Treatment of Chagas Disease 100 years after its discovery: Little to Celebrate!

The experience of Medicos sin Fronteras

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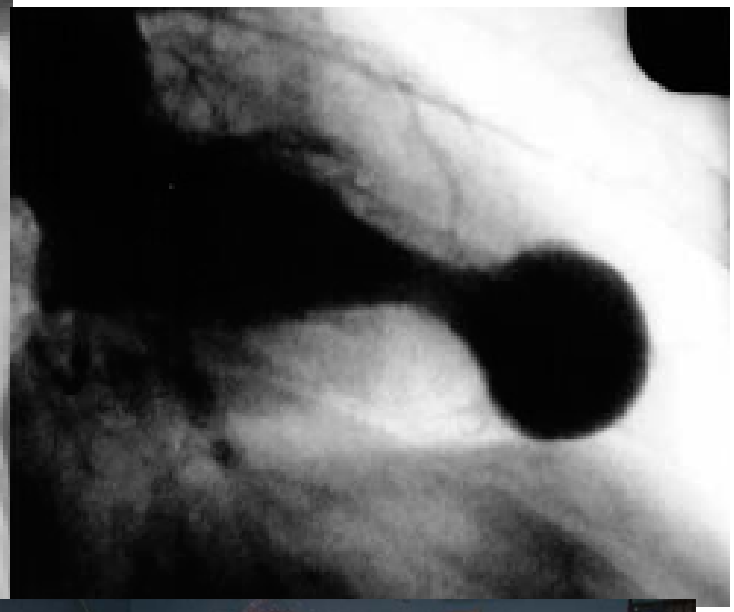
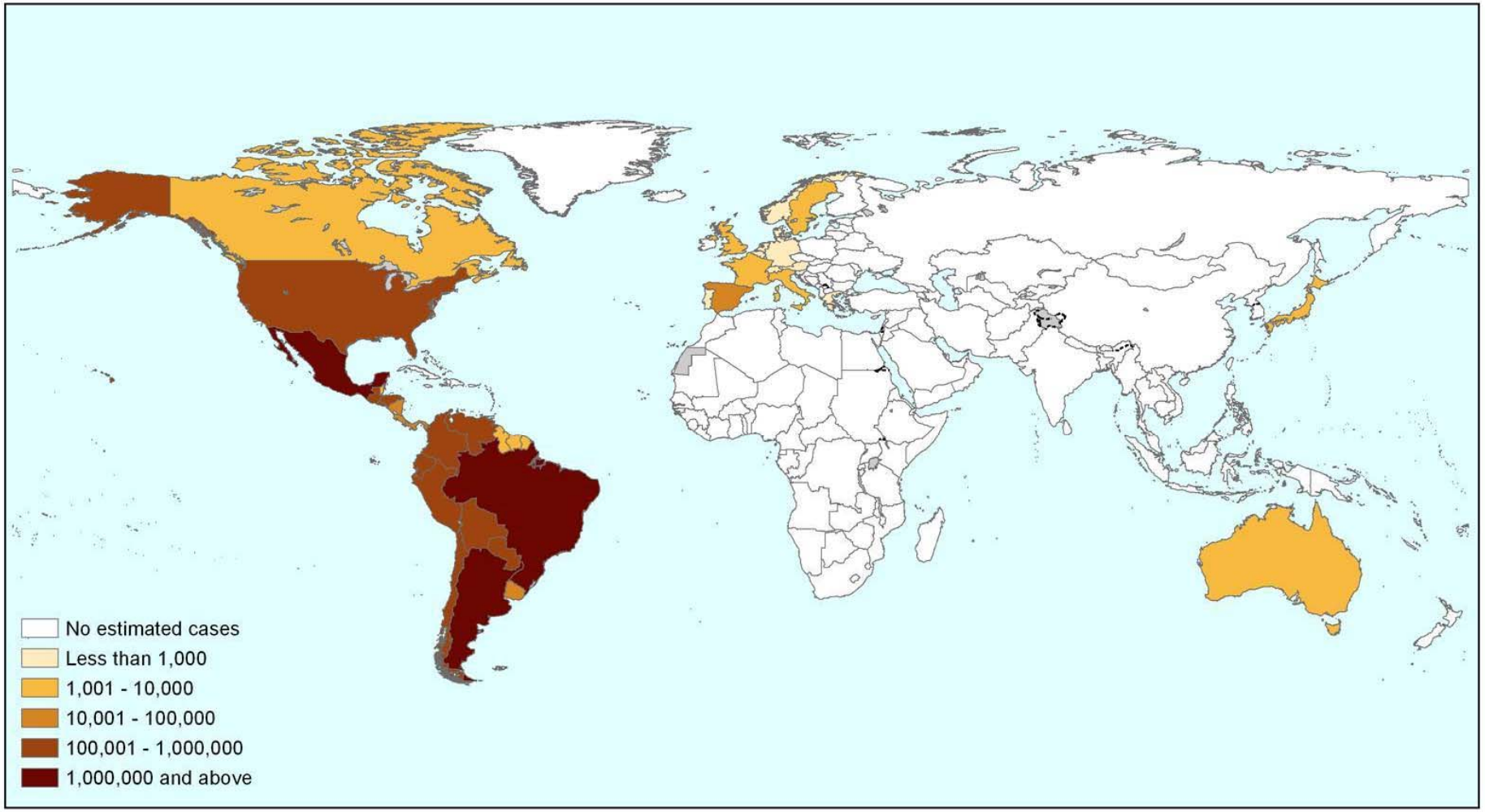


