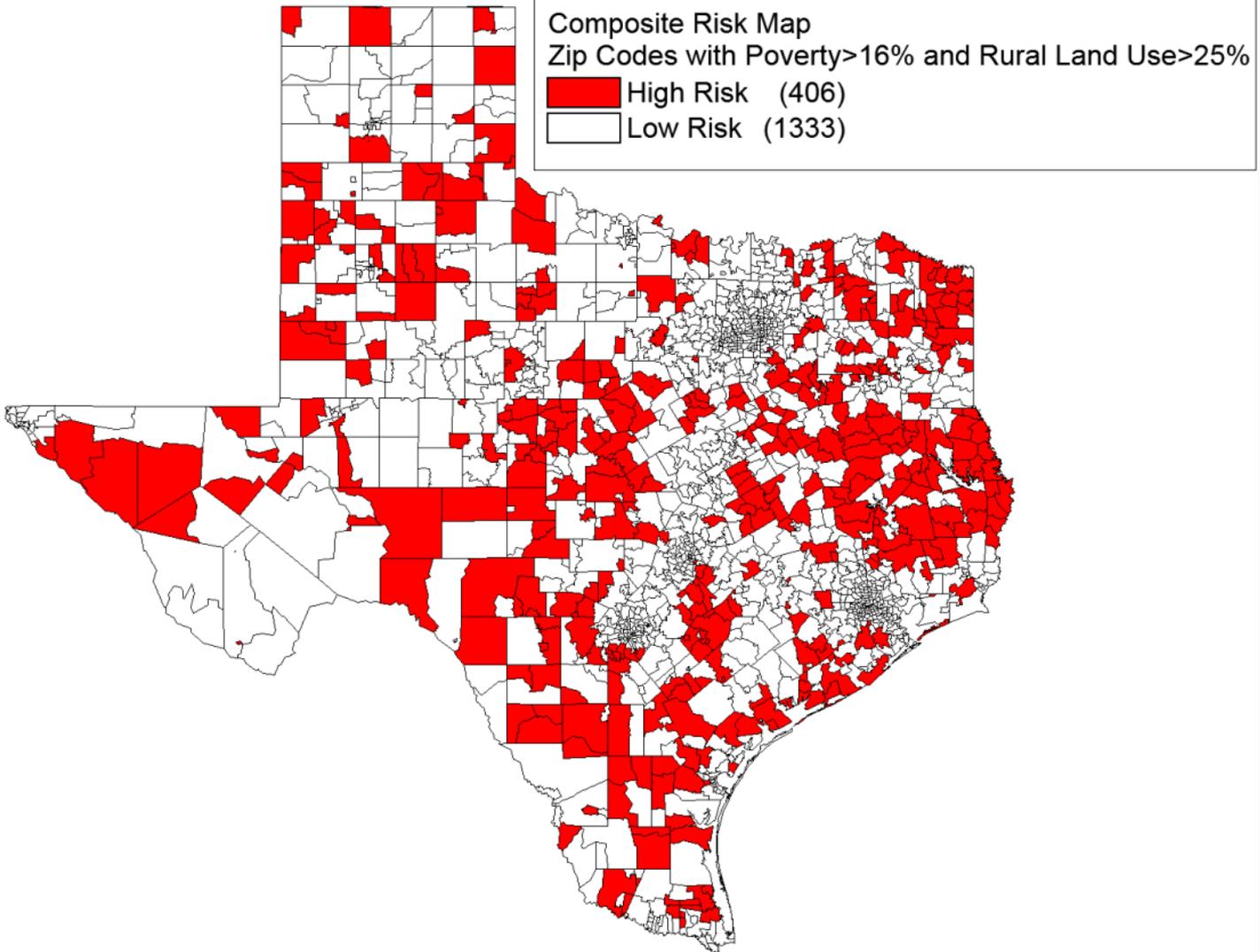
T. cruzi RIPA positive per 100,000 blood donors by Race/ Ethnicity





Percent Poverty
by Zip Code
 $p < 0.04$





Cost estimates for Texas Chagas cases

- Societal cost for healthcare & lost wages
\$2.7 million*

- Accrue 104 disability-adjusted life years lost
as a result of chronic Chagas disease*

*\$91, 531 per case; 3.57 DALYs per year- Lee et al 2013 Lancet Infect Dis
Cost estimates: 30% RIPA confirmed

What is the human source of *T. cruzi*
infection?

