Neglected Diseases (NDs) Landscape in Brazil and South America

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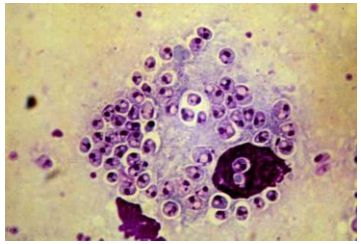
Of WHO´s 17 listed NTDs 14 occur in South America

Virus	Dengue/Severe dengue
	Rabies
Protozoa	**Chagas disease**
	Human African trypanosomiasis (sleeping sickness)
	Leishmaniases
Helminth	Cysticercosis/Taeniasis
	Dracunculiasis (guinea-worm disease)
	Echinococcosis
	Foodborne trematodiases Fasciola hot spots andes & carribbean
	Lymphatic filariasis
	Onchocerciasis (river blindness)
	Schistosomiasis
	Soil-transmitted helminthiases
Bacteria	Buruli ulcer??
	Leprosy (Hansen disease)
	Trachoma
	Yaws??

NDs are expanding and adapting in a changing world!

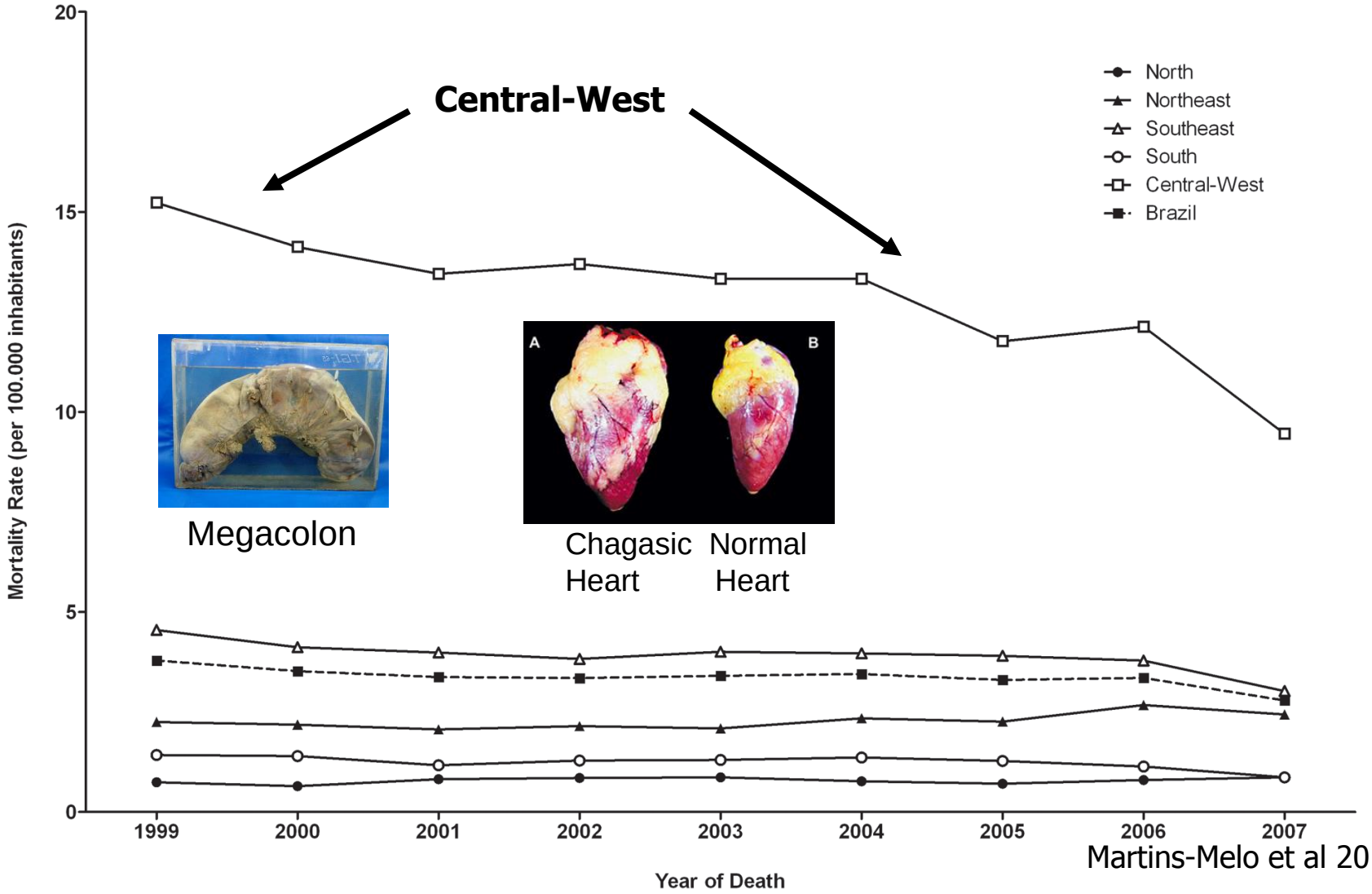
1. War - Soldiers/Civilians
2. Social unrest – Migration - individuals seeking better financial climates
3. Human Behavior – Food preparation and Drug addiction (contamination from shared syringes) - HIV global epidemic
4. Environmental aggression – Deforestation and Global warming
5. Globalization – Rapid transportation of infections (Tourism)
6. Economic recession – World wide reduction of funds for surveillance, prevention and research
7. Changing Medical Procedures – Tissue implantation (blood, organs), medication (lowering of immune response)



Chagas Disease & Leishmaniasis

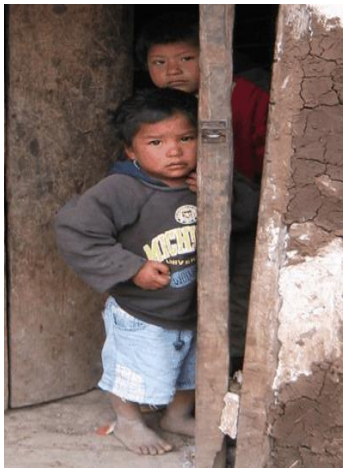
Both are **Zoonoses** so we can **never eliminate** them

Estimated that 8 million people are infected with *T.(S.) cruzi* of which around 4.5 million are from Brazil



Martins-Melo et al 2012

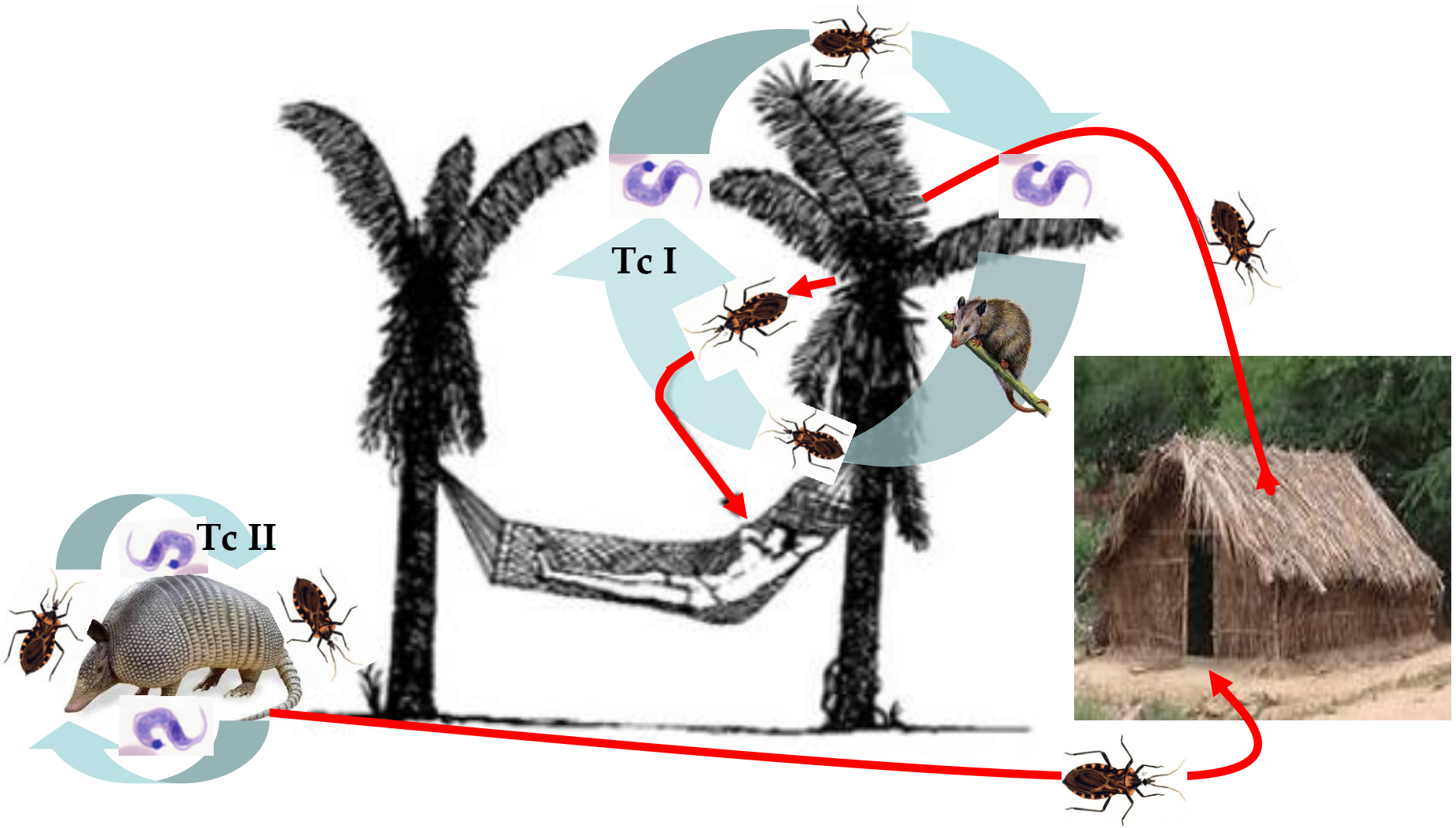
19.4% of the children in Entre Rios, Bolivia have positive Chagas serology *



