13° CONGRESO COLOMBIANO & 19° CONGRESO IBEROAMERICANO DE BANCOS DE SANGRE, MEDICINA TRANSFUSIONAL Y TERAPIA CELULAR

CONECTADOS CON EL PACIENTE

Octubre 31 a Noviembre 3 del 2024
Bogotá Colombia, Hotel Sheraton

Acobasmet
Asociación Colombiana de Bancos de Sangre y Medicina Transfusional

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NAT en LATINOAMÉRICA

JOSÉ EDUARDO LEVI

Acobasmet
Asociación Colombiana de Bancos de Sangre y Medicina Transfusional

JOSÉ EDUARDO LEVI

- Biólogo
- Doctor en Virología
- Investigador del Instituto de Medicina Tropical Universidad de São Paulo, Brasil
- Director Regional América Latina, Sociedad Internacional de Transfusión Sanguínea (ISBT), 2022-2026
- Coordinador del Comité de Enfermedades Transmisibles por la Sangre de la Asociación Brasileña de Hematología y Hemoterapia (ABHH)
- Coordinador del Comité de Diagnóstico Molecular de la Sociedad Brasileña de Patologia Clínica (SBPC)
- Superintendente de Investigación y Desarrollo dela red Dasa, Brasil

JOSÉ EDUARDO LEVI

Potential conflicto de interese: Recibí honorarios relativos a ponencias científicas das empresas Grifols y Roche nos últimos dos años.

¿QUE ES NAT?

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NUCLEIC ACID TEST o
NUCLEIC ACID AMPLIFICATION TEST (NAAT)

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)

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¿CUÁL ES LA UTILIDAD DE NAT EN EL CRIBADO DE LA SANGRE?

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1. **DONANTES EN VENTANA INMUNOLOGICA**

2. **DETECCION DE VARIANTES ANTIGENICAS Y MOLECULARES (ex. mutantes de HBsAg)**

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

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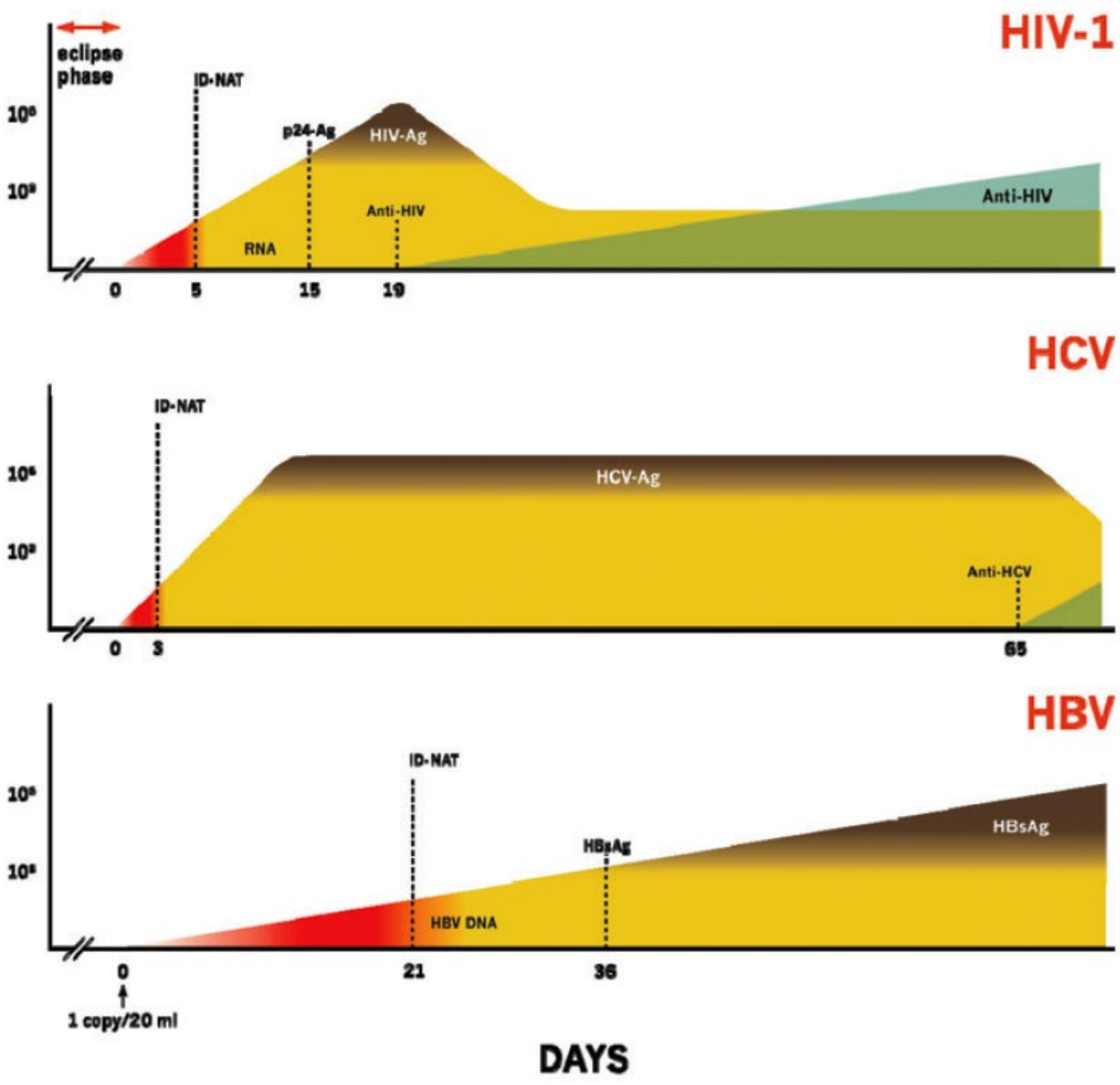
Asociación Colombiana de Bancos de Sangre y Medicina Transfusional

Kleinman SH, Lelie N, Busch MP. Infectivity of human immunodeficiency virus-1, hepatitis C virus, and hepatitis B virus and risk of transmission by transfusion. Transfusion 2009;49:2454-89.

HCV = 10.8 horas

HIV = 20.4 horas

HBV = 62.4 horas



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),

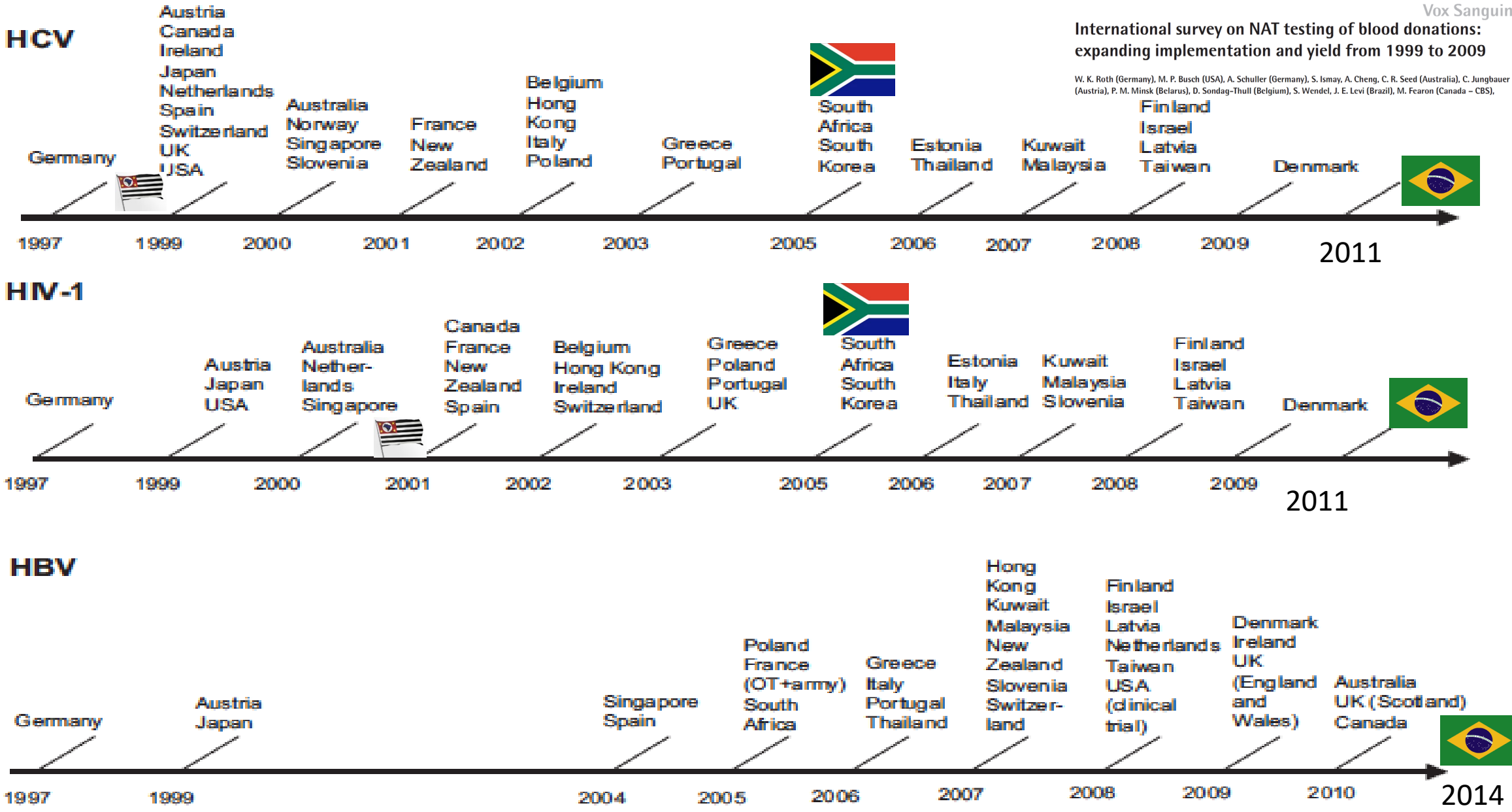
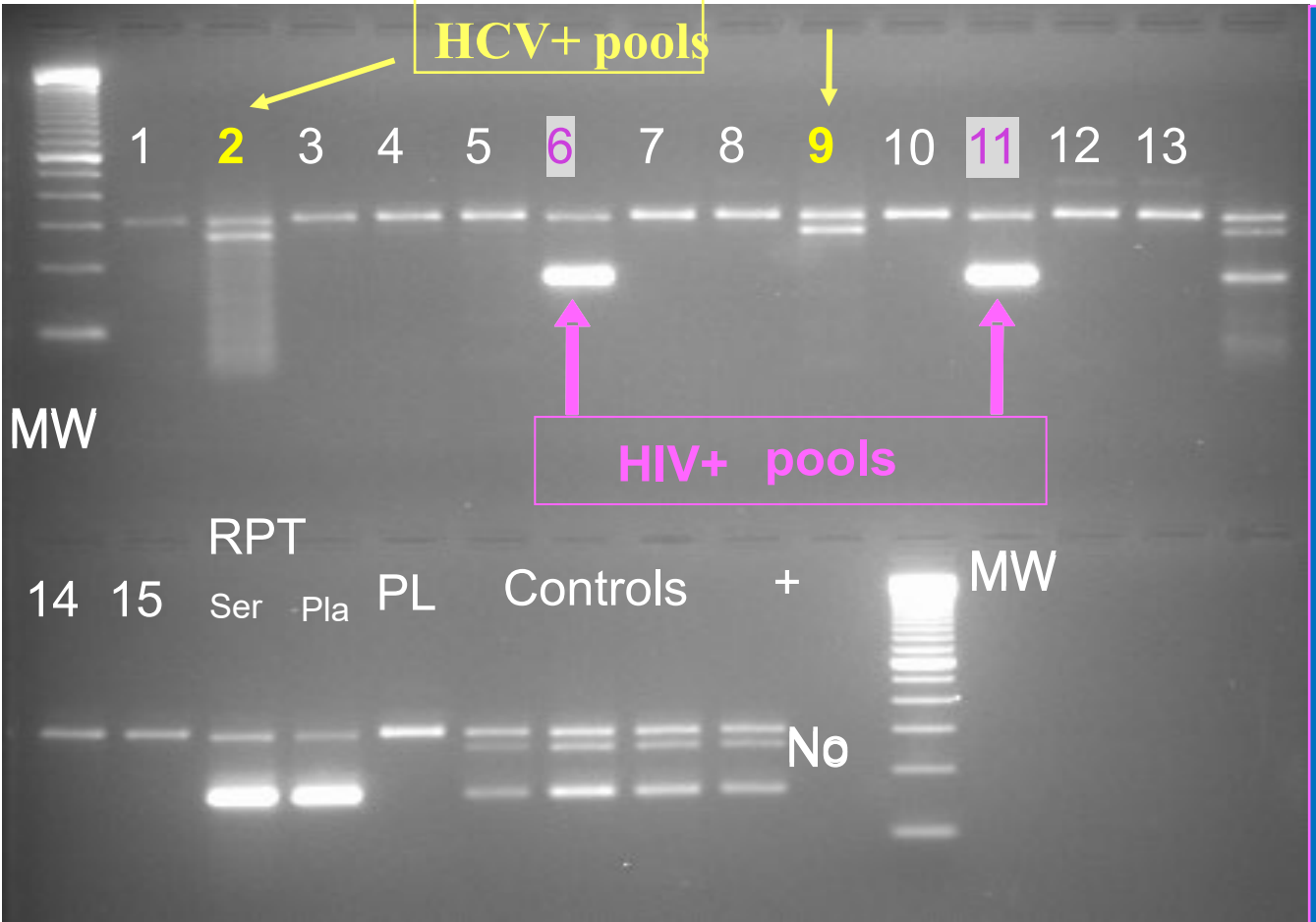


