UNIVERSITÀ DEGLI STUDI DI MILANO
FACOLTÀ DI MEDICINA E CHIRURGIA

Malattia di Chagas

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PATOLOGIA TROPICALE DI IMPORTAZIONE E AUTOCTONA
Lunedì 7 Luglio 2025, Ore 16.00-19.00

Chagas disease

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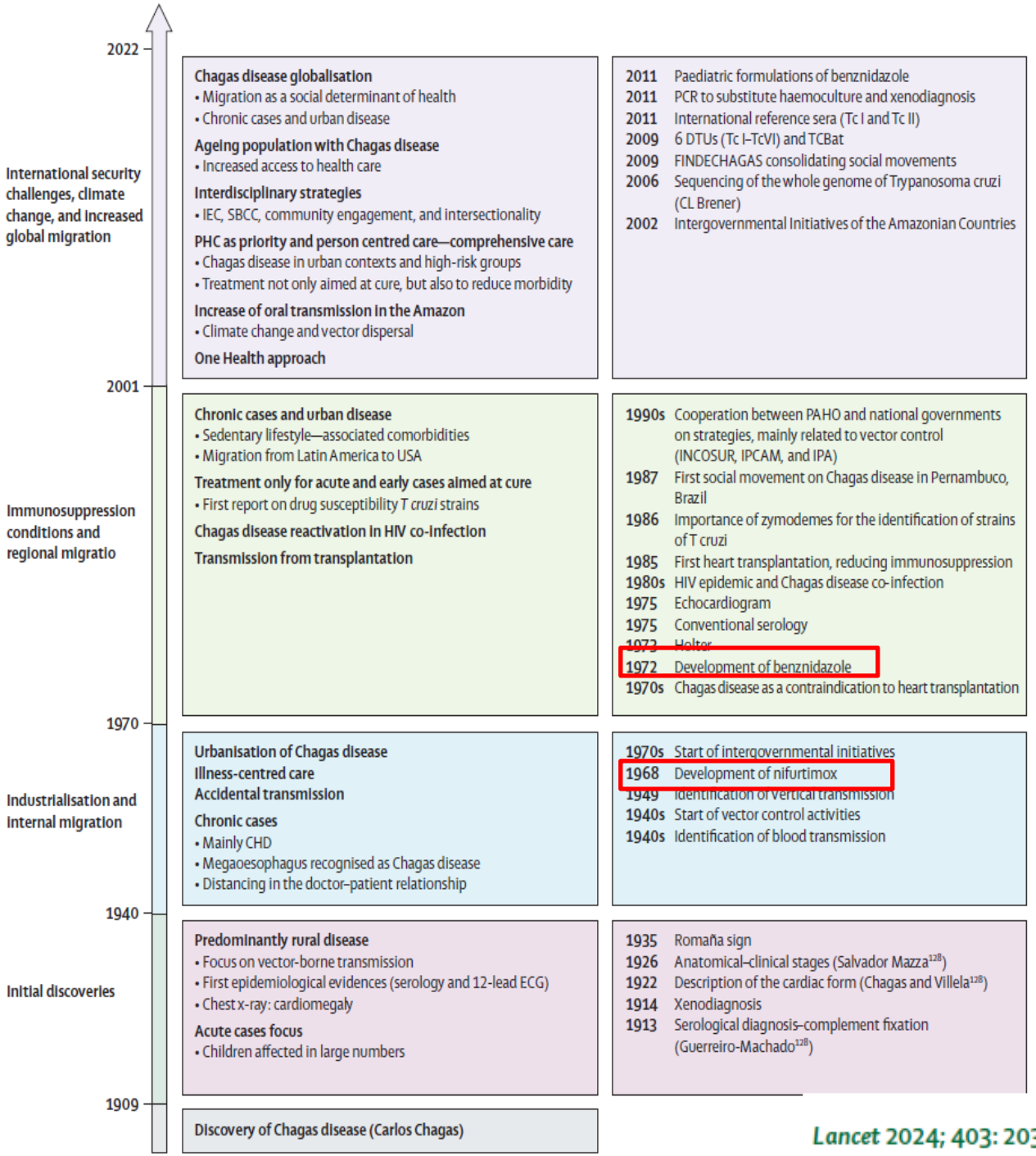

Lancet 2024; 403: 203–18

Global, Regional, and National Trends of Chagas Disease from 1990 to 2019: Comprehensive Analysis of the Global Burden of Disease Study

During the year 2019, the global prevalence of CD was 6,469,283 (95% UI = 5,658,409.78–7,374,556.70), showing a decreasing trend compared to the prevalence reported in 1990. This difference represented a 11.3% decrease in prevalence over the last three decades. Similarly, the age-standardized prevalence rate per 100,000 population in 2019 decreased to 83.61 (95% UI = 73.13–95.31) representing a 42% reduction of this value with respect to 1990 (Supplementary Figure 1). Bolivia remained the country with the highest prevalence rate per 100,000 population (4993.53; 95% UI = 4540.19 – 5483.11), followed by Venezuela (1654,73; 95% UI = 1439.50–1897.81) and Argentina (1524.07; 95% UI = 1343.16 – 1736.00) (Supplementary Figure 2). On the other hand, Brazil remained the country with the higher number of estimated CD cases, with around 2,164,570 cases (33.5% of the total). Furthermore, Argentina was the endemic country with the largest reduction in the prevalence number (–54.68%), followed Chile (–50.95%) and Uruguay (–49.95%), while Mexico (39.58%), Brazil (12.80%) and Honduras

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Global, Regional, and National Trends of Chagas Disease from 1990 to 2019: Comprehensive Analysis of the Global Burden of Disease Study

Similar to the prevalence trend, global deaths per 100,000 population due to CD decreased from (0.31; 95% UI = 0.14–0.37) in 1990 to (0.12; 95% UI = 0.07–0.21) in 2019. Furthermore, a 15.6% decrease in the absolute number of deaths was observed in this period (11,235 deaths due to CD estimated in 1990 compared to 9487 in 2019) (Supplementary Figure 3). Brazil was the country with the largest number of deaths due to CD during this period (7903 in 1990 and 6523 in 2019). On the other hand, Bolivia had the largest age-adjusted death rate per 100,000 population both in 1990 (10.93; 95% UI = 2.29–23.49) and in 2019 (7.27; 95% UI = 1.58–17.19) (Supplementary Figure 4).

The global disability-adjusted life-years (DALYs) due to CD were 360,872 (95% UI = 153,746–450,827) in 1990 and 275,377 (95% UI = 184,453–459,354) in 2019; representing an important decrease of around 23.7% DALYs over the evaluated period. Likewise, the global

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Actualización de la estimación de la enfermedad de Chagas en los países endémicos de las Américas

2018

OPS Organización Panamericana de la Salud Organización Mundial de la Salud Región de las Américas

Cuadro 1: Estimaciones de la enfermedad de Chagas en los 21 países endémicos estudiados, 2018

Indicador	No.
Población total	599 256 198
Población expuesta al vector	104 581 109
Personas con infección por *T. cruzi*	7 467 498
Prevalencia de infección por *T. cruzi* (por 100 habitantes)	1,25
Mujeres de entre 15 y 44 años con infección por *T. cruzi*	1 764 756
Nacidos vivos por año	9 872 129
Nuevos casos anuales de infección por *T. cruzi* por transmisión congénita	9129
Incidencia de infección congénita por *T. cruzi* (por 10 000 nacidos vivos)	9,25
Nuevos casos anuales de infección por *T. cruzi* por transmisión vectorial	7216
Incidencia de infección vectorial por *T. cruzi* (por 100 000 habitantes expuestos)	6,90
Personas con infección por *T. cruzi* y cardiopatía chagásica	1 537 607
Prevalencia estimada de infección por *T. cruzi* en donantes de sangre (por 100 donantes)	0,66

Nota: La lista de los 21 países considerados endémicos de la Región de las Américas es: Argentina, Belice, Bolivia (Estado Plurinacional de), Brasil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Guayana Francesa, Guyana, Honduras, México, Nicaragua, Panamá, Paraguay, Perú, Suriname, Uruguay, Venezuela (República Bolivariana de).
Fuente: elaboración propia.

Cuadro 2: Estimaciones de la enfermedad de Chagas en los 21 países endémicos estudiados, por país, 2018

País	Población total	Población expuesta al vector	Personas con infección por *T. cruzi*	Prevalencia de infección por *T. cruzi* (por 100 habitantes)	Mujeres de entre 15 y 44 años con infección por *T. cruzi*	Nacidos vivos por año	Nuevos casos anuales de infección por *T. cruzi* por transmisión congénita	Incidencia de infección congénita por *T. cruzi* (por 10 000 nacidos vivos)	Nuevos casos de infección por *T. cruzi* por transmisión vectorial	Incidencia de infección vectorial por *T. cruzi* (por 100 000 habitantes expuestos)	Personas con infección por *T. cruzi* y cardiopatía chagásica	Prevalencia estimada de infección por *T. cruzi* en donantes de sangre (por 100 donantes)
Total	**599 256 198**	**104 581 109**	**7 467 498**	**1,25**	**1 764 756**	**9 872 129**	**9129**	**9,25**	**7216**	**6,90**	**1 537 607**	**0,66**
Argentina	44 494 502	6 243 803	706 112	1,59	125 096	682 326	644	9,44	20	0,32	190 650	1,50
Belice	430 191	95 800	1895	0,44	360	7296	4	5,48	3	3,13	413	0,54
Bolivia (Estado Plurinacional de)	11 307 314	6 318 626	774 397	6,85	157 257	138 765	1698	122,37	1011	16,00	178 242	2,04
Brasil	208 494 900	27 790 041	3 913 142	1,88	940 882	2 944 932	2543	8,64	545	1,96	782 628	0,16
Chile	18 751 405	1 875 141	157 512	0,84	37 465	222 088	24	1,08	0	0,00	31 502	0,09
Colombia	48 258 494	8 138 046	405 300	0,84	103 984	645 024	809	12,54	580	7,13	113 484	0,14
Costa Rica	5 003 383	104 419	5137	0,10	1353	68 098	11	1,62	2	1,92	1130	0,12
Ecuador	18 226 512	8 226 512	158 275	0,87	49 333	251 106	494	19,67	676	8,22	30 731	0,27
El Salvador	6 643 359	235 000	152 797	2,30	38 844	90 492	110	12,16	95	40,43	28 746	1,85
Guatemala	16 346 950	5 194 614	140 584	0,86	26 581	383 263	121	3,16	1225	23,58	17 573	0,73
Guayana Francesa	301 099	102 374	2979	0,99	1474	6022	1	1,66	1	0,98	280	1,05
Guyana	785 514	285 000	7856	1,00	2	11 820	2	1,69	6	2,11	384	1,05
Honduras	9 012 229	878 692	62 184	0,69	29 808	181 165	179	9,88	237	26,97	9328	0,69
México	124 737 791	25 041 300	536 373	0,43	134 525	2 105 664	1415	6,72	685	2,74	57 928	0,34
Nicaragua	6 850 540	967 684	22 607	0,33	4513	246 646	96	3,89	241	24,90	4521	0,20
Panamá	4 158 783	925 675	15 812	0,38	3851	66 498	2	0,30	23	2,48	3320	0,26
Paraguay	7 453 695	1 046 030	134 167	1,80	37 579	123 187	370	30,04	1	0,10	21 467	1,49
Perú	32 131 400	1 070 291	144 591	0,45	35 659	562 465	145	2,58	1080	100,91	37 025	0,45
Suriname	612 985	214 600	3765	0,61	657	9809	1	1,02	5	2,33	95	0,50
Uruguay	3 427 042	0	5072	0,15	1158	40 139	1	0,25	0	0,00	355	0,20
Venezuela (República Bolivariana de)	31 828 110	9 827 461	116 941	0,37	34 375	1 085 324	459	4,23	780	7,94	27 805	0,14

Cuadro 3: Estimaciones de la enfermedad de Chagas en los 21 países endémicos estudiados, 2005, 2010 y 2018

Indicador	Año		
	2005[a]	2010[b]	2018
Población total	531 432 850	543 877 115	599 256 198
Población expuesta al vector	108 595 000	70 199 360	104 581 109
Personas con infección por *T. cruzi*	7 694 500	5 742 167	7 467 498
Prevalencia de infección por *T. cruzi* (por 100 habitantes)	1,45	1,06	1,25
Mujeres de entre 15 y 44 años con infección por *T. cruzi*	1 809 507	1 124 930	1 764 756
Nacidos vivos por año	10 832 950	N/A	9 872 129
Nuevos casos anuales por año de infección por *T. cruzi* por transmisión congénita	14 385	8668	9129
Incidencia de infección congénita por *T. cruzi* (por 10 000 nacidos vivos)	13,35	8,95	9,25
Nuevos casos anuales de infección por *T. cruzi* por transmisión vectorial	41 200	29 925	7216
Incidencia de infección vectorial por *T. cruzi* (por 100 000 habitantes expuestos)	38,00	5,05	6,90
Personas con infección por *T. cruzi* y cardiopatía chagásica	1 772 365	1 171 193	1 537 607
Prevalencia de infección por *T. cruzi* en donantes de sangre (por 100 donantes)	1,28	0,93	0,66

Nota: La lista de los 21 países considerados endémicos de la Región de las Américas es: Argentina, Belice, Bolivia (Estado Plurinacional de), Brasil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Guayana Francesa, Guyana, Honduras, México, Nicaragua, Panamá, Paraguay, Perú, Suriname, Uruguay, Venezuela (República Bolivariana de).
N/A = información no disponible.

Fuentes: elaboración propia, con base en:
a Jannin J, Salvatella R. Estimación cuantitativa de la enfermedad de Chagas en las Américas. Montevideo: OPS; 2006.
b Organización Mundial de la Salud. Chagas Disease in Latin America: An Epidemiological Update Based on 2010 Estimates. Wkly Epidemiol Rec. 2015;90(6):33-43. Disponible en: https://pubmed.ncbi.nlm.nih.gov/25671846/.

