Experiencias con tecnologías en la mitigación para reducir el ITT para diferentes patógenos - **NAT**

POTENCIAL CONFLICTO DE INTERESES:

En los últimos 2 años recibí honorarios por conferencias de las empresas Roche y Grifols.

Ponente: José Eduardo Levi

- Biólogo
- Doctor en Virología
- Investigador del Instituto de Medicina Tropical de la Universidad de São Paulo, Brasil
- Superintendente de Investigación y Desarrollo dela red Dasa
- Director Regional América Latina, Sociedad Internacional de Transfusión Sanguínea (ISBT), 2022-2024

¿QUE ES NAT?

NUCLEIC ACID TEST o
NUCLEIC ACID AMPLIFICATION TEST

Métodos de amplificación de ácidos nucleicos (ADN/ARN) con muy alta sensibilidad y especificidad

Reacción em cadena de la polimerasa (PCR)
Amplificación mediada por transcripción (TMA)

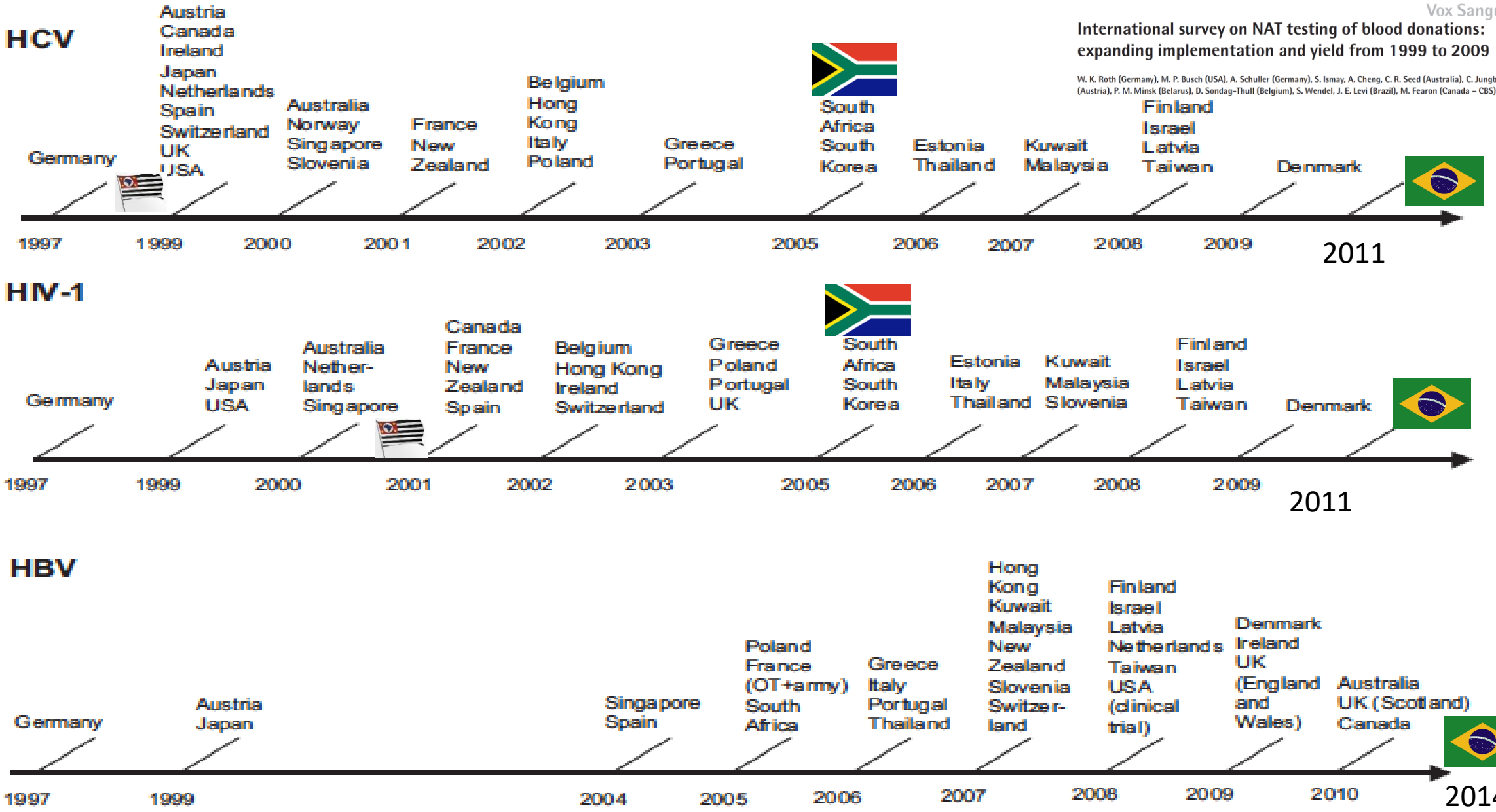
¿ CUAL ES LA UTILIDAD DE NAT EM LA TAMIZAJE DE DONANTES DE SANGRE?

1. **DONANTES EM VENTANA IMUNOLÓGICA**

2. **VARIANTES ANTIGÊNICAS (ex. mutantes HBsAg)**

3. **PORTADORES SILENCIOSOS (ex. HCV)**

Introduction of NAT testing



VoxSanguinis
The International Journal of Transfusion Medicine
ISBT International Society of Blood Transfusion
Vox Sanguinis (2012) 102, 82–90
INTERNATIONAL FORUM
© 2011 The Author(s)
Vox Sanguinis © 2011 International Society of Blood Transfusion
DOI: 10.1111/j.1423-0410.2011.01506.x
Vox Sanguinis

International survey on NAT testing of blood donations: expanding implementation and yield from 1999 to 2009

W. K. Roth (Germany), M. P. Busch (USA), A. Schuller (Germany), S. Ismay, A. Cheng, C. R. Seed (Australia), C. Jungbauer (Austria), P. M. Minsk (Belarus), D. Sondag-Thull (Belgium), S. Wendel, J. E. Levi (Brazil), M. Fearon (Canada – CBS),

Fig. 1 Introduction of nucleic acid amplification technology (NAT) testing.