Estimated global population infected by *Trypanosoma cruzi*, 2009



Sources:
1. OPS/HDM/CD/425-06 Estimación cuantitativa de la enfermedad de Chagas en las Américas.
2. Guerri-Guttenberg RA, Grana D.R., Giuseppe Ambrosio, Milei.J. Chagasic cardiomyopathy: Europe is not spared! European Heart Journal (2008); 29: 2587-2591.
3. Schmunis. G. A. Epidemiology of Chagas Disease in non-endemic countries: the role of international migration. Mem Inst Oswaldo Cruz, Rio de Janeiro, Vol. 102(Suppl. I): 75-85, 2007.
4. De Ayala A.P, Pérez-Molina J.A, Norman F., and López-Vélez R.Chagasic cardiomyopathy in inmigrants from Latin America to Spain. Emerging Infectious Disease Volume 15, Number 4–April 2009.
5. According to the numbers of inmigrants registered for 2007in the website of the Japanese Ministry of Justice and estimated seroprevalence for non endemic countries according to Paricio-Talayero J.M. Vigilancia epidemiológica de la transmisión vertical de la enfermedad de Chagas en tres maternidades de la Comunidad Valenciana. Enferm Infecc Microbiol Clin 2008;26(10):609-13.

‘Médecins Sans Frontieres’ (MSF)

- Humanitarian medical NGO, founded in 1971 by a group of French doctors
- Total independence
- Medical assistance to populations in need
- ´Temoignage´

MSF and Chagas: Evolution

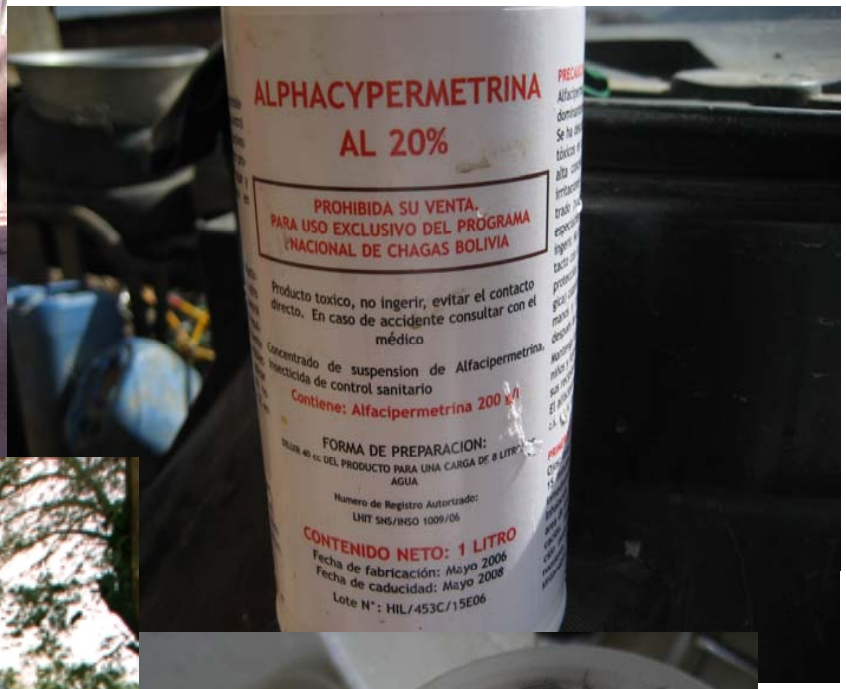
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	
Honduras	Under 5's Rural 232 treated (0.9%)										
Entre Rios - Bolivia				Under 15´s Rural 1450 treated (19.4%)							
Nicaragua				Under 15's Rural							
Guatemala					Under 14's Rural 124 treated (1.4%)						
Sucre - Bolivia							Under 18's Peri-urban 1100 treated (5.9%) Rapid test				
Cochabamba - Bolivia									Under 50's Urban and Peri-urban 600 treated to date		