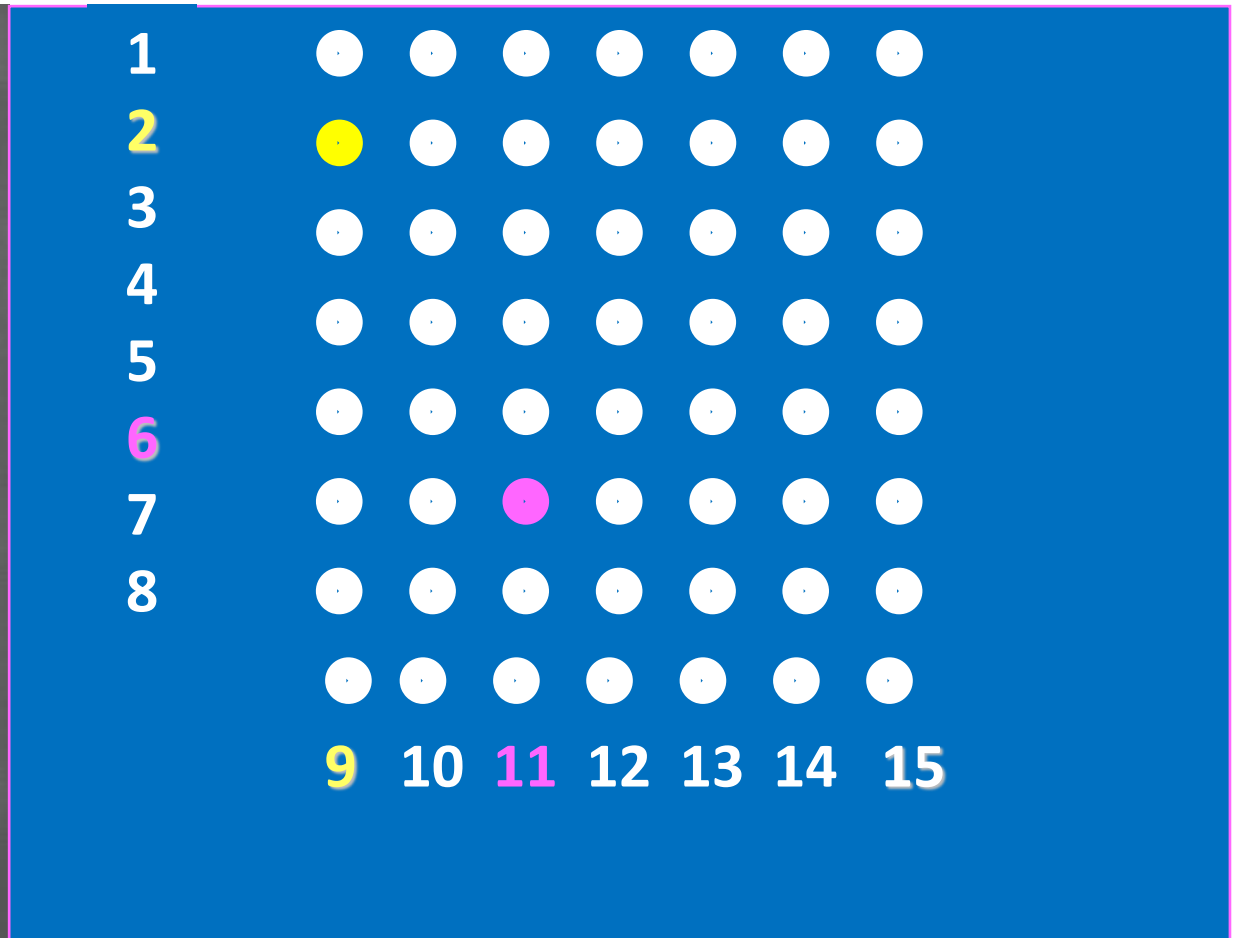
Fig. 1 Introduction of nucleic acid amplification technology (NAT) testing.

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

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

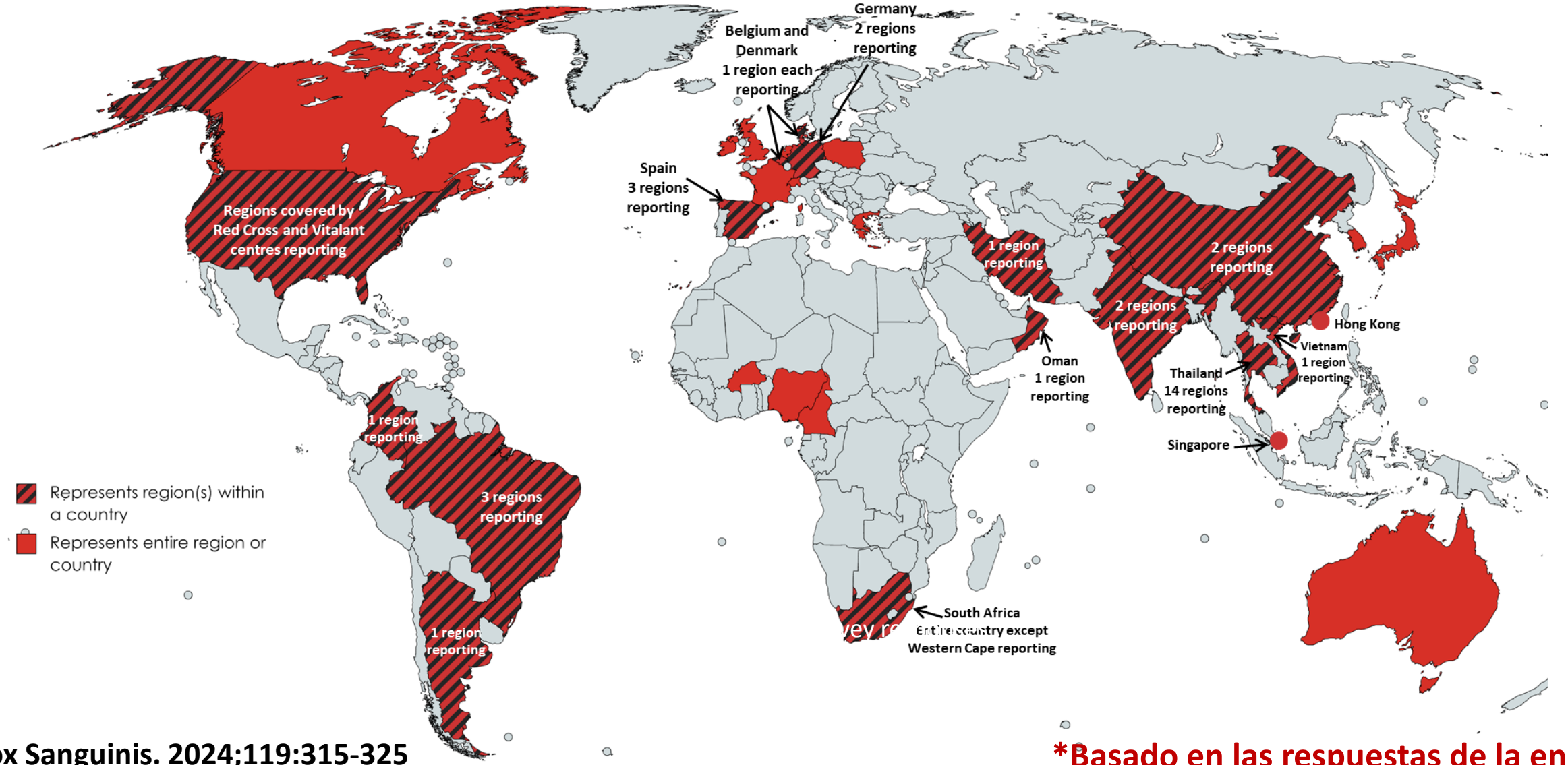
José Eduardo LEVI(1,2), Silvano WENDEL(1,2), Deise Tihe TAKAOKA(2), Isabela Cristina SILVA(2), Juliana Polachini de CASTRO(2), Mário A. TOREZAN-FILHO(1,2), Jorge GHANAME(3), Romualdo GIOACHINI(4,5), Joselito BRANDÃO(5), Evaldo Pasquini LANDI(6), Antônio César TEIXEIRA(7) & Edison Luis DURIGON(8)





International review of blood donation nucleic acid amplification testing

Regiones/países que realizan NAT*



Vox Sanguinis. 2024;119:315-325

*Basado en las respuestas de la encuesta

International review of blood donation nucleic acid amplification testing

PAÍS	CENTRO	AUTORES
COLOMBIA	Instituto Distrital de Ciencia Biotecnología e Innovación en Salud –IDCBIS, Bogotá	• Bernardo A. Camacho Rodriguez • Lisbeth J.C. Soto Coral • Paula A. Gaviria García
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	Hospital Sírio-Libanês Blood Bank, São Paulo	• Silvano Wendel
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	Regional Blood Center of Ribeirão Preto,	• Rochele Azevedo França
ARGENTINA		
	Fundación Banco Central de Sangre, Córdoba	• Sebastián Blanco
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Vox Sanguinis. 2024;119:315-325

IMPLEMENTACIÓN DE NAT EN EL TAMIZAJE SANGUÍNEO EN LATINOAMERICA -2024

PAÍS	NAT	OBLIGATORIO
Brasil	x	SÍ
Ecuador	x	SÍ
Argentina	x	EN ALGUNAS PROVINCIAS
Cuba	x	?
Panama	x	SÍ
Paraguay	x	SÍ
Chile	x	
Curazao	x	
Colombia	x	
Costa Rica	x	
República Dominicana	x	
Guatemala	x	
Honduras	x	
México	x	
Perú	x	
El Salvador	x	

Vox Sanguinis 2024;1–11.