Worldwide prevalence of chagas cardiomyopathy—an analysis from the global burden of disease dataset

Infection (2025) 53:947–952

Abdul Mannan Khan Minhas[1,2] · Rachel Marcus[3] · Salim S. Virani[4,5] · Michael D. Shapiro[6] · Robert J. Mentz[7] · Luis E. Echeverria[8] · Jonathan T. Arcobello[9] · Dmitry Abramov[10]

Table 1 Prevalence, Age Standardized Rates, and Estimated Annual Percent Change in Chagas Cardiomyopathy

	1990			2019			1990			2019			1990-2019		
	Number	95% UI		Number	95% UI		ASR	95% UI		ASR	95% UI		EAPC	95% CI	
Global	220166	139752	315866	283236	181832	407165	5.23	3.34	7.47	3.42	2.2	4.91	−0.35	−0.37	−0.32
Age groups															
25-49 years	82584	50994	122854	84705	52216	126847	4.86	3	7.23	3.12	1.92	4.67	−0.36	−0.38	−0.33
50-69 years	92358	59040	131759	127459	82264	183234	13.54	8.66	19.32	9.24	5.97	13.29	−0.32	−0.34	−0.29
70+ years	45224	30464	62006	71072	48034	97716	22.44	15.12	30.76	15.33	10.36	21.07	−0.32	−0.35	−0.29
Sex															
Male	142482	96950	194620	185477	126543	252930	7.15	4.91	9.68	4.67	3.2	6.35	−0.35	−0.37	−0.32
Female	77684	43701	123586	97759	55500	155060	3.56	2	5.65	2.27	1.29	3.6	−0.36	−0.39	−0.33
SDI															
High SDI	3149	2004	4521	3761	2422	5393	0.32	0.2	0.46	0.25	0.16	0.36	−0.23	−0.26	−0.19
High-middle SDI	89955	57869	128635	76580	49799	109055	8.23	5.31	11.76	3.87	2.51	5.52	−0.53	−0.55	−0.51
Middle SDI	68859	43323	99626	118561	75872	170684	6.16	3.93	8.86	4.64	2.99	6.64	−0.25	−0.27	−0.22
Low SDI	1486	939	2165	3075	1958	4526	0.58	0.37	0.84	0.56	0.36	0.81	−0.04	−0.12	0.06
Low-middle SDI	56711	35908	81969	81252	52212	116543	8.67	5.55	12.42	5.61	3.64	8.02	−0.35	−0.38	−0.32
Regions															
Endemic Regions															
Southern Latin America	71250	46178	101313	48812	32000	68694	153.25	99.36	217.85	61.15	40.05	86.16	−0.6	−0.62	−0.58
Andean Latin America	28915	18235	41644	32161	20744	46548	125.46	79.6	179.58	55.03	35.57	79.49	−0.56	−0.59	−0.54
Tropical Latin America	62080	39374	90263	100155	64247	145470	60.06	38.42	86.73	40.15	25.78	58.31	−0.33	−0.36	−0.3
Central Latin America	54182	33871	78296	96284	61396	137715	57.51	36.34	82.49	39.49	25.25	56.38	−0.31	−0.34	−0.29
Non-Endemic Regions															
High-income North America	2699	1717	3885	3396	2185	4873	0.84	0.53	1.21	0.67	0.43	0.96	−0.21	−0.24	−0.17
Western Europe	826	532	1172	2246	1444	3221	0.17	0.11	0.24	0.34	0.22	0.5	1.04	0.93	1.14
Australasia	116	74	164	65	42	94	0.52	0.33	0.73	0.16	0.1	0.23	−0.69	−0.71	−0.66
Caribbean	81	53	116	79	51	112	0.3	0.2	0.43	0.15	0.1	0.22	−0.49	−0.52	−0.45
High-income Asia Pacific	17	11	24	38	25	55	0.01	0.01	0.01	0.01	0.01	0.02	0.51	0.38	0.65

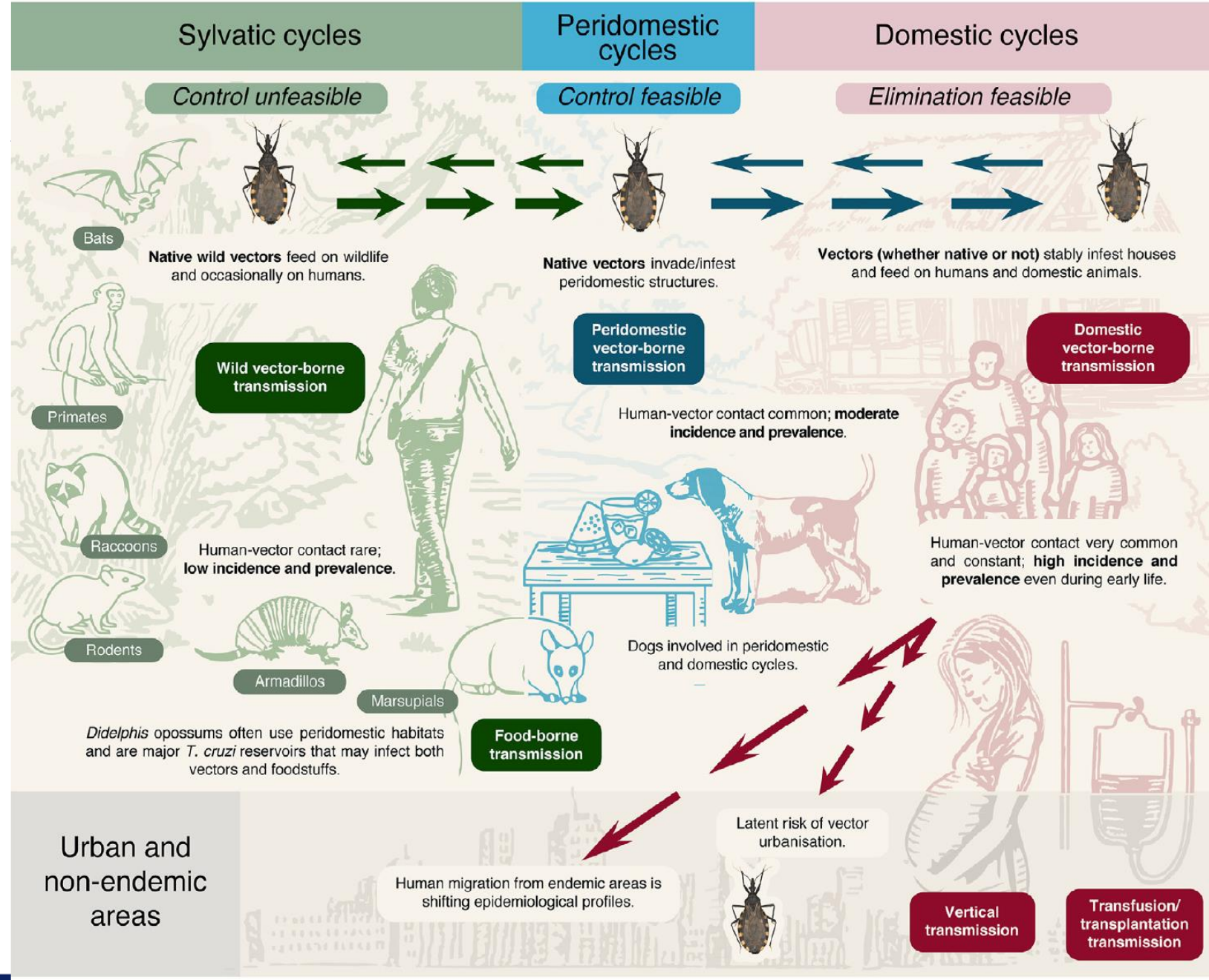
UI Uncertainty Interval, *CI* Confidence Interval, *ASR* Age standardized rate per 100,000 population, *EAPC* Estimated annual percent change, *SDI* socio-demographic index. Regional groups were defined based on Global Burden of Disease classification. Age groups are not age-standardized. Prevalence reported as 0 in 25–29 year age-group. Other geographic regions had no estimated prevalence of Chagas Cardiomyopathy (estimated prevalence of 0)

Table 2 Age standardized rates (ASR) of Prevalence per 1,00,000 Population for Chagas Cardiomyopathy in 2019

Country	ASR	95% IU	
Bolivia	185.65	118.3	267.95
Venezuela	77.95	50.67	108.51
Chile	65.94	43.32	92.72
Argentina	61.43	39.5	87.86
Mexico	45.13	28.69	64.86
Honduras	41.03	26.44	58.44
Brazil	40.48	26	58.83
Ecuador	32.56	20.73	47.16
Uruguay	32.21	20.33	45.81
Guatemala	31.81	20.44	46.03
Nicaragua	30.27	19.96	43.52
Peru	28.08	18.28	40.76
Paraguay	26.36	16.95	37.95
El Salvador	25.29	15.94	36.52
Panama	24.28	15.5	34.86
Costa Rica	21.12	13.22	30.36
Colombia	11.69	7.63	16.95
Spain	2.05	1.31	2.98
Belize	0.85	0.52	1.29
Grenada	0.76	0.34	1.41
Guyana	0.74	0.45	1.13
United States of America	0.71	0.45	1.02
Andorra	0.64	0.34	1.13
Puerto Rico	0.49	0.31	0.71
Israel	0.46	0.29	0.67
Italy	0.45	0.28	0.65
Suriname	0.4	0.24	0.62
Dominican Republic	0.38	0.24	0.55
Switzerland	0.37	0.23	0.54
Sweden	0.34	0.21	0.49
Canada	0.3	0.19	0.43
Portugal	0.22	0.14	0.31
Australia	0.19	0.12	0.28
Ireland	0.15	0.1	0.23
Antigua and Barbuda	0.1	0.05	0.21
Trinidad and Tobago	0.1	0.05	0.16
Netherlands	0.09	0.05	0.12
Denmark	0.08	0.05	0.12
Bahamas	0.07	0.03	0.12
France	0.06	0.04	0.09
Saint Lucia	0.05	0.01	0.14
Austria	0.05	0.03	0.07
Luxembourg	0.03	0.01	0.07
Iceland	0.03	0.01	0.08
Japan	0.02	0.01	0.03
Dominica	0.02	0	0.12
Germany	0.02	0.02	0.04
Cuba	0.01	0	0.01
Barbados	0.01	0.01	0.01

The epidemiology of Chagas disease in the Americas

Zulma M. Cucunubá,[a,*] Sebastián A. Gutiérrez-Romero,[a] Juan-David Ramírez,[b,c] Natalia Velásquez-Ortiz,[b] Soledad Ceccarelli,[d] Gabriel Parra-Henao,[e] Andrés F. Henao-Martínez,[f] Jorge Rabinovich,[d] María-Gloria Basáñez,[g] Pierre Nouvellet,[h] and Fernando Abad-Franch[ij,**]



g. 1: Ecoepidemiology and transmission dynamics of Chagas disease in the Americas.

The Lancet Regional Health - Americas 2024;37: 100881

Zulma M. Cucunubá,[a,*] Sebastián A. Gutiérrez-Romero,[a] Juan-David Ramírez,[b,c] Natalia Velásquez-Ortiz,[b] Soledad Ceccarelli,[d] Gabriel Parra-Henao,[e] Andrés F. Henao-Martínez,[f] Jorge Rabinovich,[d] María-Gloria Basáñez,[g] Pierre Nouvellet,[h] and Fernando Abad-Franch[ij,**]