Chagas in Bolivia

- **60% of the country is endemic**
- **Population at risk: 4,000,000**
- **Population infected: >1 million**
- **Causes 15% of adult deaths**

Prevalence of Chagas

Age Group (yrs)	Prevalence (%) -Sucre (n=19,400)	Prevalence (%) -Entre Rios (n=7,600)	Prevalence (%) -Cochabamba (n=6,500)	
0-4	1.9	5.9	2.0	
5-9	4.1	14.8	5.4	
10-14	8.6	31.0		
>15	14.2	51.7	27.5	
Total	5.9	19.4	16.0	


ALPHACYPERMETRINA
AL 20%
PROHIBIDA SU VENTA.
PARA USO EXCLUSIVO DEL PROGRAMA
NACIONAL DE CHAGAS BOLIVIA
Producto toxico, no ingerir, evitar el contacto directo. En caso de accidente consultar con el médico
Concentrado de suspension de Alfacipermetrina, insecticida de control sanitario
Contiene: Alfacipermetrina 200 g/l
FORMA DE PREPARACION:
AGUA
Numero de Registro Autorizado:
LHIT SNS/INSO 1009/06
CONTENIDO NETO: 1 LITRO
Fecha de fabricación: Mayo 2006
Fecha de caducidad: Mayo 2008
Lote N°: HIL/453C/15E06

CVO
923
CVO
924
CVO
922

Chagatest ELISA
96 det./tests

Journal of Clinical Microbiology, June 2008, p. 2022–2027 Vol. 46, No. 6
0095-1137/08/$08.00+0 doi:10.1128/JCM.02203-07
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Field Evaluation of a Rapid Immunochromatographic Assay for Detection of *Trypanosoma cruzi* Infection by Use of Whole Blood[▽]