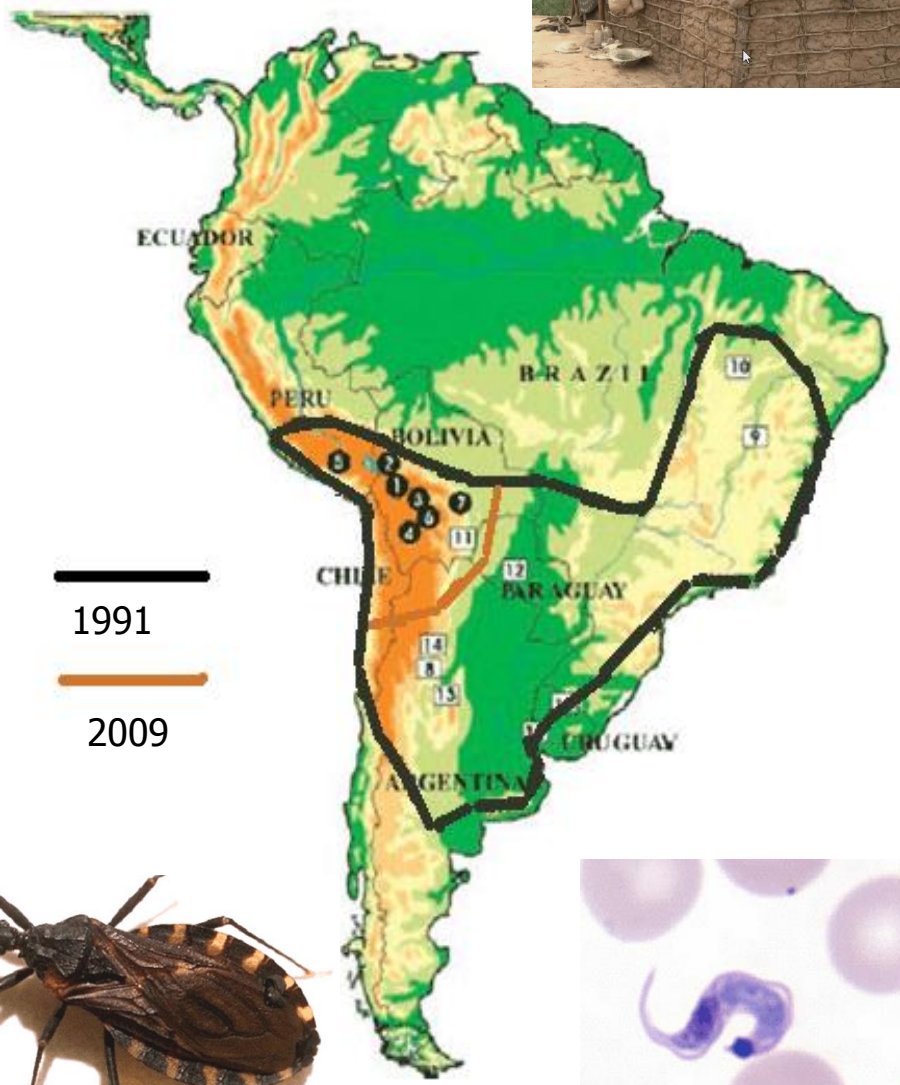
Age group	% positive
<5	5
5 - 9	14.8
10 - 14	31.0
15 - 16	51.7

* **1,475/7,618** -(2002-2007) Yun et al 2009 (MSF)

Silvatic cycles involving many wild animals and bug species

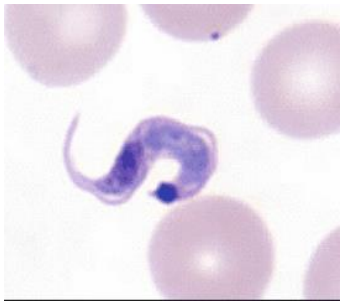


Only about 20 triatomine species are responsible for transmitting *T.(S.)cruzi* to humans



Triatoma infestans
A domesticated species
Southern Cone Initiative
1991

Sustainability?



In Brazil most cases now are due to oral transmission Açai and Sugar cane juice

Contamination with bugs during transportation

Contamination by bugs attracted to light

Congenital transmission

Mexico 2,000 per year *

USA 200 per year*

Risk estimated as being between 1-7% ** but no good data available
There may be differences between strains

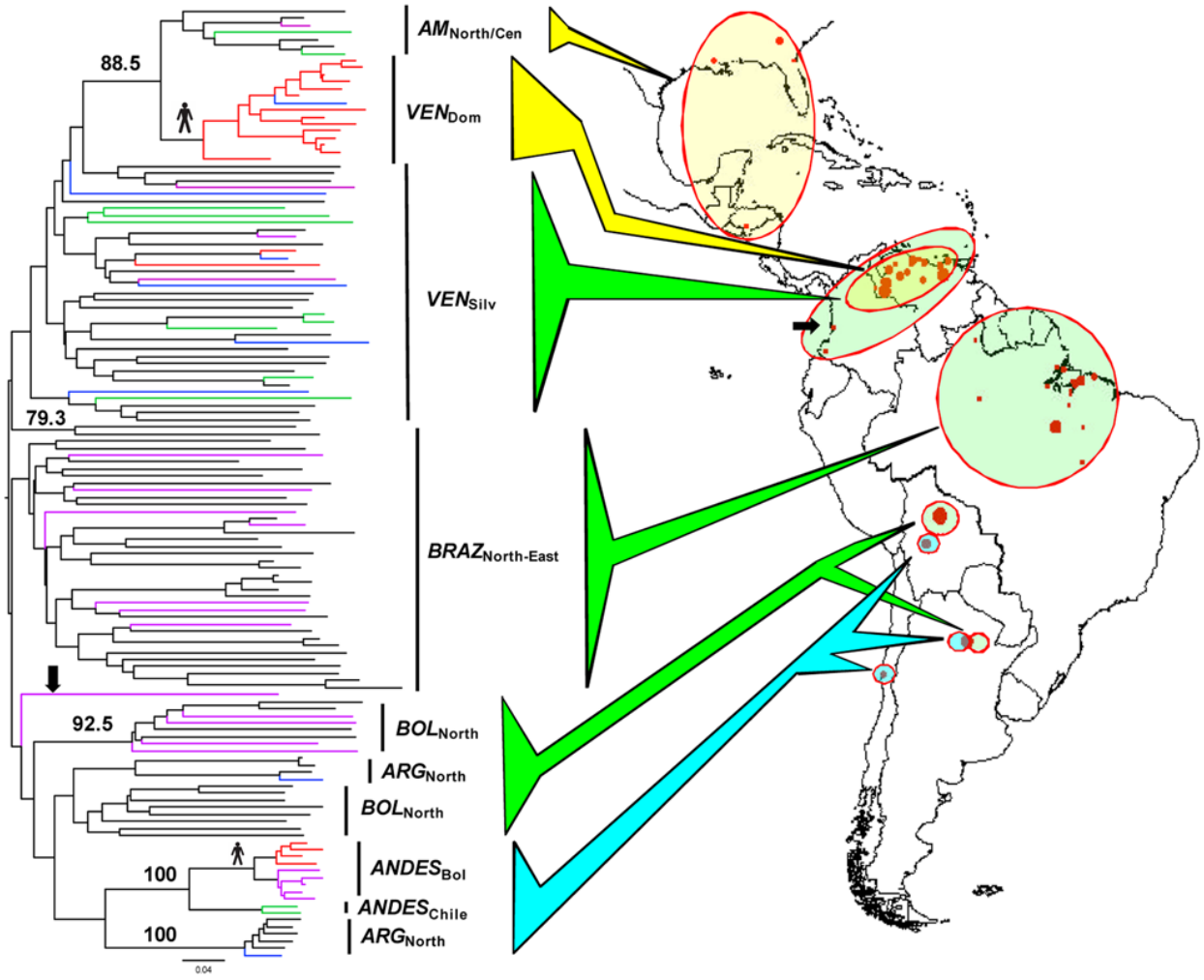
In Argentina congenital transmission has surpassed vector-transmitted acute cases **tenfold**. ***

* Beukens et al 2007
** WHO Tech Rep 2002
*** Gürtler et al 2003

Are there differences between the parasites that cause Chagas Disease?

