EFFICACY OF TESTING SCENARIOS

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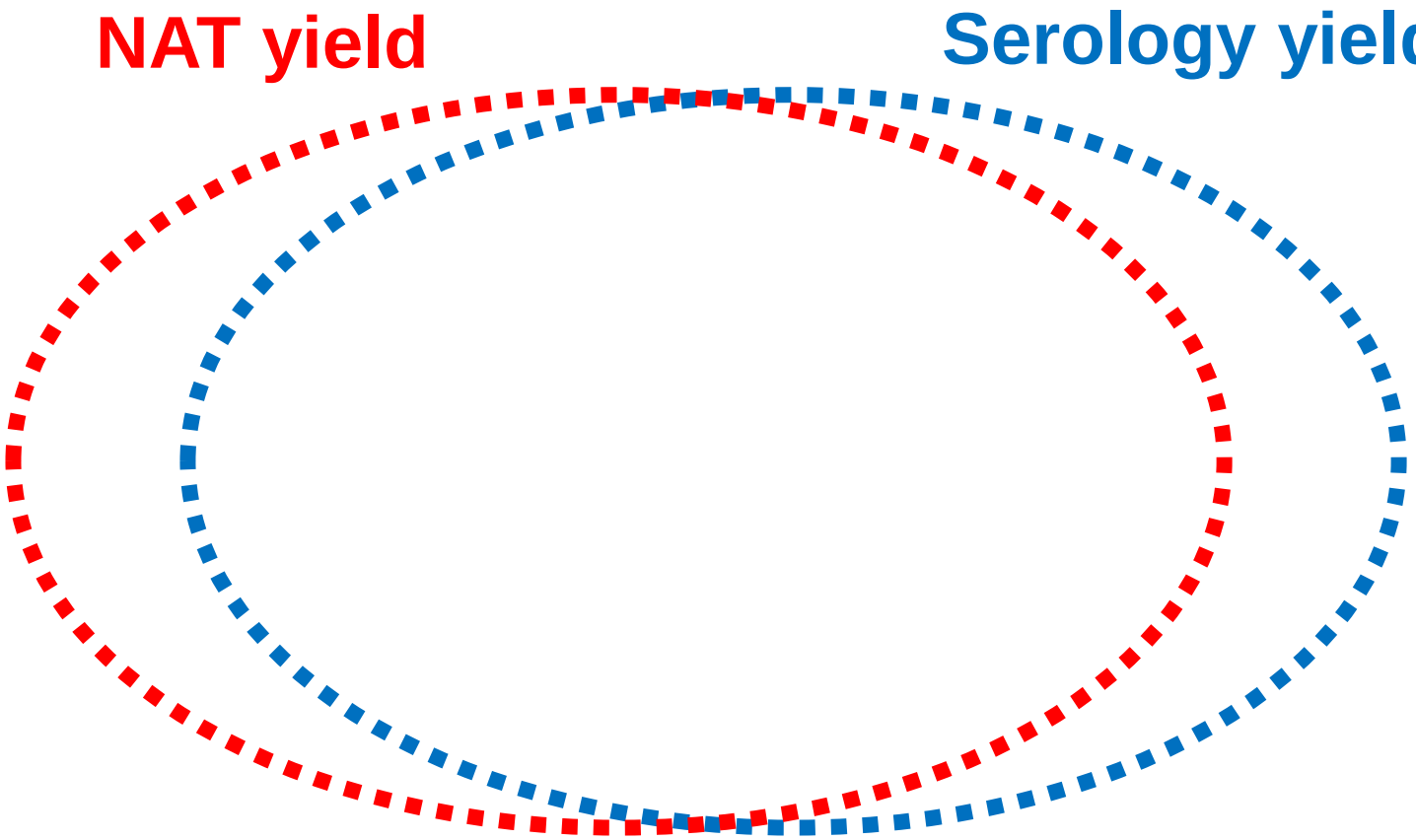
LELIE RESEARCH
BLOOD SAFETY • DIAGNOSTICS • QUALITY CONTROL

Cost Effectiveness Paradigm
NAT and Serology for HBV, HCV and HIV



Cost Effectiveness Paradigm
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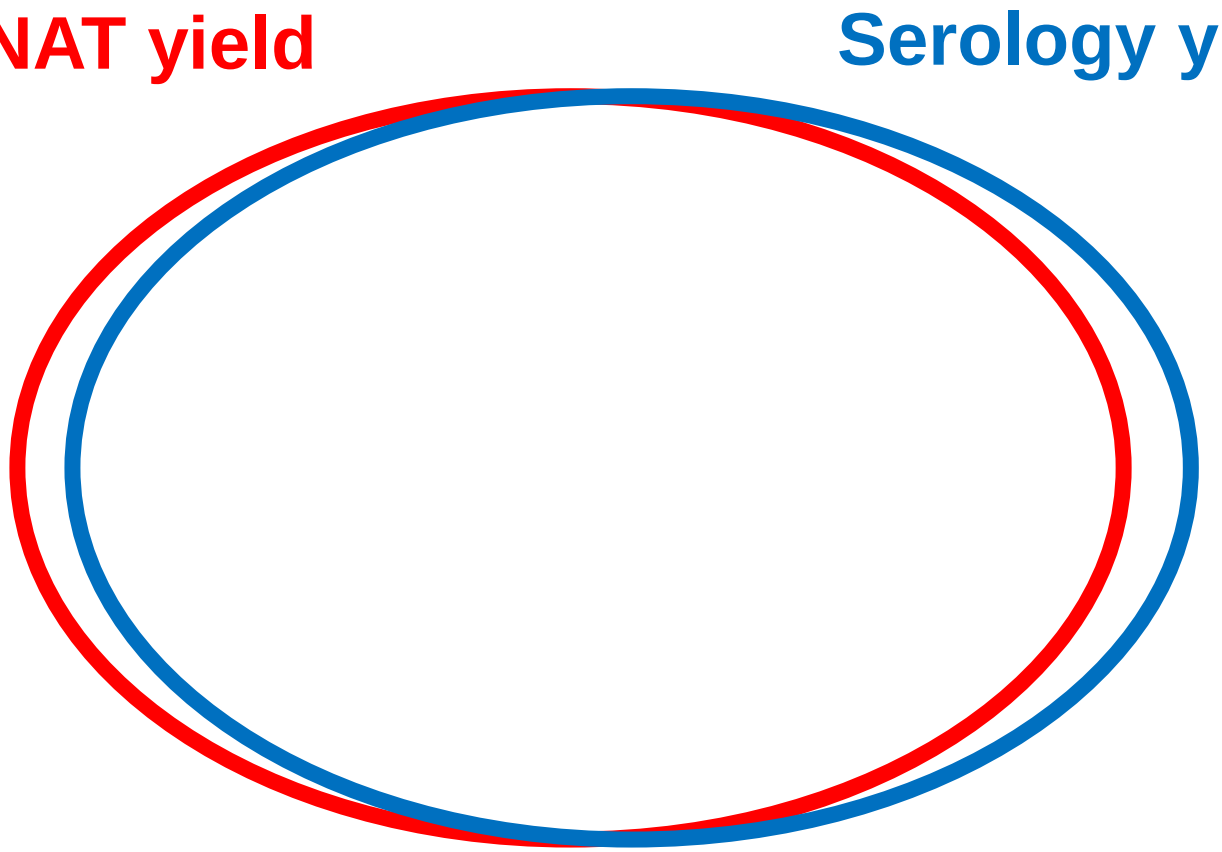