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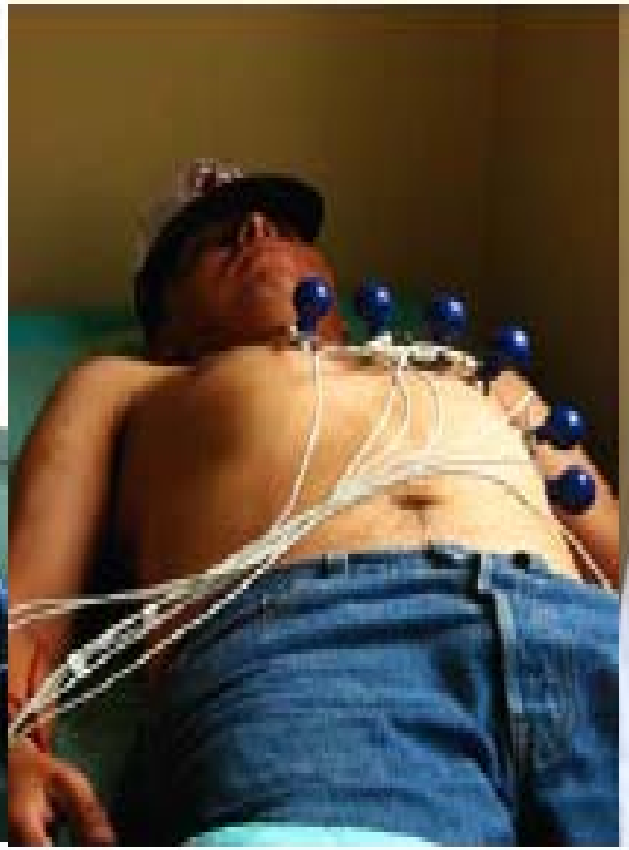
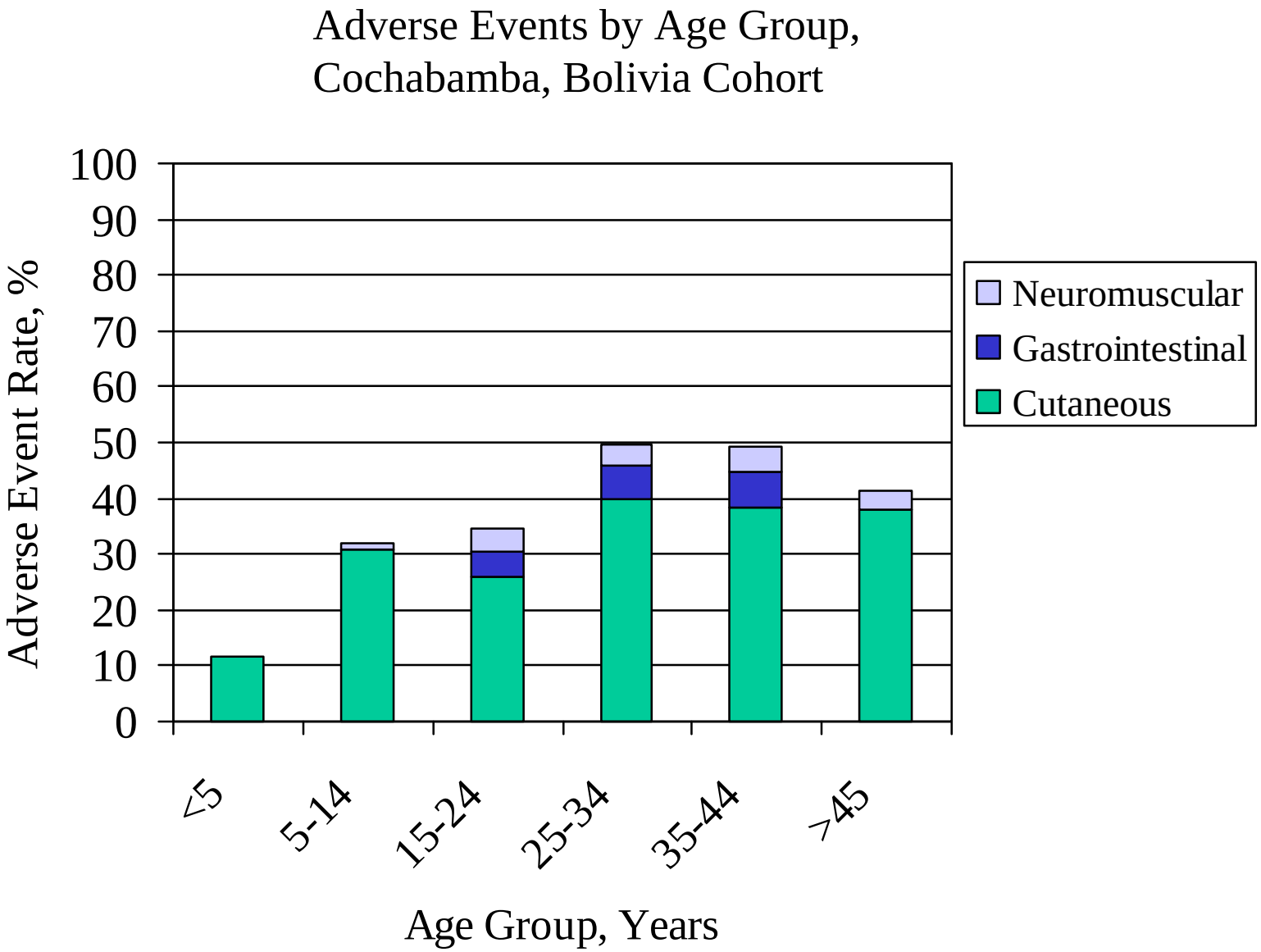
Received 30 November 2007/Returned for modification 13 February 2008/Accepted 31 March 2008