The Lancet Regional Health - Americas
2024;37: 100881

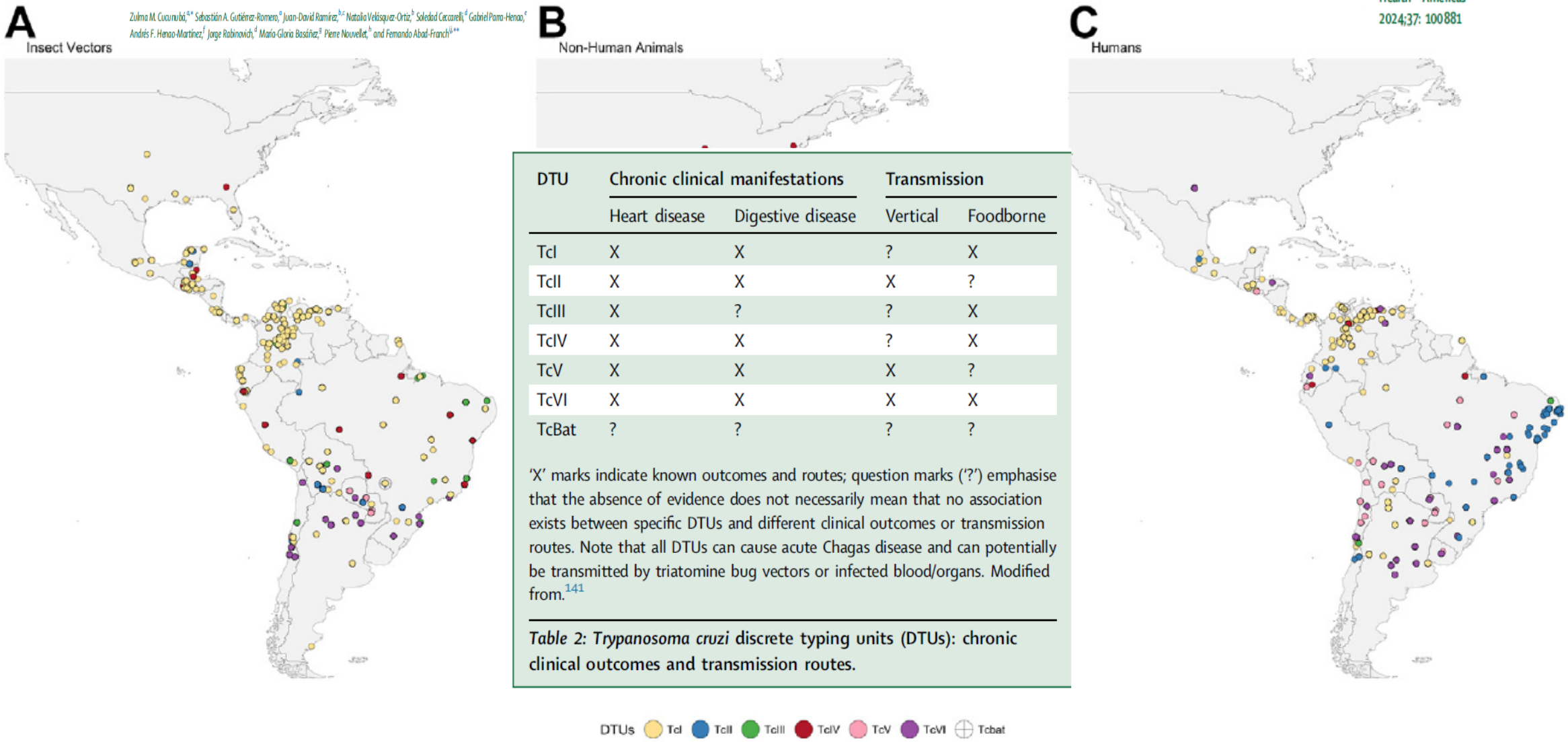
Route	Details and likelihood of infection
Vector-borne	In Chagas disease-endemic areas from the southern USA to northern Argentina and Chile, *Trypanosoma cruzi* transmission is primarily mediated by vectors.[6,25] Large-scale insecticide-spraying campaigns have drastically reduced transmission by non-native populations of *Triatoma infestans*, *T. dimidiata*, and *Rhodnius prolixus*.[25] However, house-invading and house-infesting native populations of these three 'primary' and dozens of other 'secondary' vector species maintain transmission in rural and peri-urban communities throughout the Americas.[25] Even though the underlying mechanism is rather inefficient,[26] this persistent, geographically-widespread transmission mediated by native vectors still causes thousands of new infections per year and remains the primary driver of incidence.[25] Most new vector-borne infections (up to ~95%) are asymptomatic/oligosymptomatic and remain undiagnosed and unreported.[13]
Vertical	Vertical transmission is the main source of new infections in non-endemic countries/territories and in urban settings where vectors are rare or absent.[14,25] Frequency estimates, however, are sparse and heterogeneous. The probability of transmission from infected mother to child usually ranges between ~1-2 and ~5–6%, and may be higher in endemic than in non-endemic countries.[15,16] High parasite loads likely increase, and anti-*T. cruzi* treatment of infected childbearing-aged women likely reduces, the odds of vertical transmission; the roles of maternal immune status, twin pregnancy, or parasite strains/genotypes should be better elucidated.[14,25] Not all endemic countries consistently implement screening programs.[17,25]
Oral	Oral transmission probably helps maintain enzootic infection among non-human mammals.[18,19] It may also be a relevant source of human infections, with localised outbreaks and isolated cases reported with increasing frequency from several countries.[18,20,25] Contamination of food or beverages by infected vectors (or, more rarely, opossums) is likely the main underlying mechanism, but consumption of infected mammals might also play a role.[20] High infectious loads often result in a more severe clinical picture, including more severe acute myocarditis, than what is usually seen in classical vector-borne transmission.[21] This conspicuous clinical picture, together with active contact-tracing during outbreaks, likely increases the fraction of incident cases that are diagnosed and reported.[25]
Transfusion	Transfusion-associated *T. cruzi* transmission was once a major issue, but nearly-universal donor screening in blood banks across all endemic countries has effectively brought it under control.[22,25] The risk of infection after transfusion of one unit of blood from an infected donor has been estimated at ~10–20% in endemic countries; recent evidence from non-endemic settings suggests that risk may be ~6–26% for platelets, but just ~0–4% for packed red blood cells, plasma, and cryoprecipitates.[23]
Organ transplantation	The risk of transmission associated with transplantation of an organ from an infected donor has been reported to vary between ~13 and ~75% in various cohorts and seems to be organ-specific, with transmission apparently less likely in kidney and liver recipients than in heart recipients.[24]

***Table 1: Trypanosoma cruzi* transmission routes and probability of infection.**

The Lancet Regional Health - Americas 2024;37: 100881

The epidemiology of Chagas disease in the Americas

Zulma M. Cucunubá,[a,*] Sebastián A. Gutiérrez-Romero,[a] Juan-David Ramírez,[b,c] Natalia Velásquez-Ortiz,[b] Soledad Ceccarelli,[d] Gabriel Parra-Henao,[e] Andrés F. Henao-Martínez,[f] Jorge Rabinovich,[d] María-Gloria Basáñez,[g] Pierre Nouvellet,[h] and Fernando Abad-Franch[ii,**]



DTU	Chronic clinical manifestations		Transmission	
	Heart disease	Digestive disease	Vertical	Foodborne
TcI	X	X	?	X
TcII	X	X	X	?
TcIII	X	?	?	X
TcIV	X	X	?	X
TcV	X	X	X	?
TcVI	X	X	X	X
TcBat	?	?	?	?

'X' marks indicate known outcomes and routes; question marks ('?') emphasise that the absence of evidence does not necessarily mean that no association exists between specific DTUs and different clinical outcomes or transmission routes. Note that all DTUs can cause acute Chagas disease and can potentially be transmitted by triatomine bug vectors or infected blood/organs. Modified from.[141]

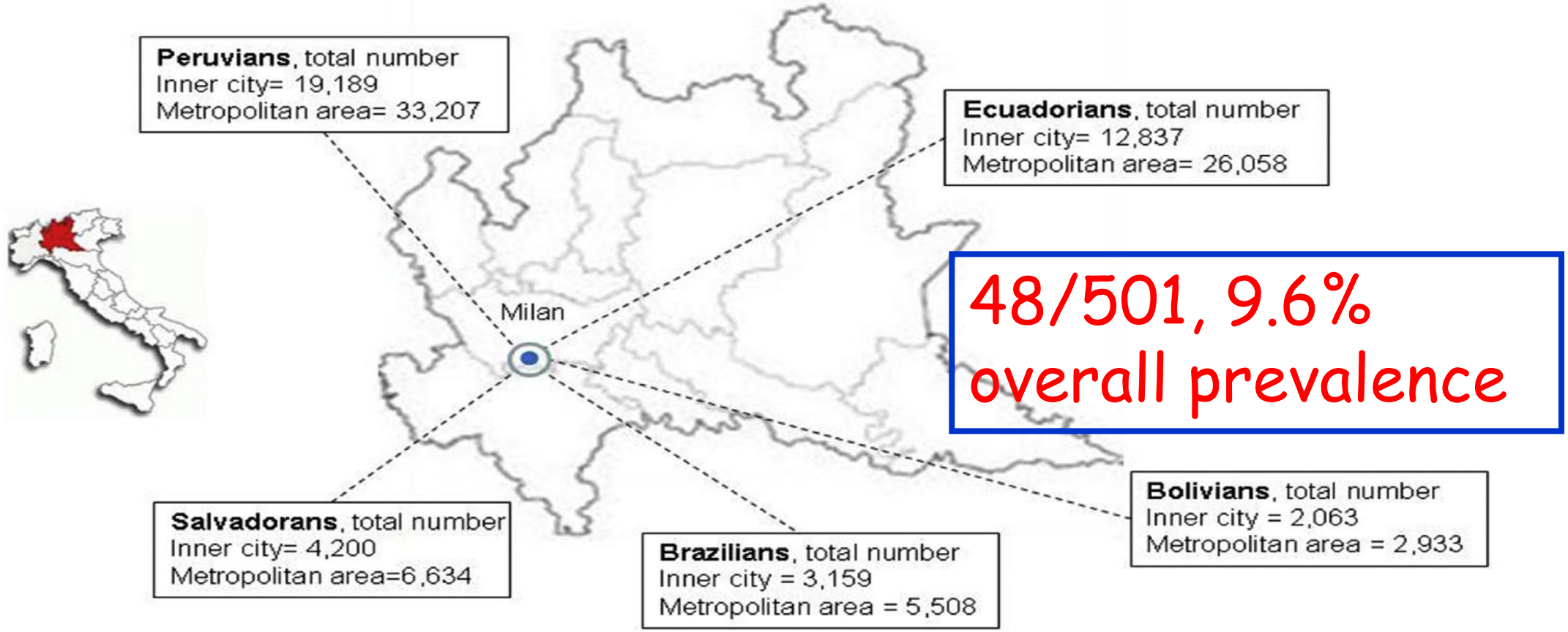
Table 2: Trypanosoma cruzi discrete typing units (DTUs): chronic clinical outcomes and transmission routes.

***Fig. 3:* Distribution of DTUs in the Americas in vectors, non-human animals, and humans.** Distribution of DTUs identified in vectors (Panel A), non-human animals (Panel B), and humans (Panel C). The size or shape of the symbols does not indicate the exact geographic location or frequency as some points may be overlapped. Map created with R Software. Data source.[137]

Original article

Chagas disease knocks on our door: a cross-sectional study among Latin American immigrants in Milan, Italy

S. Antinori [1, 2, *], L. Galimberti [2], R. Grande [3], R. Bianco [4], L. Oreni [2], L. Traversi [2], D. Ricaboni [2], G. Bestetti [2], A. Lai [1], D. Mileto [3], M.R. Gismondo [3], M. Petullà [4], S. Garelli [6], G. De Maio [6], C. Cogliati [5], D. Torzillo [5], A.M. Villa [7], A.M. Egidi [6], E.C. Repetto [6], A.L. Ridolfo [2], M. Corbellino [2], M. Galli [1, 2]

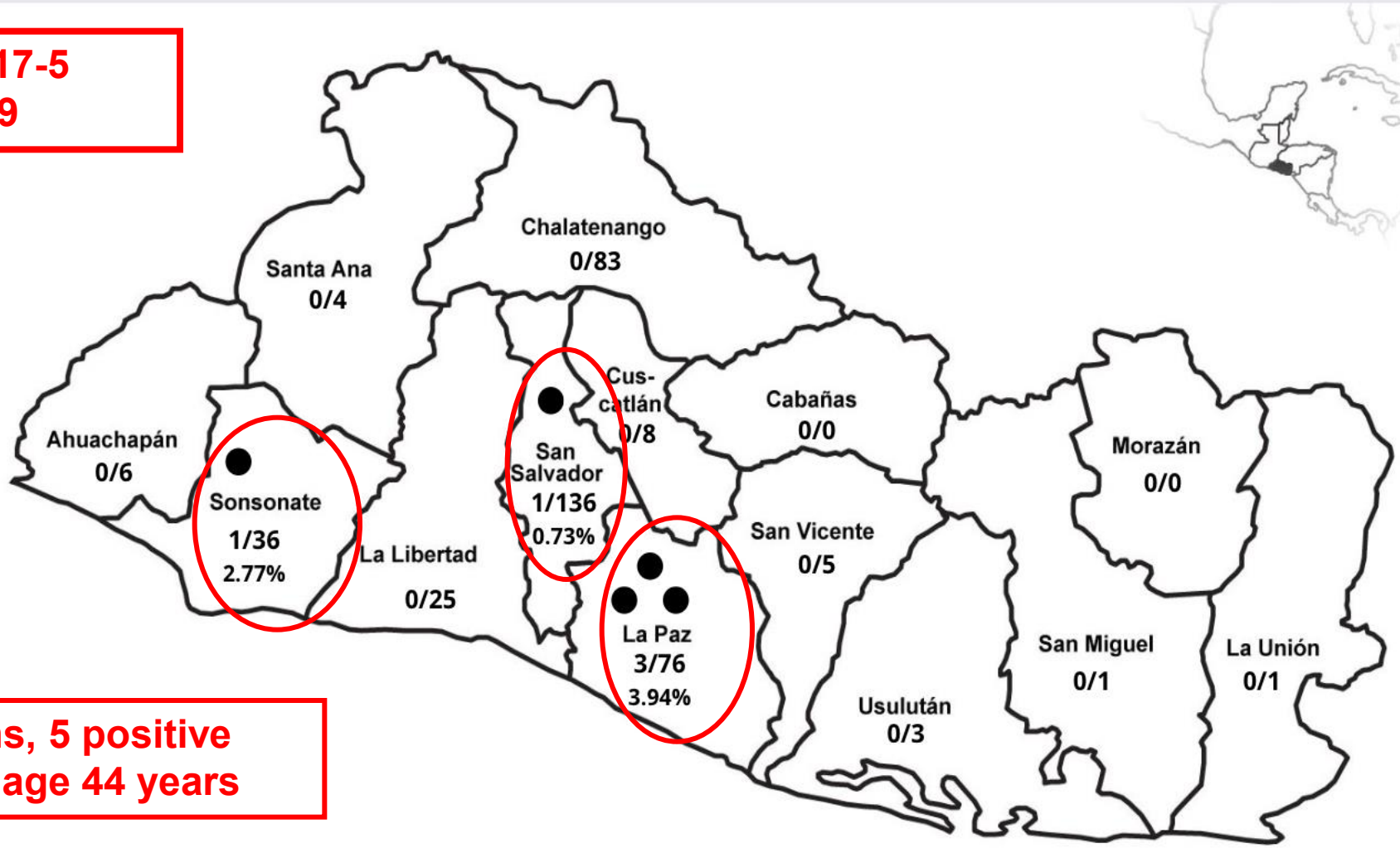


48/501, 9.6%
overall prevalence

Clin Microbiol Infect 2018;24:1340.e1-1340.e6

Chagas disease seroprevalence in immigrants from El Salvador in Milan, Italy: a cross-sectional study

13 October 2017-5 December 2019



384 Salvadorans, 5 positive (1.3%), median age 44 years

Beltrami M et al. Infect Dis 2023;55:599-66

Article

Chagas Disease and Transfusion Risk in Italy: The Results of a National Survey

Ilaria Pati *, Mario Cruciani, Francesca Masiello, Francesco Barone, Giacomo Silvioli, Massimo La Raja, Simonetta Pupella and Vincenzo De Angelis

Table 1. Percentage of participant Blood Establishments for each Italian Region/Autonomous Province.