Impact of individual-donation nucleic acid testing on risk of human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission by blood transfusion in South Africa

Transfusion. 2009;49:1115–25

Marion Vermeulen, Nico Lelie, Wendy Sykes, Robert Crookes, Johanna Swanevelder, Lilian Gaggia, Martin Le Roux, Eben Kuun, Sam Gulube, and Ravi Reddy

BACKGROUND: In 2005, the South African National Blood Service introduced individual-donation (ID) nucleic acid test (NAT) screening for human immunodeficiency virus (HIV) RNA, hepatitis C virus (HCV) RNA, and hepatitis B virus (HBV) DNA. At the same time the use of ethnic origin to prioritize the transfusion of blood according to a hierarchy of residual risk was discontinued.

VoxSanguinis
The International Journal of Transfusion Medicine
ISBT International Society of Blood Transfusion
Vox Sanguinis (2012) 102, 82–90
INTERNATIONAL FORUM

DOI: 10.1111/j.1423-0410.2011.01506.x

International survey on NAT testing of blood donations: expanding implementation and yield from 1999 to 2009

Table 3 NAT-only positives since introduction of NAT testing

Region/ country	Virus	Screened donations since implementation of NAT	NAT-only positives	NAT-only positives/ million
Africa	HIV-1	2 202 295	81	36·78
	HCV	2 202 295	4	1·82
	HBV	2 202 295	232	105·34
Asia/ Pacific	HIV-1	71 458 330	44	0·62
	HCV	71 458 330	169	2·37
	HBV	50 679 100	1091	21·53
Europe	HIV-1	110 860 111	73	0·66
	HCV	139 474 595	206	1·48
	HBV	56 342 555	550	9·76
North America	HIV-1	87 652 586	45	0·51
	HCV	89 652 687	299	3·34
	HBV	5 062 264	11	2·17
South America	HIV-1	347 374	1	2·88
	HCV	408 167	2	4·9
	HBV	No NAT testing		

Table 1. Yield of blood donation NAT testing worldwide since introduction and in 2008

Virus	Period	Tested donations, *n*	NAT-only positives, *n*	NAT-only positives/ million	Rate 2008/ total
HIV	total	272,520,696	244	0.90	2.14
	2008	37,356,757	72	1.93	
HCV	total	303,196,074	680	2.24	0.83
	2008	37,095,225	69	1.86	
HBV	total	114,286,214	1,884	16.48	0.52
	2008	19,887,649	169	8.50	

From Roth et al. [32].

Rev. Inst. Med. trop. S. Paulo
49(3):177-185, May-June, 2007

PRIMARY SCREENING OF BLOOD DONORS BY NAT TESTING FOR HCV-RNA: DEVELOPMENT OF AN "IN-HOUSE" METHOD AND RESULTS

Silvano WENDEL(1,2), José Eduardo LEVI(1,2), Deise Tihe TAKAOKA(2), Isabela Cristina SILVA(2), Juliana Polachini de CASTRO(2), Mário A. TOREZAN-FILHO(1,2), Jorge GHANAME(3), Romualdo GIOACHINI(4,5), Joselito BRANDÃO(5) & Edison Luis DURIGON(6)

Rev. Inst. Med. trop. S. Paulo
49(3):171-176, May-June, 2007

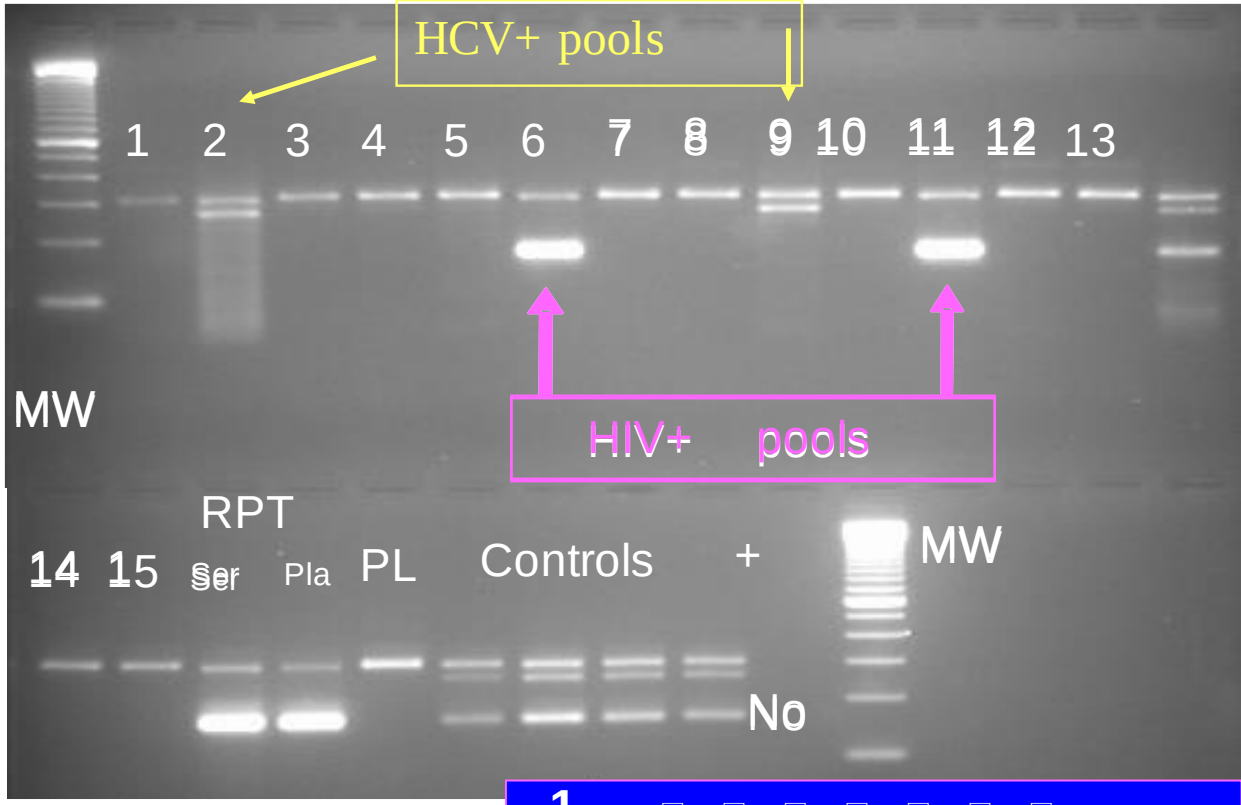
REPLACEMENT OF HIV p24 Ag TEST BY A MULTIPLEX RT-PCR METHOD FOR PRIMARY SCREENING OF BLOOD DONORS