If so is it clinically significant?

T.(S.)cruzi TcI population structure across the Americas Based on the multilocus microsatellite



Differences in response to drugs *

Region	*Number of children Under 15 years old with positive Chagas serology*	*Conversions 18 months after treatment*	*Percentage seroconversion (+ve to –ve)*	Predominant *T.cruzi* lineage
Central America	263	220	83.6%	Tc I
South America (Bolivia)	1,101	59	5.4%	Tc II

* Yun et al 2009 (MSF) !st Benznidazole; 2nd Nifurtimox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www.msf.org.br
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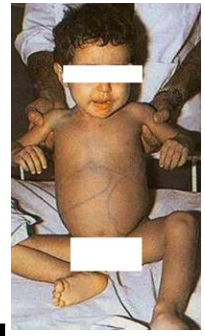
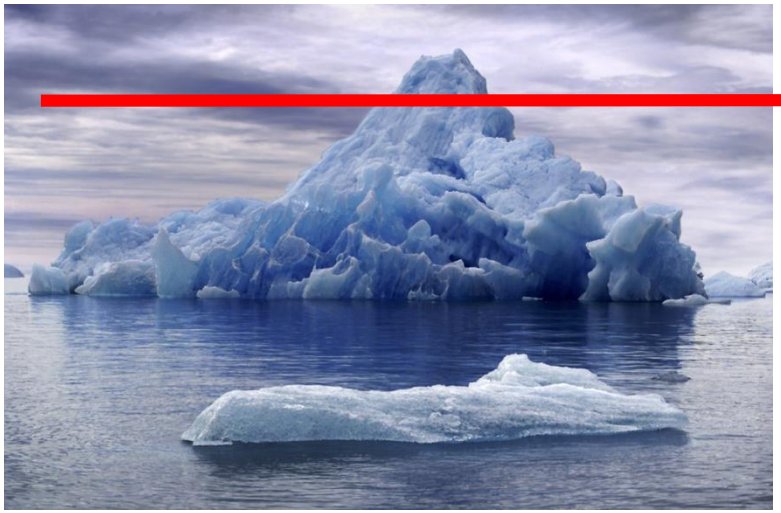
Man is not a reservoir of any South American *Leishmania*

14 named *Leishmania* species in South America infect man





Man - tip of the iceberg

Jeffrey Shaw
ICB, USP

Two distinct phylogenetic groups of *Leishmania* cause Leishmaniasis in man in South America

Subgenus (*Leishmania)* - Visceral and Cutaneous

4 species

Subgenus (*Viannia*) Cutaneous

10 species

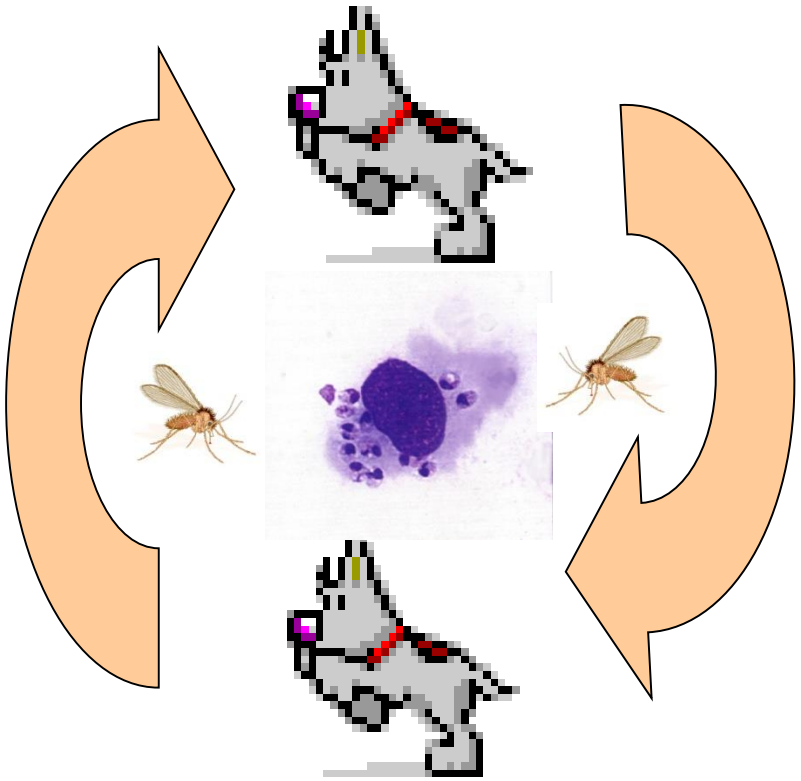
Estimates of annual* incidences of Leishmaniasis in South America

Country	Estimated annual VL Incidence		
Argentina	20	to	30
Bolivia	0		0
Brazil	**4,200**	**to**	**6,300**
Colombia	70	to	110
Paraguay	100	to	200
Venezuela	50	to	70
Total	**4,440**	**to**	**6,700**

Country	Estimated annual CL Incidence		
Argentina	730	to	1,200
Bolivia	7,400	to	12,200
Brazil	**72,800**	**to**	**119,600**
Colombia	48,800	to	80,100
French Guyana	650	to	1,100
Guyana	50	to	70
Paraguay	1,200	to	2,000
Peru	17,900	to	29,500
Suriname	8	to	14
Venezuela	6,900	to	11,400
Total	**156,438**	**to**	**257,184**

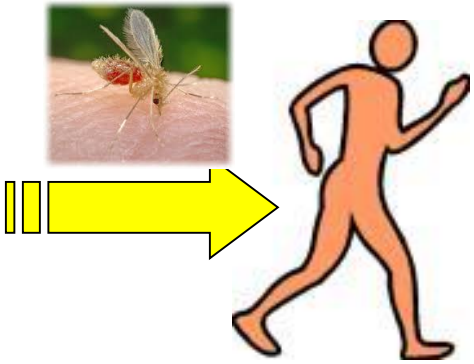
* Years 2004-2008 Adapted from **Alvar et al 2012**

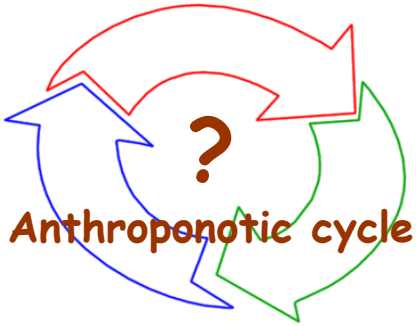
Visceral Leishmaniasis due *Leishmania* (*Leishmania*) *infantum chagasi*



Domestic/Peridomestic Enzootic cycle

Domestic/Peridomestic Zoonotic cycle





Visceral Leishmaniasis in Brazil

São Paulo State

1978 - 1st autochthonous case

1997 – 2nd autochthonous case

Between 1999 and 2013

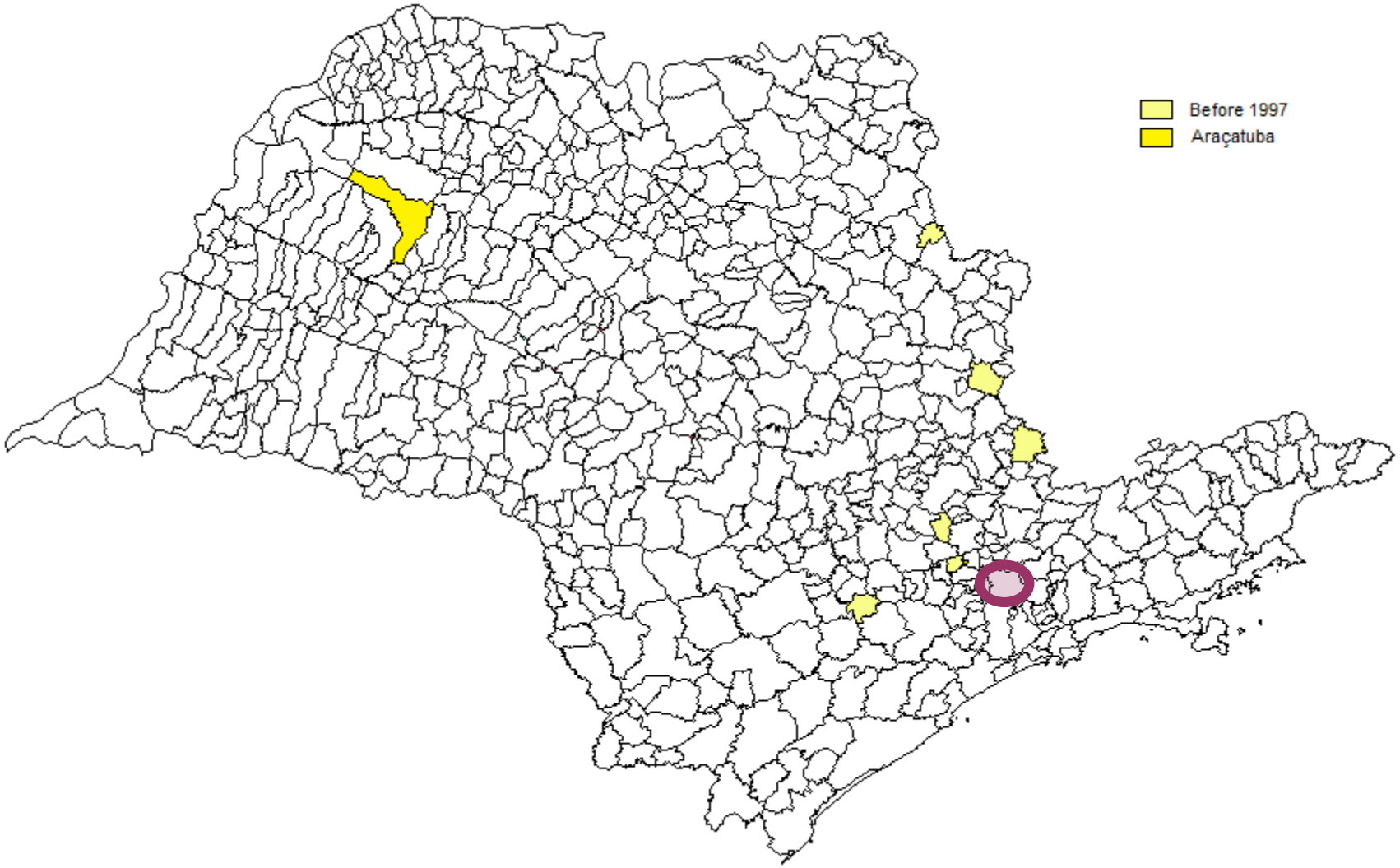
2,204 cases with 192 deaths (7.9%)