Region/A.P.	Participating BEs (%)
Abruzzo	100%
Aosta Valley	100%
Apulia	100%
Basilicata	100%
Calabria	100%
Campania	47%
Emilia Romagna	100%
Friuli Venezia Giulia	100%
Latium	100%
Liguria	100%
Lombardy	54%
Marche	58%
Molise	100%
A.P. of Bolzano	100%
A.P. of Trento	100%
Piedmont	100%
Sardinia	60%
Sicily	55%
Tuscany	93%
Umbria	100%
Veneto	100%
Mean (SD)	88.9% (±19.2%)

A.P.: Autonomous Province; BEs: Blood Establishments.

Table 2. Description of main survey results, years 2020–2021.

	2020	2021
Total donors (N.)	1,845,142	1,863,050
Tested donors for Chagas disease (N.)	15,261	9008
Tested/total donors (%)	0.8%	0.5%
Positive-inconclusive donor test (N.)	19	11
Positive-inconclusive/tested donors (%)	0.12%	0.12%
Positive donors confirmed (N.)	10	5
Positive confirmed/positive-inconclusive donor test (%)	53%	45%
Donors excluded without testing (N.)	6	14

N · number

Table 3. Risk factors for Chagas disease detected in positive blood donors confirmed.

	Birth in Endemic Areas (N.)	Travel History in Endemic Areas (N.)
2020	5	5
2021	4	1
Total	9	6

Article

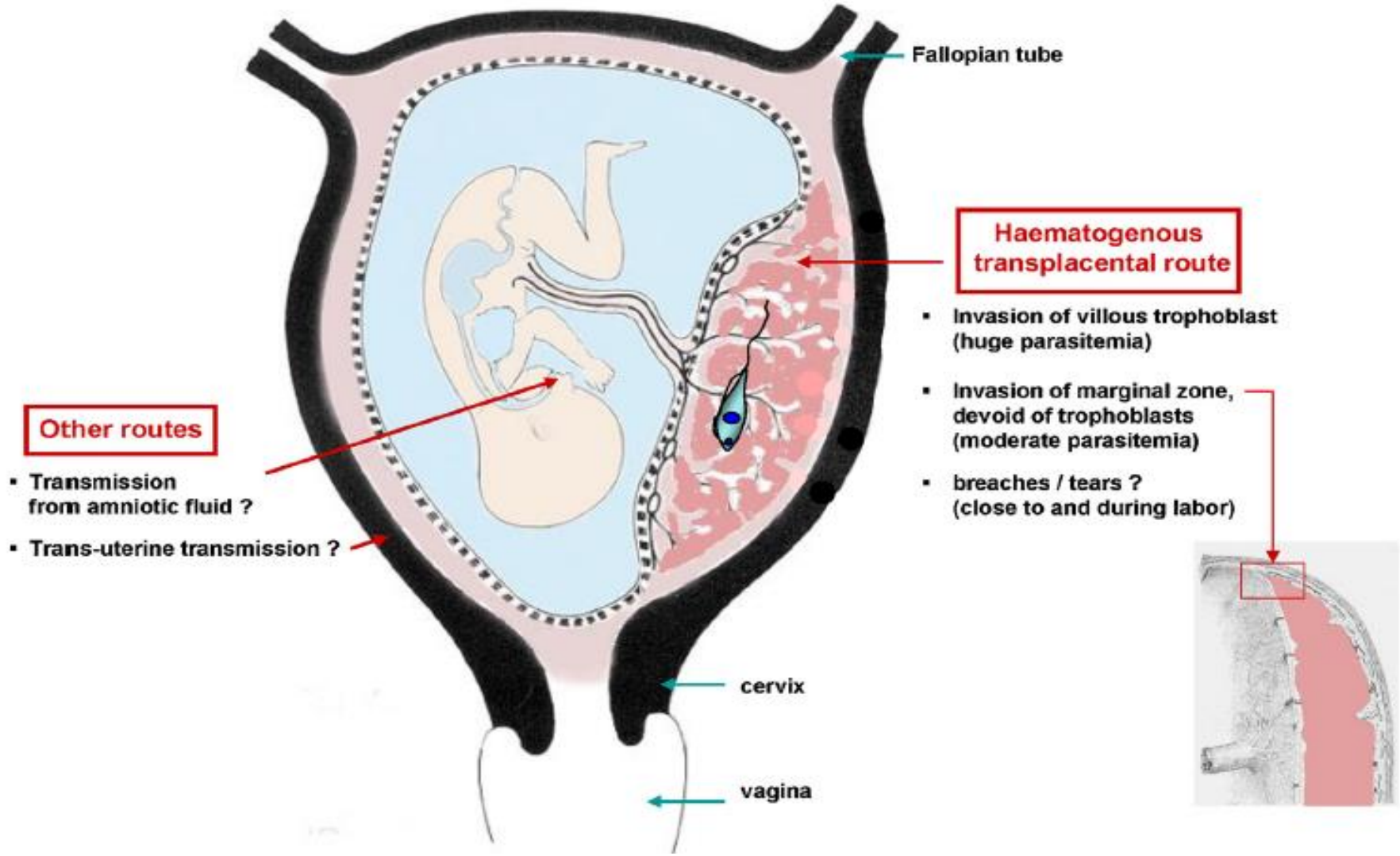
Chagas Disease and Transfusion Risk in Italy: The Results of a National Survey

Ilaria Pati *, Mario Cruciani, Francesca Masiello, Francesco Barone, Giacomo Silvioli, Massimo La Raja, Simonetta Pupella and Vincenzo De Angelis

In 2020, the regions with the highest number of positivity were Lazio, Lombardy, and Tuscany (1.4/100,000 blood donors). The Lazio Region had the highest number of positivity in 2021 (2.8/100,000 blood donors) (Figure 2).

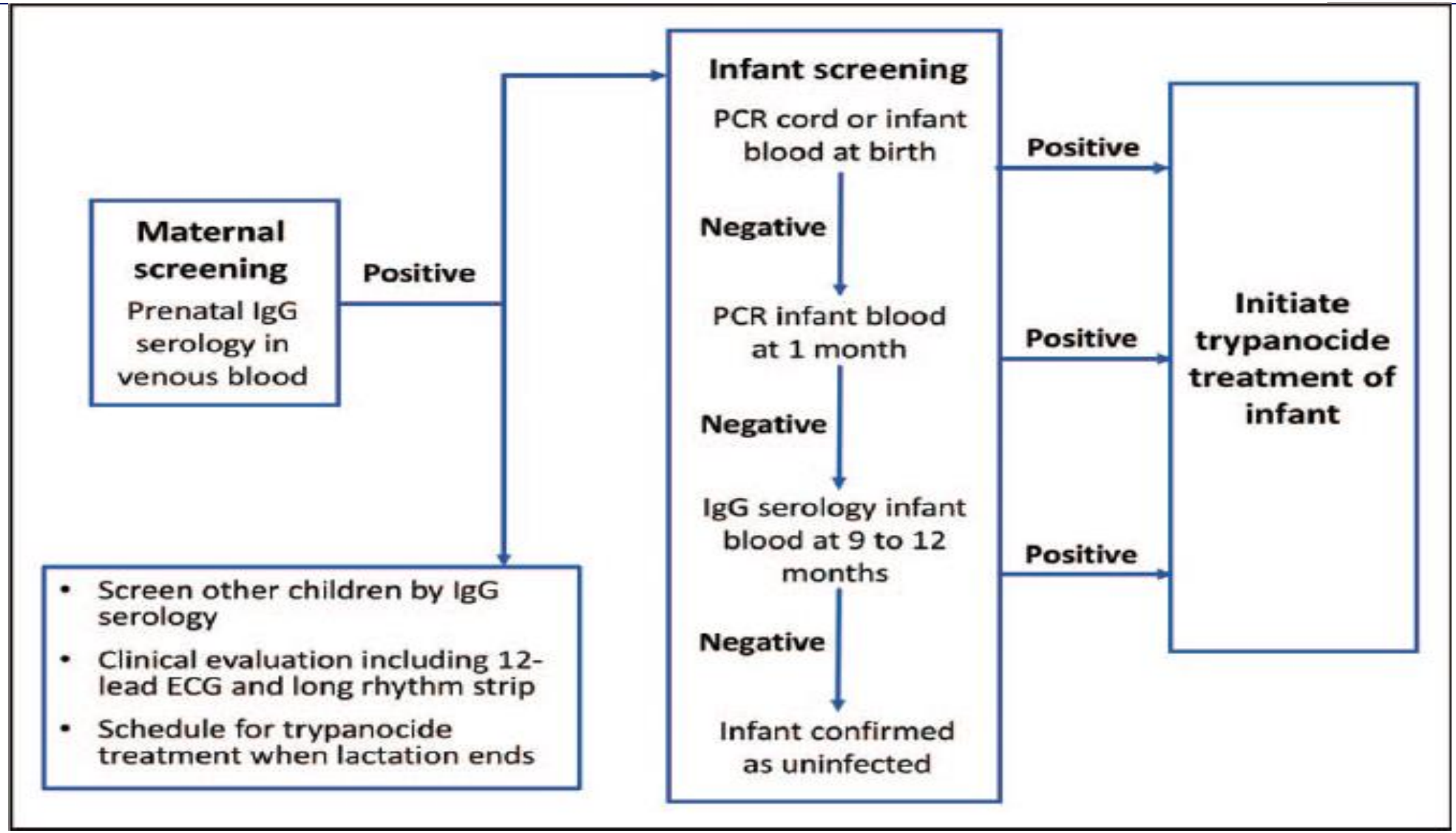
Figure 2. Distribution (on 100,000 donors) of confirmed anti-*T. cruzi* antibody positive blood donors, years 2020–2021.

Possible routes of maternal-fetal transmission of *Trypanosoma cruzi*



Carlier Y & Truyens C. Acta Tropica 2015

Congenital Chagas disease: current diagnostics, limitations and future perspectives



Messenger LA, Bern C. Curr Opin Infect Dis 2018;31:415-21

Ongoing mother-to-child transmission of Chagas disease in Italy: 2014–18 estimates

Table 1. The number of live births from women citizens continental Latin American c
the estimated number of live births from women with CD considering the prevalence

Citizenship of women from endemic countries delivering live neonates[a]	Number of live births according to mother's citizenship	Estimated numbe women with CD
Argentina	615	14 (5-19)
Belize	4	NA
Bolivia	1305	235 (181-296)
Brazil	5383	32 (9-60)
Chile	225	2 (0-5)
Colombia	1325	7 (2-12)
Costa Rica	45	0
Ecuador	6178	25 (11-44)
El Salvador	1471	54 (24-172)
Guatemala	77	1
Guyana	3	NA
Honduras	288	12 (4-21)
Mexico	472	7 (1-18)
Nicaragua	65	3 (0-7)
Panama	46	NA
Paraguay	271	15 (9-21)
Peru	8008	48 (18-94)
Suriname	3	NA
Uruguay	102	1 (0-2)
Venezuela	824	7 (1-18)
All citizenship	26 710	463 (267-792)

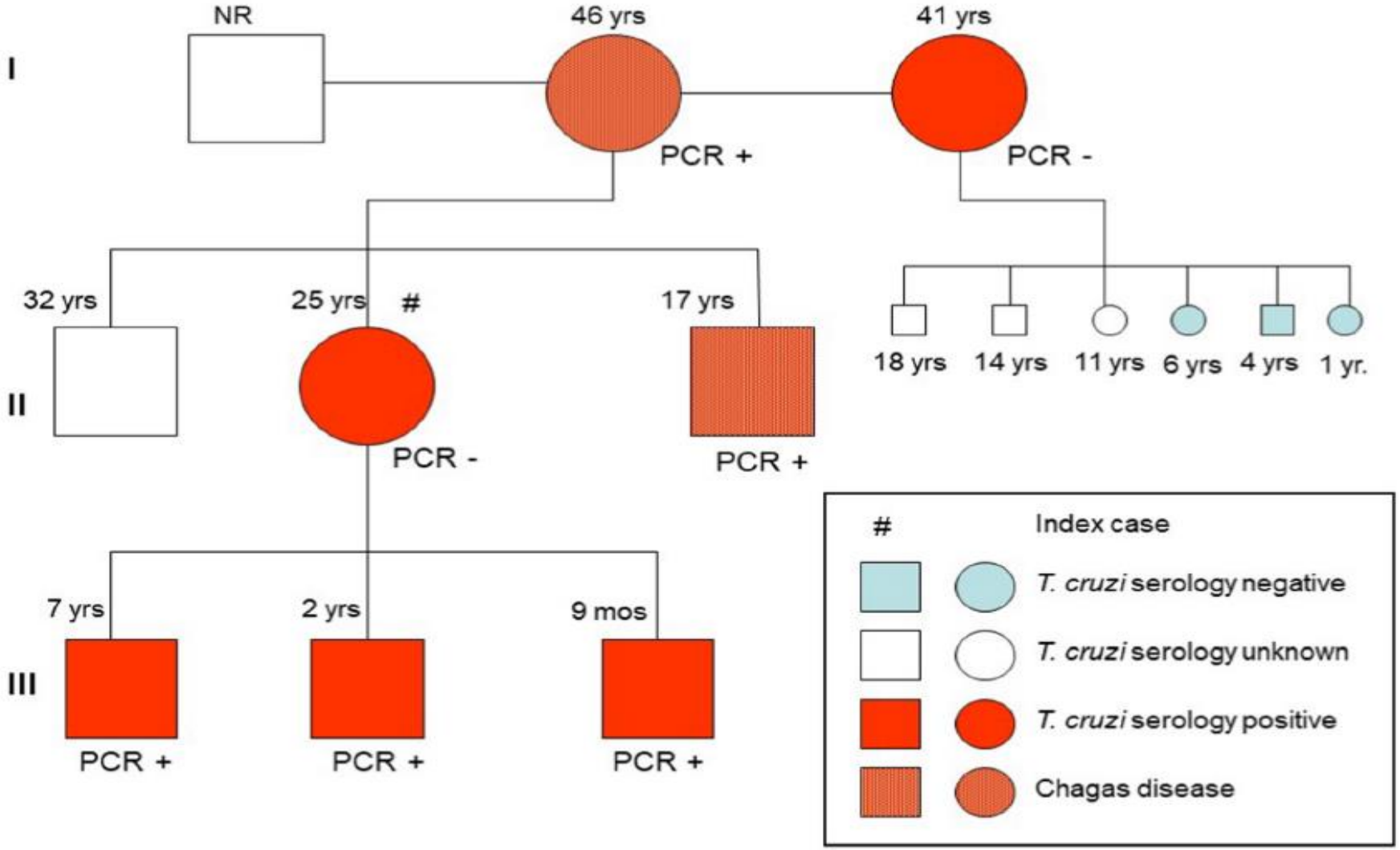
(LAn) women in Italy in the period 2014–18 provided by the National Institute of Statistics of Italy (protocol 00726/2020), the prevalence of CD in LAn migrants living in Europe[5] and the rate of congenital CD transmission provided by Colombo V {3.5% [95% confidence interval (CI):2.5-4.5]}[1], we estimated that 463 live births (95% CI 267-792) have born from women with CD (Table 1), and 16 (95% CI 12-21) congenital infections could have occurred. The prevalence of congenital CD at birth in children born from a LAn mother in Italy can be estimated to be 1:1670.