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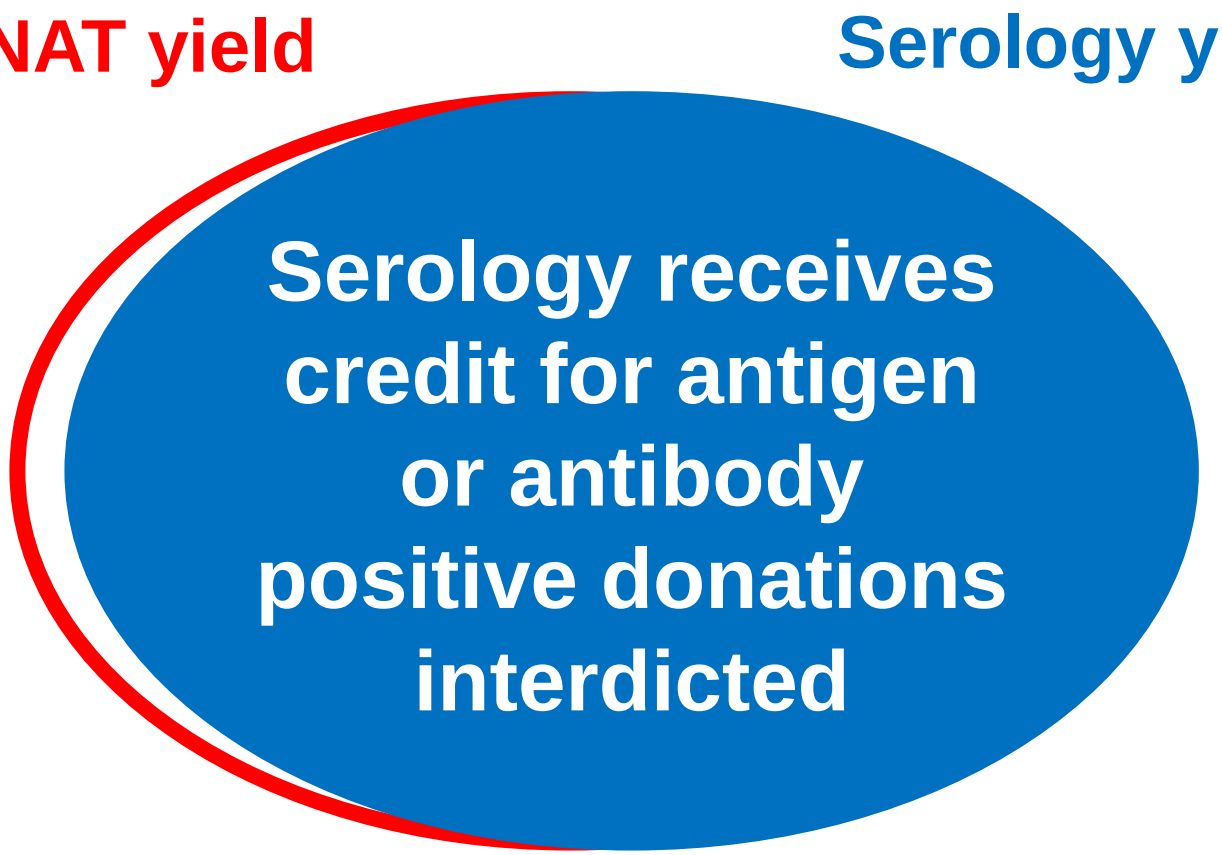
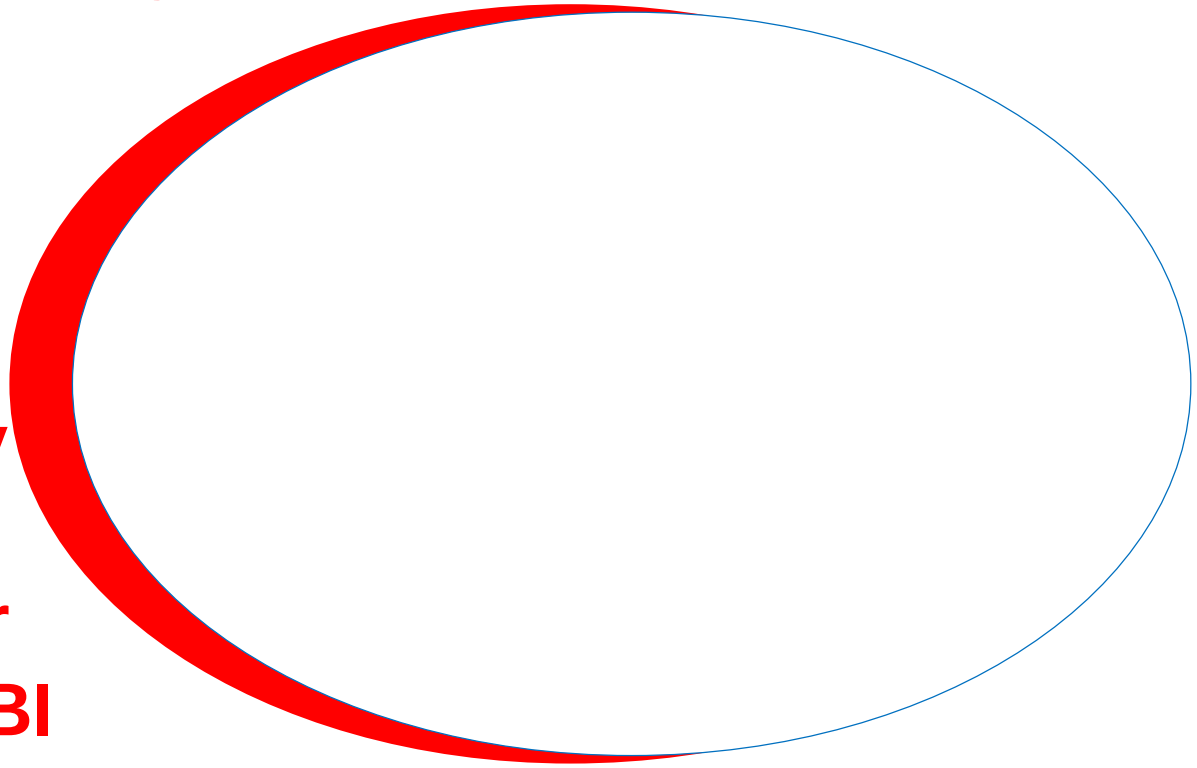


Cost Effectiveness Paradigm
NAT and Serology for HBV, HCV and HIV

NAT yield

Serology yield



NAT only receives credit for WP or OBI donations interdicted

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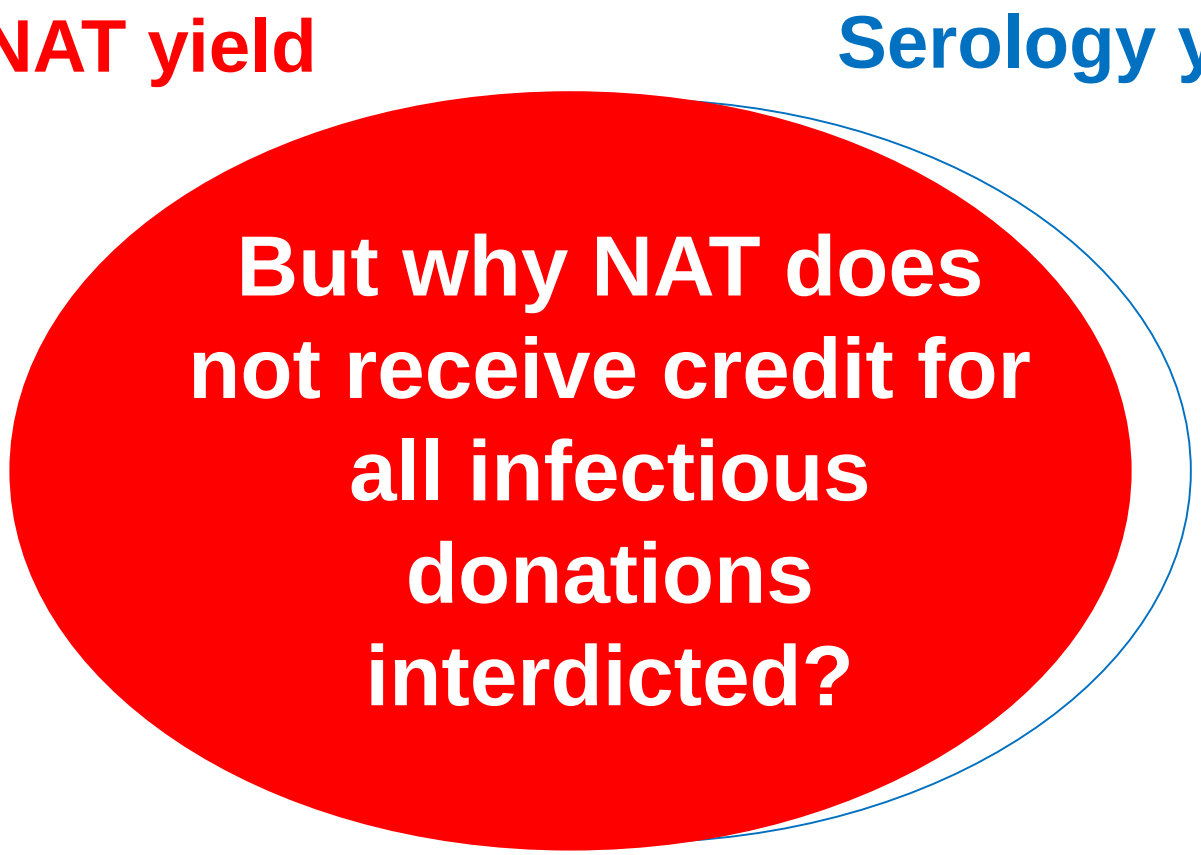
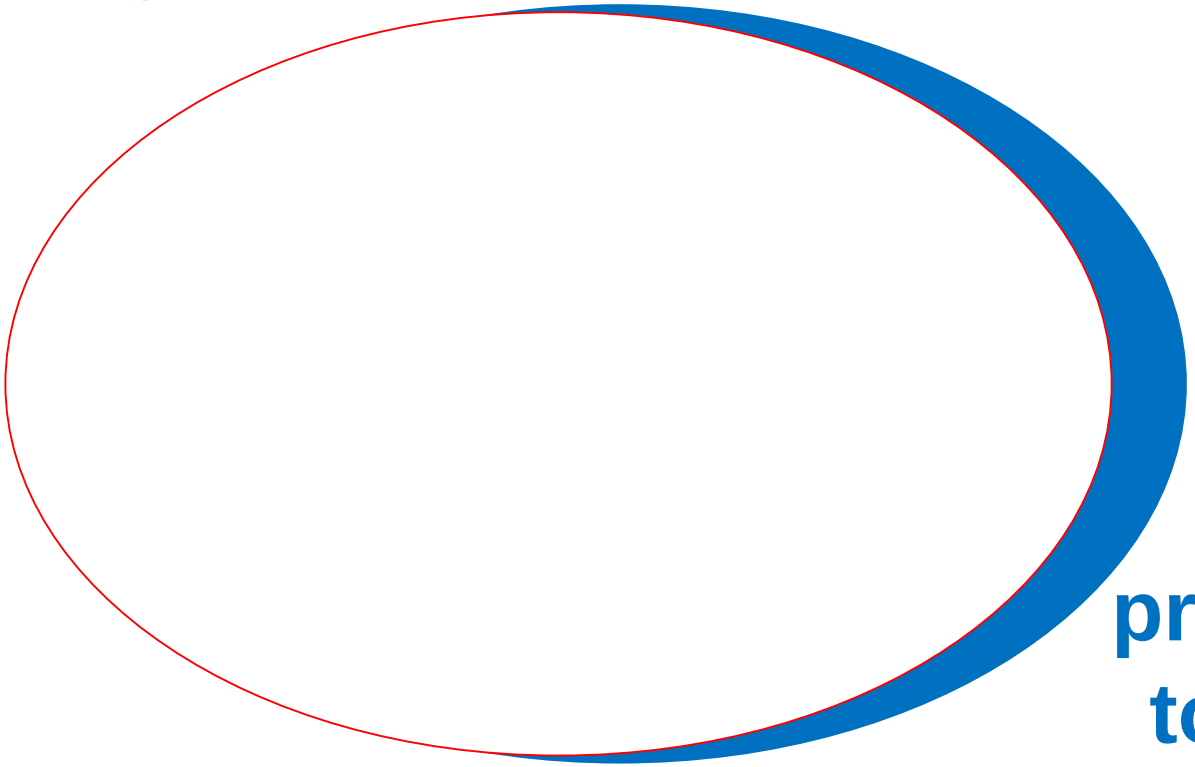
Cost Effectiveness Paradigm
NAT and Serology for HBV, HCV and HIV