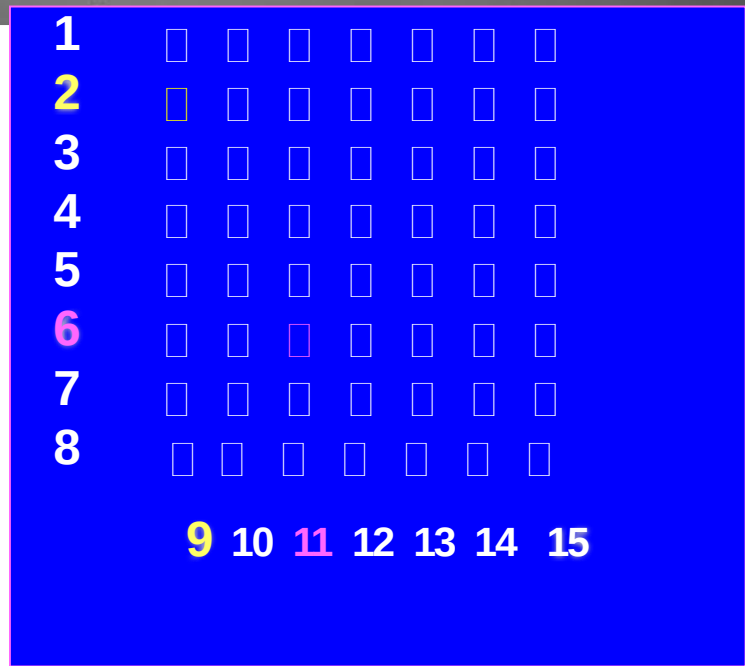
José Eduardo LEVI(1,2), Silvano WENDEL(1,2), Deise Tihe TAKAOKA(2), Isabela Cristina SILVA(2), Juliana Polachini de CASTRO(2), Mário A. TOREZAN-FILHO(1,2), Jorge GHANAME(3), Romualdo GIOACHINI(4,5), Joselito BRANDÃO(5), Evaldo Pasquini LANDI(6), Antônio César TEIXEIRA(7) & Edison Luis DURIGON(8)

Table 5
Laboratory data from a NAT+/EIA- donor, detected in the window period

Date	Anti HIV A (Abs/Cut-off)	Anti HIV B (Abs/Cut-off)	NAT	Viral load copies/mL	Western blot
27/2/6 Index donation	NRT	NRT	RT	8,310 ($\log_{10}$ = 3.92)	Ind p24+ weak Conclusion: **Indeterminate**
9/3/6	2.0/0.198 (RT)	1.91/1.00 (RT)	RT	> 750,000	Ind p24+ weak Conclusion: **Indeterminate**
20/3/6	2.0/0.181 (RT)	6.25/1.00 (RT)	RT	> 750,000	gp160 weak/gp 120 weak/p24 weak Conclusion: **Reactive**

NRT = Non Reactive; RT = Reactive





Rotina kit NAT BioManguinhos

Ministério da Saúde
FIOCRUZ
Fundação Oswaldo Cruz

Instituto de Tecnologia em Imunobiológicos
Bio-Manguinhos

Pooling 2h

Extracción 2h 20 min

”Set-up”30 min

RT-PCR 2h 30 min

7h 30 min – 8h

92 pools de 6 muestras= 552 donaciones/rutina

NAT - REDUCCIÓN SIGNIFICATIVA DEL RIESGO

The Brazilian experience of nucleic acid testing to detect human immunodeficiency virus, hepatitis C virus, and hepatitis B virus infections in blood donors

TRANSFUSION 2018;58;862–870

TABLE 5. Results of the tested blood bags and NAT-positive detection of HIV, HCV, and HBV, every year since the pilot study

Year	Blood bags screened for HIV and HCV	NAT-positive		Blood bags screened to HBV	NAT-positive
		HIV	HCV		HBV
2008 (pilot study)	5,392	0	0	NT	
2009/2010 (multicentric)	219,791	2	0	NT	
2011	471,360	0	1	NT	
2012	1,292,558	3	1	NT	
2013	2,511,092	14	4	NT	
2014	2,939,086	12	5	43,442	0
2015	3,015,848	13	6	2,596,573	18
2016	3,155,409	19	11	3,155,409	24
Total	13,610,536	63	28	5,795,424	42

NT = not tested.

TABLE 6. Geographic distribution of blood bags that are NAT positive for HIV, HCV, and HBV and NAT-yield rates per million

Geographic region	NAT positive					
	HIV (yield)		HCV (yield)		HBV (yield)	
South	14	(5.87)	8	(3.35)	2	(1.52)
Southeast	21	(3.29)	13	(2.04)	12	(4.24)
Midwest	6	(5.05)	4	(3.37)	5	(7.68)
Northeast	11	(4.01)	3	(1.09)	17	(12.11)
North	11	(12.10)	0		6	(14.14)
Total	63		28		42	

VHB = 7.24/MILLÓN
VIH = 4.62/MILLÓN
VHC = 2.05/MILLÓN

Usefulness of nucleic acid testing to reduce risk of hepatitis B virus transfusion-transmitted infection in Argentina: high rate of recent infections

Transfusion. 2017 Mar;57(3pt2):816-822. doi: 10.1111/trf.13946

Sebastián Blanco,[1,2] Marcos César Balangero,[1,2] Mildre Cledy Valle,[1] Oscar Luis Montini,[1] Luis Horacio Carrizo,[1] and Sandra Verónica Gallego[1,2]