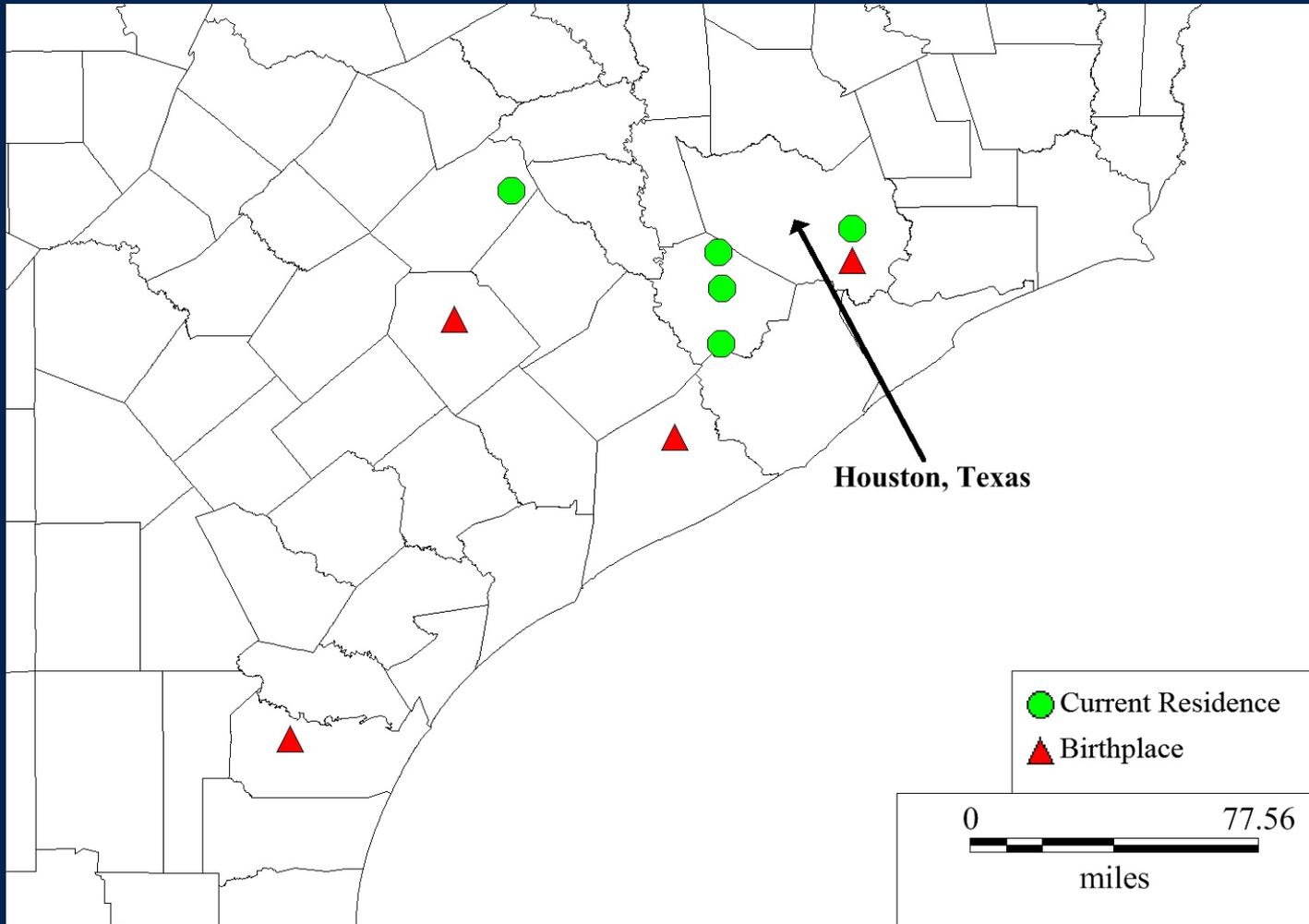
What are the routes of disease transmission?

Houston Pilot Study: Methods

- Invited RIPA + & RIPA – blood donors from GCRBC
 - 57% (17/30) of those who screened positive were confirmed
- The one-time assessment included:
 - 1) a questionnaire to evaluate risk factors for infection
 - Co-morbidities, travel history, source of disease transmission
 - 2) blood draw for biomarker evaluation
 - 3) an electrocardiogram
 - an echocardiogram for those with an abnormal ECG

36% (6/17) were locally acquired

Study ID	Age	Race	Gender	Place of Birth	Occupational Exposure	Hunter	Camper	Travel to Endemic Rural Area	Report Seeing Vector Around TX Residence
Tcruzi-002	75	Hispanic	Male	Robstown, Texas	No	No	Yes (10+ years)	No	No
Tcruzi-004	54	White	Female	Hallettsville, Texas	No	No	No	No	No
Tcruzi-006	66	White	Male	Baycity, Texas	Yes (cotton farmer 23 years)	Yes (whole life)	No	No	Yes
Tcruzi-007	75	White	Male	Rogers, Texas	No	Yes (whole life)	No	No	No
Tcruzi-012	68	Hispanic	Female	Cerralvo, Mexico	No	No	No	Yes	Yes
Tcruzi-026	23	White	Male	Pasadena, Texas	No	No	Yes (15 years)	No	No