TABLE 4 NAT-positive and NAT-yield donations by region, implementation to 2019.

	Africa ($n = 1$)	Asia and Western Pacific ($n = 11$)	Europe ($n = 15$)	North America ($n = 3$)	South America ($n = 5$)	Total ($n = 35$)
HIV						
Donations tested (*n*)	8,372,857	183,612,566	142,102,177	179,847,163	3,167,924	517,102,687
NAT-positive donations (*n*)	22,656	2575	1829	4794	1060	32,914
NAT positivity (rate[a])	2705.89	14.02	12.87	26.66	334.60	63.65
NAT yield[b] donations (*n*)	764	187	84	108	10	1153
NAT yield[b] (rate[b])	91.25	1.02	0.59	0.60	3.16	2.23
HCV						
Donations tested (*n*)	8,372,857	183,612,566	164,554,178	180,927,967	2,480,395	539,947,963
NAT-positive donations (*n*)	855	7926	10,968	54,153	1206	75,108
NAT positivity (rate[a])	102.12	43.17	66.65	299.31	486.21	139.10
NAT yield[b] donations (*n*)	50	262	191	614	4	1121
NAT yield[b] (rate[b])	5.97	1.43	1.16	3.39	1.61	2.08
HBV						
Donations tested (*n*)	8,372,857	152,221,471	102,928,968	103,272,077	2,418,536	369,213,909
NAT-positive donations (*n*)	12,462	33,093	15,975	5852	714	68,096
NAT positivity (rate[a])	1488.38	217.40	155.20	56.67	295.22	184.44
NAT yield[b] donations (*n*)	2318	11,116	897	124	10	14,465
NAT-yield[b] (rate[b])	276.85	73.03	8.71	1.20	4.13	39.18

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(4):862-870.

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	

	NAT YIELD	N CRIBADAS	TASA	TASA/ MILLÓN
HBV	42	5.795.424	1:138.000	7,24
HIV	63	13.610.536	1:216.040	4,62
HCV	28	13.610.536	1:486.000	2,05

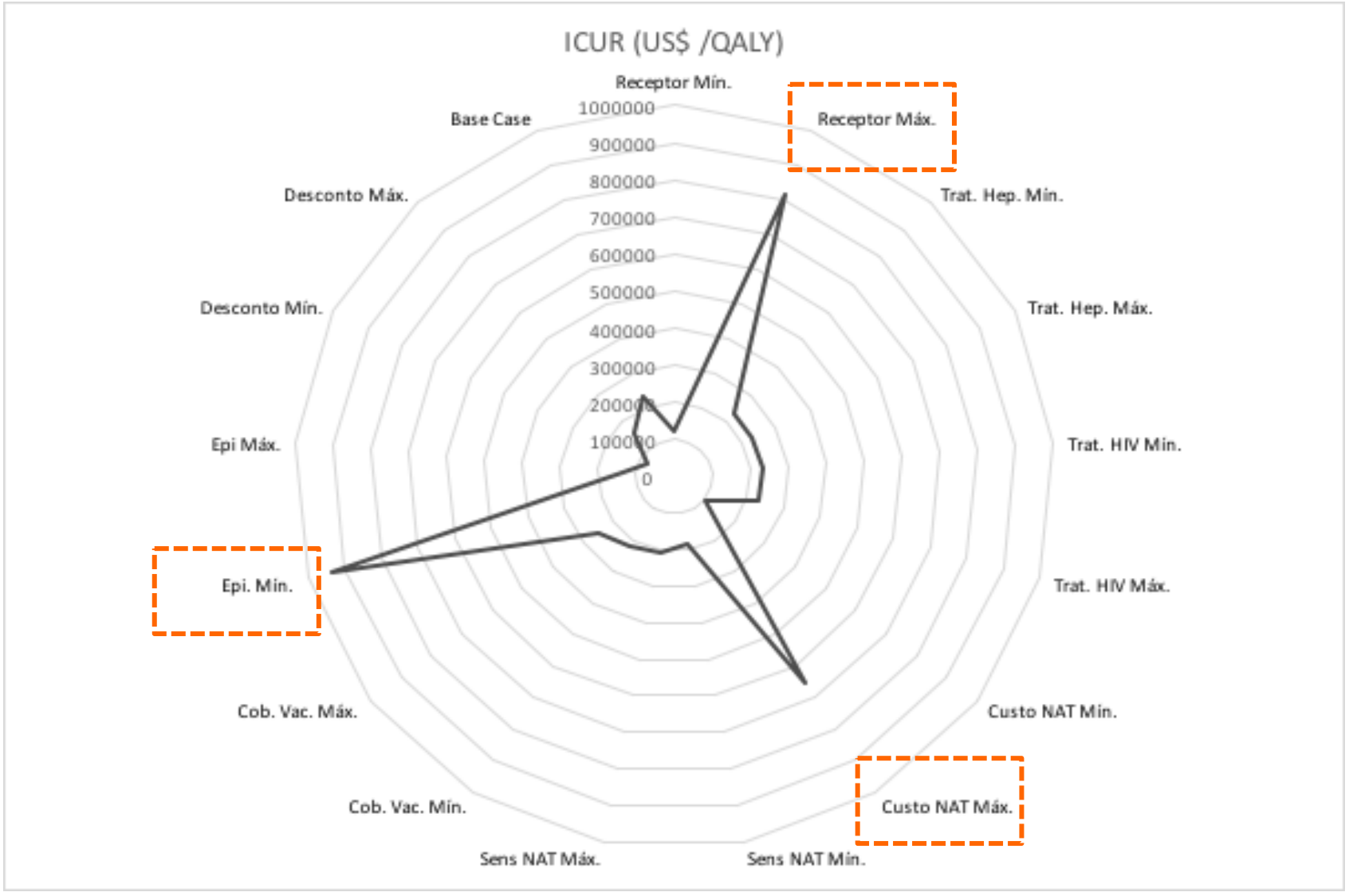
DATOS NAT-BRASIL (2011-set/2022)

	NAT+ (VENTANAS)	N Cribadas	TASA	TASA/ MILLÓN
HBV	121	**25.092.656**	1:207.377	**4.8**
HIV	171	**32.910.768**	1:192.460	**5.2**
HCV	56	**32.910.768**	1:582.335	**1.7**

Fonte: Coordenação-Geral de Sangue e Hemoderivados - Ministério da Saúde, Septiembre de 2022.

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].



pathogens

MDPI

Article

Retrospective Study of the Seroprevalence of HIV, HCV, and HBV in Blood Donors at a Blood Bank of Western Mexico

José de Jesús Guerrero-García [1,*], Alejandra Guadalupe Zúñiga-Magaña [2], Juan Carlos Barrera-De León [3,4], Rafael Magaña-Duarte [1] and Daniel Ortuño-Sahagún [2,*]

Table 4. Overview of seroprevalences based on NAT-reactive donors classified by seroreactive and seronegative (window periods) results.

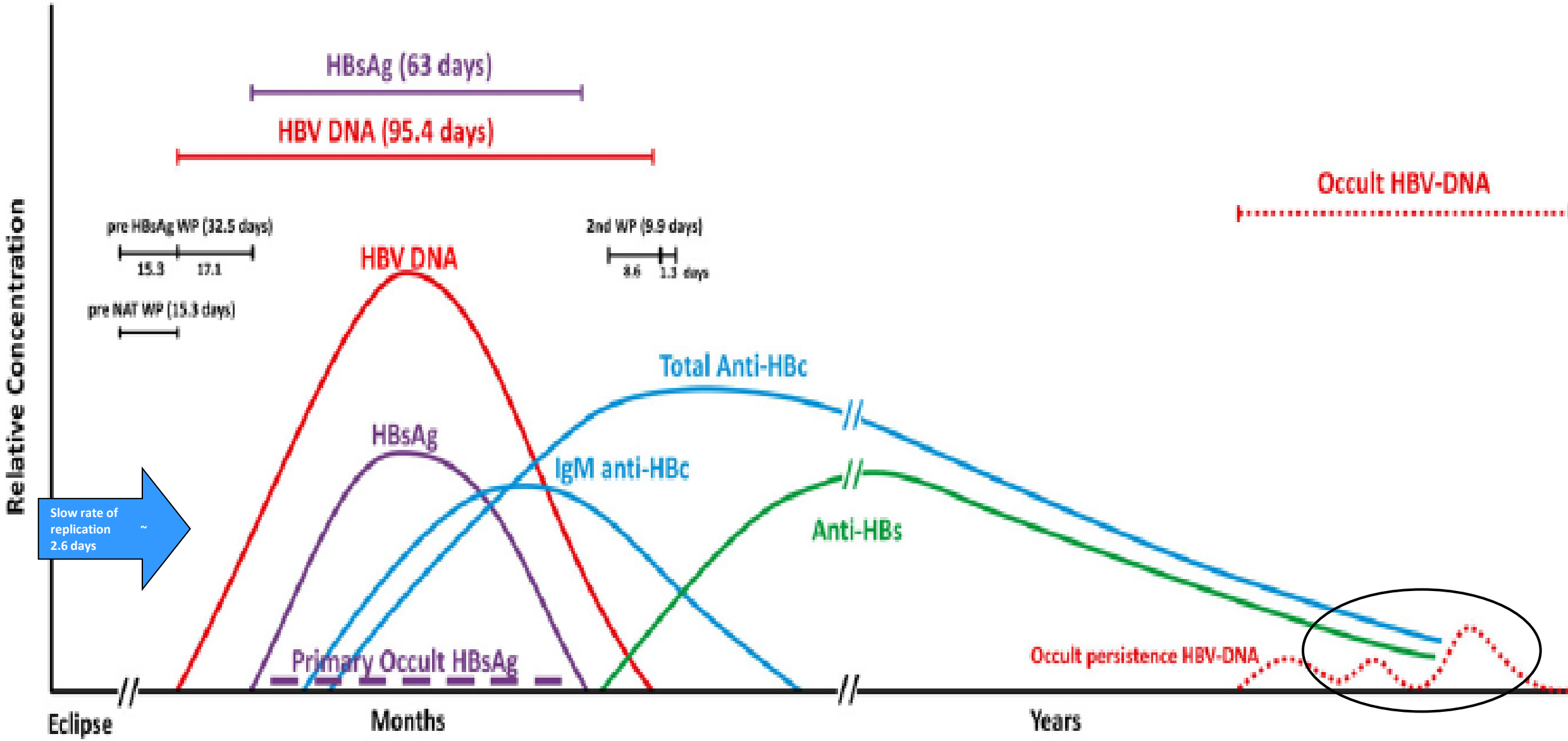
TTIs	Seroreactive + NAT-Reactive	Percentage (%)	Rate	CI (95%)	Seronegative + NAT-Reactive	Rate	CI (95%)	Total (Positive-Confirmed Seroreactive)	Percentage (%)	Rate	CI (95%)
HIV	32	0.0398	3.98	2.60–5.36	1	0.12	0.00–0.37	33	0.041	4.10	2.70–5.51
HCV	45	0.056	5.6	3.96–7.23	4	0.5	0.01–0.99	49	0.061	6.10	4.39–7.80
HBV	20	0.0249	2.49	1.40–3.58	2	0.25	0.10–0.59	22	0.027	2.74	1.59–3.88

Rates are expressed in cases per 10,000. TTIs, transfusion-transmissible infections; HIV, human immunodeficiency virus; HCV, hepatitis C virus; HBV, hepatitis B virus; CI, confidence interval (95%).