205.388 DONACIONES CRIBADAS:
155 HIV+ (TODAS Anti-HIV+)
106 HCV+ (TODAS Anti-HCV+)
76 HBV+ (168.215 CRIBADAS)

76 NAT HBV+ {
- **68 anti-HBc y HBsAg+**
- **3 anti-HBc + y HBsAg- (OBIs)**
- **3 anti-HBc- y HBsAg- (ventanas)**

RENDIMIENTO = 1,8/100.000

TABLE 1. Virologic and serologic markers of HBV infection in blood donors with suspected OBI

Donor	AgHBs*	AgHBe†	Anti-core‡	IgM core§	Anti-HBe‖	Anti-HBs¶	NAT**	VL (IU/mL)††
1	Nonreactive	Nonreactive	Nonreactive	Nonreactive	Nonreactive	Nonreactive	Reactive	294‡‡
2	Nonreactive	ND	Reactive	Nonreactive	Reactive	Nonreactive	Reactive	<29§§
3	Nonreactive	ND	Reactive	Nonreactive	Reactive	Nonreactive	Reactive	<29§§
4	Nonreactive	Nonreactive	Nonreactive	Nonreactive	Reactive	Nonreactive	Reactive	<29‡‡
5	Nonreactive	Nonreactive	Reactive	Nonreactive	Reactive	Nonreactive	Reactive	<29‖‖
6	Nonreactive	Nonreactive	Nonreactive	Nonreactive	Nonreactive	Nonreactive	Reactive	99

EXPERIENCIA NAT HEMOCENTRO DISTRITAL
Julio 2006 – Febrero 2015

Bernardo Camacho Rodríguez MD MCs

Procesado hasta 23-02-2015	Muestras analizadas	Pooles	Muestras inicialmente positivas	Muestras negativas	Muestras positivas
HCV	**304836**	**50807**	**6**	**304836**	**0**
HIV	304836	50807	11	304836	0
HBV	304836	50807	30	304831	**5**

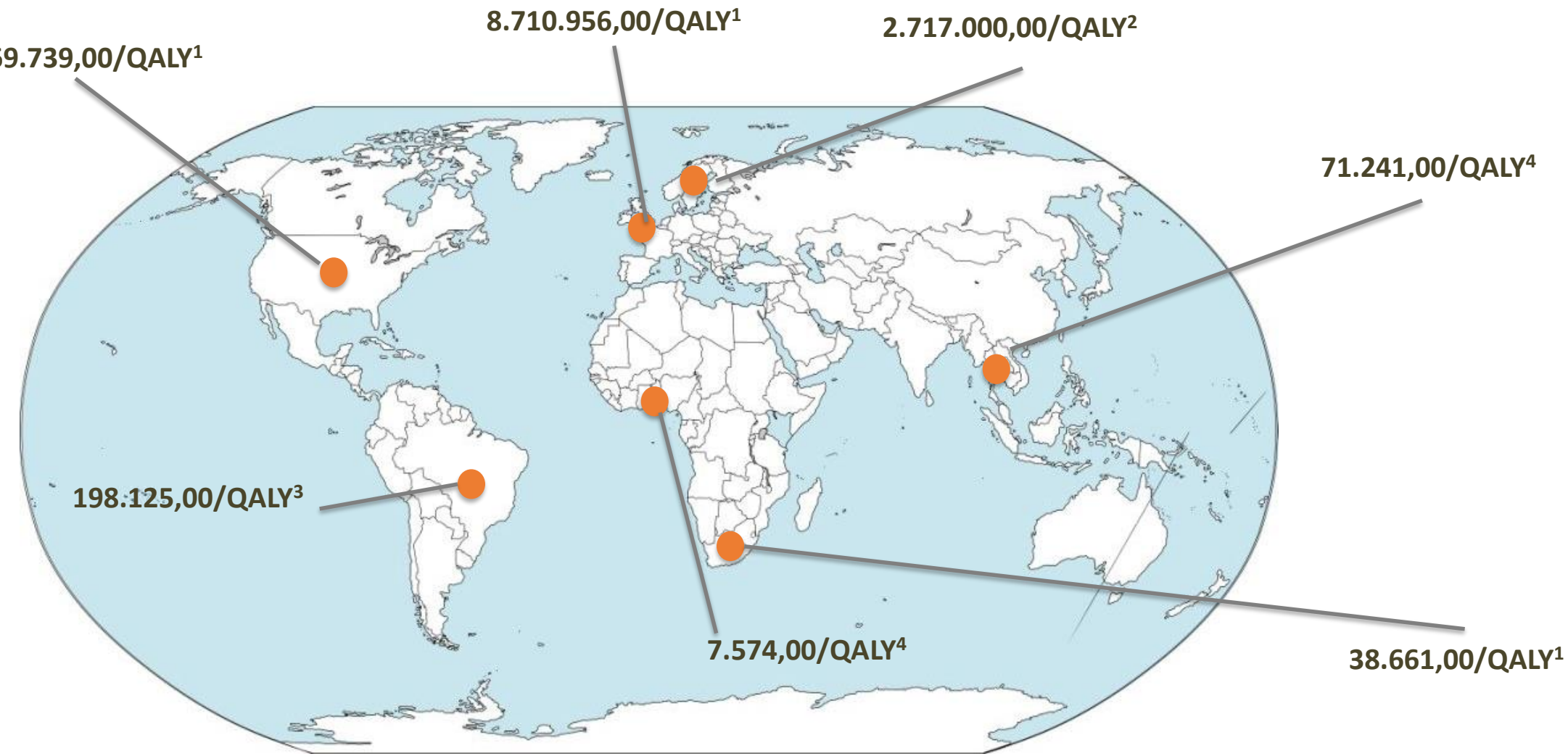
3 NAT+/ EIE Negativo 1/100.000
2 HBV ocultas: Core+ NA+ HBsAg negativo