Cost Effectiveness Paradigm
NAT and Serology for HBV, HCV and HIV

NAT yield

Serology yield



High probability to be not infectious

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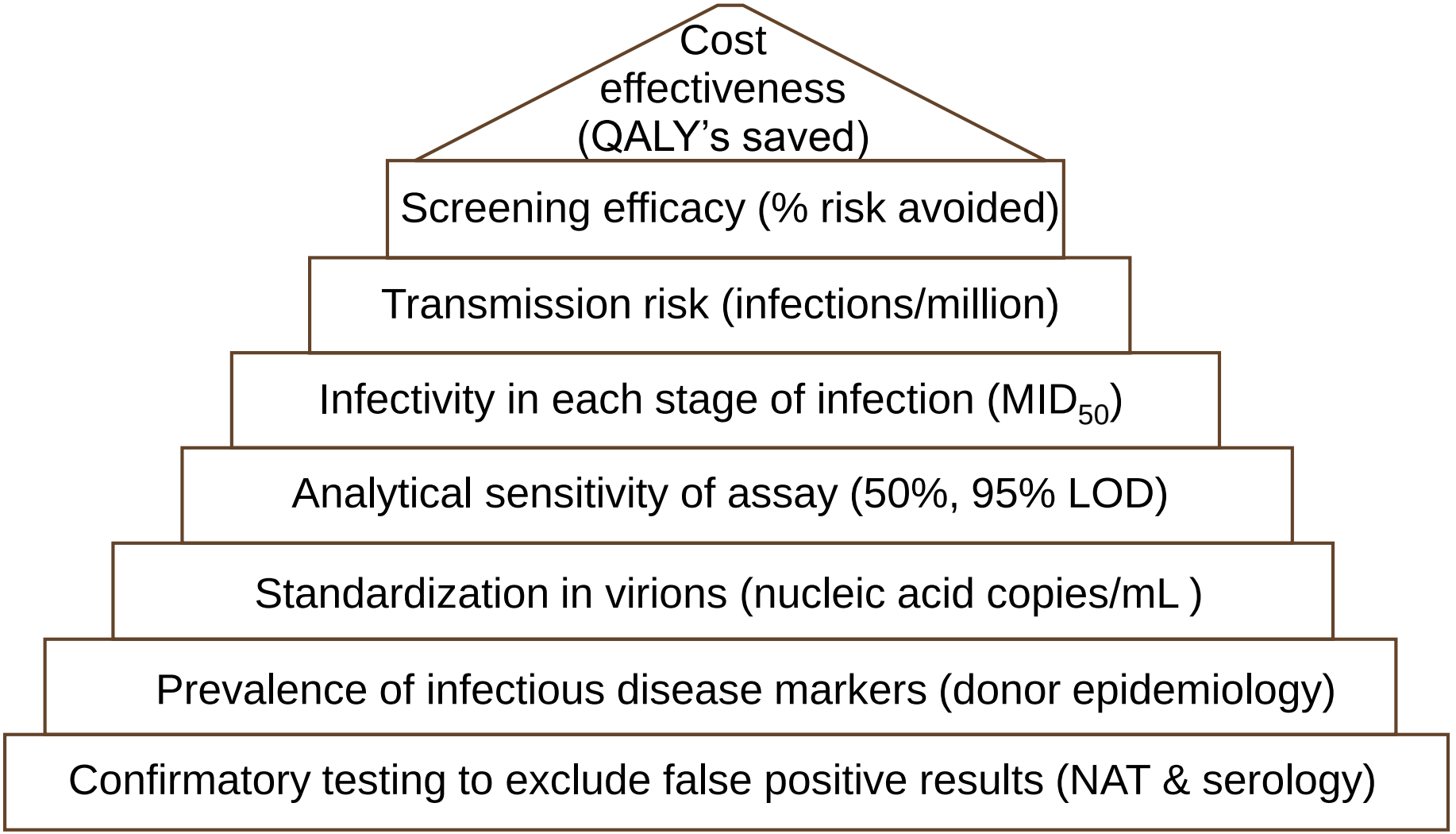
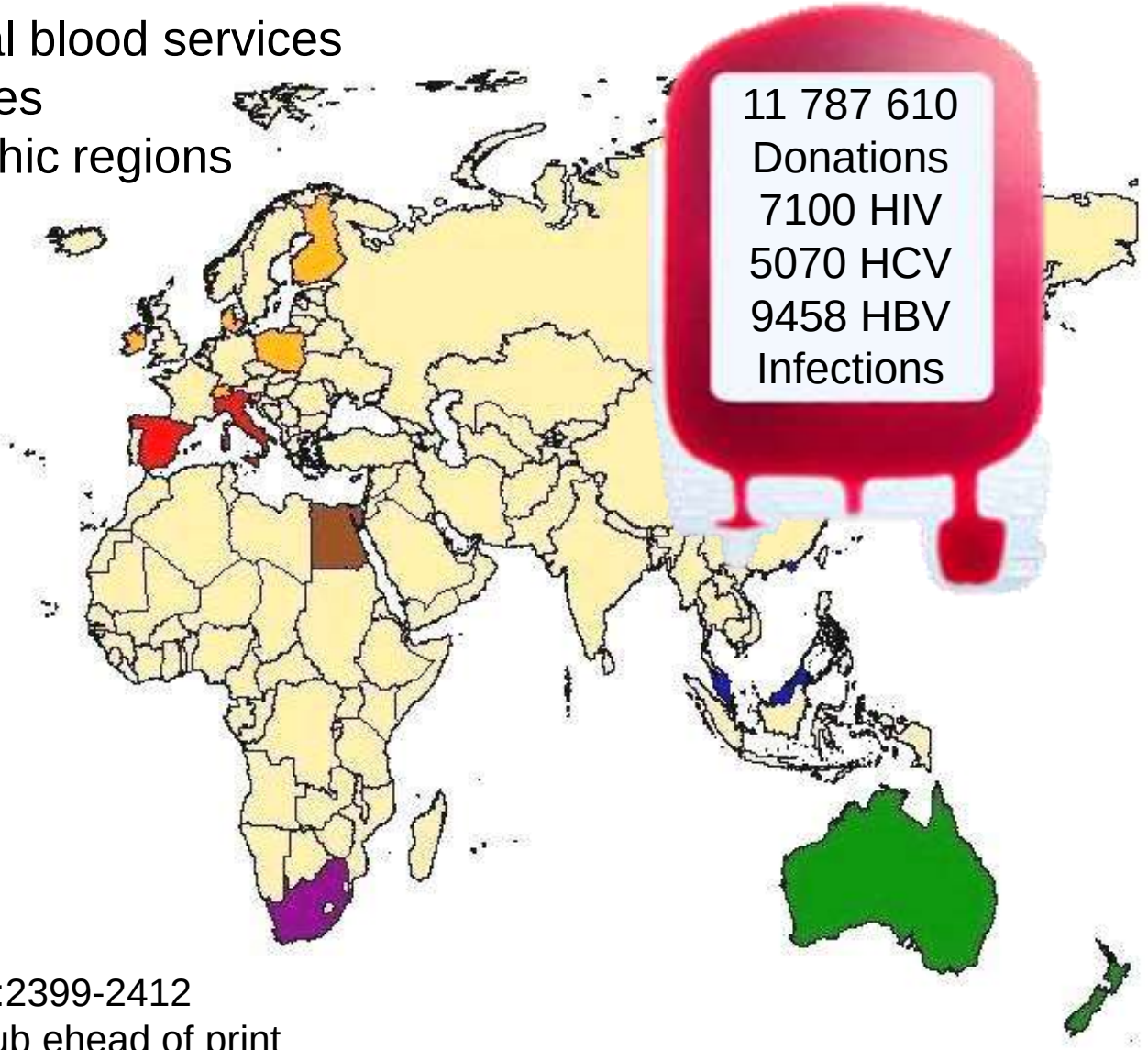
Foundations for a robust cost effectiveness analysis of screening scenarios