TASA VENTANAS NAT+ POR 100,000 DONANTES			
	MEXICO	SUDAMÉRICA	
HIV	1.2	0.3	4X
HCV	5	0.16	31X
HBV	2.5	0.4	6X

USO DEL ANTI-HBc NA TAMIZAJE SANGUÍNEA

PAÍSES QUE EMPLEAN	PAÍSES QUE NO EMPLEAN
Brasil	Ecuador
Perú	México
Argentina	Cuba
Colombia	Bolivia
Costa Rica	Chile
Alemania	China
Francia	Italia
UK (since 2022)	Portugal
EE.UU	España
Holanda	Grecia
Japón	India



Modified from Vermeulen et al, Transfusion 2012; 52, 880-892

HBsAg Non-Reactive HBV Infection in Blood Donors: Transmission and Pathogenicity

Wolfram H. Gerlich,[1]* Franz F. Wagner,[2] Michael Chudy,[3] Lene Holm Harritshoj,[4] Annette Lattermann,[5] Sandra Wienzek,[6] Dieter Glebe,[1] Mona Saniewski,[1] Christian G. Schüttler,[1] Ulrike C. Wend,[1] Wulf R. Willems,[1] Ursula Bauerfeind,[2] Christine Jork,[2] Gregor Bein,[6] Per Platz.[7] Henrik Ullum.[4] and Ebbe Dickmeiss[4]

Journal of Medical Virology 79:S32–S36 (2007)

TABLE I. HBV Markers in 55 Recipients of Blood Products From 5 Occult Infected Donors

Donor	Number of recipients	Fatal hepatitis	Anti-HBc	
			Positive[a]	Negative
A	6	1[b]	3	2
B	8	1[b]	4	3
C	13	1[c]	2	10
D red cells	13	0	5	8
D plasma	11	0	11	0
E[d]	4	0	1	3
Total	55	3	26	26

One window-period donation in two years of individual donor-nucleic acid test screening for hepatitis B, hepatitis C and human immunodeficiency virus

José Eduardo Levi
Ricardo Antonio D'Almeida Pereira
Márcia Bernardino de Carvalho Polite
Mariza Aparecida Mota
Silvia Patricia Nunez
João Renato Rebello Pinho
José Mauro Kutner

Objective: To describe general data on nucleic acid/serology testing and report the first hepatitis B-nucleic acid testing yield case of an immunized donor in Brazil.

Methods: A total of 24,441 donations collected in 2010 and 2011 were submitted to individual nucleic acid testing for hepatitis B, hepatitis C and human immunodeficiency virus using the TaqMan® MPX kit (Roche) on the Cobas s201 platform, in addition to routine screening for serological markers. Nucleic acid testing-reactive donations were further evaluated by real-time polymerase chain reaction using Cobas AmpliPrep/ Cobas TaqMan hepatitis B virus, hepatitis C virus and human immunodeficiency virus tests.

Results: Thirty-two donations were reactive by nucleic acid testing, 31 were also serologically reactive and

Table 5 - Laboratorial data from the nucleic acid testing hepatitis B virus window period donation and follow-up samples

		Nucleic acid testing																
		Syphilis			Cobas TaqScreen		Cobas TaqMan Viral Load		Hepatitis B markers						Hepatic enzymes		
Sample ID	Date	EIE	FTA-ABS	VDRL	MPX v 1.0	MPX v 2.0			anti-HBc	HBsAg	Anti-HBs	Anti-HBs QT	Anti-HBe	Ag HBe	GGT	TGO	TGP
B300111217036	May 12, 2011	POS	POS	NEG	POS	HBV POS	Undetectable below 20 IU/mL		NEG	NEG	POS	19.3 UI/mL	NEG	NEG	15 U/L	15 U/L	29 U/L
B300111217292	May 18, 2011	POS	ND	ND	POS	ND	ND	ND	NEG	NEG	POS	17.8 UI/mL	NEG	NEG	15 U/L	32 U/L	41 U/L
B300111218043	June 1, 2011	ND	ND	ND	POS	ND	ND	ND	NEG	NEG	POS	31.6 UI/mL	ND	ND	ND	ND	ND
B300112228330	January 12, 2012	ND	ND	ND	NEG	ND	ND	ND	NEG	NEG	POS	109.0 UI/mL	ND	ND	ND	ND	ND

Marked reduction in the incidence of transfusion-transmitted hepatitis B virus infection after the introduction of antibody to hepatitis B core antigen and individual donation nucleic acid amplification screening in Japan

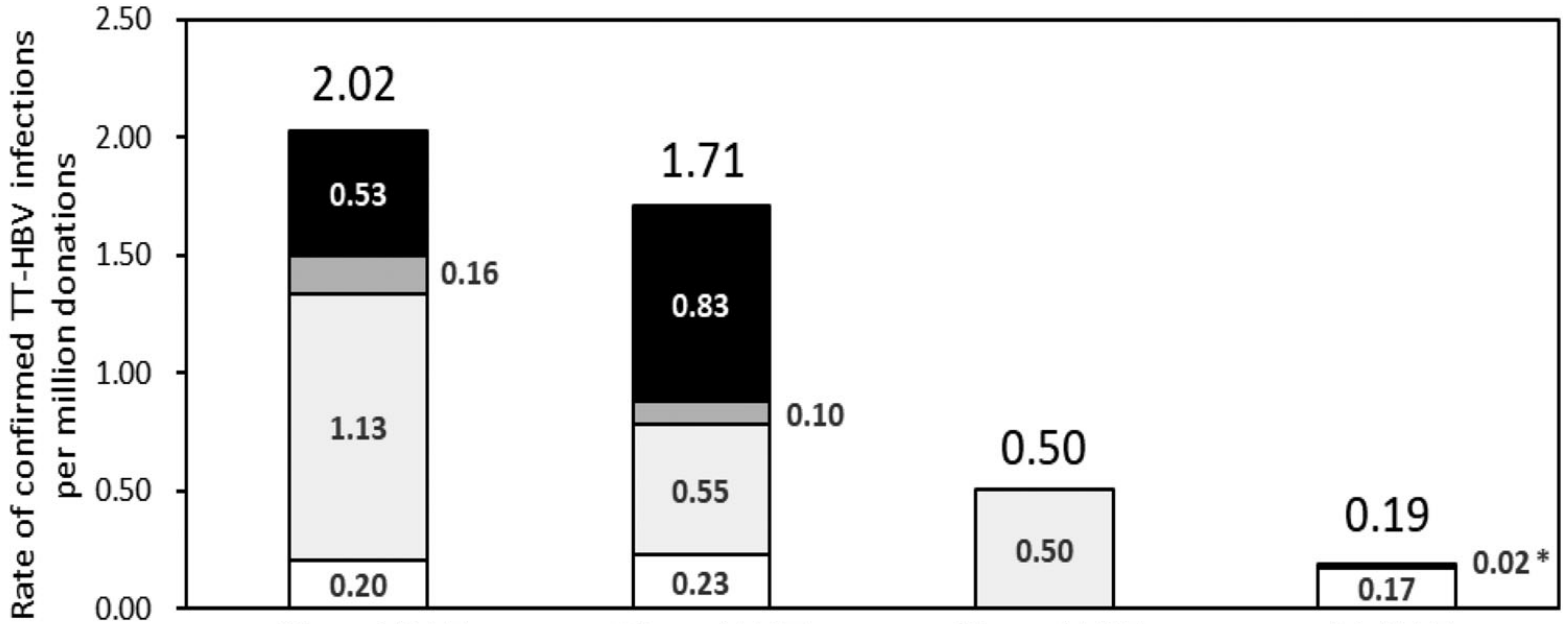
Transfusion. 2023;63:2083–2097.

Ami Tanaka[1] | Naoji Yamagishi[1] | Takashi Hasegawa[1] | Keiko Miyakawa[2] | Naoko Goto[2] | Keiji Matsubayashi[1] | Masahiro Satake[1]

TT-HBV DONANTES OBI

NAT POOL NEGATIVO

(A)

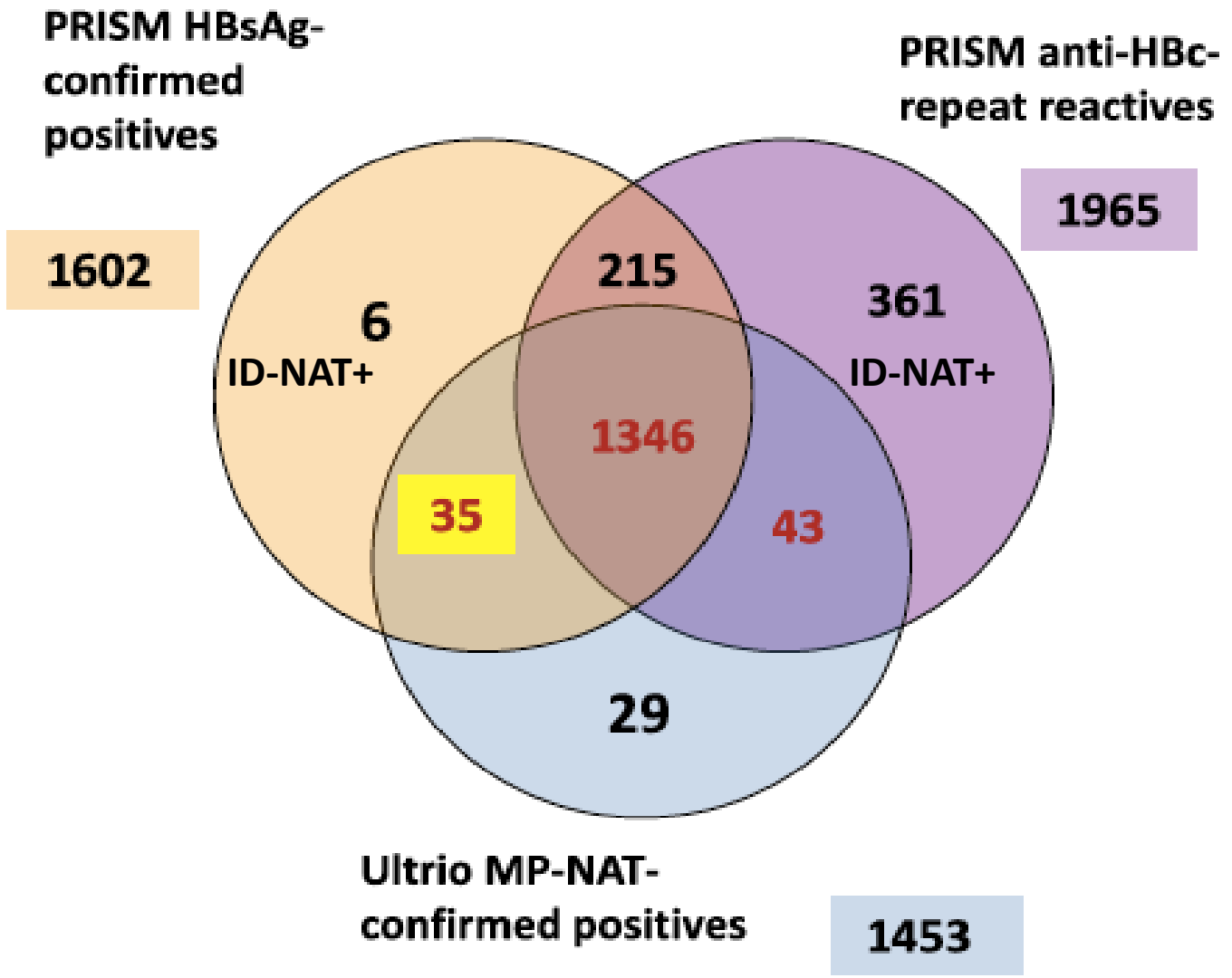


NAT system	50 pool NAT	20 pool NAT	20 pool NAT	ID-NAT
anti-HBc cutoff	Blood with weak anti-HBc accepted.		Blood positive for anti-HBc are all rejected.	
	12	12	1	1
Screening period	Feb. 2000–Jul. 2004	Aug. 2004–Jul. 2012	Aug. 2012–Jul. 2014	Aug. 2014–Dec. 2022
years	4.5	8.0	2.0	8.4
No. of donations	24,702,784	39,881,481	9,927,699	41,273,118

MX-DS3-2400001

Blood donor testing for hepatitis B virus in the United States: is there a case for continuation of hepatitis B surface antigen detection?