IMPLEMENTACIÓN DE NAT EN LA TAMIZAJE SANGUÍNEA EN BS DE LATINOAMERICA -2022

PAÍS	NAT	OBLIGATORIO
Antigua and Barbuda		
Anguilla		
Argentina	☒	EM ALGUNAS PROVINCIAS
Aruba		
Barbados		
Bermuda		
Bolivia, Plurinational State of		
Brazil	☒	**SI**
Bahamas		
Belize		
Chile	☒	
Curaçao	☒	
Colombia	☒	
Costa Rica	☒	
Cuba	☒	
Dominica		
Dominican Republic	☒	
Ecuador	☒	**SI**
Falkland Islands (Malvinas)		
Grenada		
South Georgia and the South Sandwich Islands		
Guatemala	☒	

PAÍS	NAT	OBLIGATORIO
Guyana		
Honduras	☒	
Haiti		
Jamaica		
Saint Kitts and Nevis		
Cayman Islands		
Saint Lucia		
Montserrat		
Mexico	☒	
Nicaragua		
Panama	☒	**SI**
Peru	☒	
Puerto Rico		
Paraguay		
Suriname		
El Salvador	☒	
Turks and Caicos Islands		
Trinidad and Tobago		
Uruguay		
Saint Vincent and the Grenadines		
Venezuela, Bolivarian Republic of		
Virgin Islands, British		
Virgin Islands, U.S.		

ANÁLISIS DE COSTO-EFECTIVIDAD DE NAT EN EL MUNDO



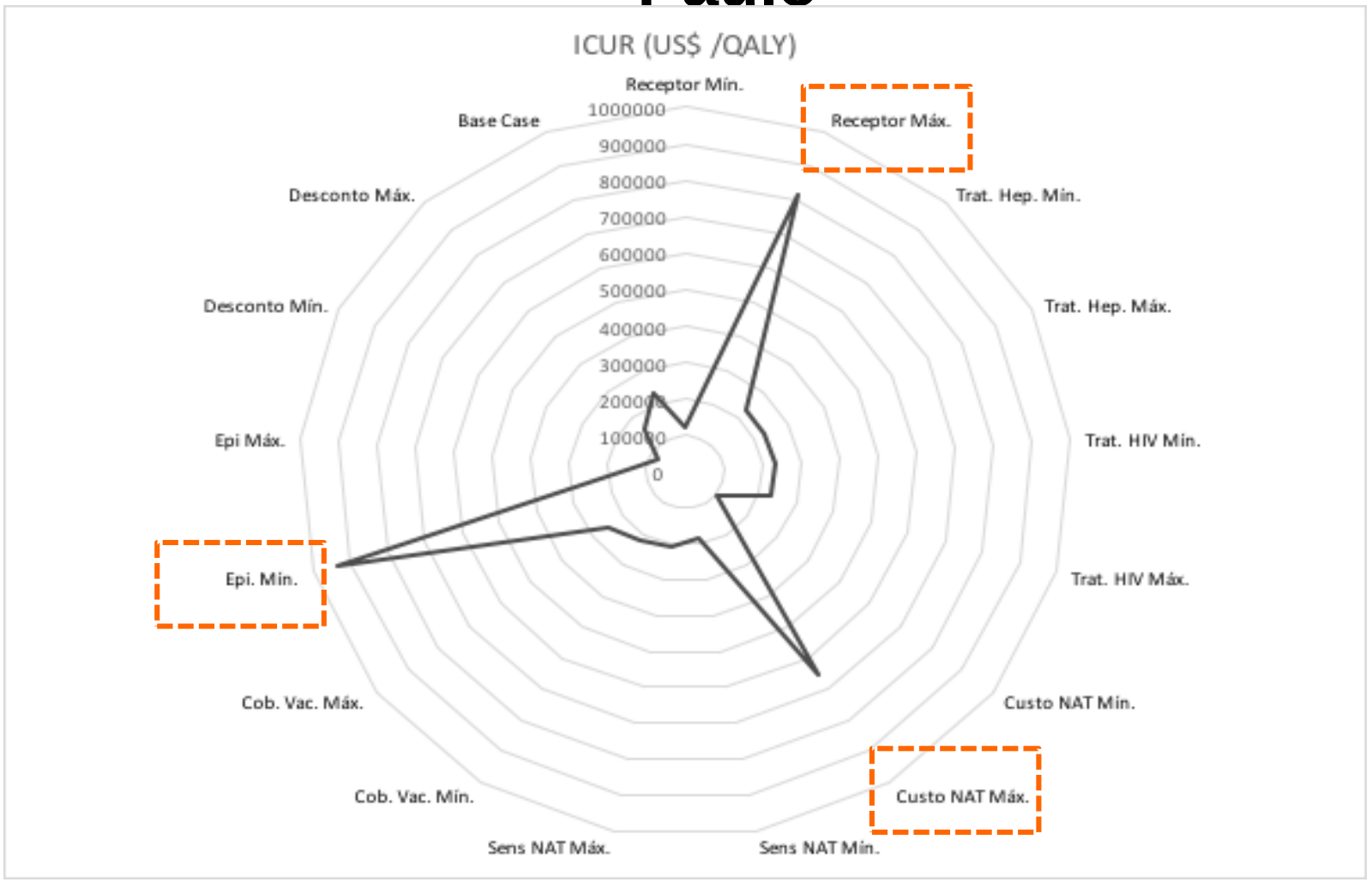
1. Custer *et al.* Vox Sanguinis 2017 – MP16 (US$ de 2014)
2. Davidson *et al.* Transfusion 2011 – ID-NAT (US$ de 2007)
3. Relatório CONITEC n.26/2012
4. van Hulst *et al*,.Transfusion 2009