Zammarchi L et al. J Travel Med 2021; 28:taaa201

Family cluster of Chagas disease among Bolivian immigrants in Italy: High rate of maternal-fetal transmission

Travel Med Infect Dis 2022;49:102370

Spinello Antinori [a,b,*], Laura Galimberti [b], Romualdo Grande [c], Davide Ricaboni [a,b], Stefania Sala [d], Vania Giacomet [e], Valeria Colombo [a,b], Mario Corbellino [b], Andrea Angheben [f],



Prevention of congenital chagas disease by trypanocide treatment in women of reproductive age: A meta-analysis of observational studies

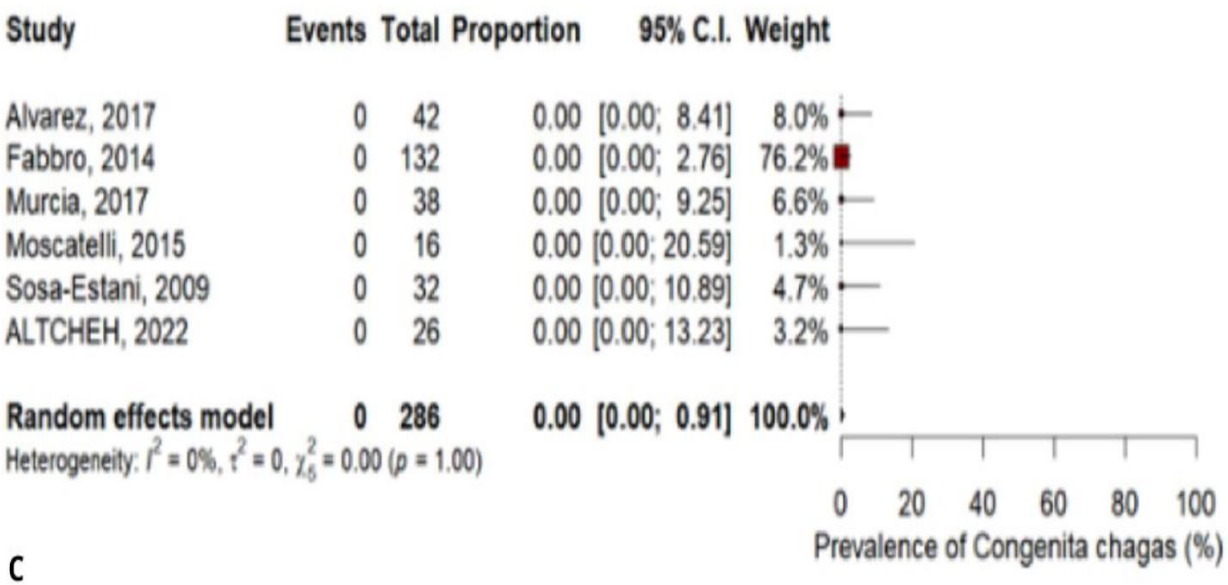
PLOS NEGLECTED TROPICAL DISEASES

Francisco Cezar Aquino de Moraes[1]*, Maria Eduarda Cavalcanti Souza[2], Lucca Dal Moro[1], Isabelle Batista Donadon[3], Emanuele Rocha da Silva[1], Dilma do Socorro Moraes de Souza[1,4], Rommel Mario Rodríguez Burbano[1,5]

Table 1. Design and Characteristics of Studies Included in the Meta-analysis.

Author	Mother Age†	Follow-up†	Confirmatory examination of Mother /child	Treatment§	Treatment duration§	N of children	Mother-child pair	Maternal geographical origin
Álvarez [21]	15–45	2–5	Serology	Bzn (5 mg/kg)	30	156	156	NA
Fabbro [22]	15–45	16,3–18,6	Serology (IHA, ELISA)	Bzn (5,16 mg/kg) and Nfx (10 mg/kg)	15–66 (Bzn) and 14–90 (Nfx)	354	354	Argentina; Bolivia; Paraguay; Uruguay
Murcia [23]	15–45	mother (1–9); children (0,6–12 months)	Serology (ELISA, IHA) and PCR	Bzn (5–7 mg/kg) and Nfx (10 mg/kg)	60 (Bzn; Nfx)	160	159	Bolivia; Paraguai; Ecuador; Argentina
Moscatelli [24]	9–34	3	Serology, PCR and ELISA	Bzn (5–7,6 mg/kg) and Nfx (9,4 mg/kg)	19–60 (Bzn; Nfx)	16	15	Argentina
Sosa-Estani [25]	21–29	14	Serology (AIE, IHA, IFI) and PCR	Bzn (6 mg/kg)	60	32	32	Argentina
ALTCHEH [26]	≤18	3	Serology (ELISA, IHA)	Nfx (NA)	30–60	26	26	NA

B



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PLoS Negl Trop Dis 18(9): e0012407. https://doi.org/10.1371/journal.pntd.0012407

Country	*Prenatal screening policy (related policies), policy implementation status* Select publicly available mother-to-child transmission related data	Refs
Argentina	*National universal screening (all previous children if (+) detected), routine* 2952 s (+) of >200,000 pregnant women screened nationally in 2021, and 136 confirmed congenital cases of 1906 suspected nationally in 2022	21–24
Bolivia	*Risk-based, high-risk departments* 13,144 s (+) of 109,238 pregnant women screened, 603 neonates born to s (+) women screened, and 47 treated nationally in 2020	17,21,25
Brazil	*Risk-based, high-risk departments* 331 confirmed cases among women of childbearing age, 23 confirmed cases among children <1 year, and 5 confirmed cases of congenital transmission nationally in 2018–2022[a]	17,21,26,27
Chile	*National universal screening, routine* 253 s (+) of 76,298 pregnant women screened, 313 neonates born to s (+) women screened, and 17 treated nationally in 2020	21,28
Colombia	*Risk-based (family follow-up if (+) detected)* 1 s (+) of 45 pregnant women among 39 s (+) of 230 total women screened in Pore, Casanare, 2015	21,29,30
Costa Rica	*Risk-based, individual risk, unknown status* 16 (+) cases among women/girls nationally among 40 total confirmed in 2022	31,32
Ecuador	*Risk-based, high-risk departments or individual risk factors* 1 s (+) among 146 pregnant women screened in hospital, Orellana Province, June–August 2016	33–35
El Salvador	*No known policy, not routine* 79 s (+) of 18,000 screened nationally in 2018	9,12,36
Guatemala	*Risk-based, endemic areas, unknown status* 37 s (+) of 134 women of childbearing age screened in Las Palmas, Chiquimula, 2017	37,38
Honduras	*Risk-based, unknown status* 1% s (+) among women of childbearing age nationally in 2015–2017	9,21,39
Mexico	*Risk-based, individual risk, unknown status* 15 s (+) postpartum women screened and 5 PCR (+) neonates of 260 mother–child pairs screened across 4 hospitals, Oaxaca, 2019–2021	40,41
Nicaragua	*Risk-based, unknown status* –	9,42
Panama	*Risk-based, unknown status* 19 s (+) among women/girls among 70 s (+) reported nationally in 2018	43,44
Paraguay	*Risk-based, high-risk departments* 296 s (+) of 14,732 pregnant women screened, 87 neonates born to s (+) women screened, 3 treated nationally in 2020	21
Peru	*No known policy, not routine* 1 s (+) of 300 pregnant women screened in Iquitos, May–June 2019	45,46
Uruguay	*National universal screening, unknown status* –	21,47
Venezuela	*Risk-based, unknown status* 78 s (+) among 1200 post-partum women screened, 6/66 PCR (+) neonates[b], 0/11 infants s (+) when screened at 9 months in Anzoátegui, 2015–2016	48,49

Note: Many countries included in this list have guidelines for screening neonates and infants born to known seropositive mothers which were not included in this table. This table is not intended to be comprehensive, and articles were selected to further contextualize national policies where possible. Countries for which no policy, guidance, or recent data could be found were also not included in this table (ie: Belize, French Guiana, Guyana, and Suriname). s (+): seropositive, –: no recent data or estimates available. [a]These data represent acute confirmed cases only, as chronic cases are not reportable to the healthcare system in Brazil. [b]3 of these six were followed at 9 months and were seronegative.

Prenatal Chagas disease screening in Latin America: the current policy landscape and potential utility of an expanded maternal-familial *Trypanosoma cruzi* testing framework

Mary K. Lynn,[a,b] Marvin Stanley Rodríguez Aquino,[b,c] Carlos Alberto Buendía Rivas,[c] Amaury Morales Landrove,[d] Alexandra Manoella Portillo de Juarez,[d] Roberto Aguila Cerón,[e] Diana García López,[e] and Melissa S. Nolan,[a,b,*] the El Salvador Congenital Chagas team[f]

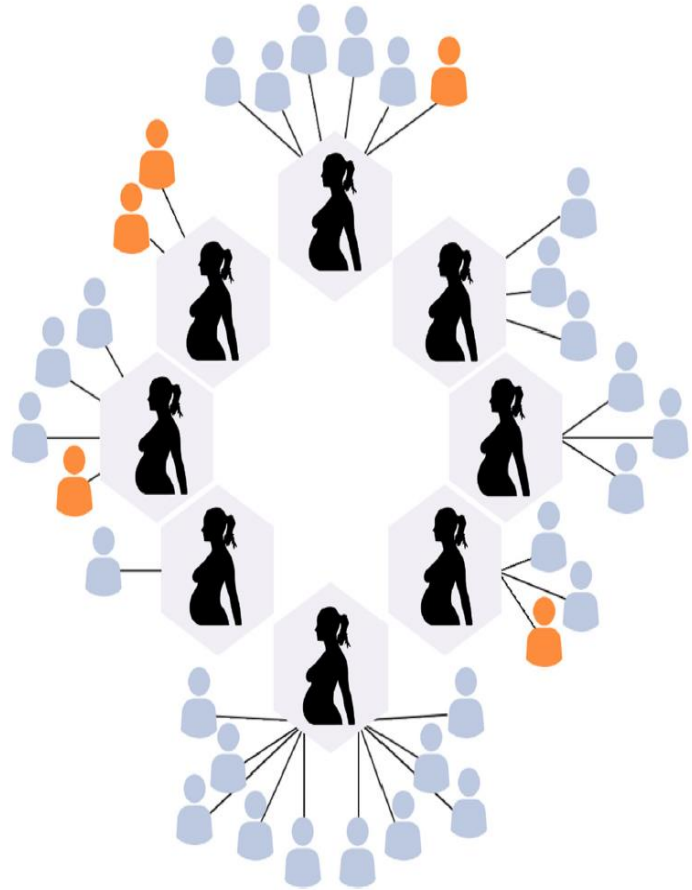

Fig. 1: Familial follow-up screening for relatives of positive and indeterminate mothers identified 16% *T. cruzi* seropositivity among familial contacts. Familial contacts screening *T. cruzi* negative are shown in blue-gray, and those screening positive are shown in orange.

The Lancet Regional Health - Americas 2025;47: 101139

Table 1. Summary of Chagas disease manifestation differences following vector-borne or foodborne transmission (references and greater detail included in the text below).