TRANSFUSION 2018;58;2166–2170



Blood donor screening in the Netherlands: Universal anti-HBc screening in combination with HBV nucleic acid amplification testing may allow discontinuation of hepatitis B virus antigen testing

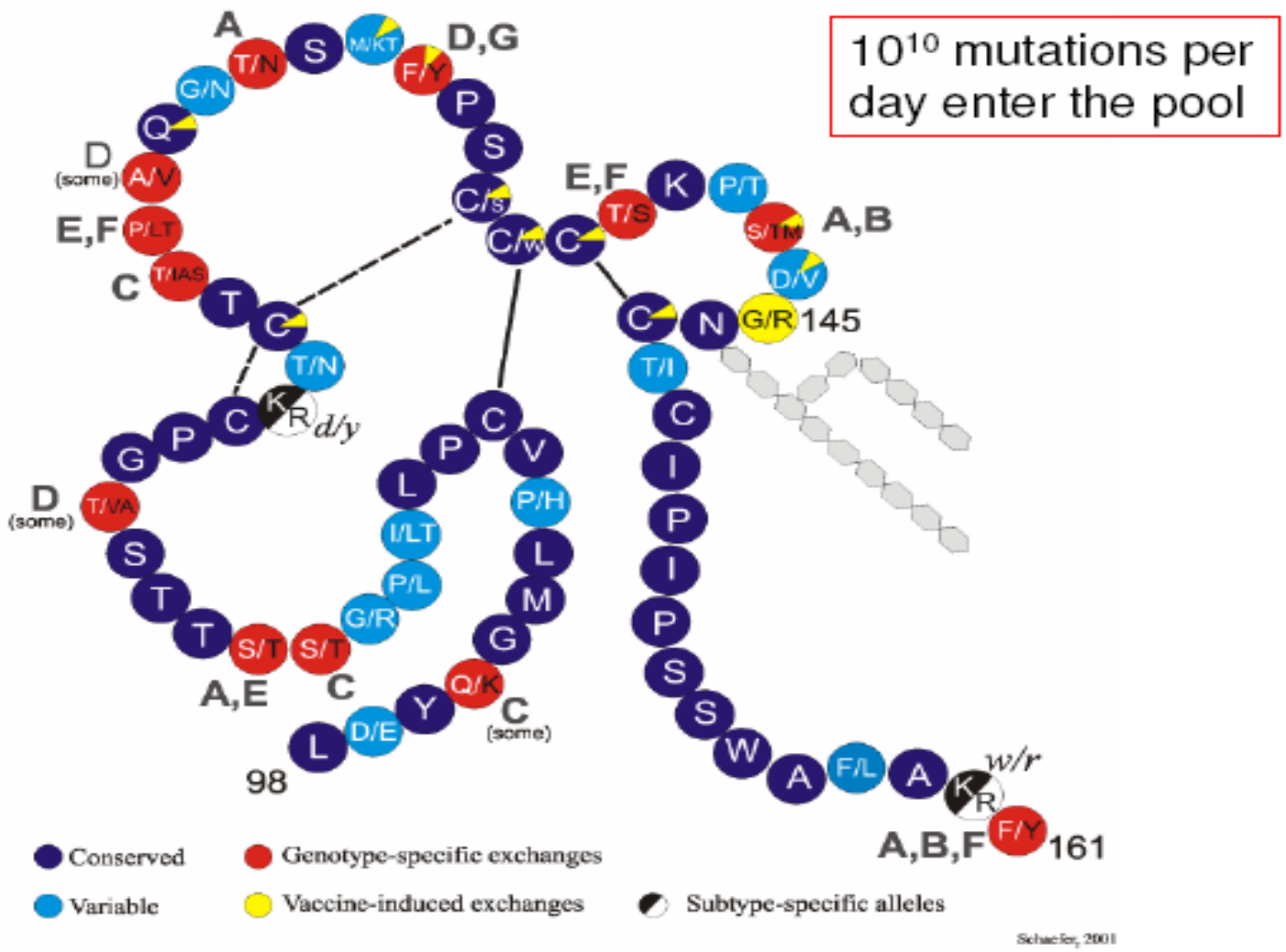
Transfusion. 2021;1–9.

Conclusión: **El cribado de donantes para HBV podría limitarse a MP-NAT y anti-HBc.** MP-NAT y anti-HBc mejoraron la seguridad de la sangre al interceptar donaciones de donantes con infección reciente u OBI, mientras que HBsAg no lo hizo. La pérdida innecesaria de donantes relacionada con el cribado anti-HBc es sustancial, pero no pone en peligro la continuidad del suministro de sangre.

A Novel Insertion in the Hepatitis B Virus Surface Protein Leading to Hyperglycosylation Causes Diagnostic and Immune Escape

Viruses **2023**, *15*, 838. https://doi.org/10.3390/v15040838

Genotype- and vaccine-escape induced specific exchanges in the *a* determinant of SHBs



10^{10} mutations per day enter the pool

JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 2006, p. 662–665 Vol. 44, No. 2
0095-1137/06/$08.00+0 doi:10.1128/JCM.44.2.662–665.2006

Group O Human Immunodeficiency Virus Type 1 Infection That Escaped Detection in Two Immmunoassays

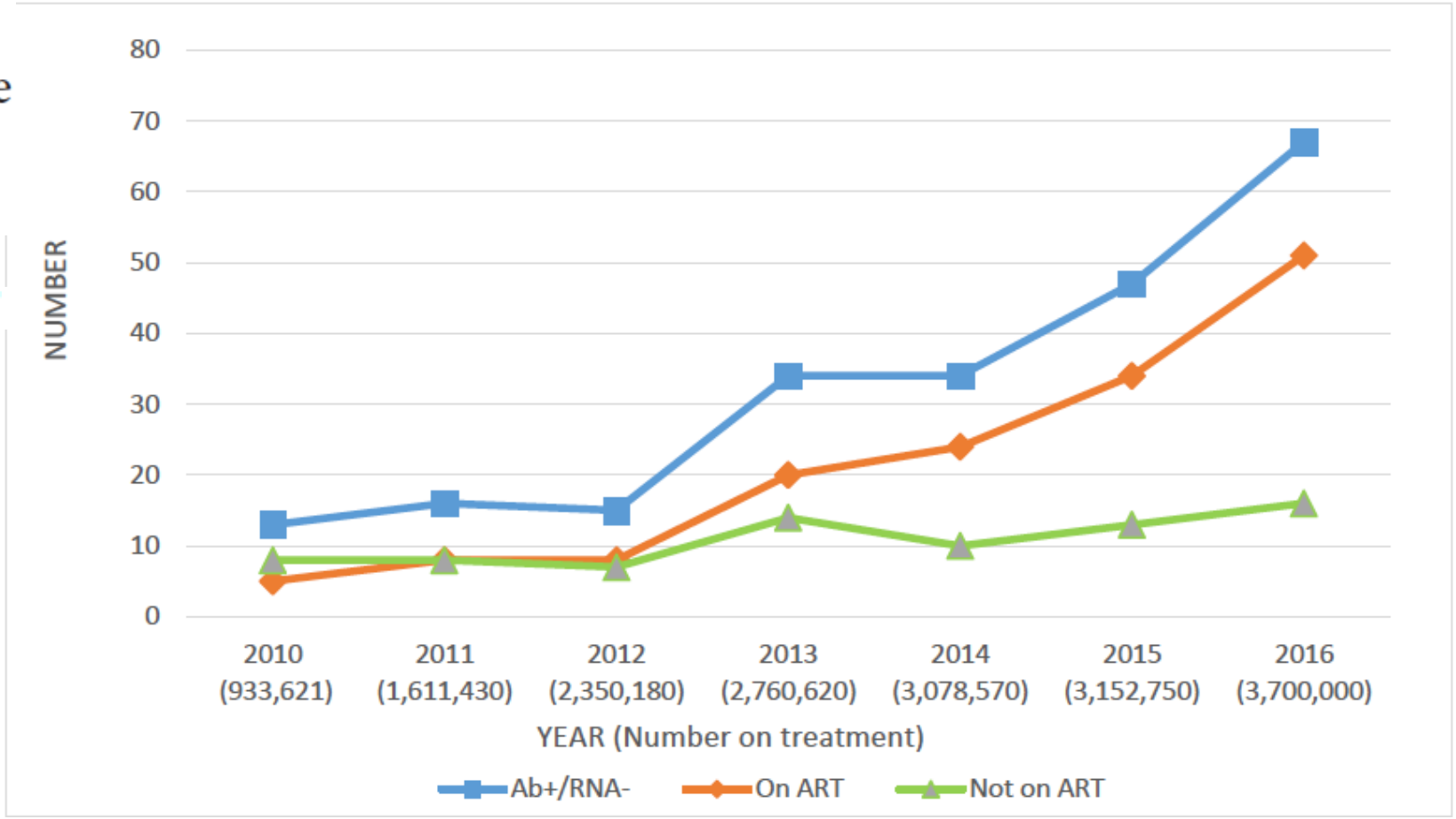
TABLE 2. Sequences of the immunodominant region (IDE) of gp41

Fragment	Sequence[a]
Group M consensus	.....RVLAVERYLKDQQLLGIWGCSGKLICTTAV
Group O consensus	.....RLLALETLIQNQQLLNLWGCKGRLVCYTSV
Case	.....RLLALETLLQNQQLLNLWGCKG**TR**ICYTSV

[a] The unusual dipeptide motif is in bold and underlined.

Discovery of False Elite Controllers: HIV Antibody-Positive RNA-Negative Blood Donors Found To Be on Antiretroviral Therapy

The Journal of Infectious Diseases® 2019;220:643–7



Results: 150 (66.4%) of 226 potential EC had detectable ART with increasing prevalence by year (OR=7.57 for 2016 vs. 2010, 95% CI 1.96-32.17).

Discussion: False presumptive EC status due to undisclosed ART represents a growing proportion of potential EC donors in South Africa coincident with the country's ART rollout.