1992 India 77,102 cases 1,049 deaths (1.4%)

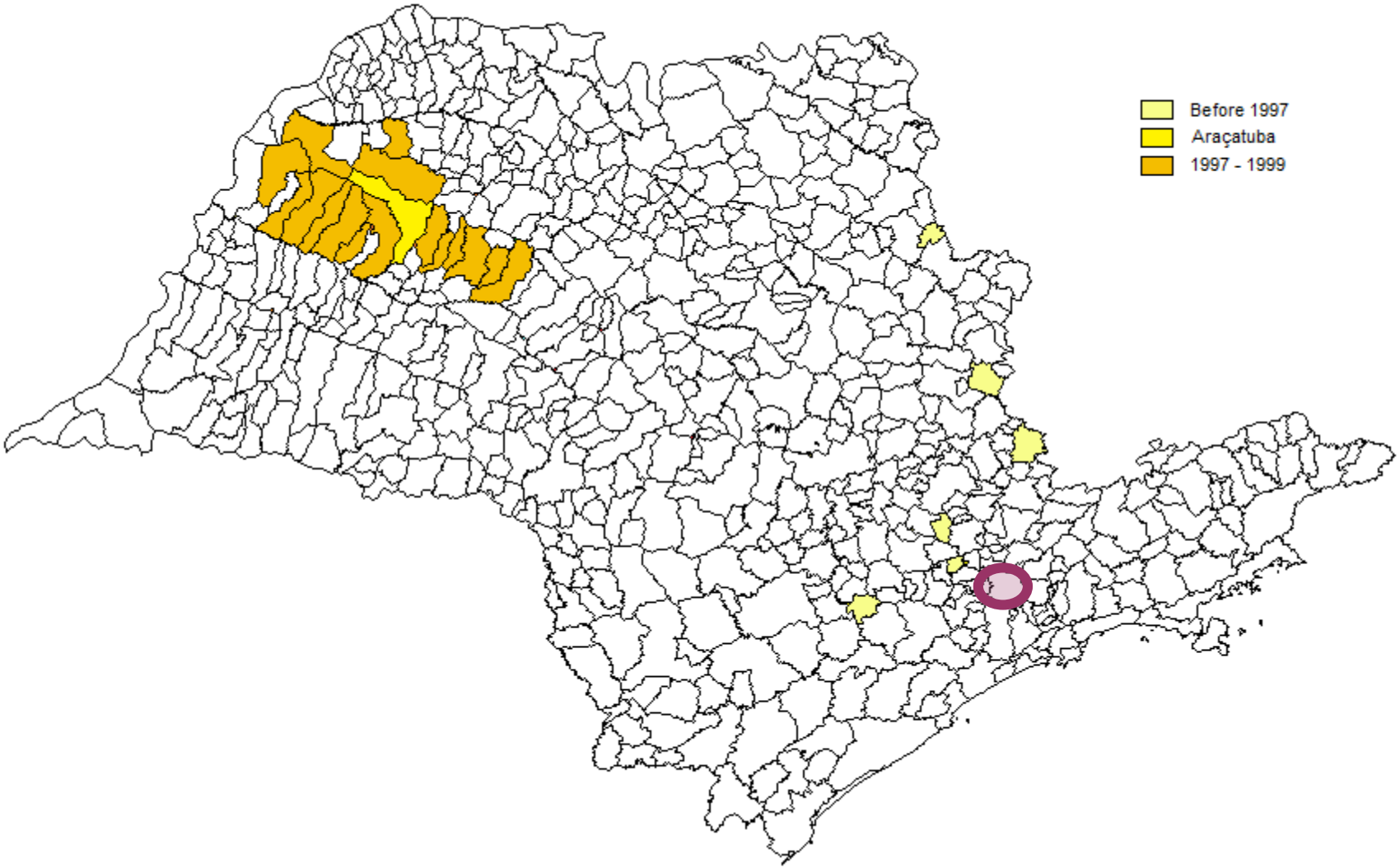
An alarmingly fast expansion of the vector of visceral leishmaniasis followed by the spread of the disease in dogs then man