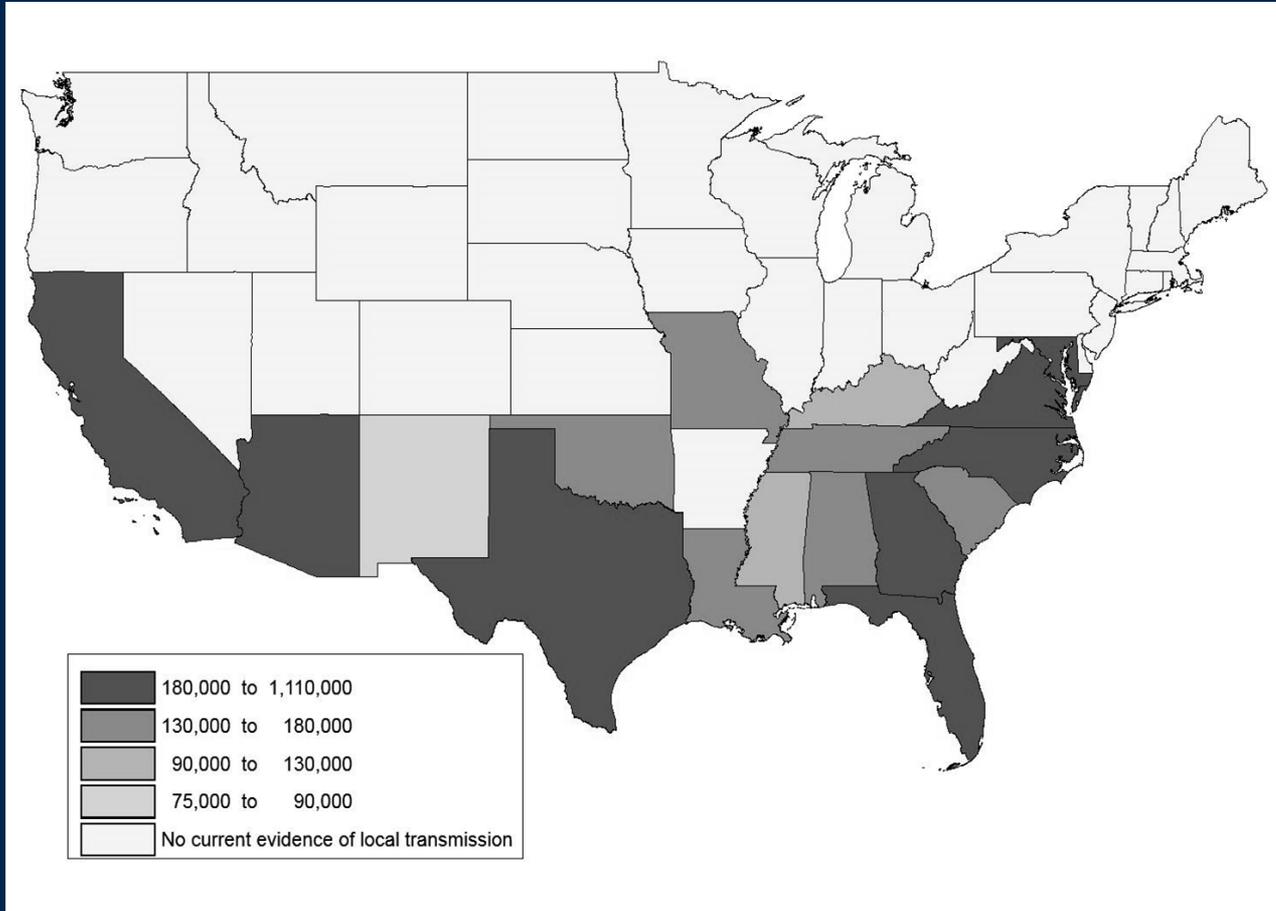
Implications for Hunting as a High-risk activity for transmission

- Direct blood-to-blood transmission via skinning
- Inadequate lodging
- Increased exposure to vector