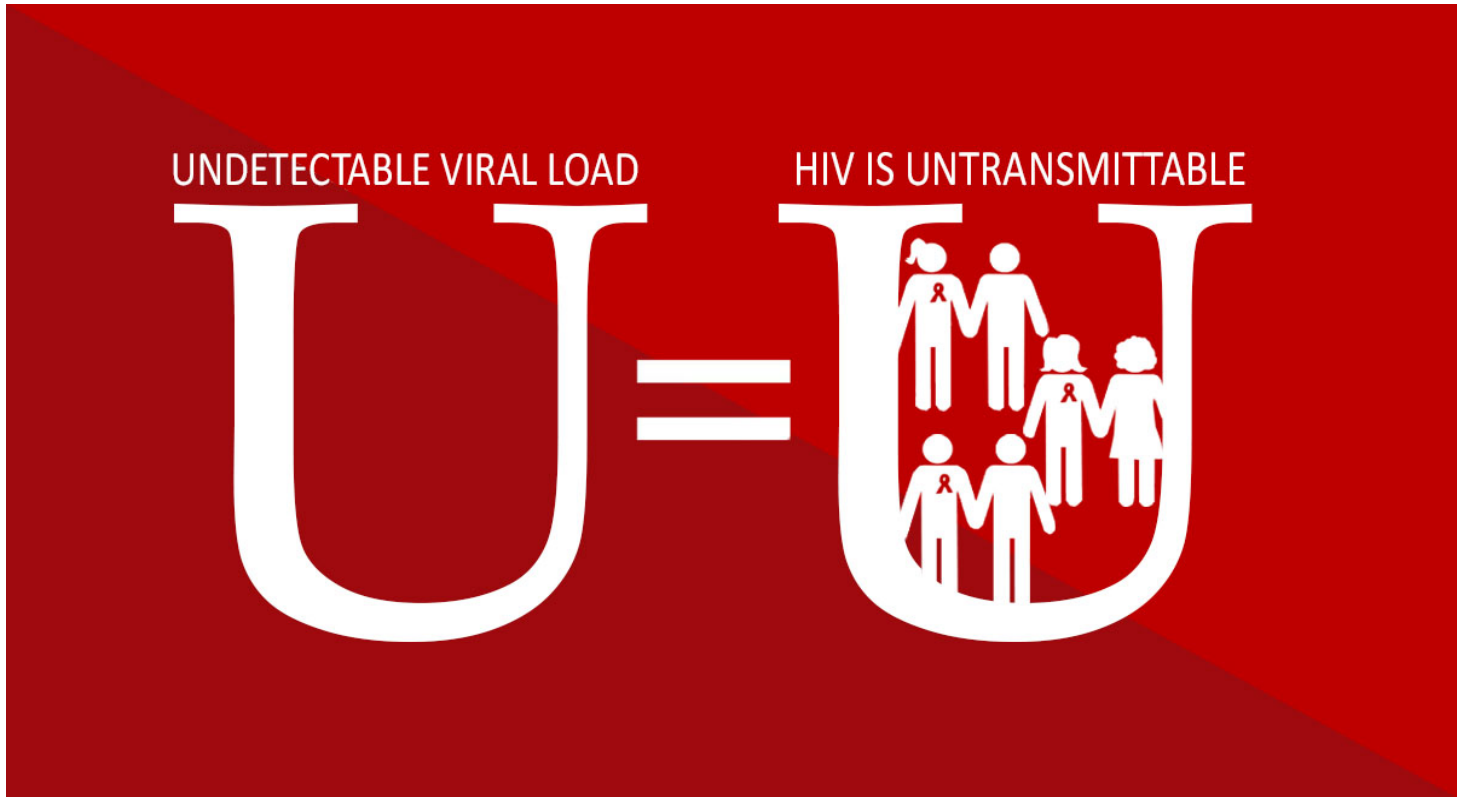
Robert W. Eisinger, PhD
Office of the Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.

Carl W. Dieffenbach, PhD
Division of AIDS, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.

Anthony S. Fauci, MD
Office of the Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.

HIV Viral Load and Transmissibility of HIV Infection

Undetectable Equals Untransmittable



NO PARA NOSOTROS EN SERVICIOS DE TRANSFUSIÓN DE SANGRE!!!

The HIV epidemic in Latin America: accomplishments and challenges on treatment and prevention

Curr Opin HIV AIDS 2019, 14:366–373

Table 1. Latin American countries that have either implemented a demonstration project or have made preexposure prophylaxis available through a national policy as of December 2018

Country	Guidelines	Demonstration project	National policy	Private sector
Argentina	Drafted	Planning	–	Yes[a]
Bahamas (The)	Available	–	Yes	–
Barbados	Available	–	Yes	Yes[a]
Bolivia	–	Planning	–	–
Brazil	Available	Implemented	Yes	–
Chile	Available	Planning	Planning	Yes[a]
Colombia	–	Planning	–	–
Cuba	Available	–	Yes	–
Dominican Republic	Drafted	Implemented	Planning	Yes[b]
Guatemala	Available	Planning	Planning	Yes[b]
Haiti	Available	Planning	Yes	–
Jamaica	–	Planning	–	–
Mexico	Available	Implemented	–	–
Paraguay	–	Planning	Planning	Yes[b]
Peru	Available	Implemented	–	Yes[a]

Source: WHO.
[a]Through private physicians.
[b]Through nongovernmental organizations.

¿Qué es PrEP? = PreExposure Prophylaxis

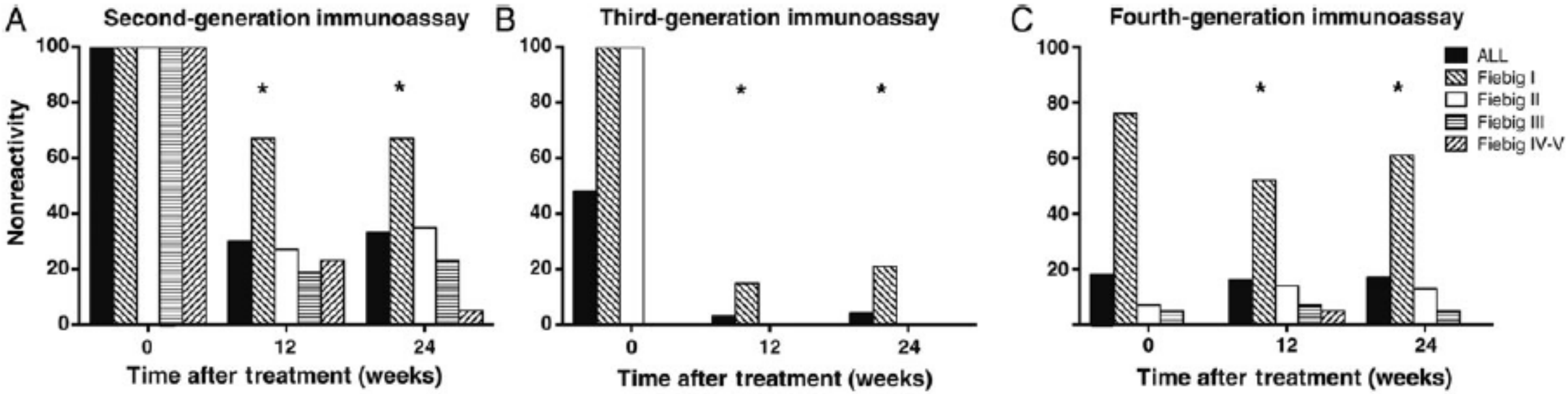
¿Qué es PEP? = PosExposure Prophylaxis

Truvada o Descovy (FTC+TDF) son una combinación de emtricitabina (FTC) y tenofovir disoproxil fumarato (TDF).

Los dos medicamentos pertenecen a la clase de Inhibidores de la transcriptasa reversa (Nucleoside/Nucleotide Reverse Transcriptase Inhibitors)

Initiation of Antiretroviral Therapy During Acute HIV-1 Infection Leads to a High Rate of Nonreactive HIV Serology

Clinical Infectious Diseases® 2016;63(4):555–61



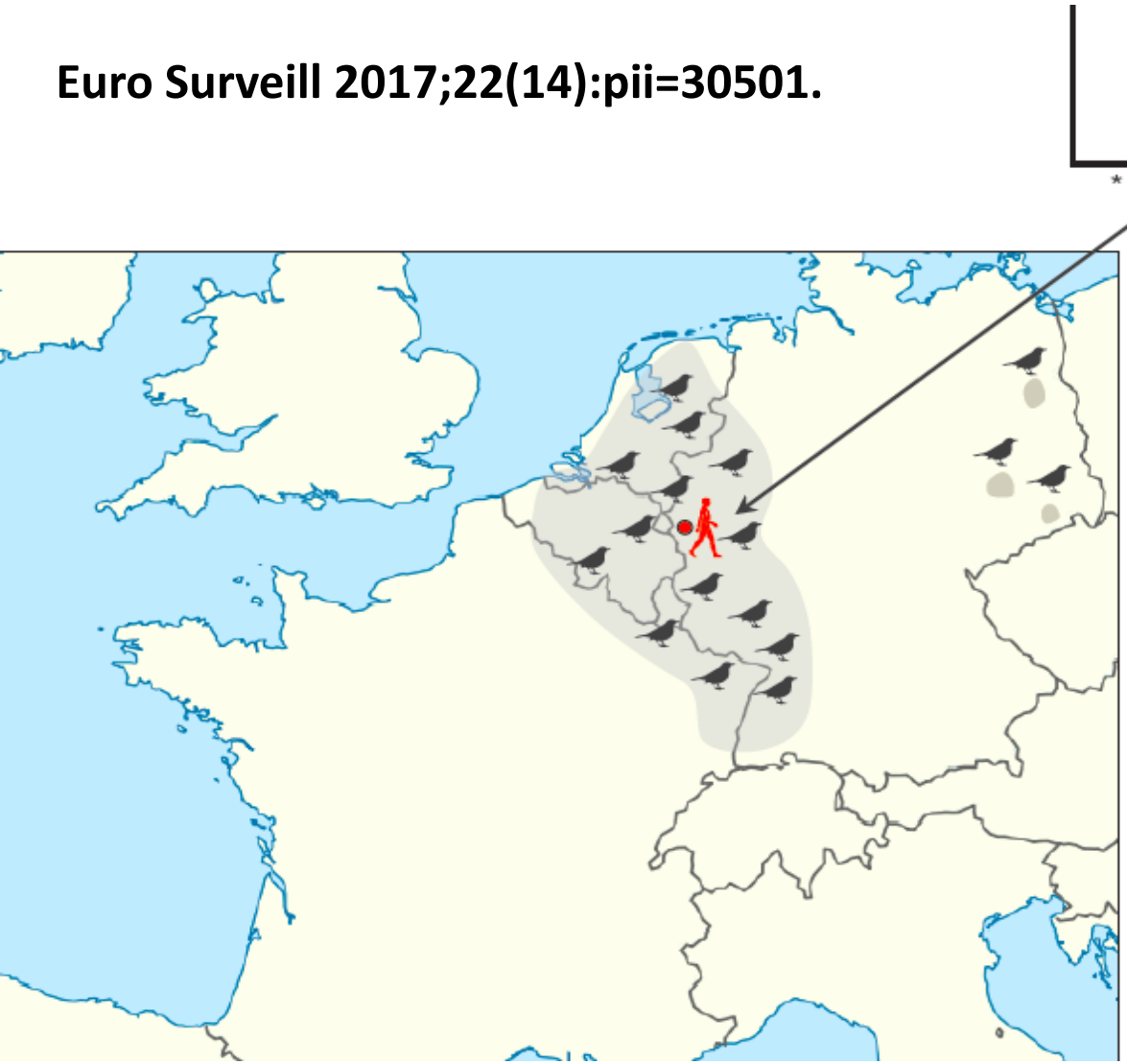
Influence of unreported HIV prophylaxis on the kinetics of post-blood donation HIV seroconversion