Disease phase	Vector-borne transmission	Foodborne transmission
Acute	Largely asymptomatic; 3% to 60% cases mild symptoms such as fever	Close to 100% experience fever—other common symptoms include myalgia, headache, and oedema
Acute	Romaña's sign or chagoma often seen	Facial oedema in around 90% of cases
Acute	Cardiac manifestation in up to 10%, particularly in children	Early myocardial involvement occurs frequently (up to 100%)—often severe; cardiac tamponade associated with mortality
Chronic	Symptomatic phase (years or decades after infection) • For 60% to 70%: asymptomatic or indeterminate • For: 20% to 30% cardiac or digestive form (megaoesophagus/megacolon) • Both forms in 5% to 15%	Undefined—but rapid progression to long-term cardiac or gastrointestinal dysfunction indicated
Mortality	Estimated 5% to 10%	Estimated 8% to 40%

Chagas disease

Andréa Silvestre de Sousa, Debbie Vermeij, Alberto Novaes Ramos Jr, Alejandro O Luquetti

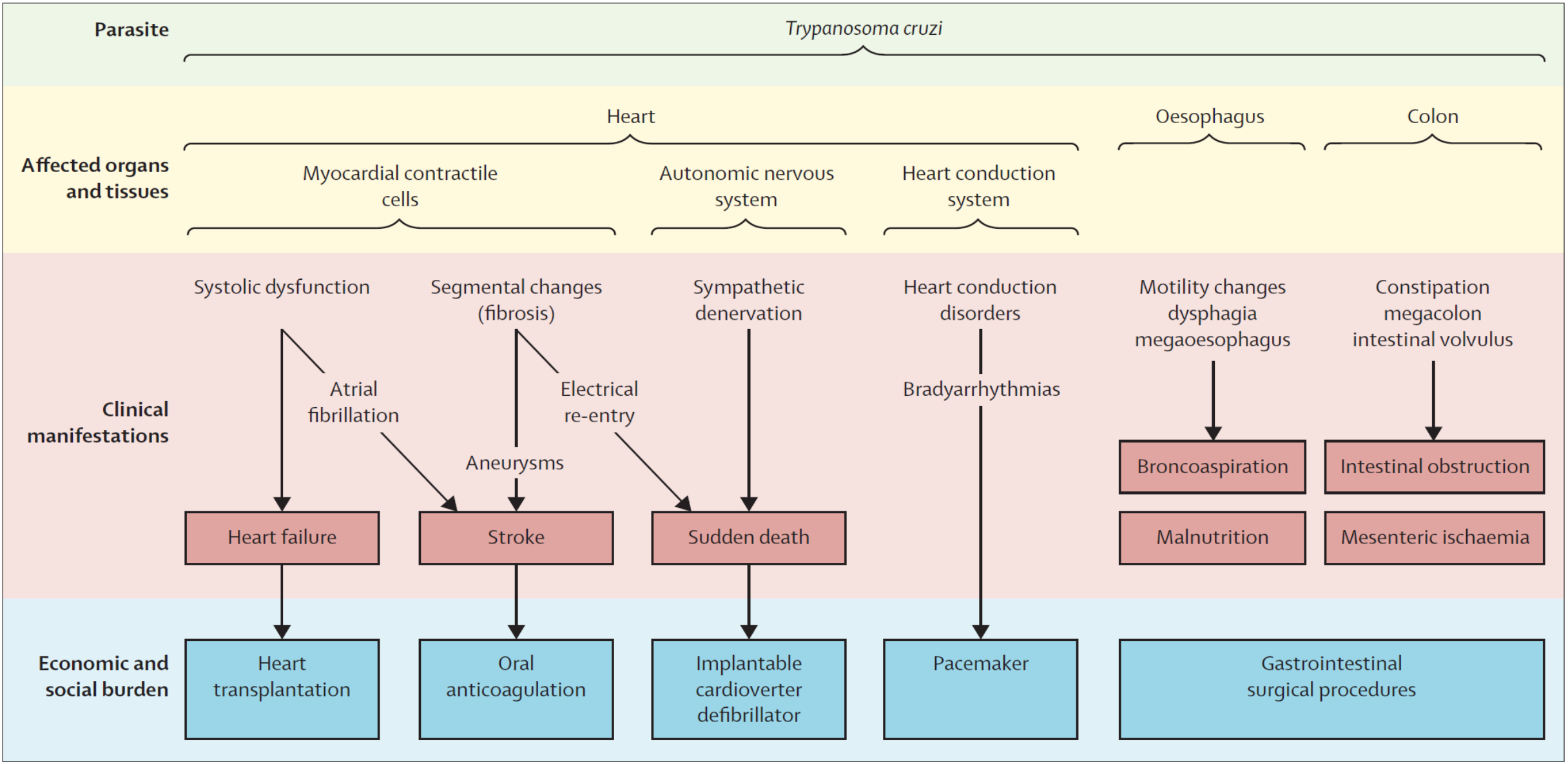

Figure 1: Clinical manifestations, and economic and social burden of chronic Chagas disease

Lancet 2024; 403: 203-18

Original article

Chagas disease knocks on our door: a cross-sectional study among Latin American immigrants in Milan, Italy

S. Antinori [1, 2, *], L. Galimberti [2], R. Grande [3], R. Bianco [4], L. Oreni [2], L. Traversi [2], D. Ricaboni [2], G. Bestetti [2], A. Lai [1], D. Mileto [3], M.R. Gismondo [3], M. Petullà [4], S. Garelli [6], C. De Maio [6], C. Cogliati [5], D. Torzillo [5], A.M. Villa [7], A.M. Egidi [6], F.C. Repetto [6]

Table 4

Clinical characteristics of 29 subjects with Chagas disease who underwent clinical staging

Characteristic	*n* (%)
Country of origin	
Bolivia	26 (89.7)
El Salvador	2 (6.9)
Argentina	1 (3.4)
Median age (IQR)	37.5 (17–67)
Gender	
Male	7 (24.1)
Female	22 (75.9)
Clinical stage	
Indeterminate	18 (62.1)
Chagas cardiomyopathy	4 (14.3)
Digestive Chagas	5 (17.8)
Chagas cardiomyopathy + digestive disease	1 (3.6)

Trypanosoma cruzi infection in a non-endemic country: epidemiological and clinical profile

F. Salvador[1], B. Treviño[2], E. Sulleiro[3], D. Pou[2], A. Sánchez-Montalvá[1], J. Cabezos[2], A. Soriano[2], N. Serre[2], J. Gómez i Prat[2], A. Pahissa[1] and I. Molina[1]

TABLE 2. Main clinical series of chronic Chagas disease patients in non-endemic areas

Reference of publication	Muñoz [18]	Lescure [19]	Pérez-Ayala [20]	Valerio [21]	Jackson [22]	Ramos [23]
Country	Spain	France	Spain	Spain	Switzerland	Spain
Country of origin of patients	Bolivia 86.6%	Bolivia 87.4%	Bolivia 97%	Bolivia 95%	Bolivia 93.4%	Bolivia 78.9%
Study period	2004–2007	2008–2009	2003–2009	2005–2009	1979–2011	2002–2011
Number of patients	202	60	357	100	258	128
Mean age (years)	36	33	36	38.2	41	35
Provenance of patients	TMU	TMU	TMU, PCC, blood bank	TMU, PCC	PCC, blood bank	Hospital with no TMU
Immunosuppressed patients	3 HIV, 3 oncological patients	No data	4 HIV	No data	1 heart transplantation	1 HIV
Cardiac assessment	ECG, chest X-ray	Clinical symptoms	ECG, echocardiogram	ECG, echocardiogram	No data	ECG, chest X-ray, echocardiogram
Cardiac form prevalence	19%	23.6%	18.6%	49%	20.1%	24.1%
Gastrointestinal assessment	Barium enema and oesophagogram, only in symptomatic patients	Clinical symptoms	Barium enema, oesophagogram and oesophageal manometry, only in symptomatic patients	No data	No data	Barium enema and oesophagogram, only in symptomatic patients
Gastrointestinal form prevalence	9%	22%	5.1%	No data	0.7%	0.9%
Number of treated patients	No data	No data	195 (54.6%)	No data	129 (50%)	76 (59.3%)

TMU, Tropical Medicine Units; PCC, Primary Care Centres; MTCTPP, mother to child transmission prevention programme; HIV, human immunodeficiency virus; ECG, electrocardiogram.

Clin Microbiol Infect 2014;20:706-12

Mechanisms behind the high mortality rate in chronic Chagas cardiomyopathy: Unmasking a three-headed monster

Luis E. Echeverría[1]*, Angie Yarlady Serrano-García[1], Lyda Z. Rojas[2], Enrique A. Berrios-Bárcenas[3], Juan Esteban Gómez-Mesa[4], and Sergio A. Gómez-Ochoa[1,5]*

ESC European Society of Cardiology

European Journal of Heart Failure (2024)
doi:10.1002/ejhf.3460

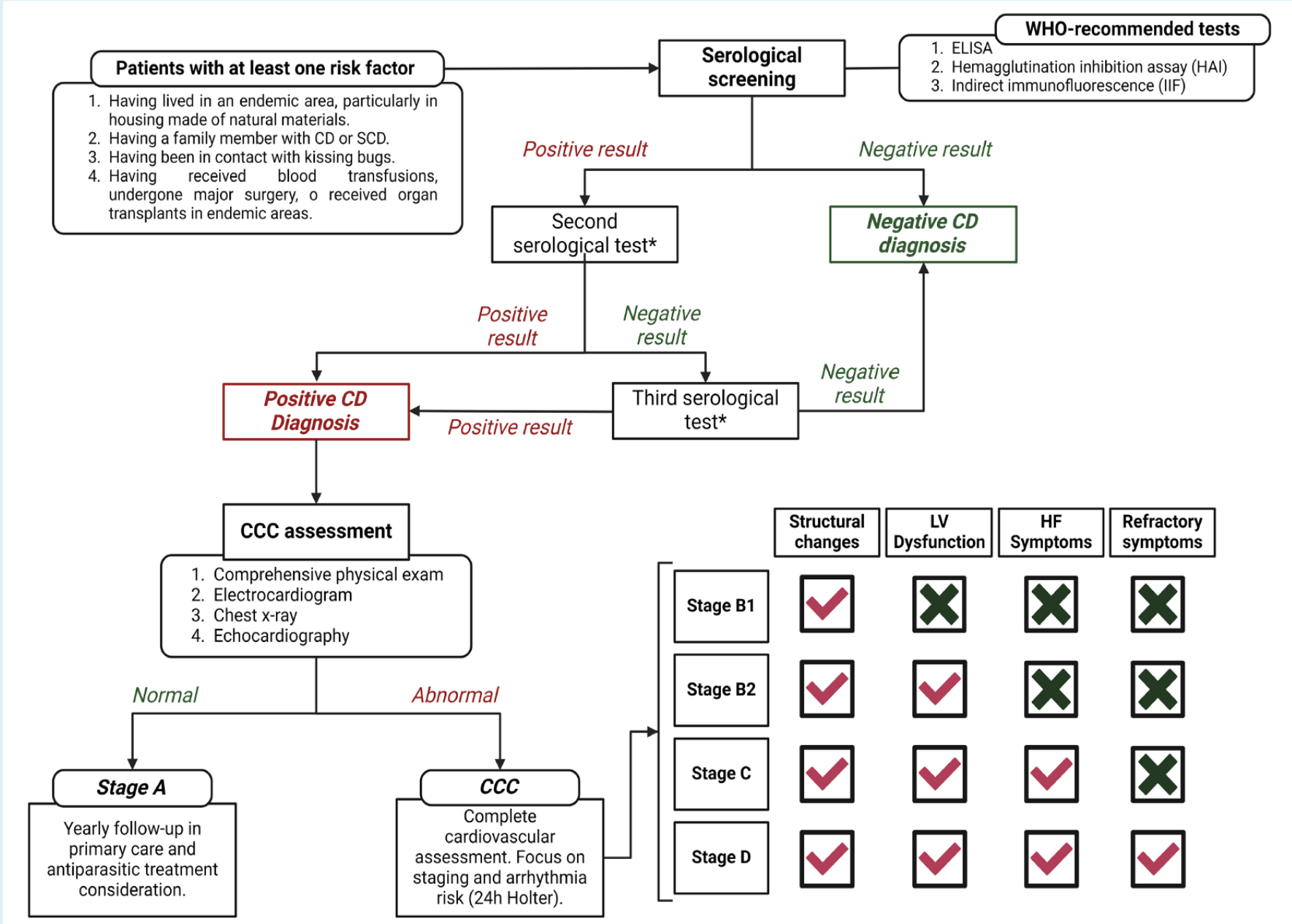

Figure 2 Algorithm for the serological diagnosis and clinical staging of patients at risk of Chagas disease (CD) in non-endemic countries. CCC, chronic Chagas cardiomyopathy; HF, heart failure; LV, left ventricular; SCD, sudden cardiac death; WHO, World Health Organization.

Mechanisms behind the high mortality rate in chronic Chagas cardiomyopathy: Unmasking a three-headed monster

Luis E. Echeverría[1]*, Angie Yarlady Serrano-García[1], Lyda Z. Rojas[2], Enrique A. Berrios-Bárcenas[3], Juan Esteban Gómez-Mesa[4], and Sergio A. Gómez-Ochoa[1,5]*

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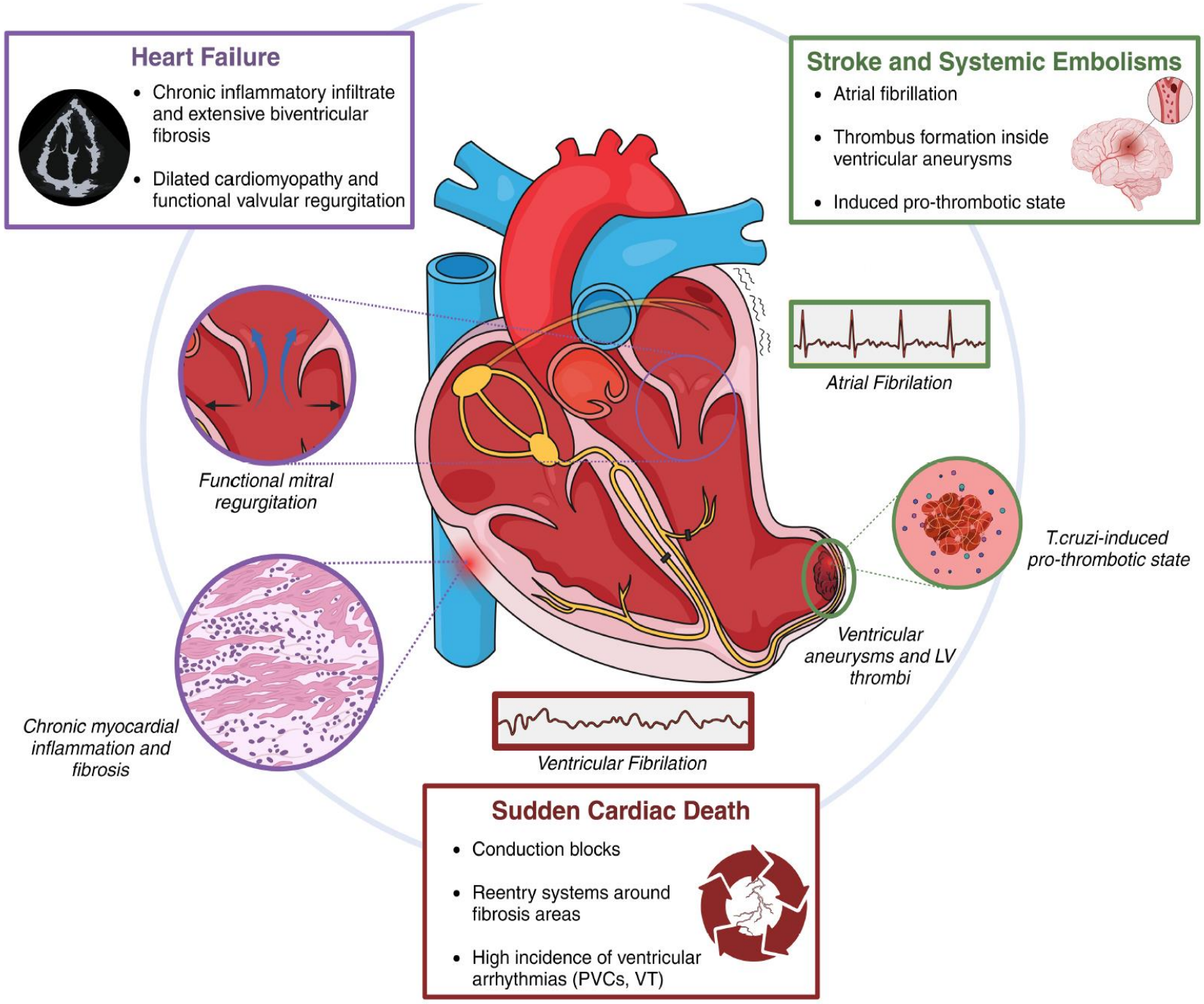