International ID-NAT Survey

Switzerland
Slovenia
Poland
Finland
Denmark
Ireland
Italy
Spain
Egypt
South Africa
Malaysia
Singapore
Hong Kong
Australia
New Zealand

20 national blood services
15 countries
6 geographic regions



Bruhn et al. Transfusion 2013:53:2399-2412
Bruhn et al Transfusion 2015 Epub ehead of print

HIV manuscripts

ORIGINAL ARTICLE

Comparison of human immunodeficiency virus assays in window phase and elite controller samples: viral load distribution and implications for transmission risk

Marion Vermeulen, Charl Coleman, Josephine Mitchel, Ravi Reddy, Harry van Drimmelen, Tracy Fickett, Michael Busch, and Nico Lelie

Prevalence of human immunodeficiency virus RNA and antibody in first-time, lapsed, and repeat blood donations across five international regions and relative efficacy of alternative screening scenarios

*Roberta Bruhn, Nico Lelie, Brian Custer, Michael Busch, Steven Kleinman, and the International NAT Study Group**

HCV manuscripts

ORIGINAL RESEARCH

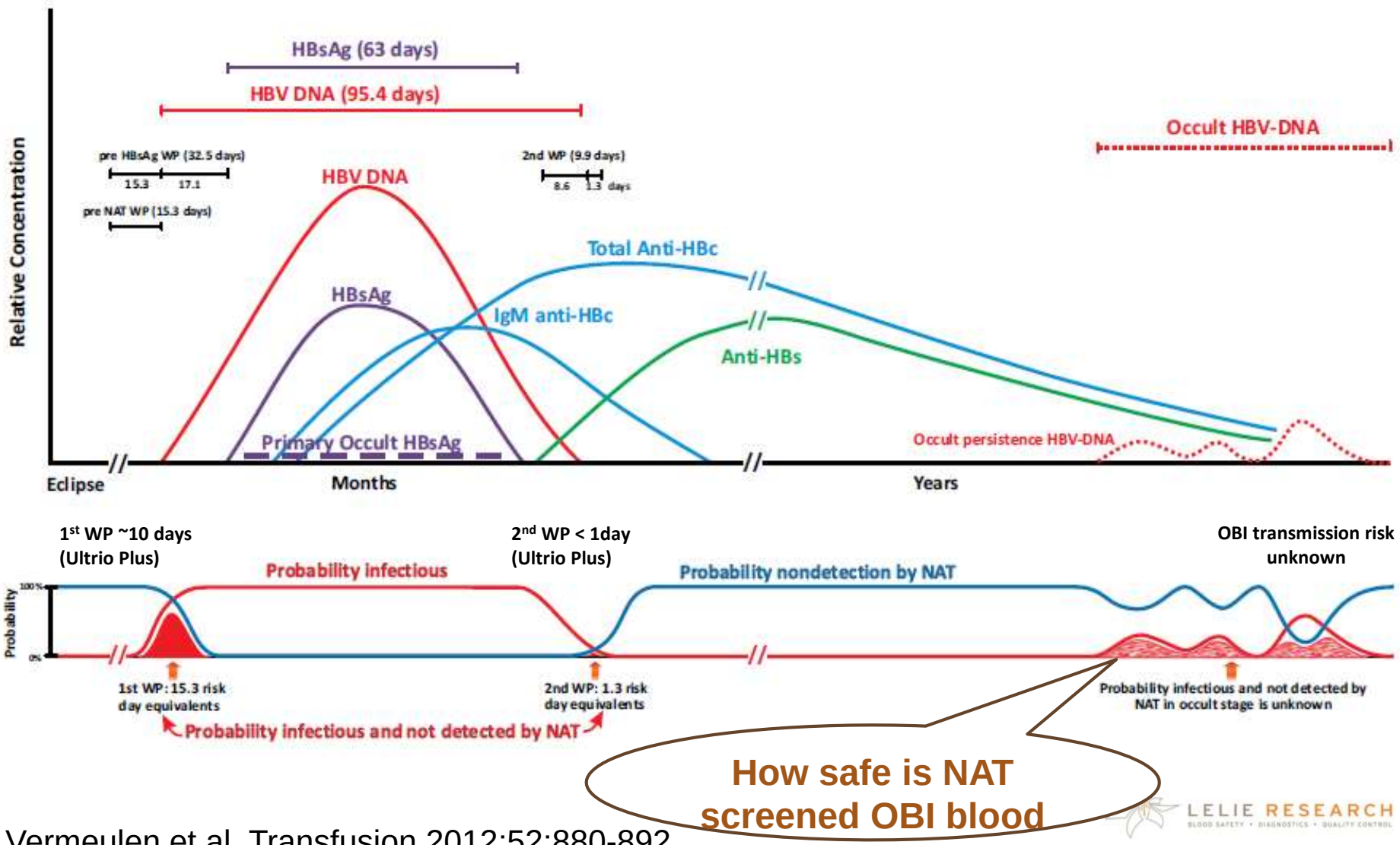
Viremia levels in hepatitis C infection among Egyptian blood donors and implications for transmission risk with different screening scenarios

Magdy El Ekiaby,[1] Faten Moftah,[2] Heidi Goubran,[2] Harry van Drimmelen,[3] Syria LaPerche,[4] Steve Kleinman,[5] Michael Busch,[6] and Nico Lelie[7]

Relative efficacy of nucleic acid amplification testing and serologic screening in preventing hepatitis C virus transmission risk in seven international regions

Roberta Bruhn,[1] Nico Lelie,[2] Michael Busch,[1] Steven Kleinman,[3] and the International NAT Study Group

Course of HBV markers and residual transmission risk in ID-NAT



Vermeulen et al, Transfusion 2012;52:880-892.