Recorded distribution of *Lu.longipalpis* in São Paulo before 1997

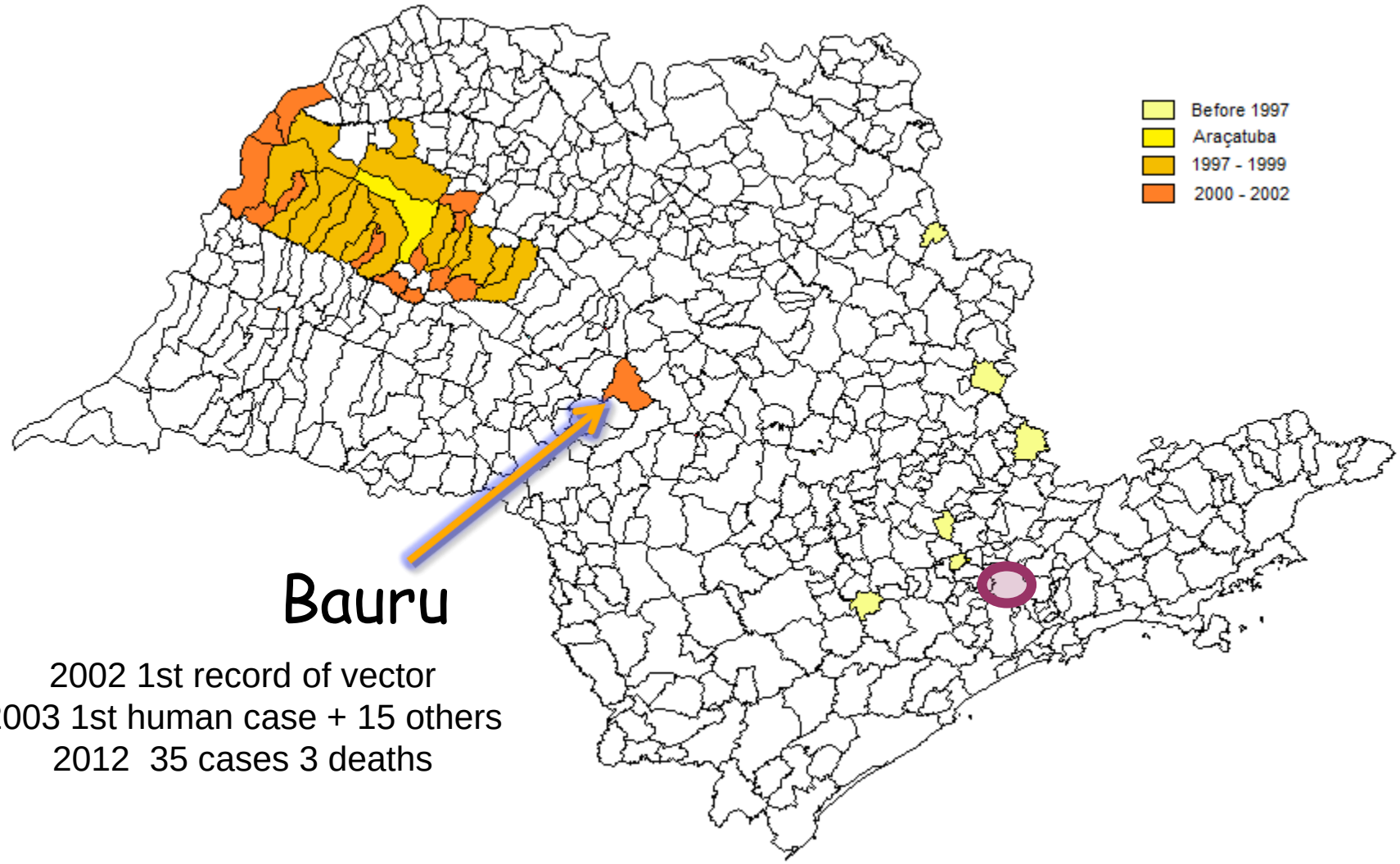
L. longipalpis found in Araçatuba 1997



2 years later 1999



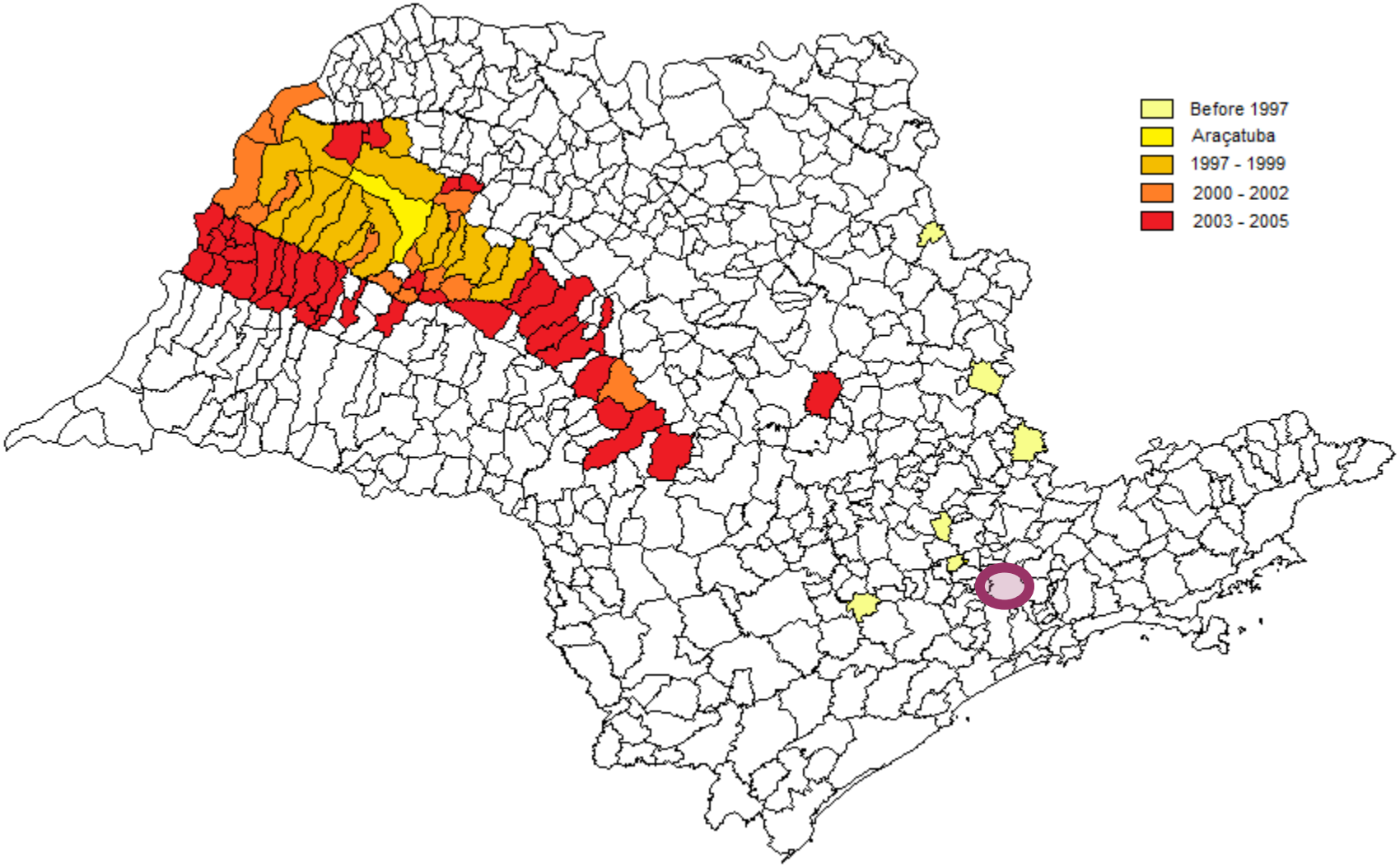
5 yrs later 2002



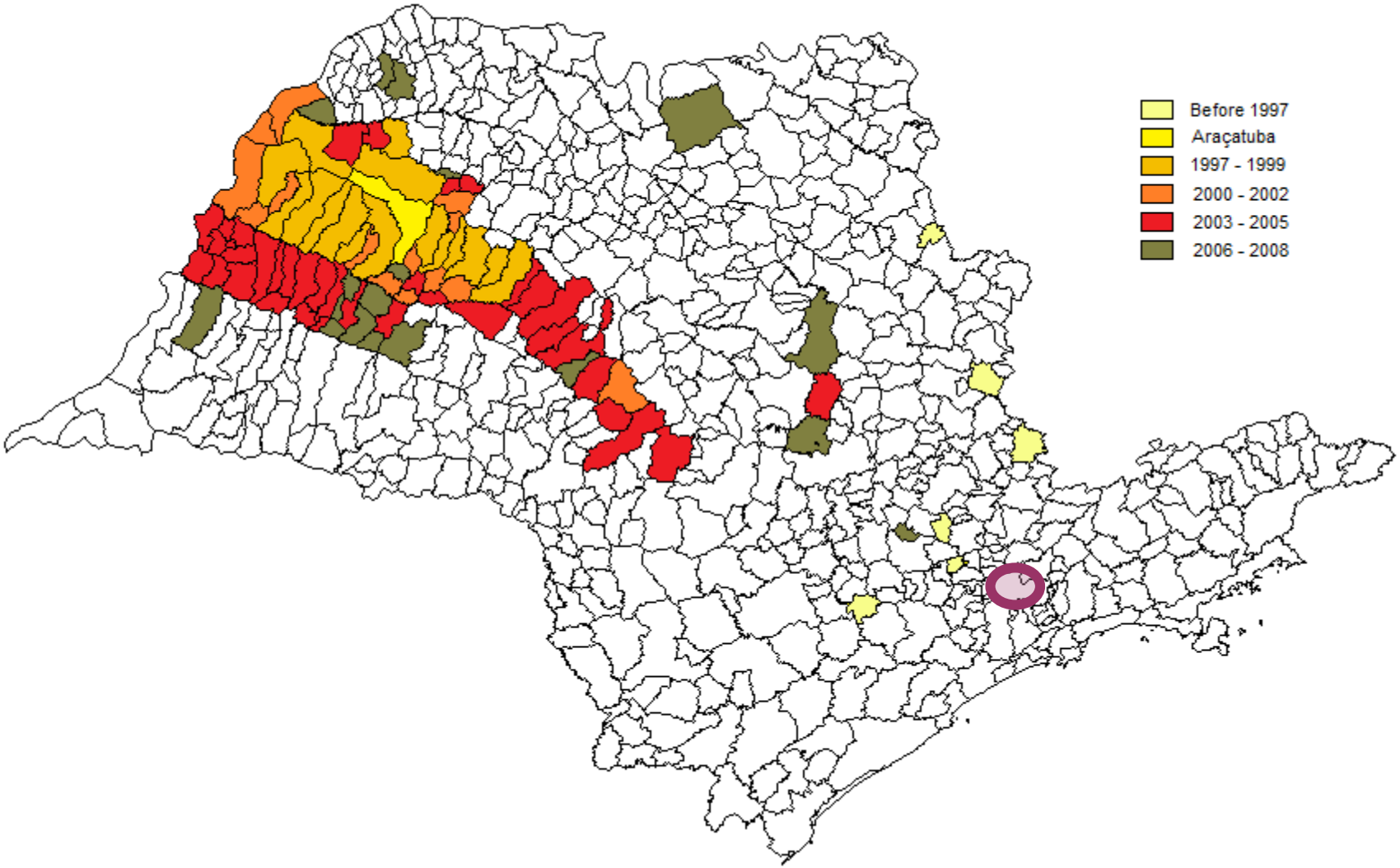
Bauru

2002 1st record of vector
2003 1st human case + 15 others
2012 35 cases 3 deaths

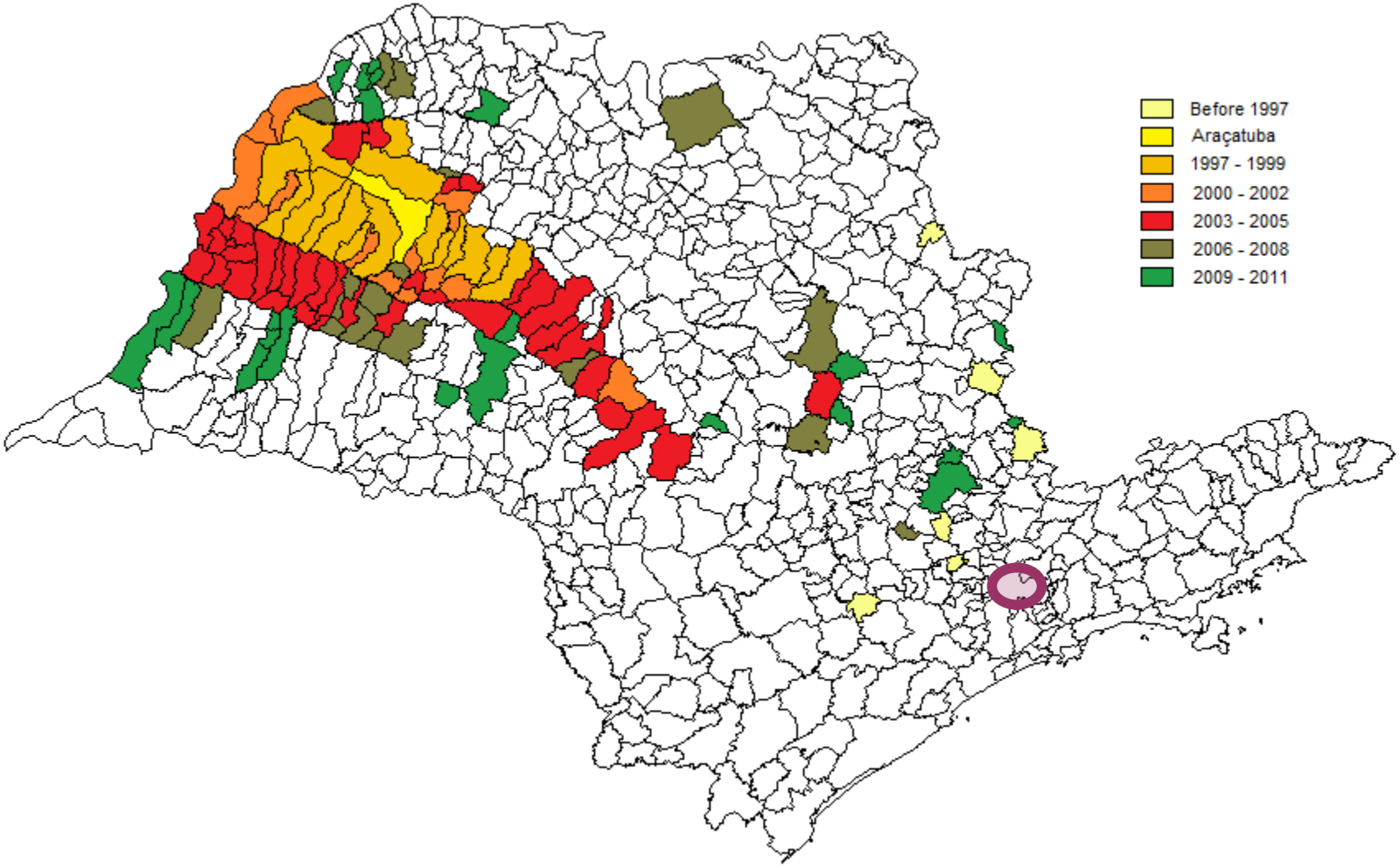
8 yrs later - 2005