Acute Heart Failure in Patients with Chagas Cardiomyopathy: Results of the I Brazilian Heart Failure Registry (BREATHE)

Pedro Gabriel Melo de Barros e Silva,[1,2,3] Denilson Campos Albuquerque,[4,5] Renato Delascio Lopes,[2,6,7] Paulo Roberto Nogueira,[8] Aguinaldo F. Freitas Jr,[9] Carlos Vieira Nascimento,[10] Charles Mady,[11] Elizabete Silva dos Santos,[12] Mauro Esteves Hernandes,[13] Maria Alayde Mendonça Rivera,[14] João David de Souza Neto,[15] Alvaro Rabelo,[16] Manoel Fernandes Canesin,[17] Helder Reis,[18] Anderson da Costa Armstrong,[19] Conrado Hoffmann,[20] Renato Hideo Nakagawa Santos,[1] Isabella de Andrade Jesuino,[1] Luis Eduardo Rohde,[21,22] Lidia Zytinsky Moura,[23] Fabiana Goulart Marcondes-Braga,[4,11] Evandro Tinoco Mesquita,[4,24] José Albuquerque de Figueiredo Neto,[25] Ricardo Mourilhe-Rocha,[26,27] Luís Beck-da-Silva,[21,22] Mucio Tavares Oliveira Junior,[4,11] Marcus Vinicius Simões,[28] on behalf of the BREATHE Investigators

Central Illustration: Acute Heart Failure in Patients with Chagas Cardiomyopathy: Results of the I Brazilian Heart Failure Registry (BREATHE)

BACKGROUND

- Chronic Chagas cardiomyophaty (CCC) is a common etiology of heart failure in Latin America with very specific clinical features
- The Brazilian Heart Failure Registry (BREATHE) enrolled a total of 3,013 patients hospitalized due to heart failure from February 2011 to july 2018 which were followed for one year

METHODS

Current analysis compared clinica, demographic information, and cardiac structure/function data on echocardiogram, and outcomes during hospital stay and after discharge in patients with CCC versus other etiologies

RESULTS

261 (8.7%) CCC
2,752 (91.3%) other etiologies

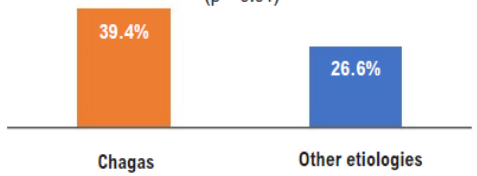
Baseline: Patients with CCC were five years younger and had less comorbidities

Hospital admission:
- More than 50% had signs of right-sided heart failures
- Almost 3 times more "cold and wet" profile[1]
- Nt-proBNP more than 2 times higher[1]
- Median left ventricle ejection fraction of 25%
- More than 25% had severe atrioventricular regurgitation

[1] Compared to other etiologies

Prognosis

Incidence of death in 12 months
(p = 0.01)



**CCC was indpendently associated with 2 times higher odds of mortality in 12 months*

CONCLUSIONS

Patients with CCC hospitalized due to acute heart failire, as compared with other etiologies, were younger and had less comorbidities. However, these patients had a higher risk profile at admission, with worse outcomes during one-year follow-up.

Arq Bras Cardiol. 2025; 122(5):e20240555

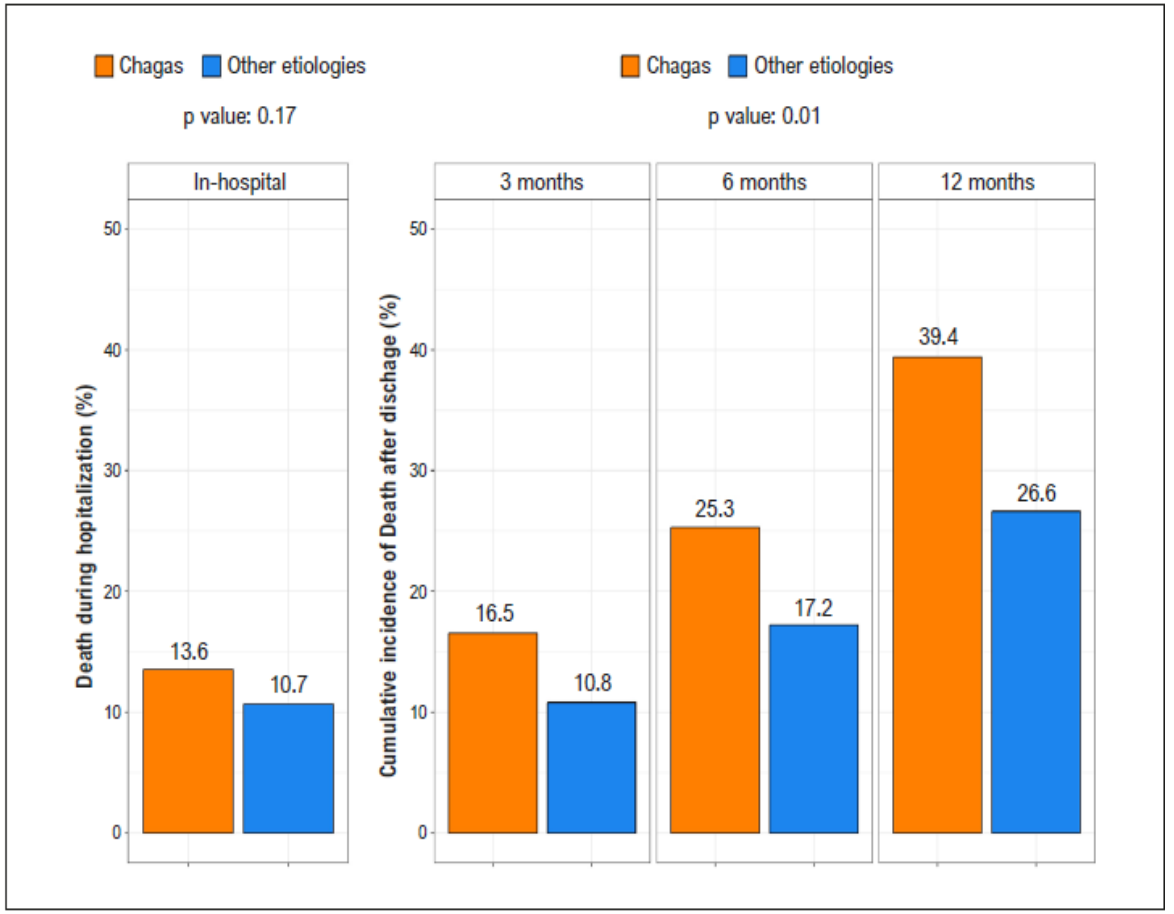


Figure 1 – *In-hospital mortality and cumulative incidence of mortality after discharge, in both groups.*

Prevalence of clinical forms of Chagas disease: a systematic review and meta-analysis – data from the RAISE study

Bruno Ramos Nascimento,[a,b,c,*] André Dias Nassar Naback,[b] Beatriz Marino Pena Santos,[d] Yvonne Geissbühler,[f] Caroline Demacq,[f] Monica Quijano,[f] Pablo A. Perel,[e] Israel Molina,[g,l] Isis Eloah Machado,[h] Ewerton Cousin,[i] Jonathan F. Mosser,[i] Pedro Emanuel de Paula Carvalho,[a] Francisco Rogerlândio Martins-Melo,[j,k] and Antonio Luiz Pinho Ribeiro,[a,b] On behalf of the RAISE investigators

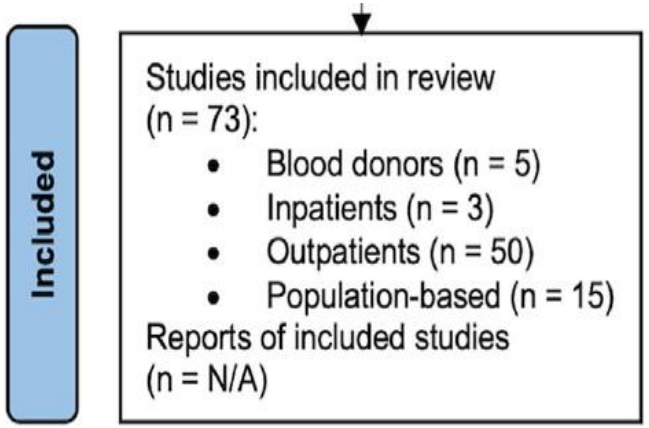


Fig. 1: PRISMA flowchart of article

Type of analysis:	Indeterminate form, N = 46 (%, 95% CI):	Chronic Chagas cardiomyopathy, N = 71 (%, 95% CI):	Digestive form, N = 44 (%, 95% CI):	Mixed form, N = 26 (%, 95% CI):
Overall:	42.6% (36.9–48.6), I^2 = 95.1%	42.7% (37.3–48.3), I^2 = 96.1%	17.7% (14.9–20.9), I^2 = 90.2%	10.2% (7.9–13.2), I^2 = 87.5%
Study setting:				
Blood donors:	48.2% (40.0–56.5), I^2 = 0.0% (2 studies)	33.9% (24.9–44.1), I^2 = 75.1% (5 studies)	23.1 (16.8–30.8), I^2 = 0.0% (2 studies)	8.7% (2.5–26.3), I^2 = 75.0% (2 studies)
Inpatients:	13.3% (0.1–96.5), I^2 = 92.5% (2 studies)	52.9% (34.5–70.6), I^2 = 89.9% (3 studies)	35.8 (7.2–80.1), I^2 = 94.4% (2 studies)	12.4% (3.8–33.8), I^2 = 73.1% (2 studies)
Outpatients:	41.8% (35.3–48.5), I^2 = 95.8% (38 studies)	47.1% (39.5–54.9), I^2 = 97.5% (48 studies)	16.0 (13.3–19.2), I_2 = 89.7% (36 studies)	10.7% (7.9–14.4), I^2 = 89.8% (19 studies)
Population studies:	47.2% (39.0–55.5), I^2 = 62.0% (4 studies)	31.2% (24.4–38.9), I^2 = 96.1% (15 studies)	25.4% (16.0–37.7), I^2 = 85.4% (4 studies)	7.2% (4.8–10.7), I^2 = 0.0% (3 studies)
P-value for comparison:	P = 0.55	P = 0.01*	P = 0.07	P = 0.44
Endemic vs. non endemic countries:				
Endemic:	36.8% (31.9–42.0), I^2 = 92.8% (38 studies)	48.0% (42.3–53.8), I^2 = 96.8% (57 studies)	21.7% (18.4–25.4), I^2 = 88.6% (38 studies)	12.6% (9.8–16.0), I^2 = 86.6% (21 studies)
Non-endemic:	70.8% (61.1–79.0), I^2 = 88.7% (8 studies)	23.1% (12.7–38.1), I^2 = 98.7% (14 studies)	8.5% (5.5–12.8), I^2 = 83.4% (8 studies)	2.0% (0.6–6.1), I^2 = 69.4% (5 studies)
P-value for comparison:	P < 0.001*	P = 0.004*	P < 0.001*	P < 0.001*

Abbreviation: CI: confidence interval. * P-value <0.05.

Table 2: Prevalence of the clinical forms of Chagas disease, in all studies included, by study setting and by endemicity, with between-group comparison.