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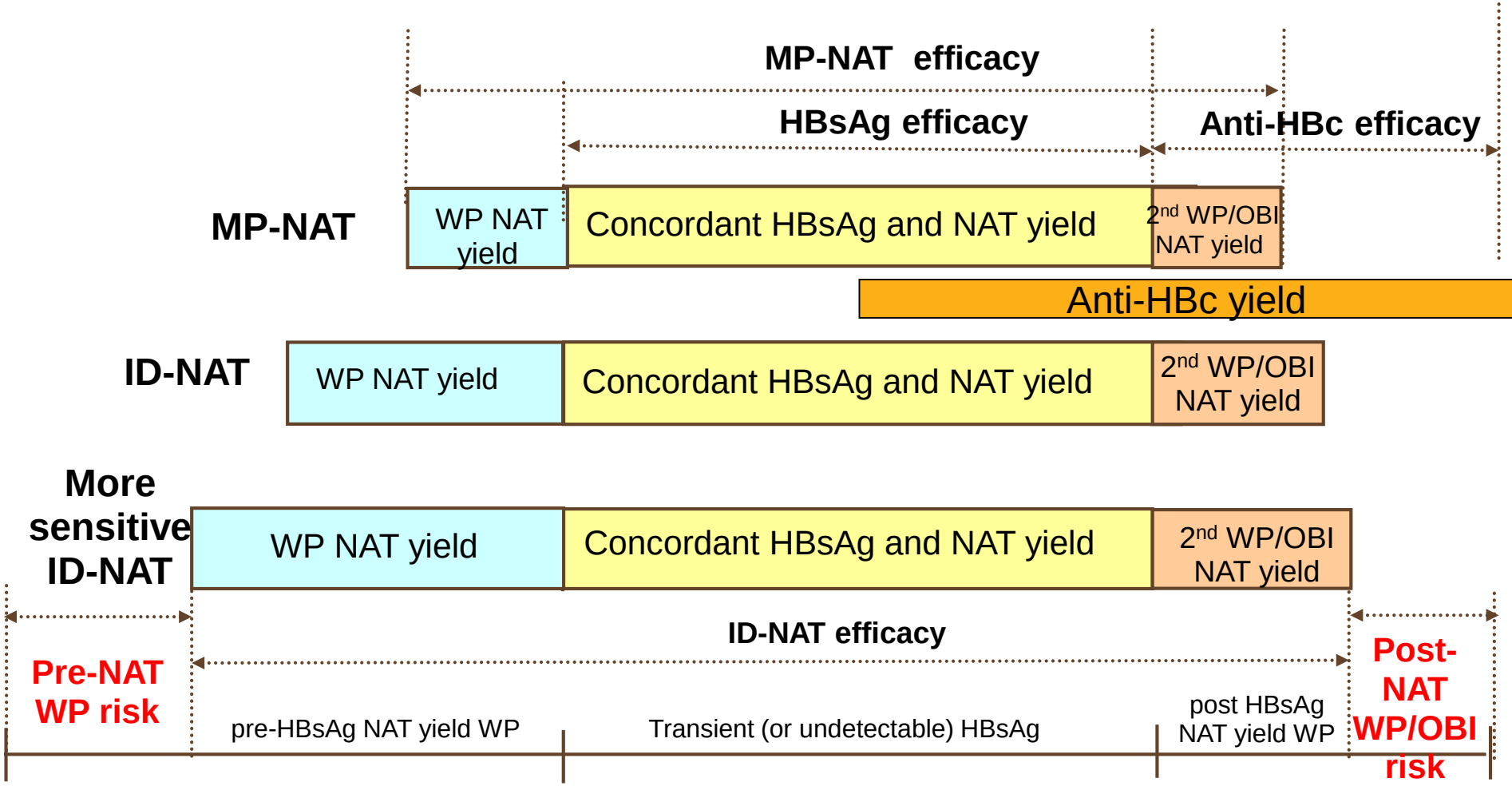
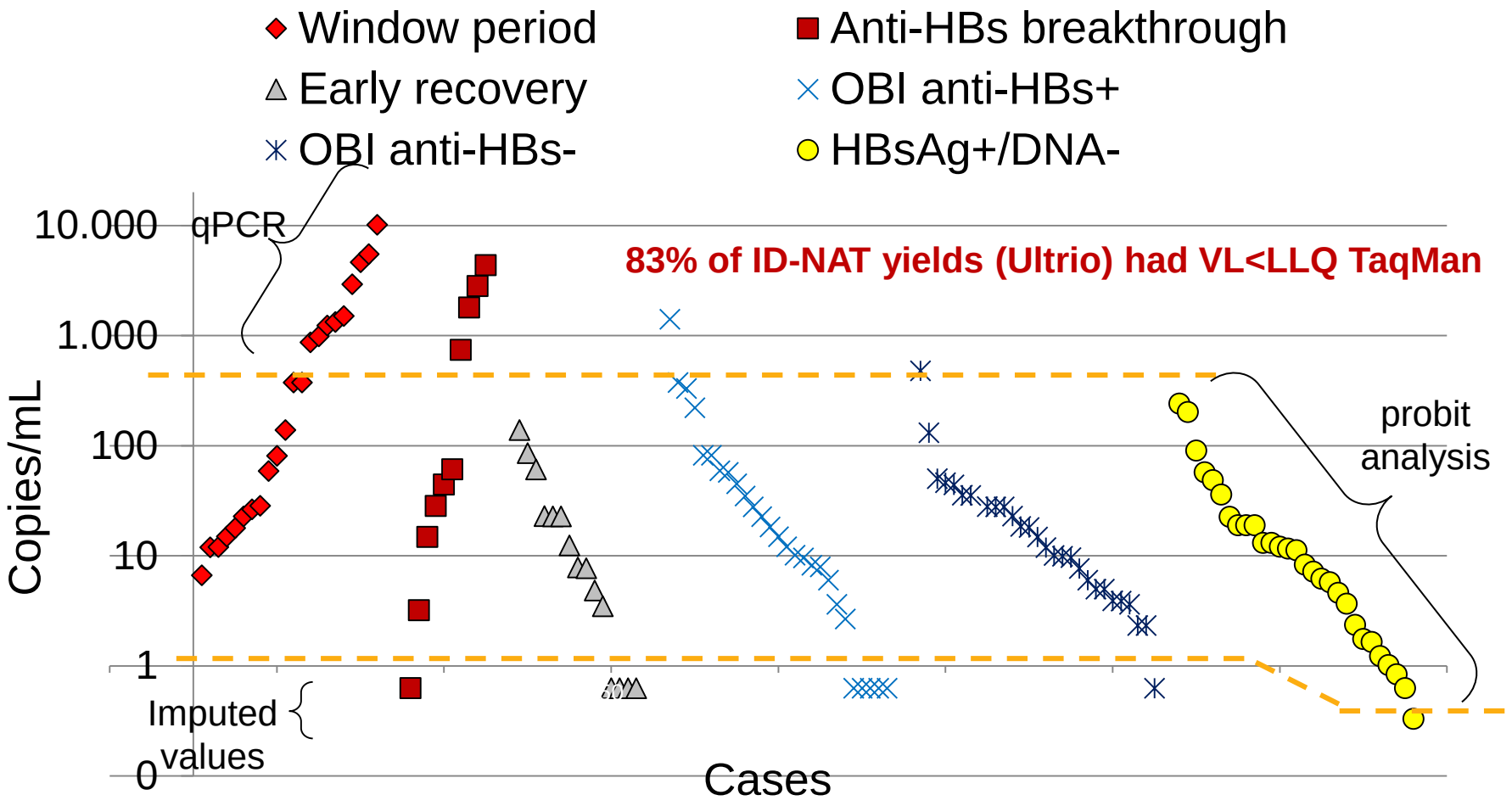
Efficacy of HBV screening assays