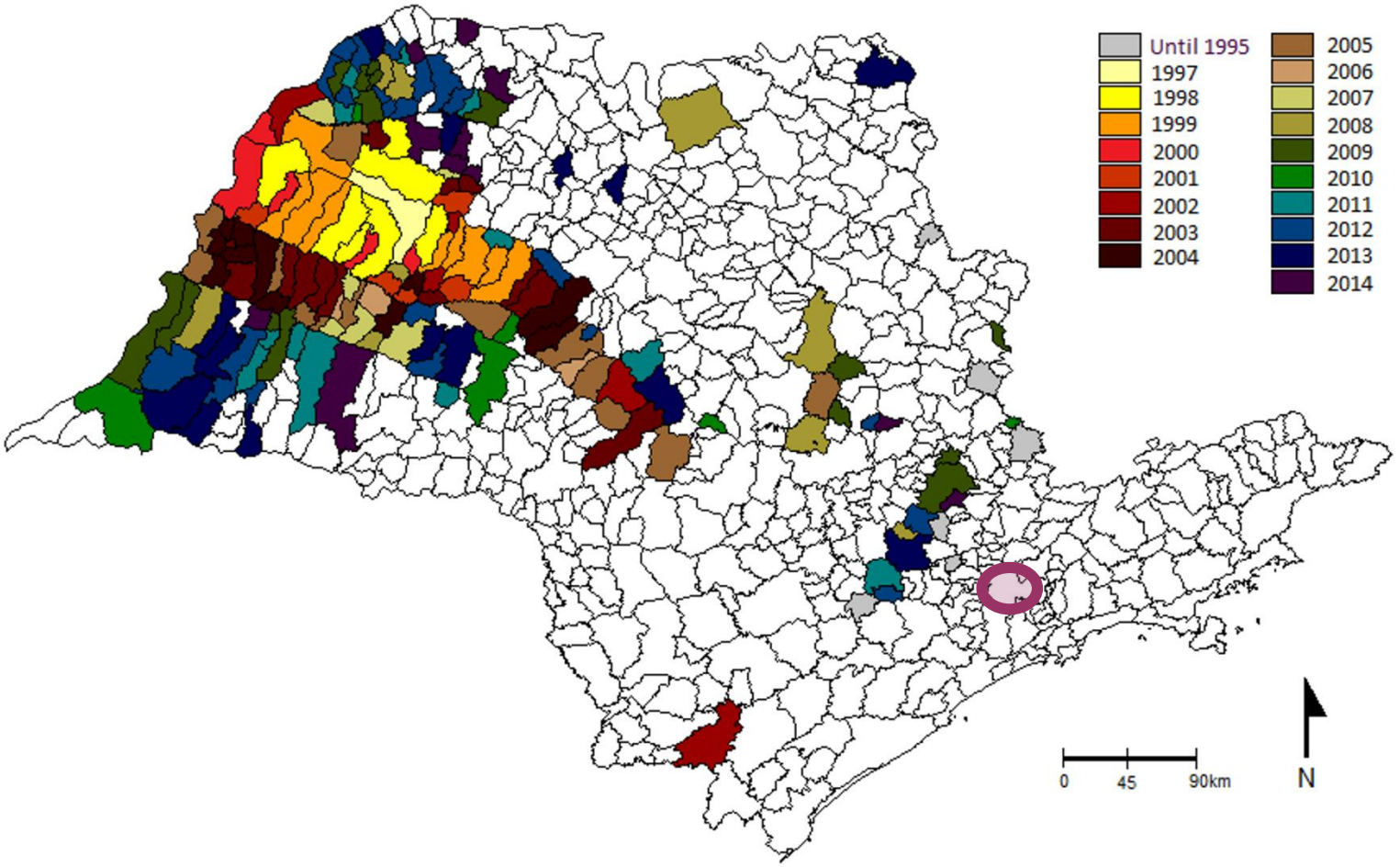
11 yrs later - 2008



14 yrs later - 2011

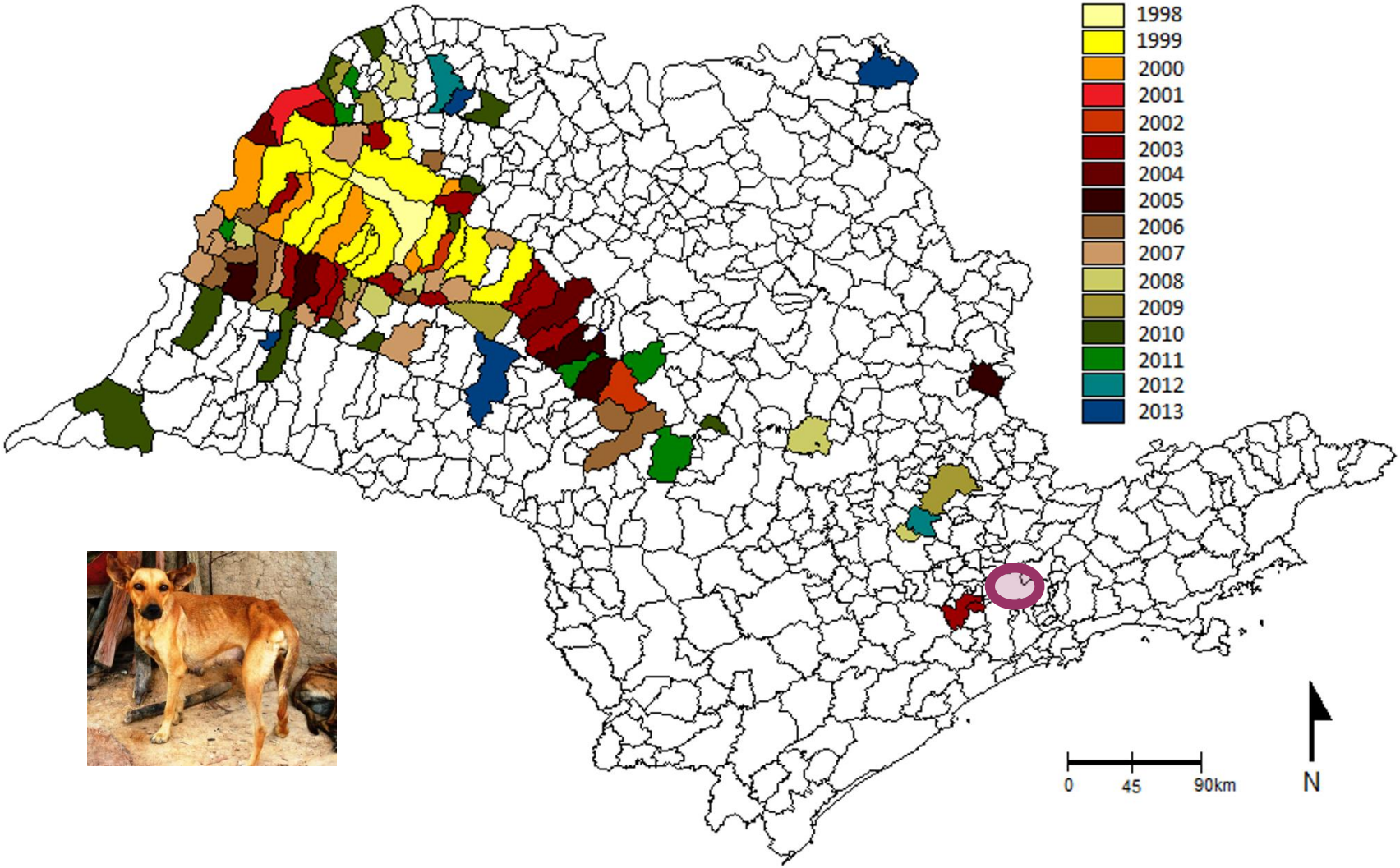


17 yrs later - 2014

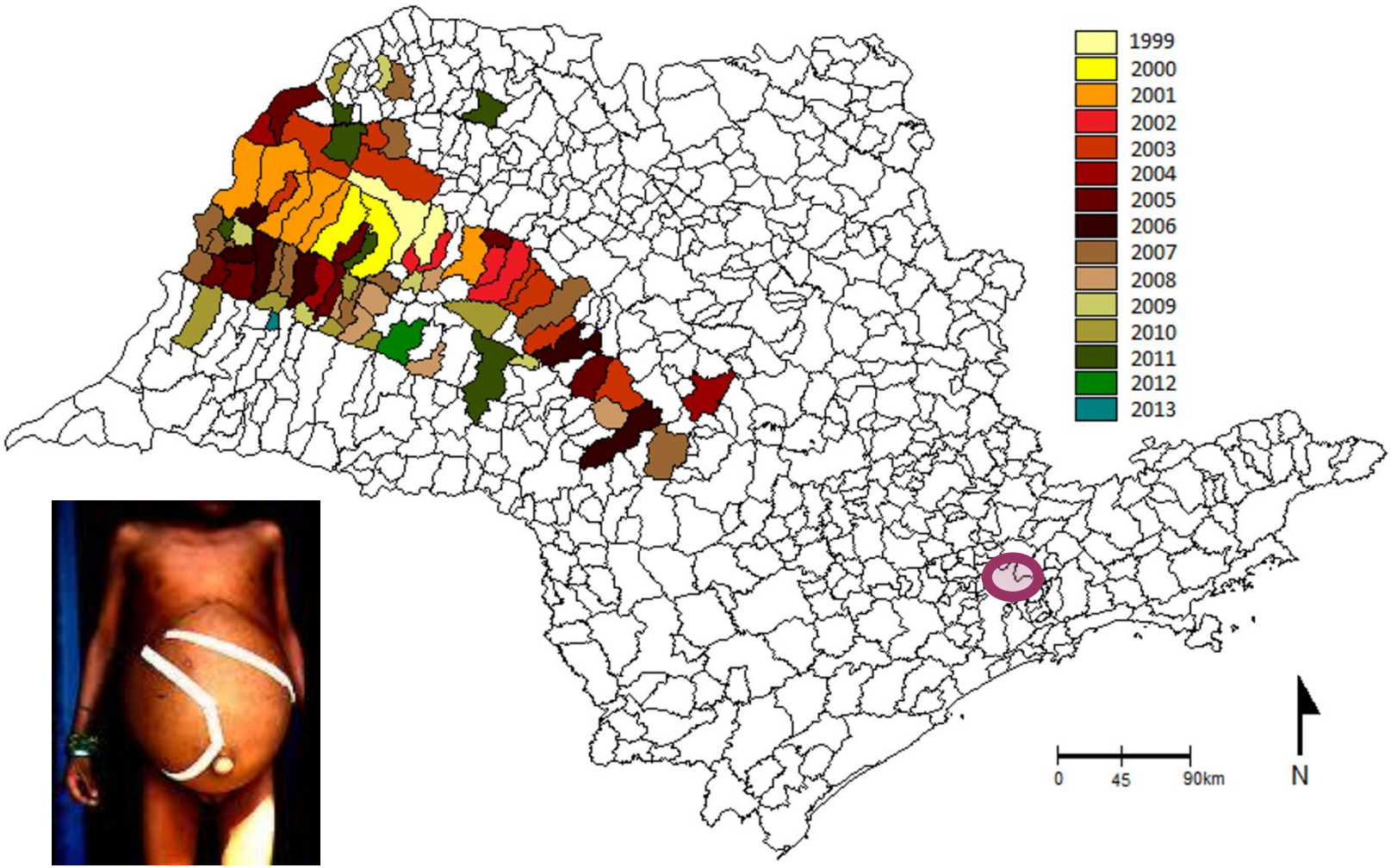


Casanova et al in press

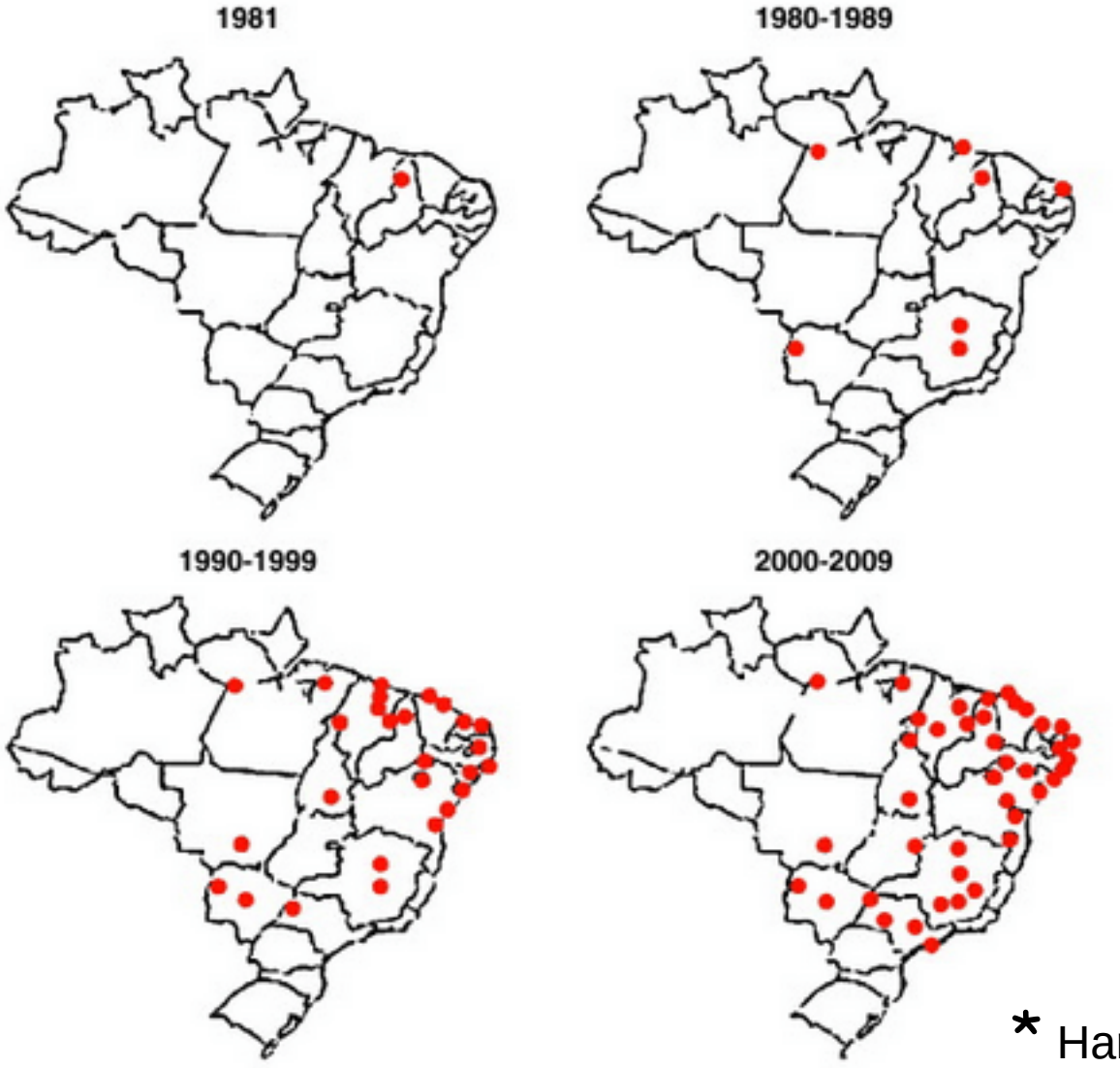
The spread of canine VL in SP



The spread of human VL in SP



The urbanization of Visceral Leishmaniasis in Brazil *: Adaptation of the vector to the urban environment



* Harhay et al 2011

Cutaneous Leishmaniasis

In South America it is caused by 13 different species

Some species are rare in man others are very common

Clinical repercussions

Very many different clinical forms that respond differently to treatment

Bolivia has the highest incidence of cutaneous & mucocutaneous leishmaniasis in the Americas being twice that of Brazil

Based on 2008 Estimates

Bolivia	75 /100,000
Brazil	37 /100,000
(Brazilian Amazonia	58 /100,000!)