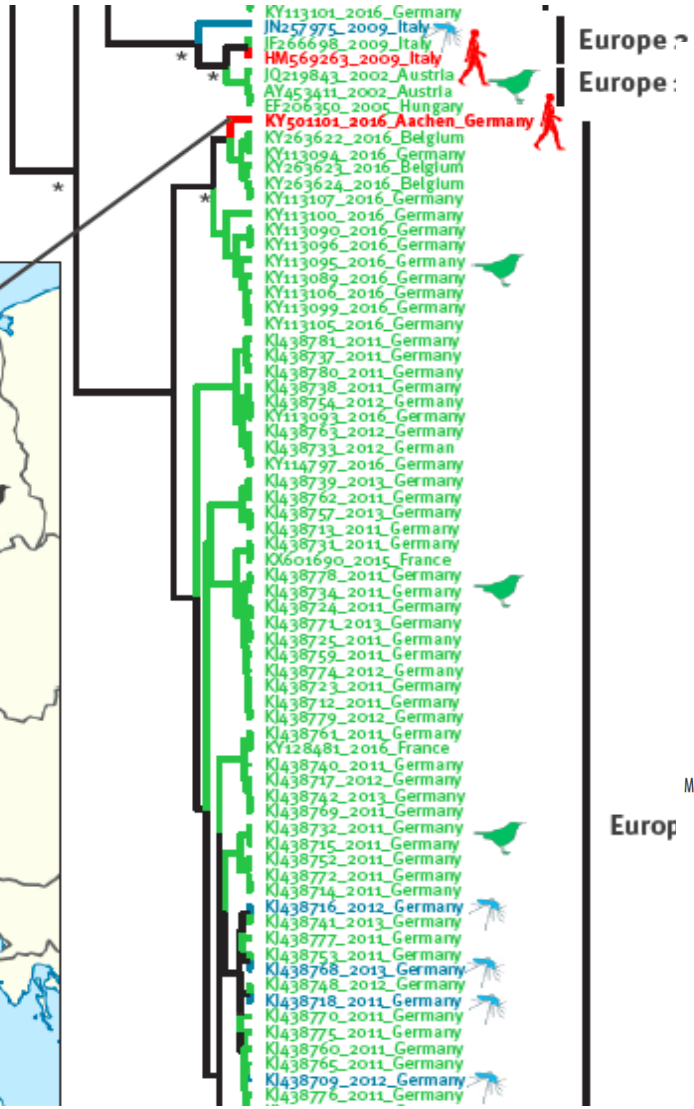
Transfusion. 2021;1–5.

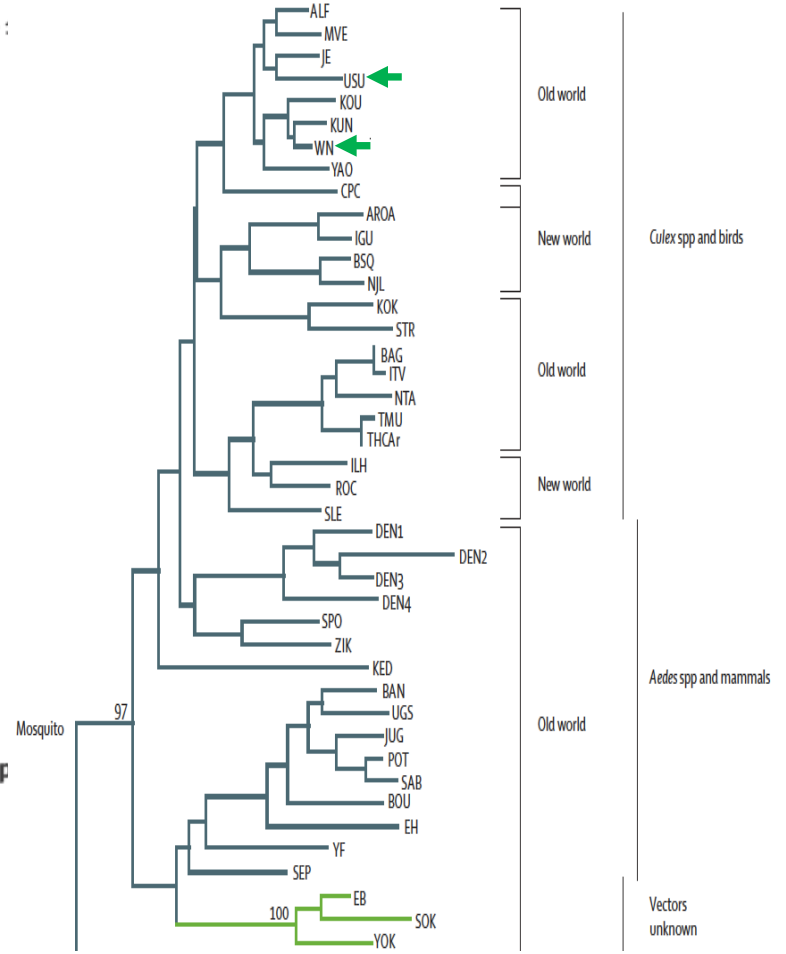
Donor	Time (days)	CMIA serology[a]	Pooled qualitative RT-PCR	Individual qualitative RT-PCR	Quantitative RT-PCR[b]
One	Index	Negative	Borderline	Positive	<10
PeP	48	Negative	ND	Negative	Negative
	70	1.13	ND	Negative	Negative
	105	35.4	ND	Positive	151
Two	Index	Negative	Positive	Positive	4774
	6	Negative	ND	ND	6080
	25	Positive	ND	Positive	ND

Blood donor screening for West Nile virus (WNV) revealed acute Usutu virus (USUV) infection, Germany, September 2016

Euro Surveill 2017;22(14):pii=30501.

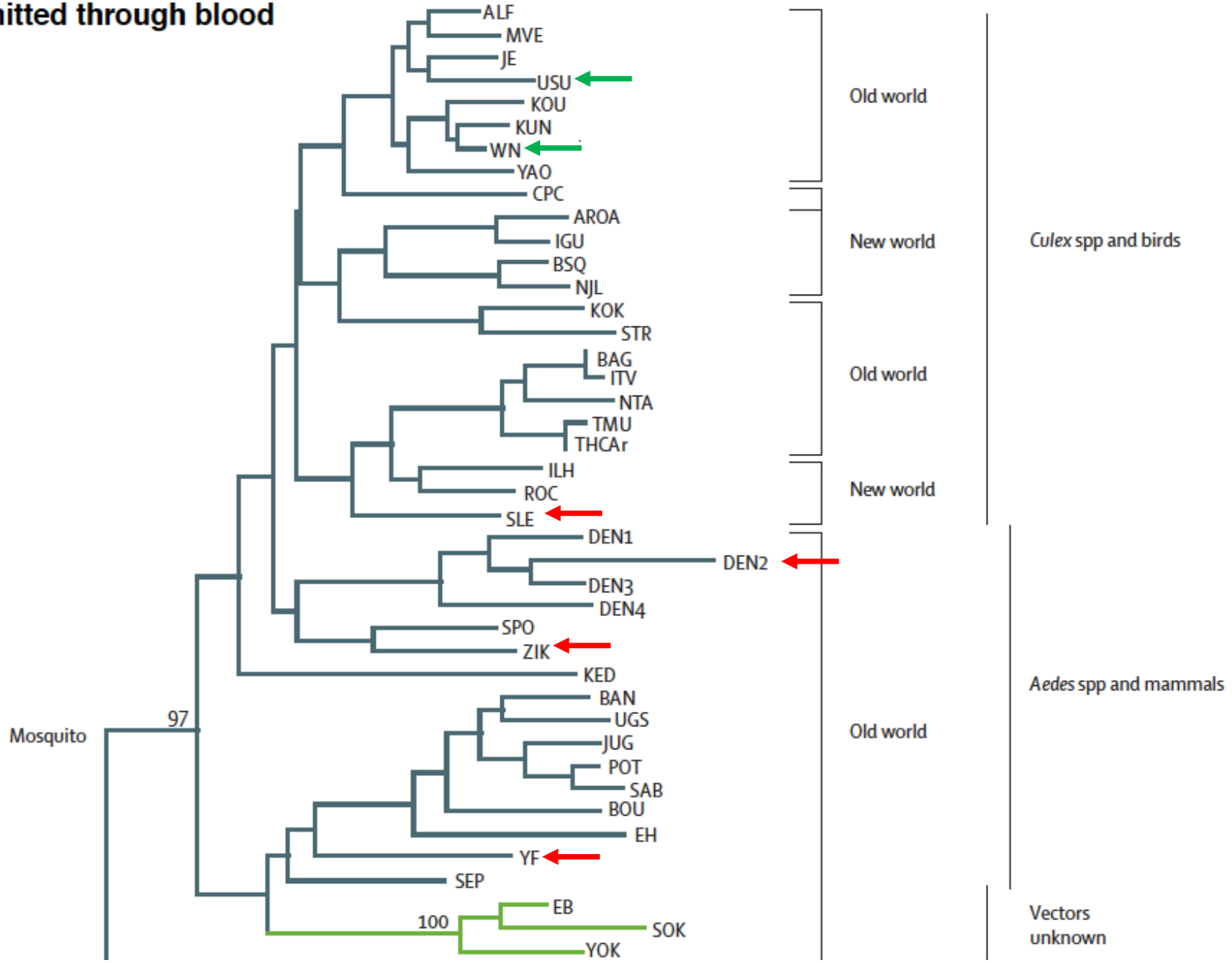






St. Louis encephalitis virus possibly transmitted through blood transfusion—Arizona, 2015

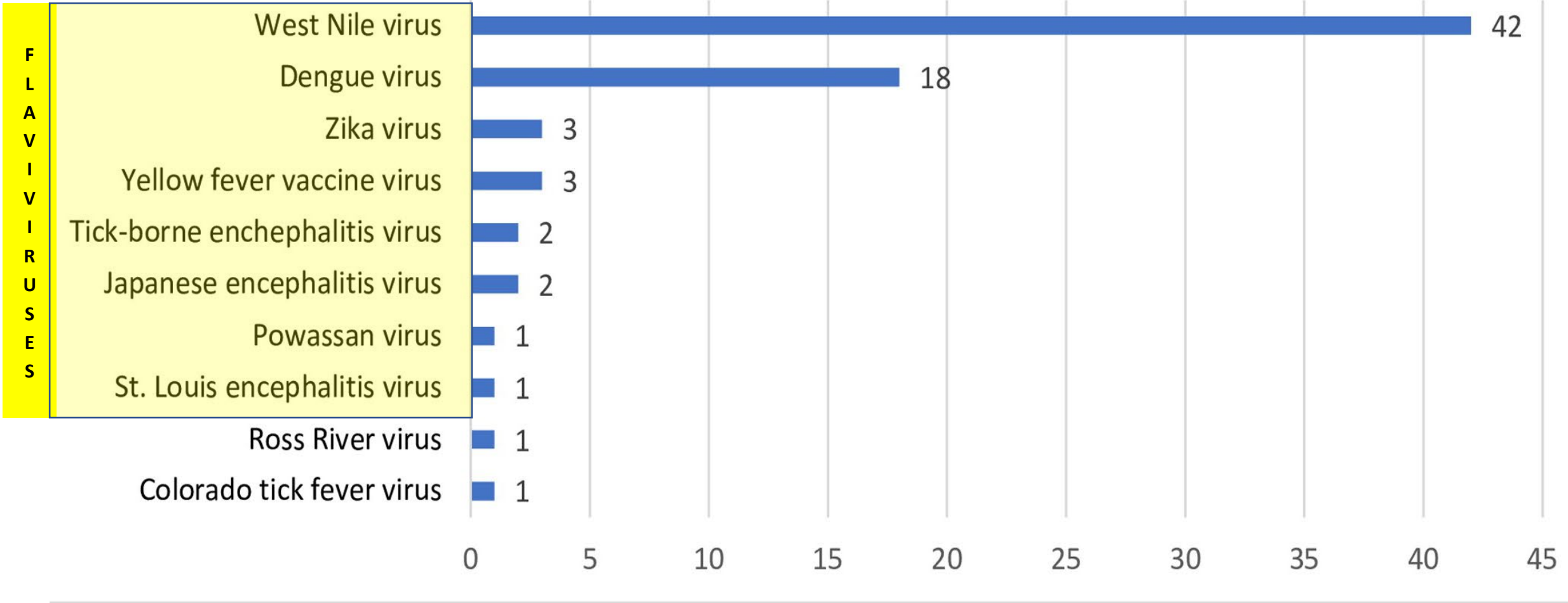
Transfusion. 2017 December ; 57(12): 2987–2994.