*

Viral load distribution in different stages of HBV infection



Vermeulen M. et al, Transfusion 2014;54:2496-2504

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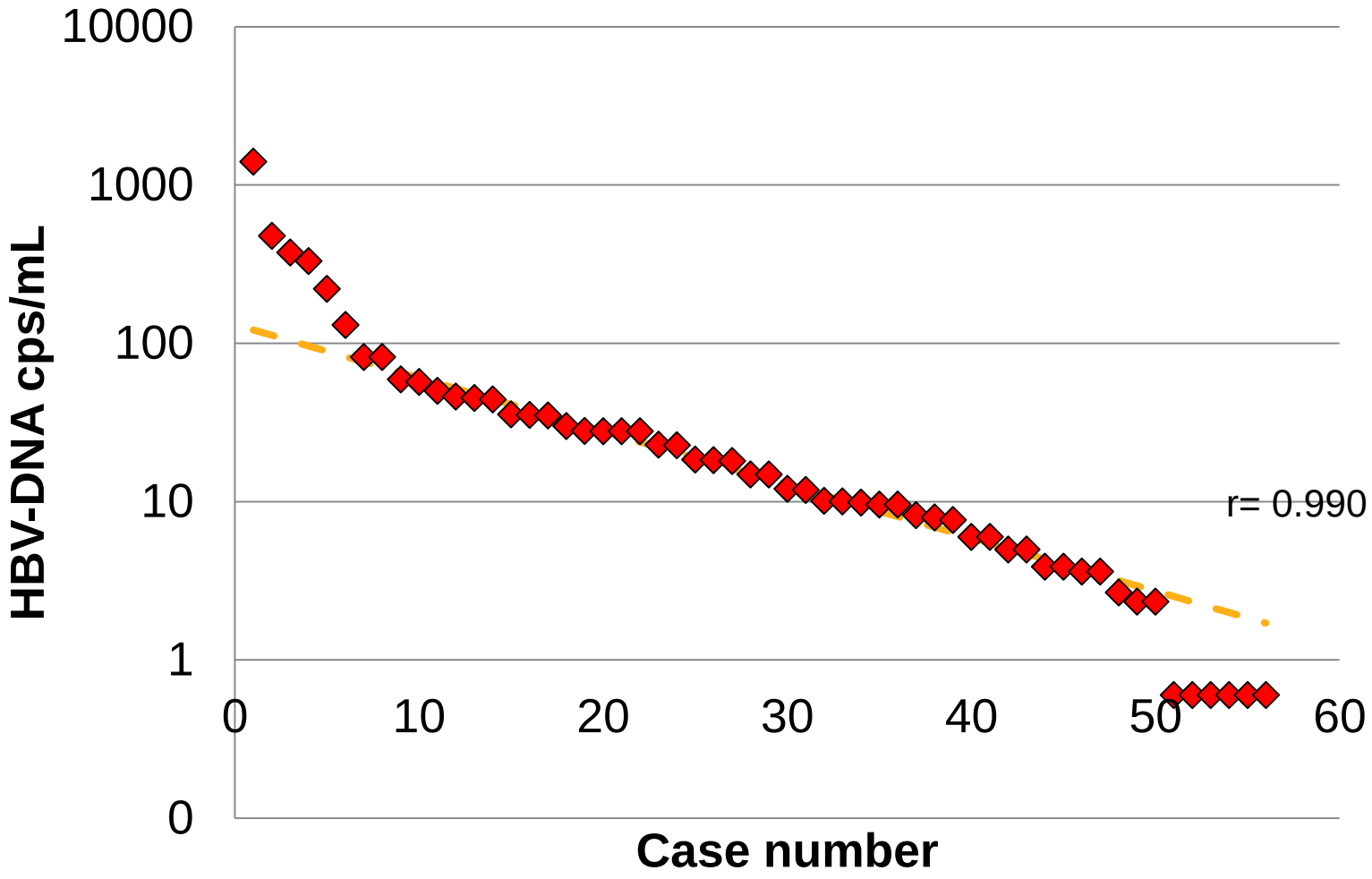
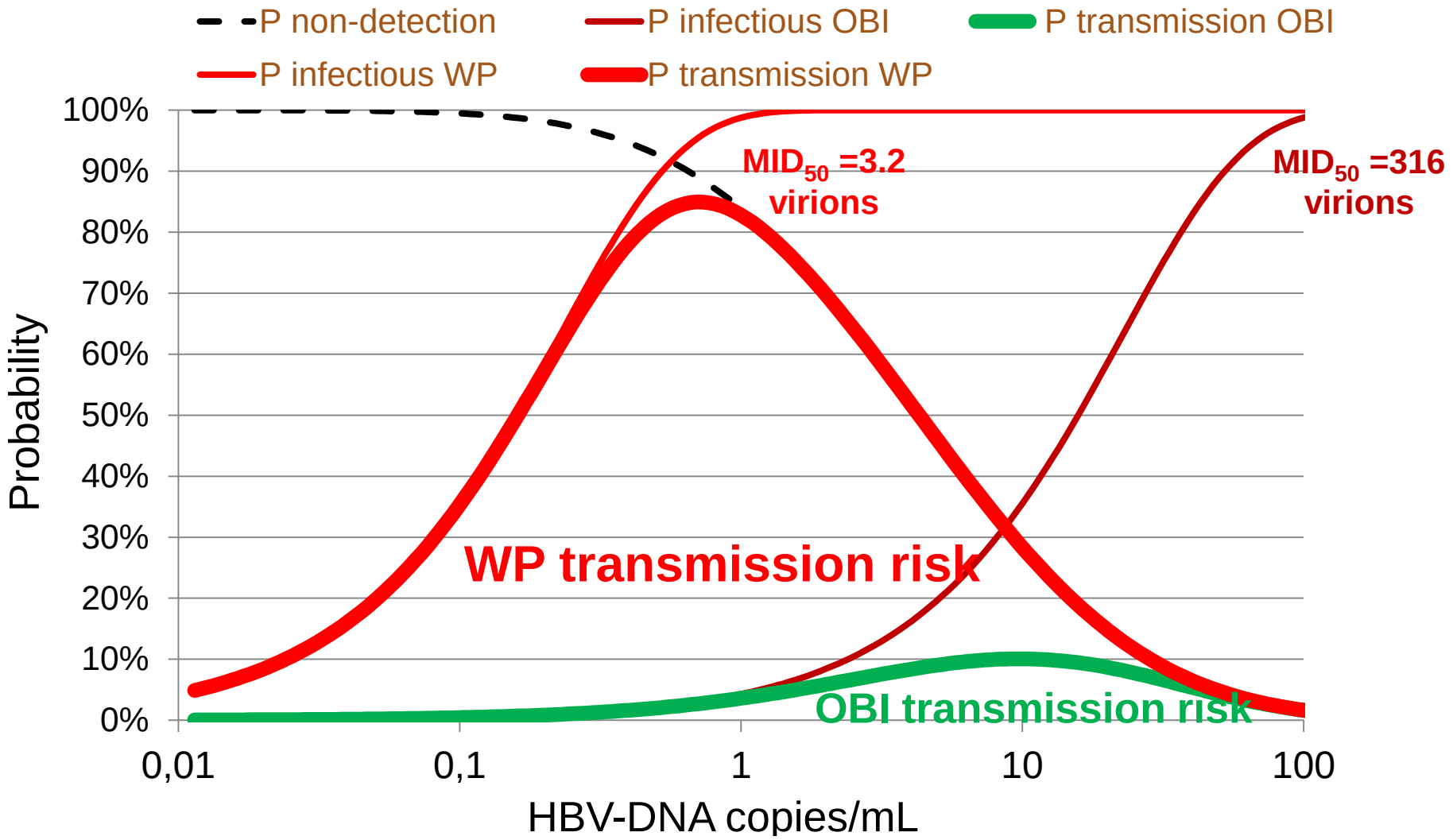
Viral load distribution in OBI



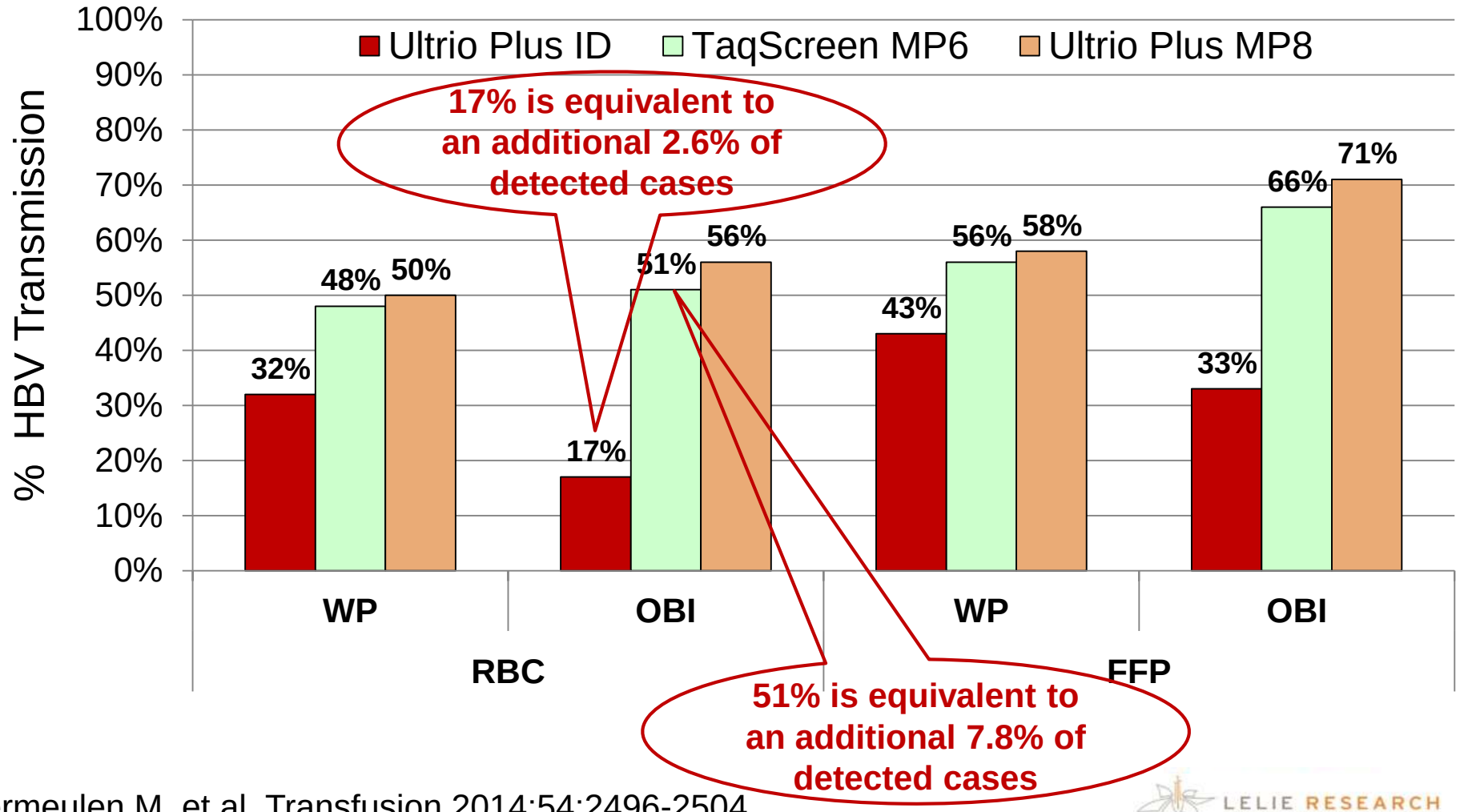
Vermeulen M. et al, Transfusion 2014;54:2496-2504

WP and OBI transmission risk by ID-NAT (Ultrio Plus) screened donations (RBCs)



Weusten J et al, Transfusion 2011;51:203-15. Lelie et al. Proceedings OBI conference Guangzhou
Vermeulen M. et al, Transfusion 2014;54:2496-2504

Estimated percentage of donations that are predicted to cause infection but not detected by ID and MP-NAT options