Retrospect, advances and challenges in Chagas disease diagnosis: a comprehensive review

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Type of test	Diagnostic use	Reagents storage and transportation	Sample	Limit of detection	Quantitative results	Clinical sensitivity	Clinical specificity	Observations	Refs.
Parasitological									
Fresh blood	Acute CD	NA	5–10 mL peripheral whole blood	>500 par/mL	No	<40%	>98%	Low complexity, but microscopy required; 15–30 min per preparation.	26
Strout	Acute CD	NA	5–10 mL peripheral whole blood	NA	No	<50%	>98%	Low complexity. Involves two centrifugation steps before microscopy. Ideally, it should be done within 2 h of blood collection.	27,28
MH/MM	Acute CD, congenital CD	NA	0.3–0.6 mL whole blood	>50 par/mL	No	50%	>98%	Same as the other parasitological methods, it is microscopy-based, operator dependent, has a low throughput (15–30 min per determination), and the time elapsed between sample collection and examination is critical.	29,30
Molecular									
PCR	a) Acute CD and infection reactivation, congenital CD b) Post-treatment follow-up	Reagents must be transported and stored at -20 °C	a) 1–5 mL whole blood (EDTA or GEB treated), biopsy samples, cerebrospinal fluid b) 1–5 mL whole blood (EDTA anticoagulated)	0.5 to 1 par/mL depending on DTU	Yes, upon including standard curve	70–98% Acute and congenital CD; 50–65% in untreated chronic CD	>98%	rtPCR assays based on satDNA or kDNA sequences. Require expensive equipment and molecular biology level facility, highly trained personnel, and the cost of reagents is high (single determination 35–70 USD).	31–33
LAMP	Acute CD, including congenital CD	Room temperature, no cold chain required	a) 30 µL liquid whole blood anticoagulated with heparine b) Single 3–6 mm punch of whole blood DBS in filter paper	a) 1 to 5 par/mL depending on DTU b) 10 to 20 par/mL depending on DTU	No	93–97%	>94%	LAMP assay based on satDNA sequence. POC test, no major or expensive equipment required. Feasible at low-resource settings. ASSURED compliance. Still need to be validated as a tool for treatment follow-up. Estimate cost range 8–12 USD per determination.	34,35

Serological[a]									
HAI	Congenital CD > 9 months Chronic CD	Refrigerated	Serum	NA	Yes	73–99%	60–97%	Lower cost and no need of equipment make of HAI a first diagnostic option in vast areas endemic to CD. But poorer performance than ELISA o IIF assays described.	36
ELISA	Congenital CD > 9 months Chronic CD	Refrigerated	Serum or plasma	NA	Yes	28–99%	>96%	Better to use spectrophometer for read out. Generally have a high performance with Se/Sp > 95%; in regions like Bolivia the agreement between ELISAs is nearly perfect, but in Central America and Mexico Se is <80%. Market cost per determination <3 USD.	36,37
IIF	Congenital CD > 9 months Chronic CD	Refrigerated	Serum or plasma	NA	Yes	NA[b]	NA[b]	Low throughput. Requires of fluorescent microscope and trained personnel. Used as tiebreaker test in reference laboratories; it is labor-intensive and often based on in-house protocols.	-
CMIA	Congenital CD > 9 months Chronic CD Blood bank screening	Refrigerated	Serum or plasma	NA	Yes	>99%	>99%	High throughput capacity, operator-independence, and automated functionality make it highly suitable for blood bank screening. High cost of equipment and reagents limits its use to centralized blood banks and high-resource settings.	38
RDTs	Congenital CD > 9 months Chronic CD	No cold chain	5–100 µL whole blood finger-pricked	NA	No	27–99%	87–97%	POC tests with results turnaround within 1 h; easy-to-use and no equipment required. Performance feasible at low-resource settings (ASSURED compliance), and market costs ranging 2 to 8 USD per single test.	37,39,40

Impact of antiparasitic therapy on cardiovascular outcomes in chronic Chagas disease. A systematic review and meta-analysis

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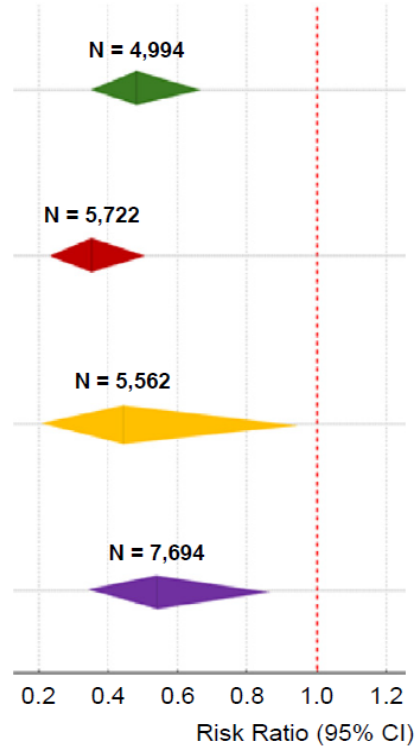
Outcomes	Mean follow-up* (years)	Nº of participants (studies)	Control group event rate	Relative effect (95% CI)	Treatment group event rate† (95% CI)	I^2	NNT (95% CI)
ECG changes	9.9	4,994 (17 studies,4 RCT and 13 observational studies)	37.2 per 100	RR 0.48 (0.36 to 0.66)	17.9 per 100 (13.4 to 24.6)	76%	5 (4 to 8)
Disease progression	7.9	5,722 (12 studies, 3 RCT and 9 observational studies)	24.0 per 100	RR 0.35 (0.23 to 0.51)	8.4 per 100 (5.5 to 12.2)	72%	6 (5 to 8)
CV death	7.2	5,662 (7 studies, 2 RCT and 5 observational studies)	8.3 per 100	RR 0.44 (0.21 to 0.95)	3.7 per 100 (1.7 to 7.9)	50%	22 (15 to 250)
Overall mortality	6.2	7,694 (10 studies, 2 RCT and 8 observational studies)	9.6 per 100	RR 0.54 (0.34 to 0.87)	5.2 per 100 (3.2 to 8.3)	60%	23 (16 to 77)



Forest plots: Each color represents an individual outcome. The center of the diamond plot represents the risk ratio and both ends, the 95% confidence intervals. The control group event rate was calculated by summing the number of events from all included studies (number of events out of number of total control patients).
ECG, electrocardiogram. CV, cardiovascular. I^2, the heterogeneity statistic. NNT, number needed to treat (NNT is calculated as 100 divided by the absolute risk difference—i.e., (Control group event rate minus Treatment group event rate) when expressed as a percentage, or as 1 divided by the absolute risk difference when given as a proportion). RCT, randomized control trials. RR, risk ratio. *Weighted means were used for the pooled estimates of the mean follow-up, taking into account each study's sample size. †Was calculated based on the relative effect and its 95% CI applied to the control group event rate.

Table 2: **Summary of the results of meta-analysis comparing antiparasitic treatment versus control on major cardiovascular outcomes in patients with chronic Chagas disease.**

Efficacy of three benznidazole dosing strategies for adults living with chronic Chagas disease (MULTIBENZ): an international, randomised, double-blind, phase 2b trial

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Methods The MULTIBENZ trial was an international, randomised, double-blind, phase 2b trial performed in Argentina, Brazil, Colombia, and Spain. We included participants aged 18 years and older diagnosed with Chagas disease with two different serological tests and detectable *T cruzi* DNA by qPCR in blood. Previously treated people, pregnant women, and people with severe cardiac forms were excluded. Participants were randomly assigned 1:1:1, using a balanced block randomisation scheme stratified by country, to receive benznidazole at three different doses: 300 mg/day for 60 days (control group), 150 mg/day for 60 days (low dose group), or 400 mg/day for 15 days (short treatment group). The primary outcome was the proportion of patients with a sustained parasitological negativity by qPCR during a follow-up period of 12 months. The primary safety outcome was the proportion of people who permanently discontinued the treatment. Both primary efficacy analysis and primary safety analysis were done in the intention-to-treat population. The trial is registered with EudraCT, 2016-003789-21, and ClinicalTrials.gov, NCT03191162, and is completed.

Findings From April 20, 2017, to Sept 20, 2020, 245 people were enrolled, and 234 were randomly assigned: 78 to the control group, 77 to the low dose group, and 79 to the short treatment group. Sustained parasitological negativity was observed in 42 (54%) of 78 participants in the control group, 47 (61%) of 77 in the low dose group, and 46 (58%) of 79 in the short treatment group. Odds ratios were 1·41 (95% CI 0·69–2·88; p=0·34) when comparing the low dose and control groups and 1·23 (0·61–2·50; p=0·55) when comparing short treatment and control groups. 177 participants (76%) had an adverse event: 62 (79%) in the control group, 56 (73%) in the low dose group, and 59 (77%) in the short treatment group. However, discontinuations were less frequent in the short treatment group compared with the control group (2 [2%] *vs* 11 [14%]; OR 0·20, 95% CI 0·04–0·95; p=0·044).

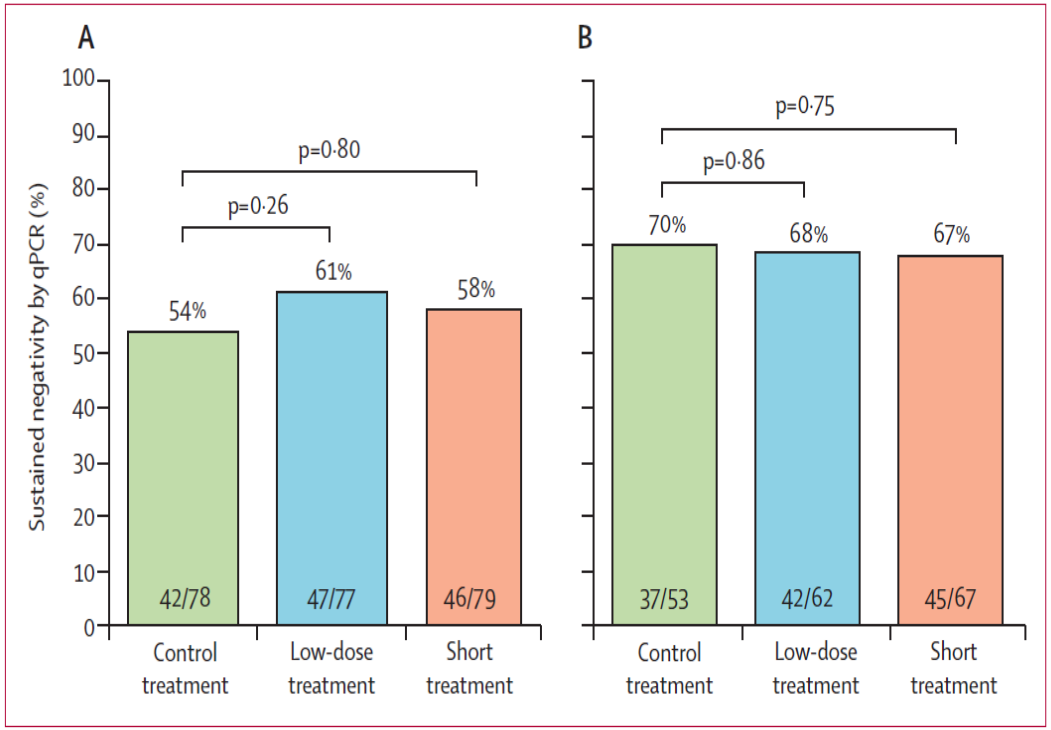

Figure 2: Efficacy outcomes
(A) Intention-to-treat analysis. (B) Per-protocol analysis.

Efficacy and safety of fexinidazole for treatment of chronic indeterminate Chagas disease (FEXI-12): a multicentre, randomised, double-blind, phase 2 trial

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	Fexinidazole 6·0 g (N=15)	Fexinidazole 3·6 g (N=15)	Fexinidazole 6·6 g (N=15)	All fexinidazole (N=45)	Placebo* (N=47)
Median age (IQR), years	38 (35–44)	42 (35–47)	42 (35–44)	41 (35–45)	30 (23–40)
Sex					
Male	5 (33%)	2 (13%)	3 (20%)	10 (22%)	10 (21%)
Female	10 (67%)	13 (87%)	12 (80%)	35 (78%)	37 (79%)
Nationality, Bolivian	14 (93%)	14 (93%)	15 (100%)	43 (96%)	47 (100%)
Body-mass index, kg/m²	27·23 (3·00)	28·06 (3·17)	25·95 (3·58)	27·08 (3·31)	26·11 (3·72)
Trypanosoma cruzi parasite load, (eq-p/mL)	3·67 (9·56)†	1·29 (2·56)	3·83 (7·24)	2·92 (6·95)	0·95 (2·37)
Medical history					
Diabetes mellitus	1 (7%)	0	0	1 (2%)	0
Dyslipidaemia	2 (13%)	1 (7%)	0	3 (7%)	0
Hypercholesterolaemia	2 (13%)	1 (7%)	0	3 (7%)	0
Obesity	1 (7%)	0	0	1 (2%)	4 (9%)
Hypertension	0	1 (7%)	0	1 (2%)	0
Anxiety	1 (7%)	1 (7%)	1 (7%)	3 (7%)	1 (2%)
Insomnia	1 (7%)	0	0	1 (2%)	0

Data are n (%) or mean (SD) unless otherwise specified. *Historical control group.[16] †One patient did not have a screening sample due to being incorrectly assigned.

Table 1: Baseline characteristics

	Fexinidazole 6·0 g (N=15)	Fexinidazole 3·6 g (N=15)	Fexinidazole 6·6 g (N=15)	Placebo (N=47)
Sustained parasite clearance until month 4 (intention to treat)*†	4/14 (29%; 0·17)	3/15 (20%; 0·39)	1/14 (7%; 0·86)	6/46 (13%)
Sustained parasite clearance until month 12 (intention to treat)†	4/14 (29%; 0·077)	1/15 (7%; 0·77)	1/14 (7%; 0·75)	4/46 (9%)
Sustained parasite clearance until month 4 (per protcol)*	3/11 (27%; 0·23)	3/13 (23%; 0·31)	1/11 (9%; 0·80)	6/46 (13%)
Sustained parasite clearance until month 12 (per protocol)*	3/11 (27%; 0·12)	1/13 (8%; 0·73)	1/11 (9%; 0·67)	4/46 (9%)

Data are n/N (%; p value) or n/N (%). p values are for comparison with placebo. *The fexinidazole 6·0 g and 6·6 g groups and the historical control placebo group each had one patient with missing data for these endpoints. †Against placebo; sustained parasite clearance means negative serial qualitative PCR (three negative PCR results from three samples collected on the same day) results on all assessments from end of treatment through the follow-up period.

Table 2: Sustained *T cruzi* clearance

Shorter treatment in chronic Chagas disease: a new promise?

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The results of these studies should be carefully placed in the saga of research into the treatment of *T cruzi* infection. The disappointment with fexinidazole is in line with the high rate of failure in the search for new drugs effective in halting *T cruzi* infection. Conversely, the efficacy of the short benznidazole regimen with low rate of treatment discontinuation indicate that a phase-3 randomised trial testing this therapeutic approach is needed, as the authors have suggested. Additionally, it is imperative to introduce

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