Laboratory and clinical diagnostic classification of seropositive individuals, followed by treatment and supportive therapy, is an established component of Chagas' disease control in areas where this disease is endemic. However, most Chagas' disease patients live in remote areas where neither equipped laboratories nor skilled human resources are widely available. Employing a rapid diagnostic test (RDT), when using whole blood samples, is the best option for Chagas' disease control. A high sensitivity and specificity for the Chagas Stat-Pak RDT (Chembio Diagnostic Systems, Inc., Medford, NY) has been reported for assays using serum and plasma, but its validity for the detection of antibodies to *Trypanosoma cruzi* infection in whole blood is unknown. This cross-sectional study measured the sensitivity and specificity of the Chagas Stat-Pak with whole blood, using conventional serological assays for comparison. The interobserver reliability in the interpretation of the Chagas Stat-Pak results and "ease-of-use" criterion needed to perform the Chagas Stat-Pak and conventional assays were also measured. The Chagas Stat-Pak yielded a high specificity (99.0%, 95% confidence interval [CI] = 98.4 to 99.4%) but a relatively low sensitivity (93.4%, 95% CI = 87.4 to 97.1%). The interobserver reliability was excellent (kappa [n = 1,913] = 0.99, $P < 0.0001$), and the quantified ease-of-use criterion suggested that the RDT is simple to perform. Despite the attributes of the Chagas Stat-Pak, it is not an ideal diagnostic test for the population investigated in the present study due to its relatively low sensitivity and high cost. The RDT manufacturer is called upon to improve the test if the international community hopes to make progress in controlling Chagas infections in areas where this disease is endemic.



Side Effects in Sucre

AGE GROUP	PATIENTS	CUTANEOUS		GASTROINTESTINAL		NEUROMUSCULAR	
		nº	%	nº	%	nº	%
0 - 4 years	67	9	**13,4%**	0	0,0%	0	0,0%
5 - 10 years	297	64	**21,5%**	25	8,4%	7	2,4%
11 - 15 years	435	120	**27,6%**	31	7,1%	19	4,4%
> 16 years	245	92	**37,6%**	25	10,2%	6	2,4%
Total	**1044**	285	27,3%	81	7,8%	32	3,1%


Adverse Events by Age Group,
Cochabamba, Bolivia Cohort
Adverse Event Rate, %
100
90
80
70
60
50
40
30
20
10
0
<5
5-14
15-24
25-34
35-44
>45
Age Group, Years
Neuromuscular
Gastrointestinal
Cutaneous