Vermeulen M. et al, Transfusion 2014;54:2496-2504

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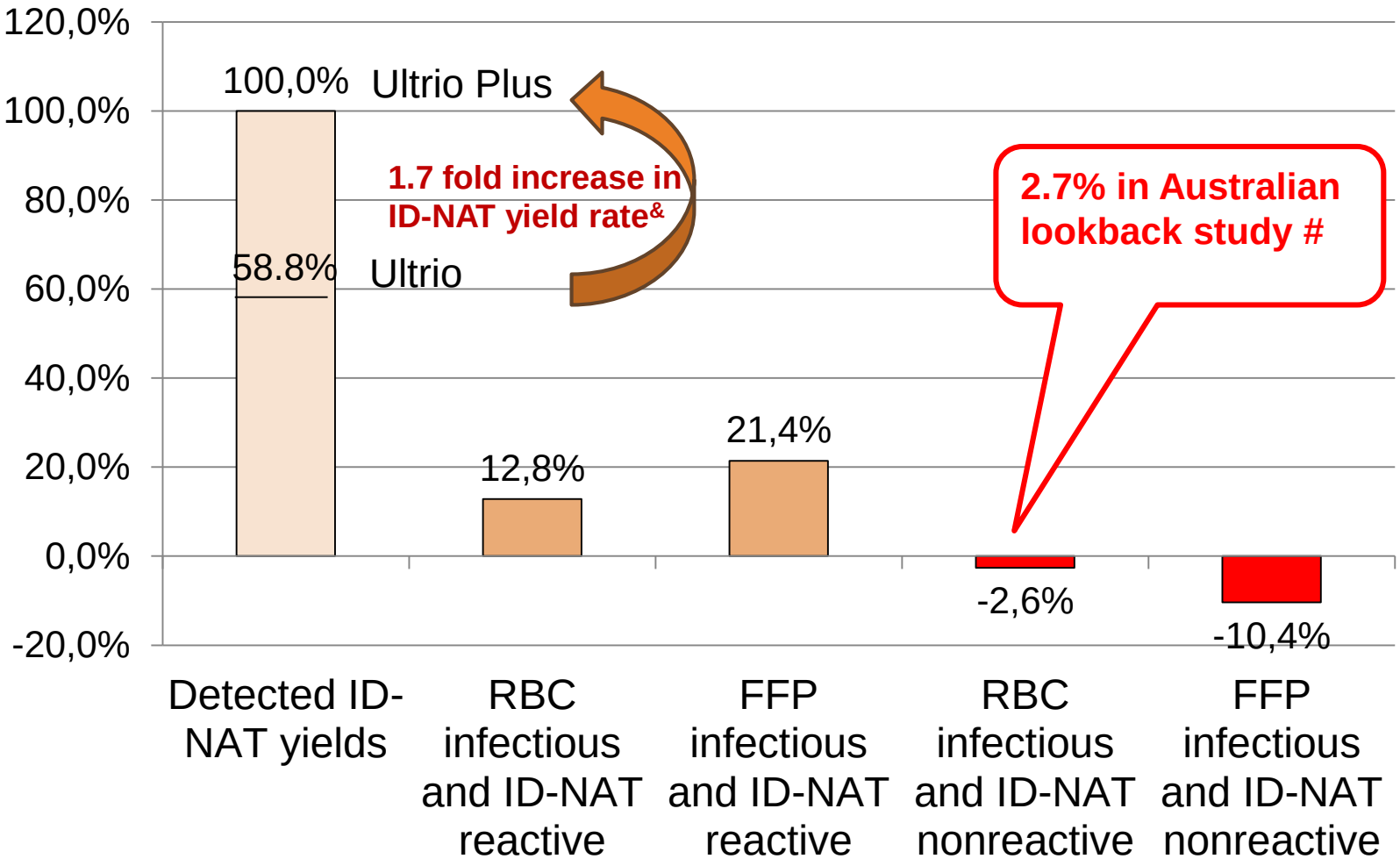
OBI transmission risk by ID-NAT screened blood



Data adapted from Vermeulen M. et al, Transfusion 2014;54:2496-2504

 # Seed et al. Vox Sanguinis 2015;108:113-22

&Vermeulen M. et al, Vox Sang 105 Suppl. 1;56 (Abstract 4A-S32-02)

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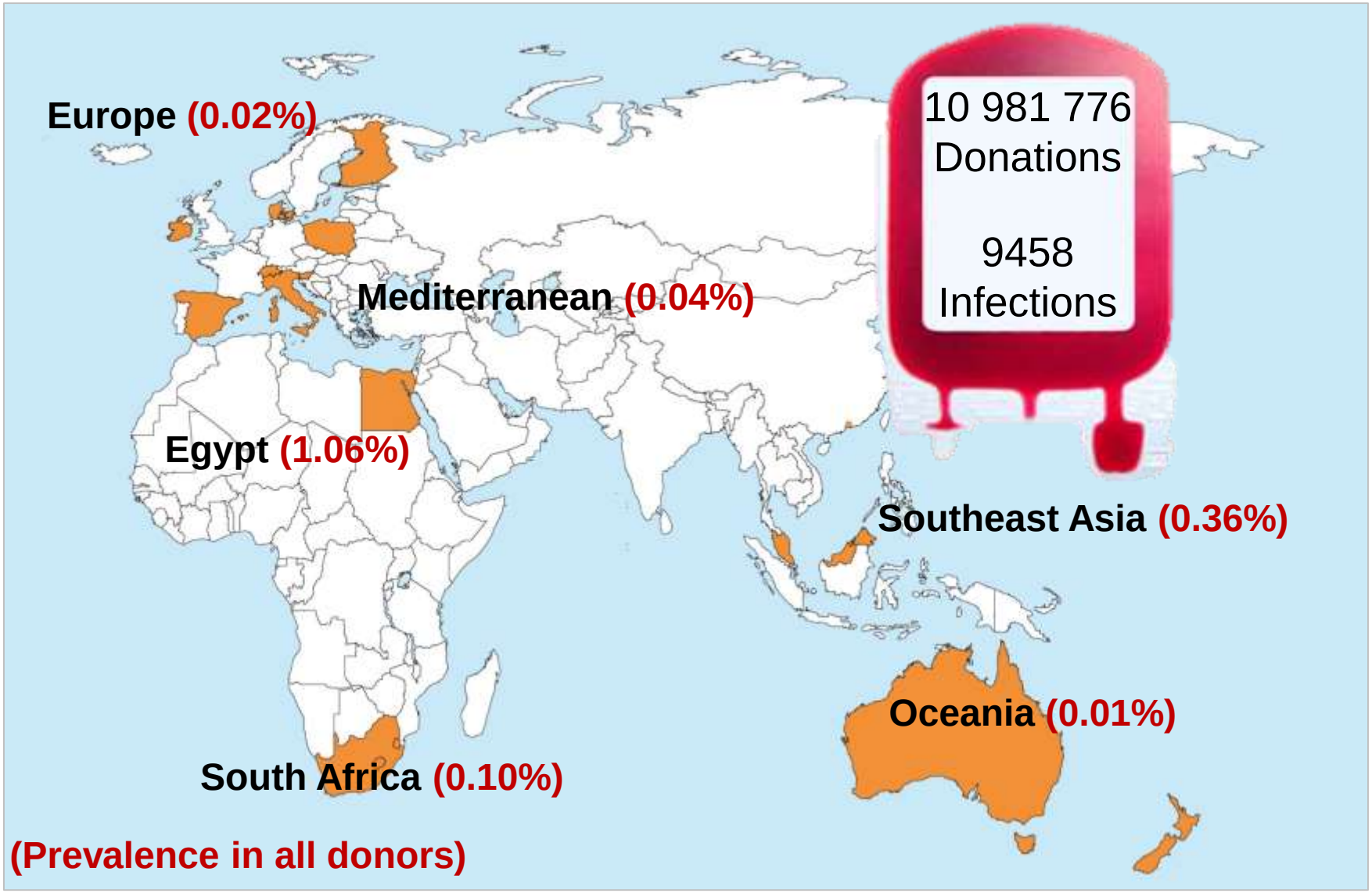
HBV ID-NAT survey



Lelie et al, manuscript in preparation

LELIE RESEARCH
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Types of confirmed HBV infections (n=9458) in international survey among ID-NAT (Ultrio) users

Infection stage	HBV-DNA	HBsAg	anti-HBc	IgM-anti-HBc	n	%
Early WP	+	-	-	-	168	1.8%
HBsAg+/DNA+	+	+			8016	84.8%
Late WP	+	-	+	+	54	0.6%
HBsAg+/DNA-	-	+	+		610	6.4%
OBI	+	-	+	-	587	6.2%
Unclassified	+	-			23	0.2%

Lelie N et al.. Vox Sanguinis 2013;105 (Suppl. 1): 55-6.

Types of acute HBV NAT yields identified in international survey

Acute HBV NAT yields	HBV-DNA	HBsAg	anti-HBc	IgM-anti-HBc	anti-HBs	n	%
Pre-HBsAg WP	+	-	-	-	-	137	61.7%
Acute occult*	+	-	-	-	-	9	4.1%
Anti-HBs breakthrough[#]	+	-	-	-	+	22	9.9%
Post-HBsAg WP	+	-	+	+	+/-	54	24.3%

*Acute occult = acute viremia in multiple follow up samples without HBsAg ever detectable

[#]Anti-HBs breakthrough = viremia followed by rise in anti-HBs and later conversion to anti-HBc in vaccinated or unvaccinated individual

Lelie N et al.. Vox Sanguinis 2013;105 (Suppl. 1): 55-6.