Transfusion-transmitted arboviruses: Update and systematic review

Ángel Giménez-Richarte[1]*, María Isabel Ortiz de Salazar[1], María-Paz Giménez-Richarte[2], Miriam Collado[1], Pedro Luís Fernández[1], Carlos Clavijo[1], Laura Navarro[1], Cristina Arbona[1], Pascual Marco[3,4], Jose-Manuel Ramos-Rincon[4]*

PLOS Neglected Tropical Diseases | https://doi.org/10.1371/journal.pntd.0010843 October 6, 2022

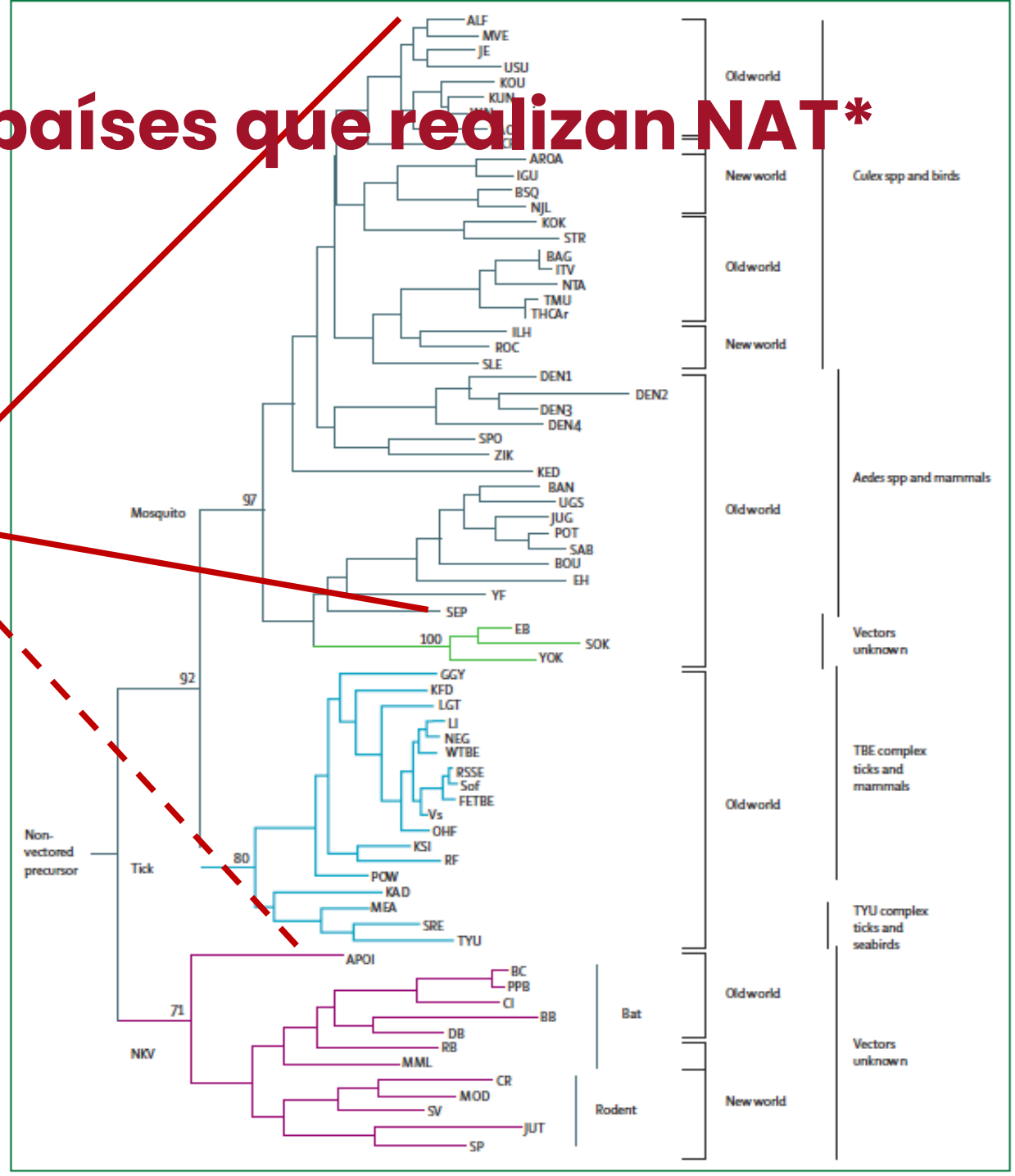


Pathogenic flaviviruses

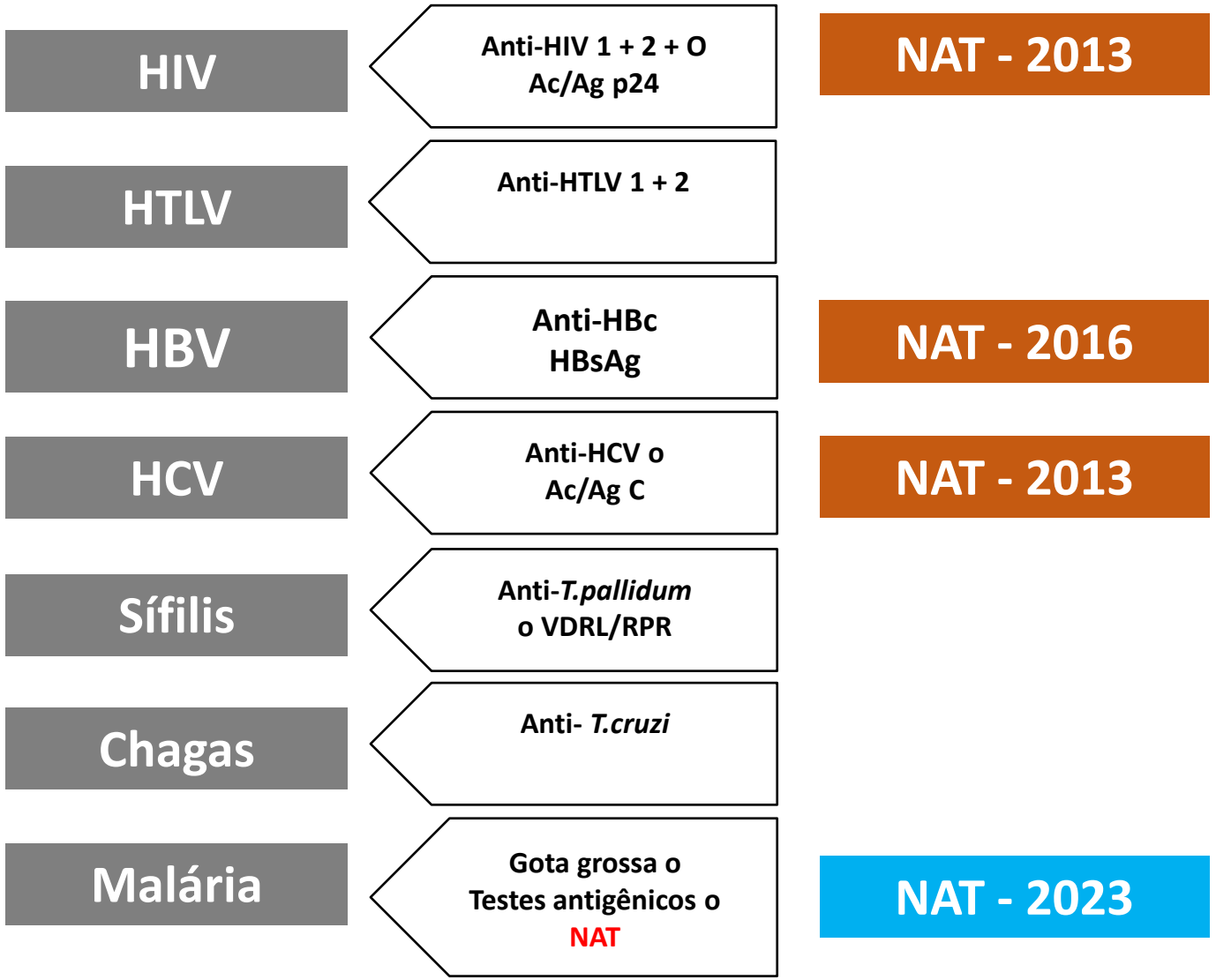
Lancet 2008; 371: 500–09

Regiones/países que realizan NAT*

PanFlavivirus NAT?



PRUEBAS OBLIGATORIAS DONACIONES DE SANGRE, BRASIL 2024



EXPERIENCIA BRASILEÑA CON NAT MALARIA 2023-SET.2024

	Donaciones cribadas	NAT+	Prevalencia
Total*	**3.602.813**	**57**	**1 / 63.207**
HEMOAM	94.415	8	**1 / 11.802**
HEMOSC	155.349	4	**1 / 38.807**
HEMORIO*	667.973	10	**1 / 66.797**

Fontes: Coordenação-Geral de Sangue e Hemoderivados - Ministério da Saúde, Setembro/2023
***Aula Luiz Amorim, HEMO 2024**

AGENTES EMERGENTES TRANSMISIBLES POR TRANSFUSIÓN PARA LOS QUE SE HA INSTITUIDO ALGÚN TIPO DE INTERVENCIÓN (>año 2000)

AGENTE	TIPO	VIA DE EXPOSICIÓN	AÑO INICIO	INTERVENCCIÓN
WEST NILE	VÍRUS	MOSQUITO	2003	NAT
CHIKUNGUNYA	VÍRUS	MOSQUITO	2005/2006	NAT y PRT
ZIKA	VÍRUS	MOSQUITO	2016	NAT
BABESIA	PROTOZOÁRIO	GARRAPATAS	2020	NAT
HEPATITE E	VÍRUS	AGUA/ALIMENTOS	2020	NAT
MALÁRIA	PROTOZOÁRIO	MOSQUITO	2023	NAT

MUCHAS GRACIAS!

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