Photo credit: Victor Quispe-Machaca

Implications for High-risk Occupational Exposure in US

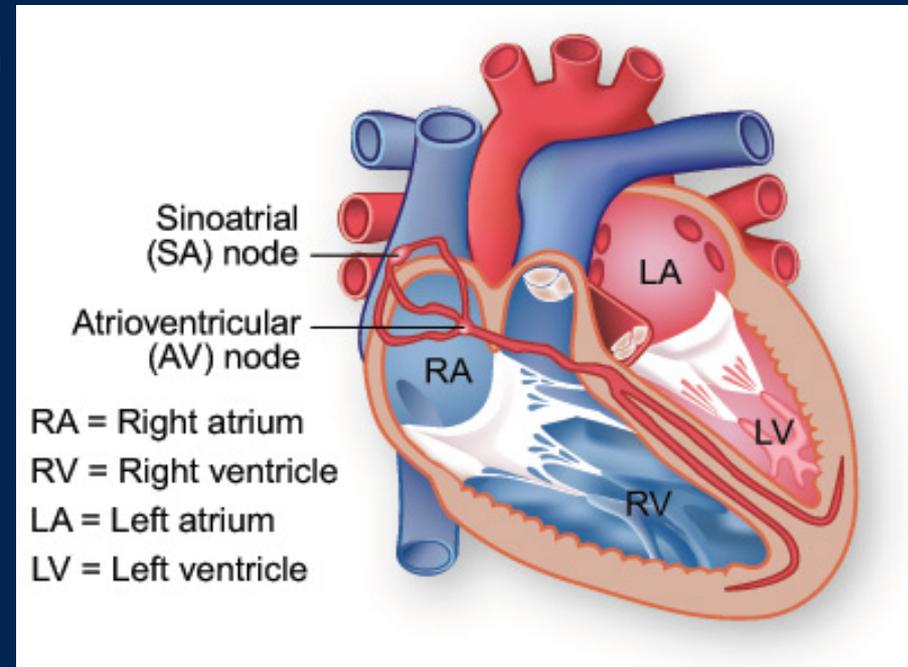


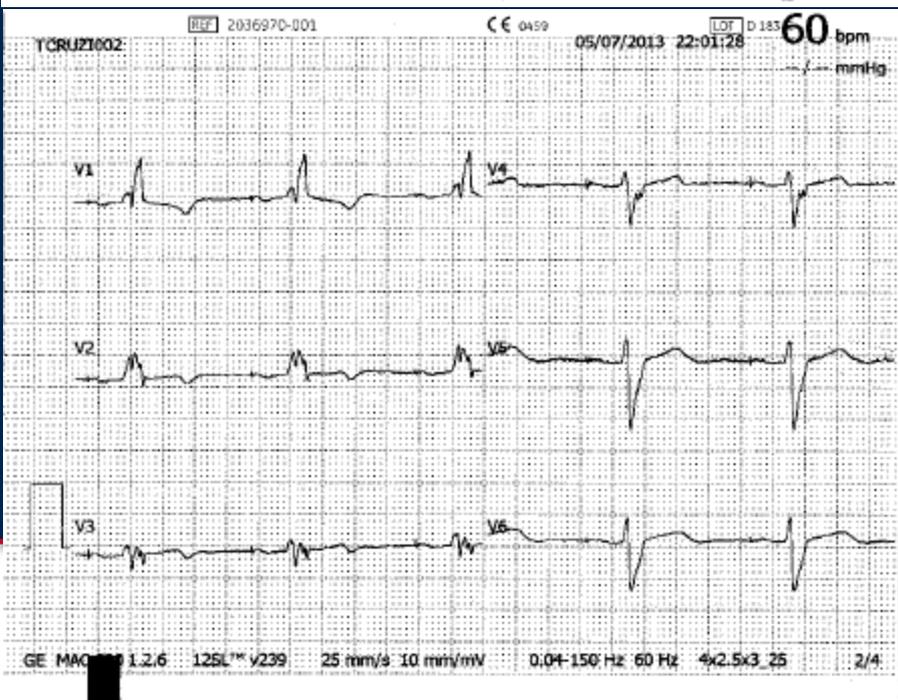
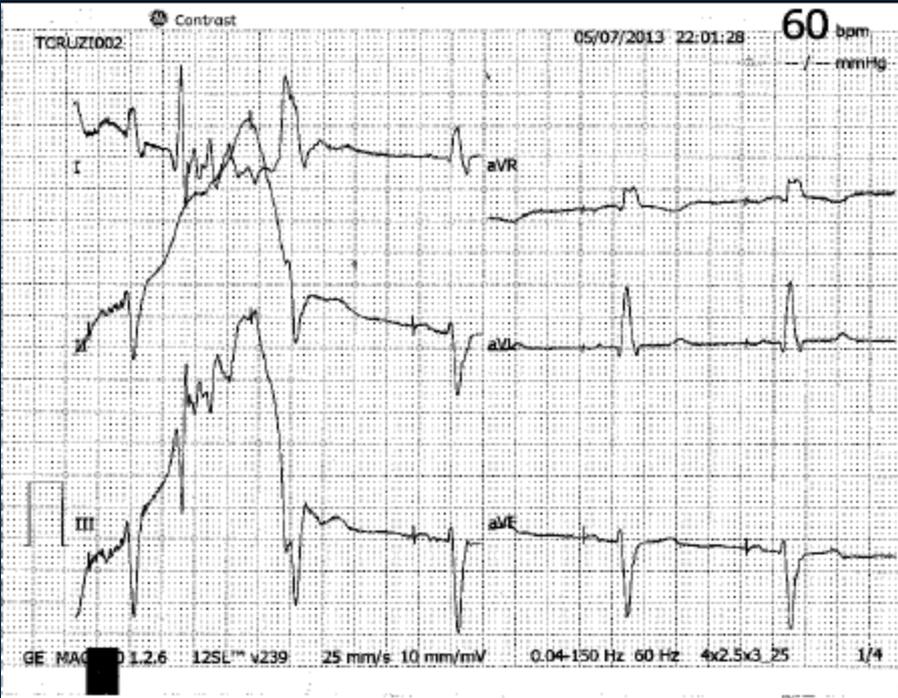
- 5 million with extensive time outdoors
- 178,000 working during nocturnal feeding time

Are those infected with *T. cruzi* in
Texas developing cardiac
disease?