Types of chronic HBV NAT yields identified in international survey

Chronic HBV NAT yields	HBV-DNA	HBsAg	anti-HBc	IgM-anti-HBc	anti-HBs	n	%
OBI anti-HBs-	+	-	+	-	-	278	47,4%
OBI anti-HBs+	+	-	+	-	+	281	47,9%
OBI anti-HBs only	+	-	-	-	+	26	4,4%
OBI no marker	+	-	±	-	-	2	0,3%

Lelie N et al. Vox Sanguinis 2013;105 (Suppl. 1): 55-6.

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Comparison of WP and OBI NAT yield rates in first time versus lapsed + repeat donations

	SE Asia	South Africa	Mediterranean	ECN Europe	South Pacific
FT donations	**324 665**	**360 818**	**290 042**	**294 367**	**152 961**
WP NAT yields (rate)	14 (1:23 190)	47 (1:7677)	10 (1:29 004)	1 (1:294 367)	1 (1:152 961)
OBI NAT yields (rate)	43 (1:7 750)	93 (1:3 880)	24 (1:12 085)	5 (1:58 873)	5 (1:30 592)
LPD+RPT donations	**726 716**	**3 210 497**	**1 806 690**	**2 323 315**	**1 389 519**
WP NAT yields (rate)	18 (1 :40 373)	106 (1:30 288)	20 (1:90 335)	5 (1 :464 663)	0 (1 :?)
OBI NAT yields (rate)	118 (1 :6159)	101 (1 :31 787)	110 (1 :16 424)	36 (1 :64 537)	40 (1 :34 738)
WP yield ratio FT/LPD+RPT (p value)	**1.74 (0.11)**	**3.95 (<0.00001)**	**3.11 (0.00194)**	**1.58 (0.67)**	**?**
OBI yield ratio FT/LPD+RPT (p value)	**0.82 (0.28)**	**8.19 (<0.00001)**	**1.36 (0.33)**	**1.10 (0.84)**	**1.14 (0.79)**

Proportion of HBV infection types and clinical sensitivity of HBsAg and HBV-DNA detection

Classification	First Time	Lapsed	Repeat
All HBV infections	8354	378	700
WP NAT yields	74 (0.9%)	34 (9.0%)	115 (16.4%)
OBI NAT yields	178 (2.1%)	107 (28.3%)	298 (42.6%)
HBsAg+/DNA+	7523 (90.1%)	218 (57.7%)	275 (39.3%)
HBsAg+/DNA-	579 (6.9%)	19 (5.0%)	12 (1.7%)
All HBsAg+	8102 (97.0%)*	237 (62.7%)	287 (41.0%)§
All HBV-DNA+	7775 (93.1%)*	359 (95.0%)	688 (98.3%)§

*p<0.0001

*p<0.0001

Lelie N et al. Vox Sanguinis 2013;105 (Suppl. 1): 55-6.

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Parameters HBV risk day equivalent (RDE) model

- 50% minimum infectious dose (MID_{50})
  - WP: MID_{50} 3.16 (1-10) virions or copies
  - Late WP and OBI: 316 (100-1000) virions or copies
- Geomean[#] 50% LODs[1,2] → early and late WP days
  - Ultrio - 63 copies/mL → 23.2 and 4.0 days
  - Ultrio Plus - 4.1 copies/mL→13.1 and 0.8 days
  - TaqScreen - 3.9 - copies/mL→(MP6) 20.0 days
- Incidence rate adjustment factor[1]
  - HBsAg – 2.0
  - Ultrio – 1.08
  - Ultrio Plus – 1.0

#Geometric mean of a) Ultrio NAT yield dilutions and b) HBsAg+/DNA- samples

1. Vermeulen M. et al, Vox Sang 105 Suppl. 1;56 (Abstract 4A-S32-02)
2. Vermeulen et al Transfusion 2013; 53: 2459-06

Parameters HBV NAT yield ratio model

- Ultrio Plus to Ultrio ID-NAT yield improvement factors[1]
  - Early WP – 1.70
  - Late WP – 1.67
  - OBI – 1.72
  - HBsAg+/DNA –(seroyield) – 0.42
- Probability RBC infectivity[2,3]
  - **Pre ID-NAT (Ultrio Plus) WP residual risk – +45.5%**
  - Early WP ID-NAT yield – 100%
  - HBsAg+/HBV-DNA+ concordant – 100%
  - Late WP and OBI ID-NAT yield – 12.8%
  - **Late WP and OBI ID-NAT residual risk – +2.6%**
  - **Late WP and OBI MP6-NAT residual risk – +7.8%**
  - HBsAg+/HBV-DNA –(seroyield) – 17.2%

1. Vermeulen M. et al, Vox Sang 105 Suppl. 1;56 (Abstract 4A-S32-02)
2. Vermeulen et al, Transfusion 2014;54:2496-2504.
3. Lelie N. Proceedings OBI conference Guangzhou.

Estimated residual HBV WP and OBI transmission risk with ID-NAT* in South Africa as calculated by ratio modelling

Donation category	pre-WP	post-WP	OBI	HBsAg+/ DNA-
First time	1:17941	1:395,712	1:86,757	1:47,006
Lapsed	1:29,206	1:2,774,520	1:269,387	~
Repeat	1:50,454	1:4,686,925	1:897,317	~
Lapsed + Repeat	1:46,642	1:4,349,442	1:710,803	~
All	1:40.149	1:2,164,486	1:411,647	1:465,295

~ no HBsAg+/DNA- in lapsed and repeat donors observed with Ultrio Plus in one year analysis of Vermeulen M. et al (Vox Sang 105 Suppl. 1;56 (Abstract 4A-S32-02))

*Residual risk estimated for Ultrio Plus on Ultrio prevalence data

Estimated residual HBV transmission risk per million RBC transfusions in South Africa with different screening scenarios

Testing scenario	FT	LPD	RPT	LPD + RPT	All
HBsAg	219.8	133.6	71.2	78.3	96.8
HBsAg + anti-HBc	136.6	109.5	63.4	68.6	79.6
HBsAg + anti-HBc + MP16-NAT	100.9	62.0	35.9	38.8	45.1
HBsAg + MP6-NAT	127.5	64.6	34.3	37.7	46.8
HBsAg + anti-HBc + MP6-NAT	85.3	52.4	30.3	32.8	38.1
ID-NAT only	49.4	38.3	21.1	23.1	29.9
HBsAg + ID-NAT	28.1	38.3	21.1	23.1	27.8
HBsAg + anti-HBc + ID-NAT*	14.1	34.2	19.8	21.4	24.9

* Equivalent to anti-HBc + ID-NAT

FT= first time, LPD=lapsed RPT= repeat donations

Efficacy (%) in removing HBV transmission risk by RBC transfusions in South Africa with different screening scenarios

Testing scenario	FT	LPD	RPT	LPD + RPT	All
HBsAg	97.1	71.1	50.5	56.5	89.7
HBsAg + anti-HBc	98.2	76.3	56.0	61.9	91.6
HBsAg + anti-HBc + MP16-NAT	99.2	86.6	75.1	78.4	95.2
HBsAg + MP6-NAT	98.9	86.0	76.1	79.0	95.0
HBsAg + anti-HBc + MP6-NAT	99.4	88.7	78.9	81.7	96.0
ID-NAT only	99.4	91.7	85.3	87.2	96.8
HBsAg + ID-NAT	99.6	91.7	85.3	87.2	97.1
HBsAg + anti-HBc + ID-NAT*	99.8	92.6	86.2	88.1	97.4

* Equivalent to anti-HBc + ID-NAT

FT= first time, LPD=lapsed RPT= repeat donations

Incremental efficacy (%) in reducing HBV transmission risk by RBC transfusions in South Africa achieved by addition of ID-NAT to serology and vice versa

Addition of:	FT	LPD	RPT	LPD + RPT	All
ID-NAT to HBsAg	2.49	20.6	34.8	30.7	7.31
ID-NAT to HBsAg & anti-HBc	1.59	16.3	30.3	26.2	5.81
HBsAg to ID-NAT	0.28	0.0	0.0	0.0	0.23
anti-HBc to ID-NAT	0.46	0.88	0.92	0.91	0.53

FT= first time, LPD=lapsed RPT= repeat donations

Efficacy of NAT and Serology for HBV, HCV and HIV
Conclusions and discussion

- An ID-NAT alone screening scenario is more efficacious than MP-NAT and serology together
  - and could be a cost effective strategy, particularly for lapsed and repeat donors (e.g. in a setting where platelets and FFP are subjected to pathogen inactivation technology)
- An Ag/Ab (combo) assay testing* strategy is far less efficacious than ID-NAT alone
- The international data base of the ID-NAT user group is instrumental to calculate cost effectiveness of different screening (or blood safety) scenarios

*also HBsAg combined with anti-HBc

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- Heidi Goubran, Faten Moftah, National Blood Transfusion Service, Cairo, Egypt
- Magdy El Ekiaby, Shabrawishi Hospital, Dokki, Egypt
- Silvia Sauleda, Banc de Sang I Teixits, Barcelona, Spain
- Roberto Roig, Manolo Alvarez, Valencia Regional Blood Tx Center, Valencia, Spain
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- Paola Manzini, University of Turin, Turin, Italy
- Cecilia Peduzzi, S.O.D University of Careggi, Florence, Italy
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