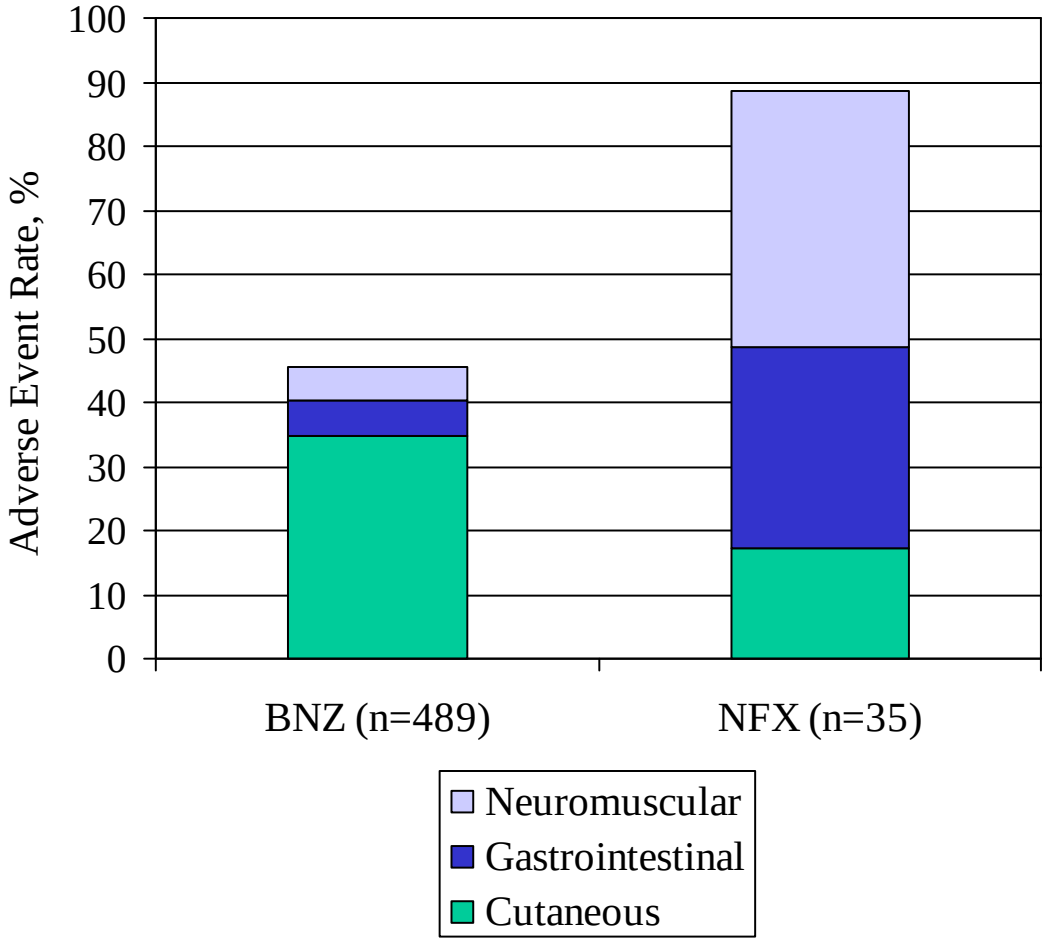
Important Side Effects

- Mortality
  - 0/3300 patients
- Hospitalisation
  - 4/3300 patients (1 SJS, 1 TEN)
- Loss to Follow-Up
  - 0-15%

Important Side Effects

	ENTRE RIOS <15	SUCRE <18	COCHA <15	COCHA MALE >15	COCHA FEMALE >15
Diagnosed Positive	1464	1102	151	219	573
Started Treatment	1434 (97.9%)	1044 (94.7%)	**109 (72.2%)**	**130 (59.3%)**	**264 (46%)**
Completed >55 Days	1356 (94.6%)	894 (85.6%)	82 (75.2%)	101 (77.7%)	174 (65.9%)
Stop due to Side Effects	28 (2.0%)	61 (5.8%)	**12 (11.0%)**	**9 (6.9%)**	**56 (21.0%)**
Stop for Unknown Reason	49 (3.4%)	83 (8.0%)	**12 (11.0%)**	**20 (15.4%)**	**25 (9.5%)**

BNZ (first-line) vs NFX (second-line): Adverse events in adults >15 years old



Moderate:

- **22.9% NFX vs 9.2% BNZ**

Severe:

- **5.8% NFX vs 0.2% BNZ**

Treatment Efficacy (% Seronegativisation)

- Entre Rios, Bolivia
  - 59 out of 1,101
  - **5.4% at 36-60 months**
- Sucre, Bolivia
  - 0 out of 276
  - **0% at 18 months**
- Yoro, Honduras
  - 87% at 18 months
- Olopa, Guatemala
  - 58% at 18 months

Impact of the projects?

- Prevention and Treatment
- Protocols
- Retained trained staff
- Publications
- In 5 health centres
  - 50% non-MSF staff are ‘involved’
  - 90% of treatment contacts by non-MSF doctors
  - 50% of screening done by non-MSF nurses
  - 30% of diagnosis done by non-MSF lab staff

- In Entre Rios:
  - Less than 100 children diagnosed and treated in 3 years since project closure
- In Sucre:
  - 1040 of 1080 children diagnosed before MSF departure remain untreated.
- In Bolivia:
  - **>99% of adult need unmet**
  - **95% of children need unmet**

‘Pathology’ of Neglect

- Failure of Government
- Poverty (**Lack of human resources**)
- Few people (..or too many people!)
- **Invisibility** (No symptoms, chronic effects, not photogenic, anonymous death)
- Difficult/Costly prevention, diagnosis, treatment
- **‘Unsatisfying’ treatment**
- Difficult research
- False beliefs and stigma
- **No demand for treatment by community**

‘...every study, every experience, points a finger towards a ...population which lives in extreme poverty, and produces irritation in their governments, being testament to their incapacity to resolve huge economic and social problems.’

Carlos Chagas

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What is needed?

- **Better tools**
  - Insecticides
  - Vaccine
  - Diagnostics
  - Drugs and Formulations
  - Test of Cure
  - **R&D system that is fit for purpose**
- **Better approaches**
  - Innovative Integrated Models
  - ‘Sustainability science’

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A ‘new’ model

- Community engagement and **motivation**
- Concept of ‘PLC’
- Treatment Preparedness
- Integrate prevention and treatment
- Compromise with **reality**
- **‘Task-shifting’** to mitigate human resource crisis

Muito obrigado

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www.msf.org.br/chagas