•41% (7/17) Abnormal ECG Finding

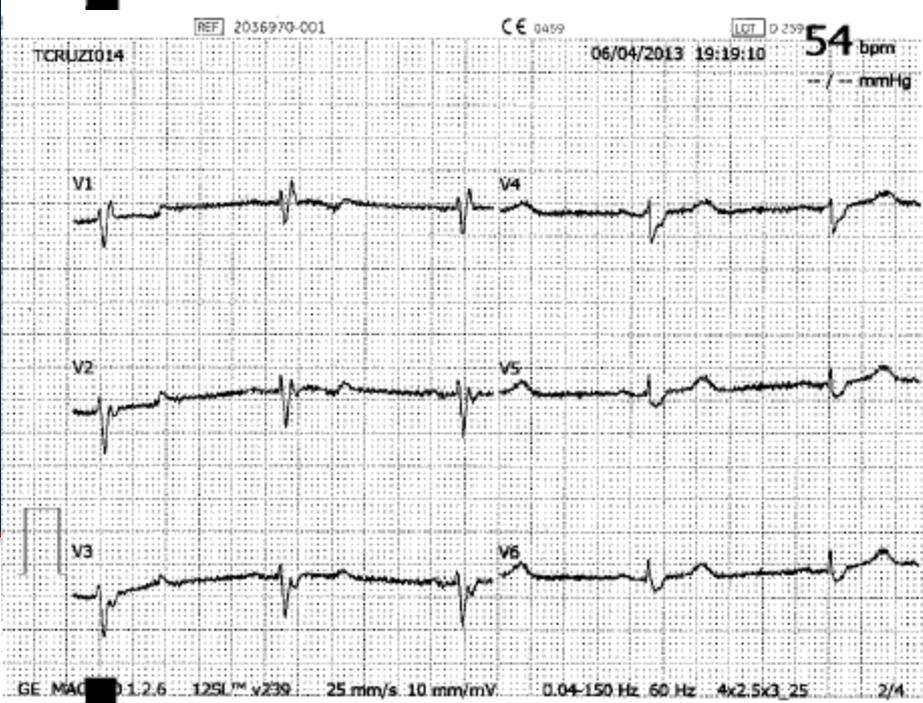
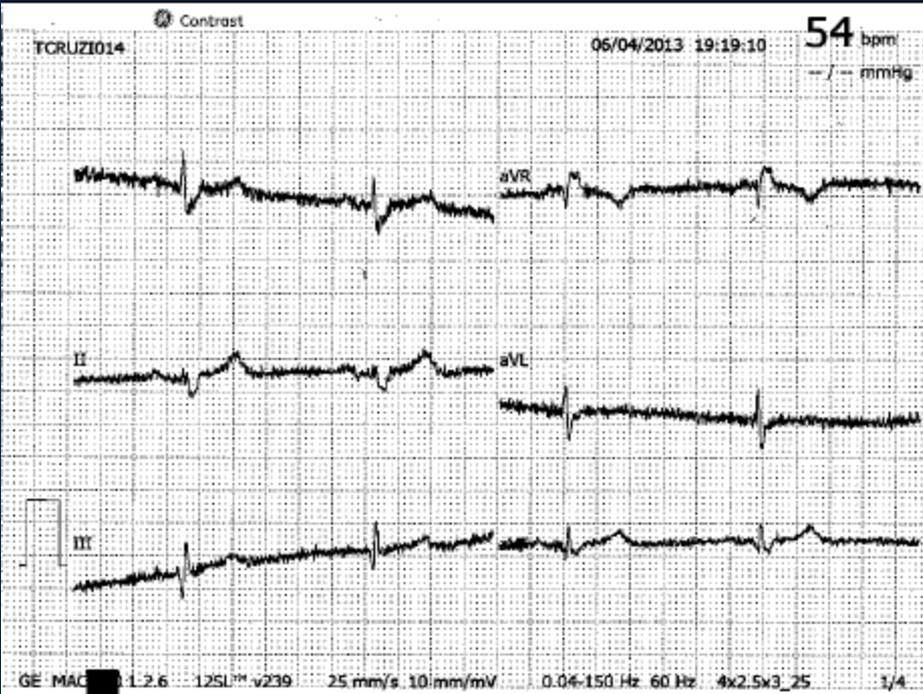
- 72% (5/7) were major abnormalities
- 57% (4/7) were potentially locally acquired
- 14% (1/7) had ECHO abnormality
- 57% (4/7) had Hypertension
- 14% (1/7) had Diabetes
- None have received treatment prior to study





Tcruzi-002 ECG

- 75 year old Hispanic Male
- Atrial paced with right bundle branch block
- Left anterior fascicular block
- 1st degree atrioventricular block