Evaluación Económica del NAT en Brasil

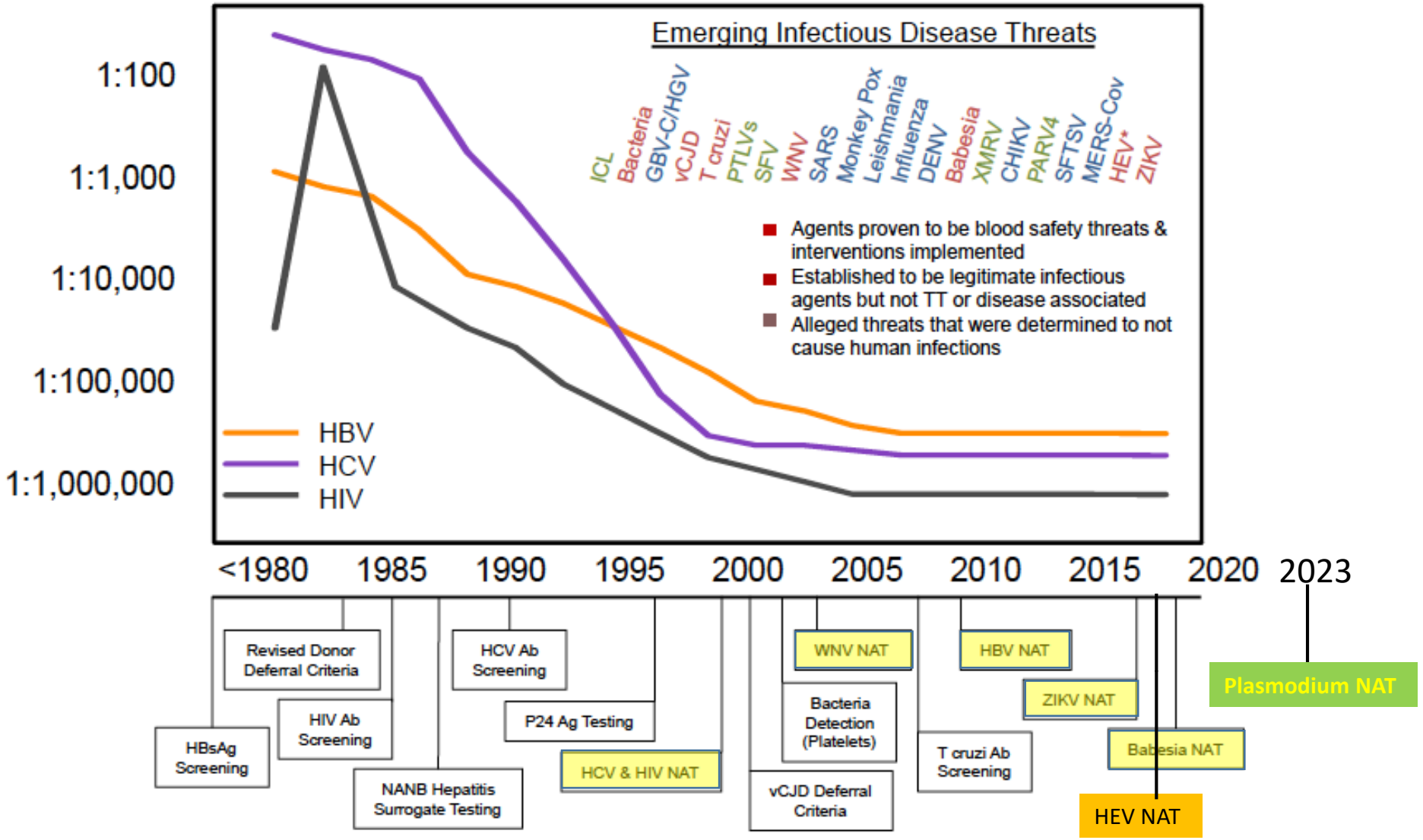
PhD Thesis, Rafael Leme Souza,

Instituto de Medicina Tropical da Universidade de São Paulo

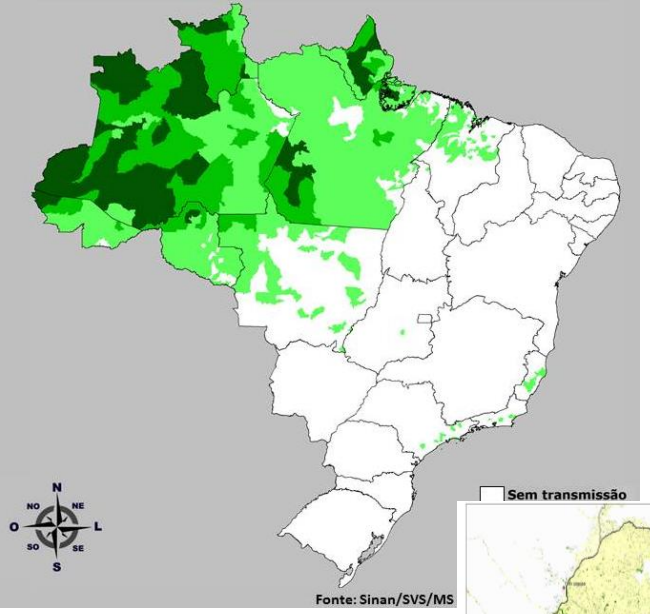
Análise de sensibilidade univariada da razão de custo-utilidade incremental para cada estratégia de triagem de sangue [em dólares para o ano de 2018 por QALY].



Risks of major transfusion-transmitted viral infections and emerging infectious agents of concern to blood safety



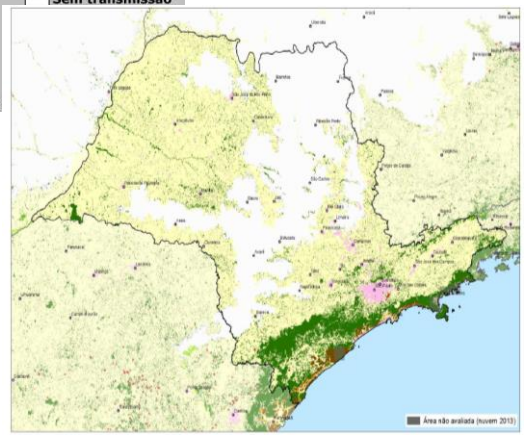
Busch MP, Bloch EA, Kleinman S. Prevention of Transfusion Transmitted Infections. Blood 2019