Isiboro Secure
Lu. shawi
Domestic &
Peridomestic
L.(V.)braziliensis

85% *L.(V.) braziliensis*

20% Mucocutaneous

Relationship of *Leishmania* species to treatment

A comparison of Sodium Stiboglucanate (S) & Ketoconazole (K)*.

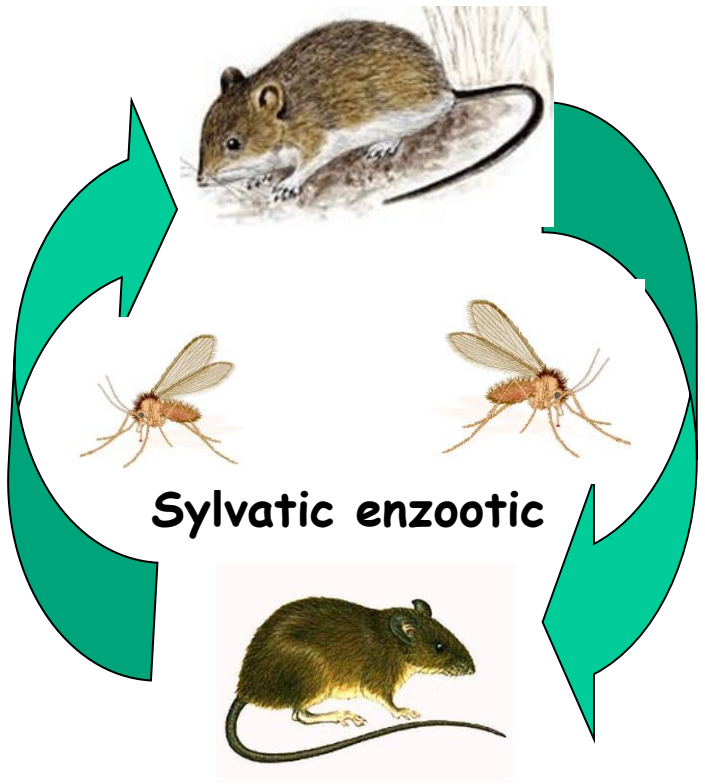
Parasite	S	K
L.(V.) braziliensis	96%	30%
L.(L.) mexicana	57%	89%

After Navin et al., 1992

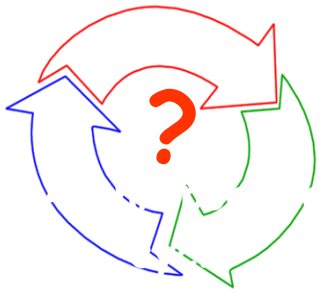
L (V.) braziliensis infections of man occur in every South American country except Chile

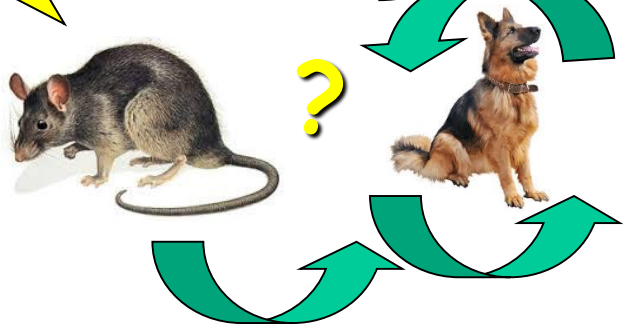
24 sand fly species have been implicated in its transmission

Present understanding of *L.* (*V.*) *braziliensis* transmission cycles

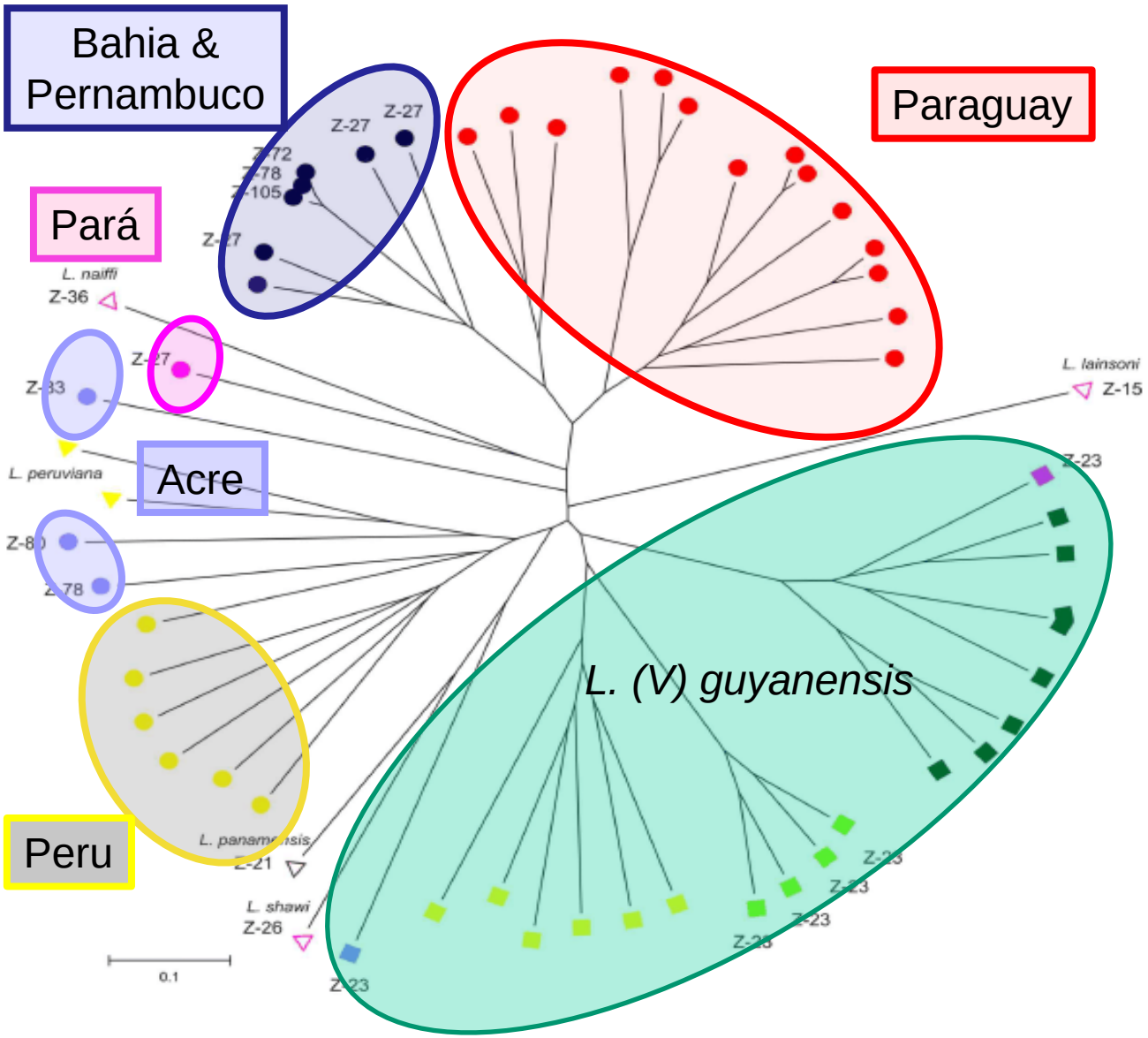


Sylvatic enzootic





Discrimination of *L. (V.) braziliensis* * strains using microsatellite



* Oddone et al 2009

Where are we now?

Control measures for Chagas Disease and the different forms of Leishmaniasis are ineffective

No vaccines for these diseases suitable for use in man will be available in the foreseeable future

Presently available drugs for these diseases cause undesirable side effects and are difficult to administer

The solution: new less toxic easily administered drugs