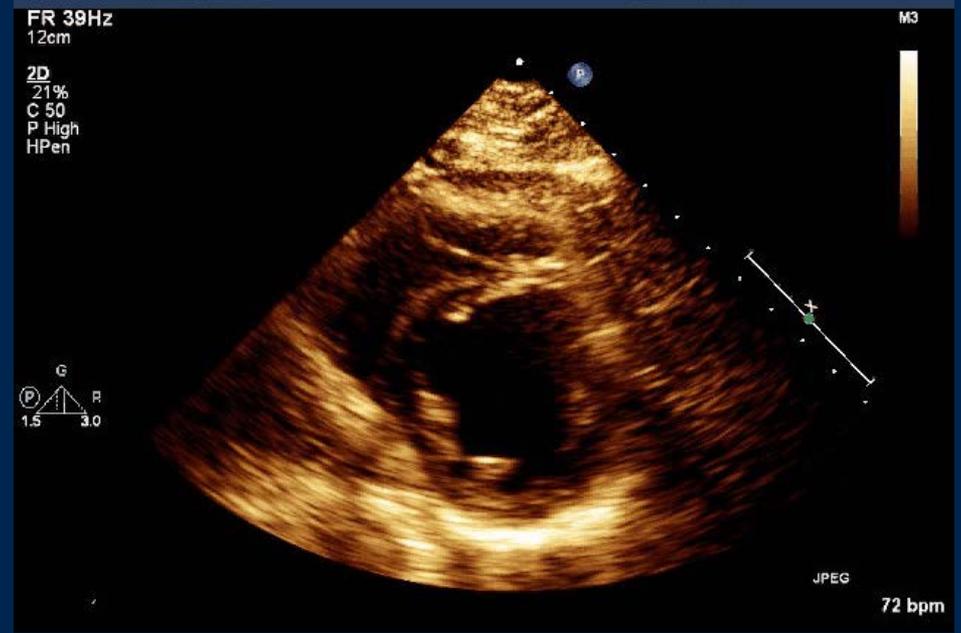
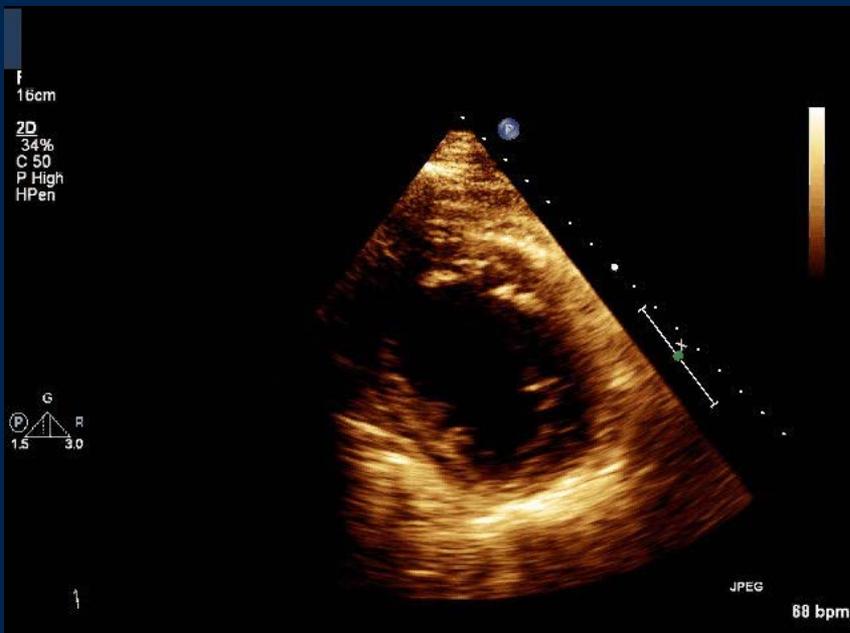