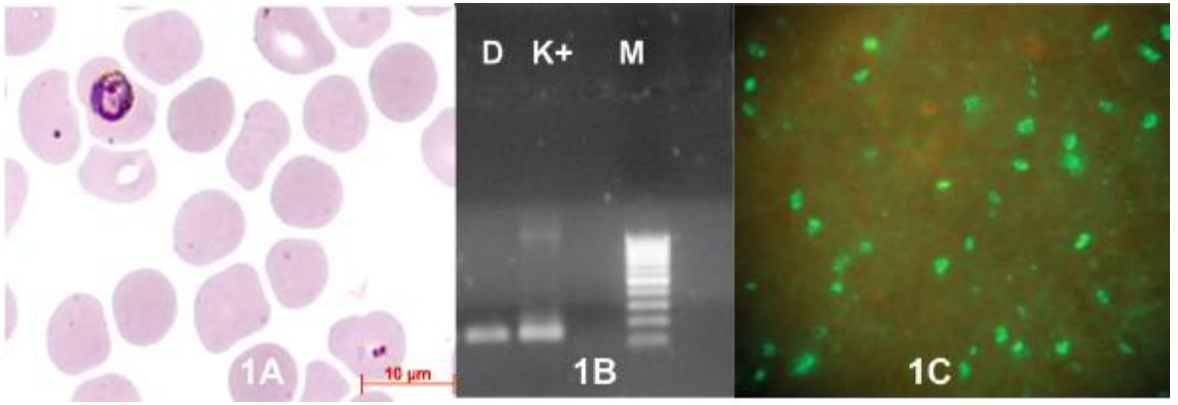
The hidden *Plasmodium malariae* in blood donors: a risk coming from areas of low transmission of malaria

Rev Inst Med Trop São Paulo. 2020;62:e100

Mariana Aschar[1], José Eduardo Levi[1,2], Maria L. R. N. Farinas[1], Sandra C. Montebello[3], Alfredo Mendrone-Junior[3], Silvia Maria Di Santi[1,4,5]



TRANSFUSION-TRANSMITTED MALARIA: CASE REPORT OF ASYMPTOMATIC DONOR HARBORING *Plasmodium malariae*

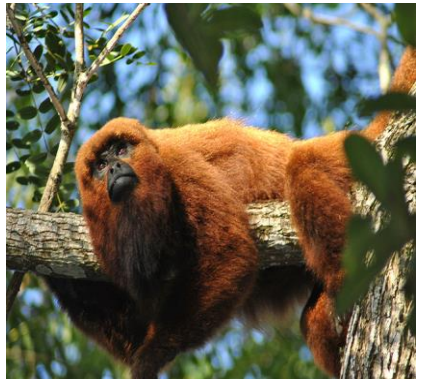


Rev. Inst. Med. Trop. Sao Paulo
53(1):55-59, January-February, 2011

Neoregelia johannis

Anopheles (Kerteszia) cruzii

Allouata sp.



Journal of Infectious Diseases Advance Access published July 9, 2015

MAJOR ARTICLE

Transfusion-Transmitted Dengue and Associated Clinical Symptoms During the 2012 Epidemic in Brazil

Ester C. Sabino,[1] Paula Loureiro,[2] Maria Esther Lopes,[3] Ligia Capuani,[1] Christopher McClure,[4] Dhuly Chowdhury,[4] Claudia Di-Lorenzo-Oliveira,[5] Lea C. Oliveira,[1] Jeffrey M. Linnen,[6] Tzong-Hae Lee,[7] Thelma Gonçalez,[7] Donald Brambilla,[4] Steve Kleinman,[7,8] Michael P. Busch,[7,9,a] and Brian Custer[7,9,a]; for the International Component of the NHLBI Recipient Epidemiology and Donor Evaluation Study-III

Rio de Janeiro and Recife were successfully tested. Rates of confirmed infection with DENV, all of which typed as DENV-4, were 0.51% in Rio de Janeiro and 0.80% in Recife. The peak of the epidemic occurred in week 19 (early May) of 2012 in Rio de Janeiro and week 14 (early April) in Recife, with rates of confirmed DENV RNA detection of >1% and >2%, respectively.

TASA DE TRANSMISIÓN = 37.5%

Conclusions. During a large epidemic of DENV-4 infection in Brazil, >0.5% of donations were RNA positive, and approximately one third of components resulted in TT. However, no significant clinical differences were evident between RNA-positive and RNA-negative recipients.

Real-time symptomatic case of transfusion-transmitted dengue

TRANSFUSION 2015;55:961–964

José Eduardo Levi,[1,2] Anna Nishiya,[1] Alvina Clara Félix,[2] Nanci Alves Salles,[1] Luciana Ribeiro Sampaio,[1] Fátima Hangai,[1] Ester Cerdeira Sabino,[3] and Alfredo Mendrone Jr[1]

NAT-ZKV

Information for Blood Establishments Regarding FDA's Determination that Zika Virus is no Longer a Relevant Transfusion-Transmitted Infection, and Withdrawal of Guidance titled "Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components" **12 MAYO 2021**

DONACIONES NAT ZKV+ EE.UU

2016 - 1.8% (PUERTO RICO)