Tcruzi-014 ECG

- 43 year old Hispanic Female
- Right bundle branch block
- Left axis deviation

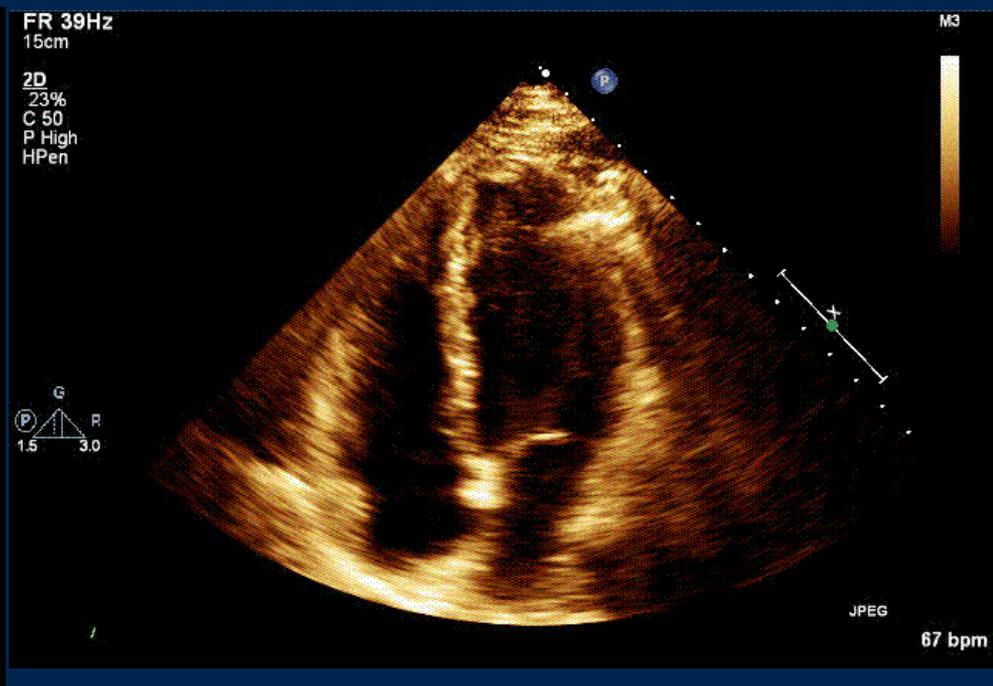
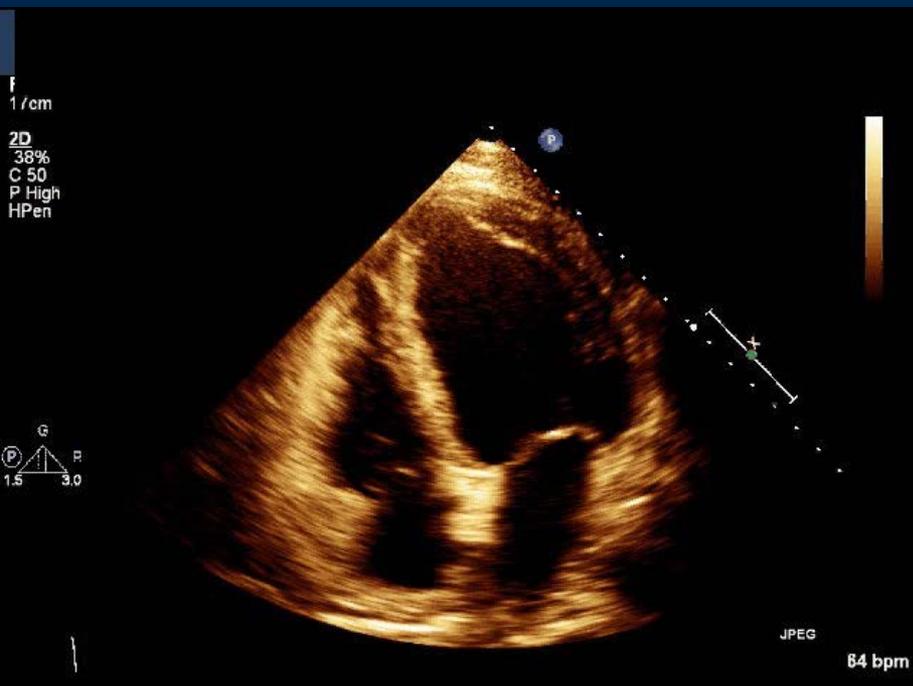
Tcruzi-003