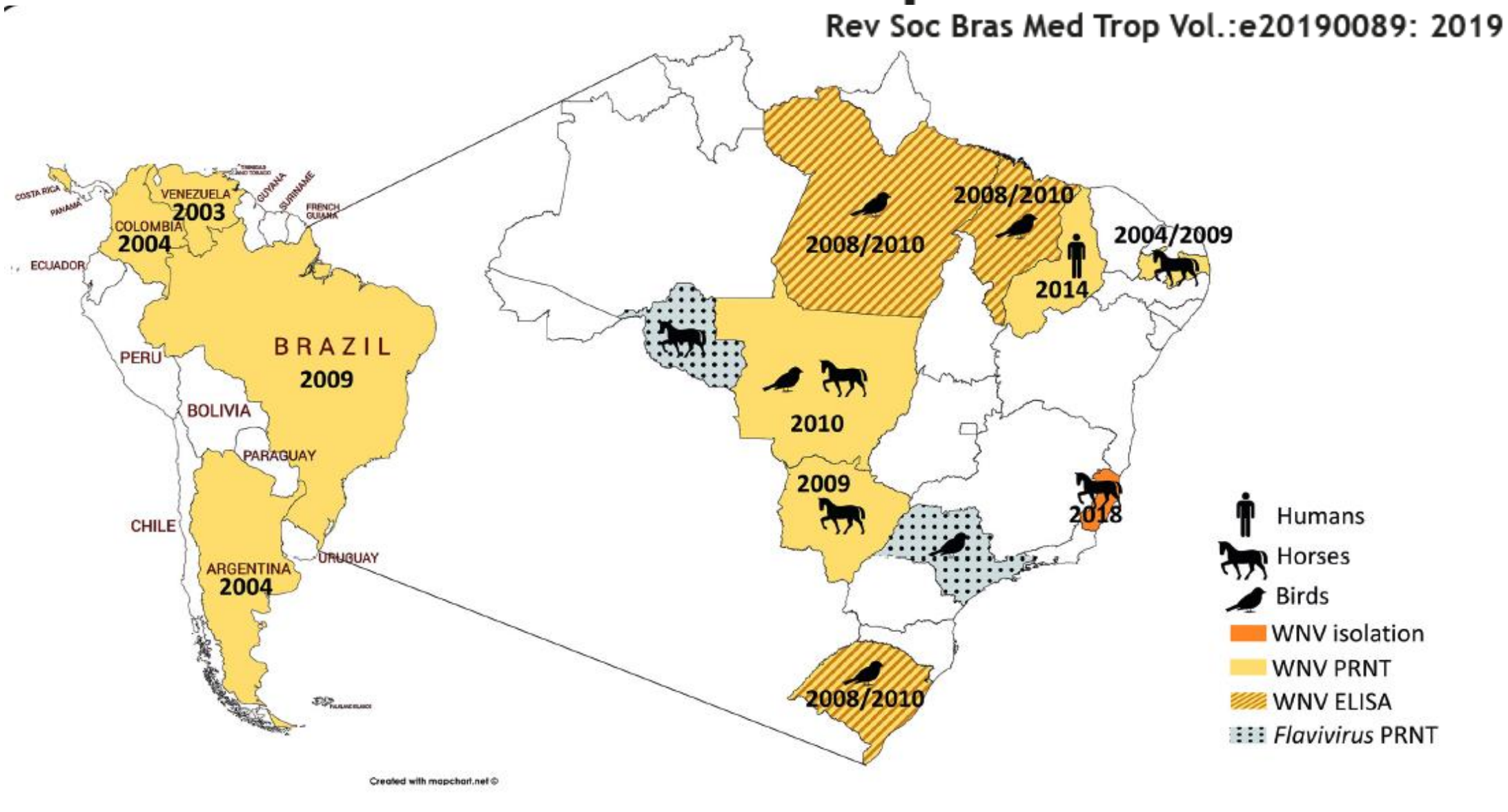
ABRIL 2016 - DECIEMBRE 2017 = 400

2017 =17 DONACIONES

2018 = 2 DONACIONES

MARZO 2018 - ABRIL 2019 = 0

West Nile virus infections are here! Are we prepared to face another flavivirus epidemic?



Mitigating the risk of transfusion-transmitted infections with vector-borne agents solely by means of pathogen reduction

Transfusion. 2022;1–11.

TABLE 3 Percentage of donations in which infectious titers would be within PRT inactivation capacity

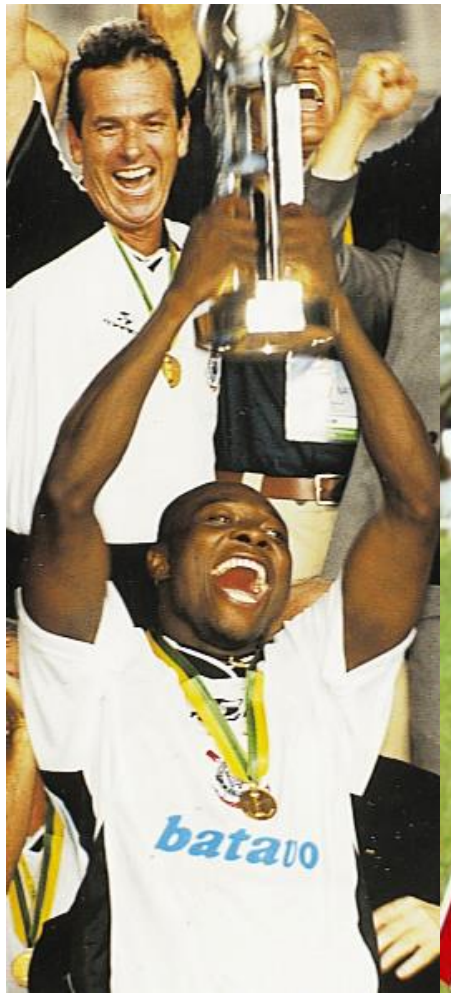
Pathogen	A/UVA P RTs			S-303/GSH PRT Red blood cells
	Plasma	Platelets in 100% plasma	Platelets in 65%PAS/35% plasma	
WNV	100%	100%	100%	N/A
DENV	100%	100%	100%	100%
ZIKV	100%	100%	100%	100%
CHIKV	100%	100%	100%	>98.2%
Babesia microti	100%	100%	100%	100%

TABLE 4 Number of donors deferred for risk of infection with or testing reactive for vector-borne pathogens at the American Red Cross in 2019[a]

Vector-borne agent	Available U.S. mitigation options	Number of deferred donors	Number of additional platelet donations with A/UVA PRT[b]	Number of additional RBC donations with S-303/GSH PRT[b]
WNV	MP-NAT/ID-NAT	45	5	40
Babesia	Deferral, ID-NAT, PRT	89	9	80
Plasmodium	Deferral due to travel, PRT	26,673	2667	24,006
Trypanosoma cruzi	Deferral, first time serology	951	95	856
Total		27,758[c]	2776	24,982

MUCHAS GRACIAS!

dudilevi@usp.br



Acobasmet
Asociación Colombiana de Bancos de Sangre y Medicina Transfusional

GCIAMT
Grupo Cooperativo Iberoamericano de Medicina Transfusional

Join us next year at ISBT Gothenburg 2023!

ISBT Gothenburg 2023

June 17 - 21, 2023

Gothenburg, Sweden

Registration and Abstract submission opening in January 2023