Control



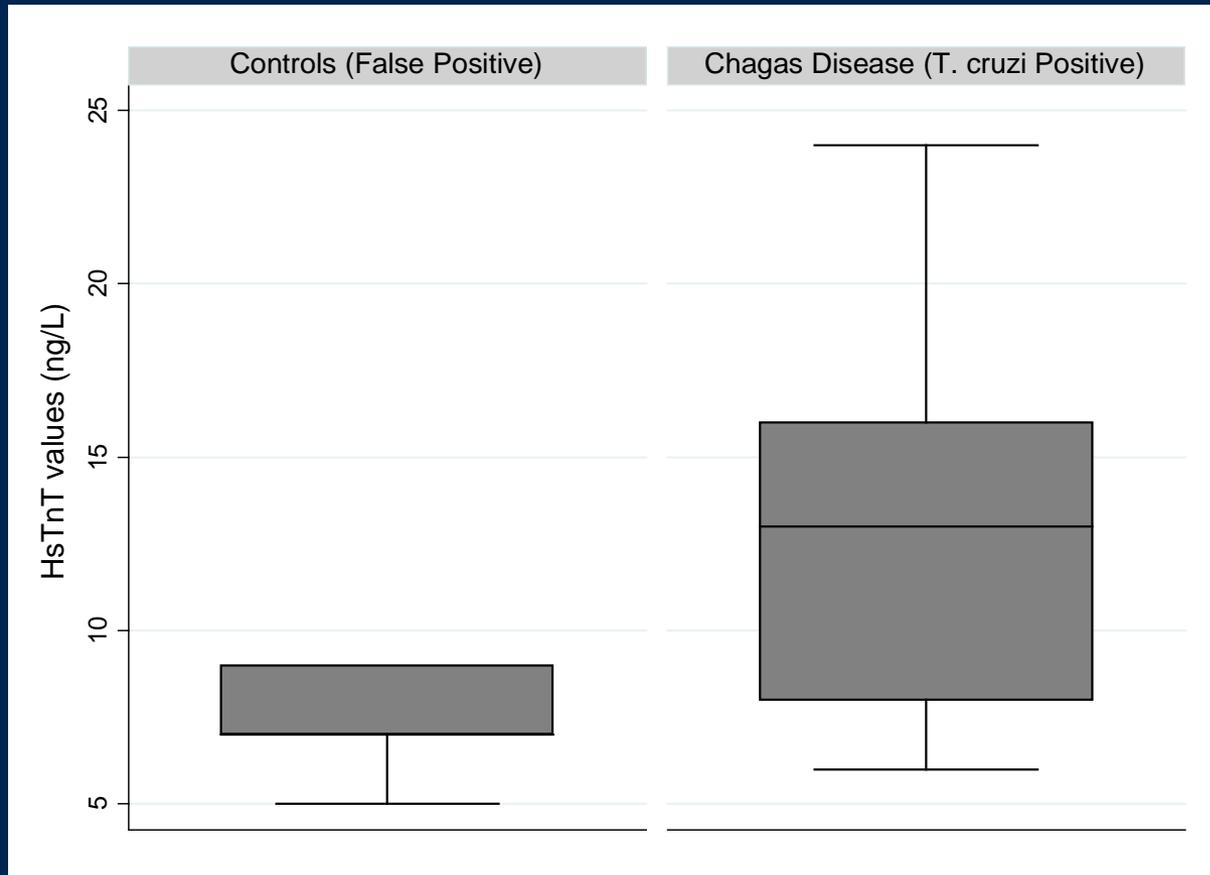
Tcruzi-003

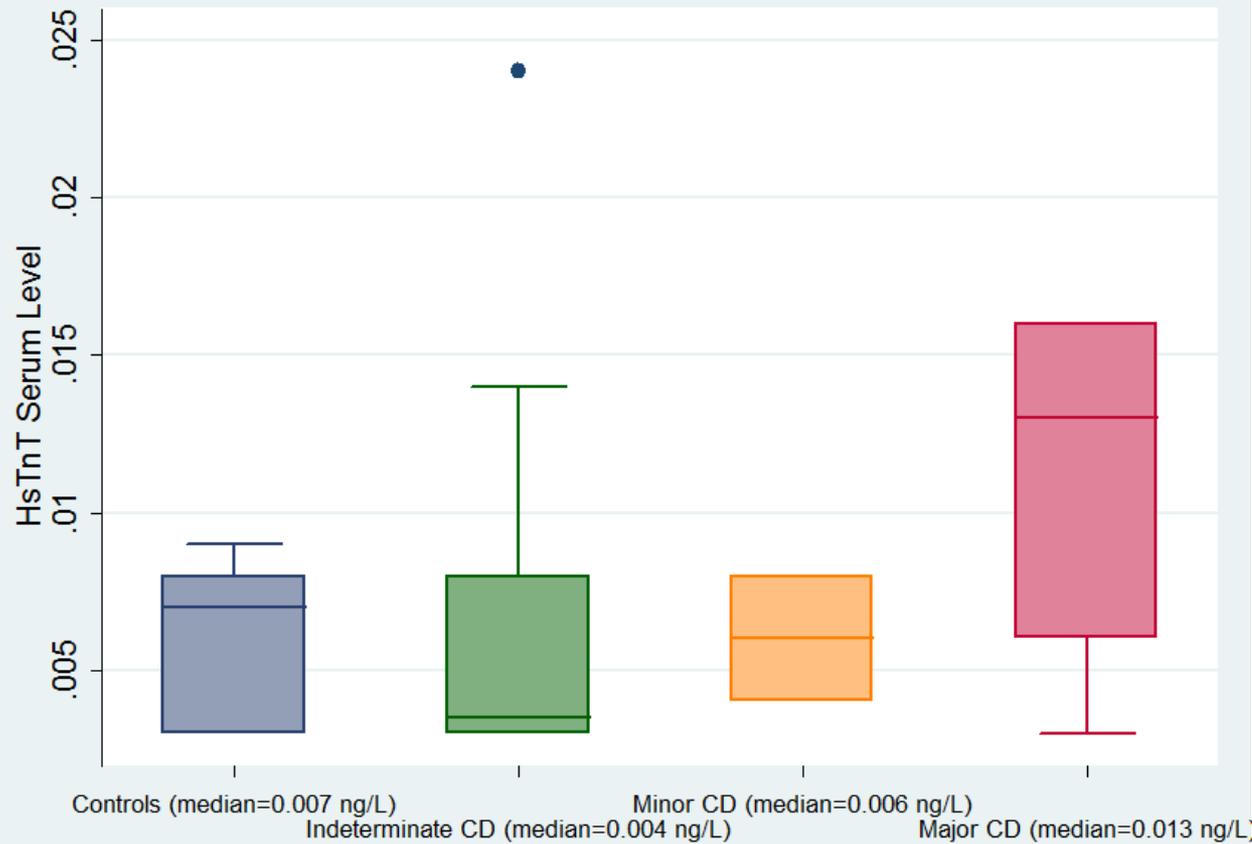
Control



Can we predict who is at risk for developing cardiac disease?

HsTnT biomarker levels by disease status





High Sensitivity Troponin T could be an important biomarker for advanced Chagas cardiomyopathy

Conclusions

- Substantial disease burden in Texas (1 per 6,500)
- *T. cruzi* infection can cause cardiac manifestations, even in persons without travel to Latin & South America
- High risk populations for transmission
 - Hunters (multiple sources)
 - Nocturnal occupations
- High Sensitivity Troponin T could be an important biomarker for stratifying cardiac disease severity

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