Efficacy of testing scenarios in reducing HBV transmission risk

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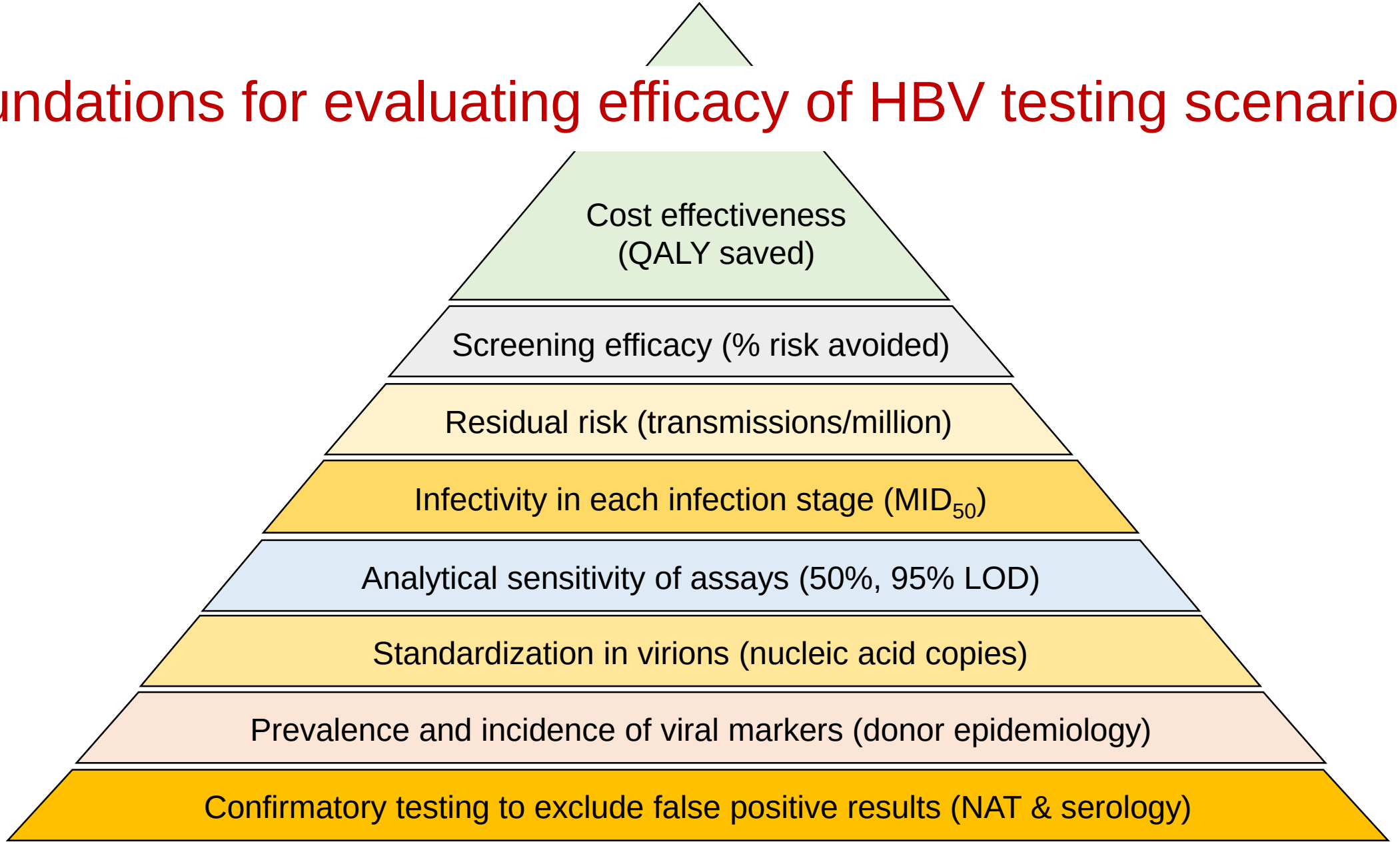
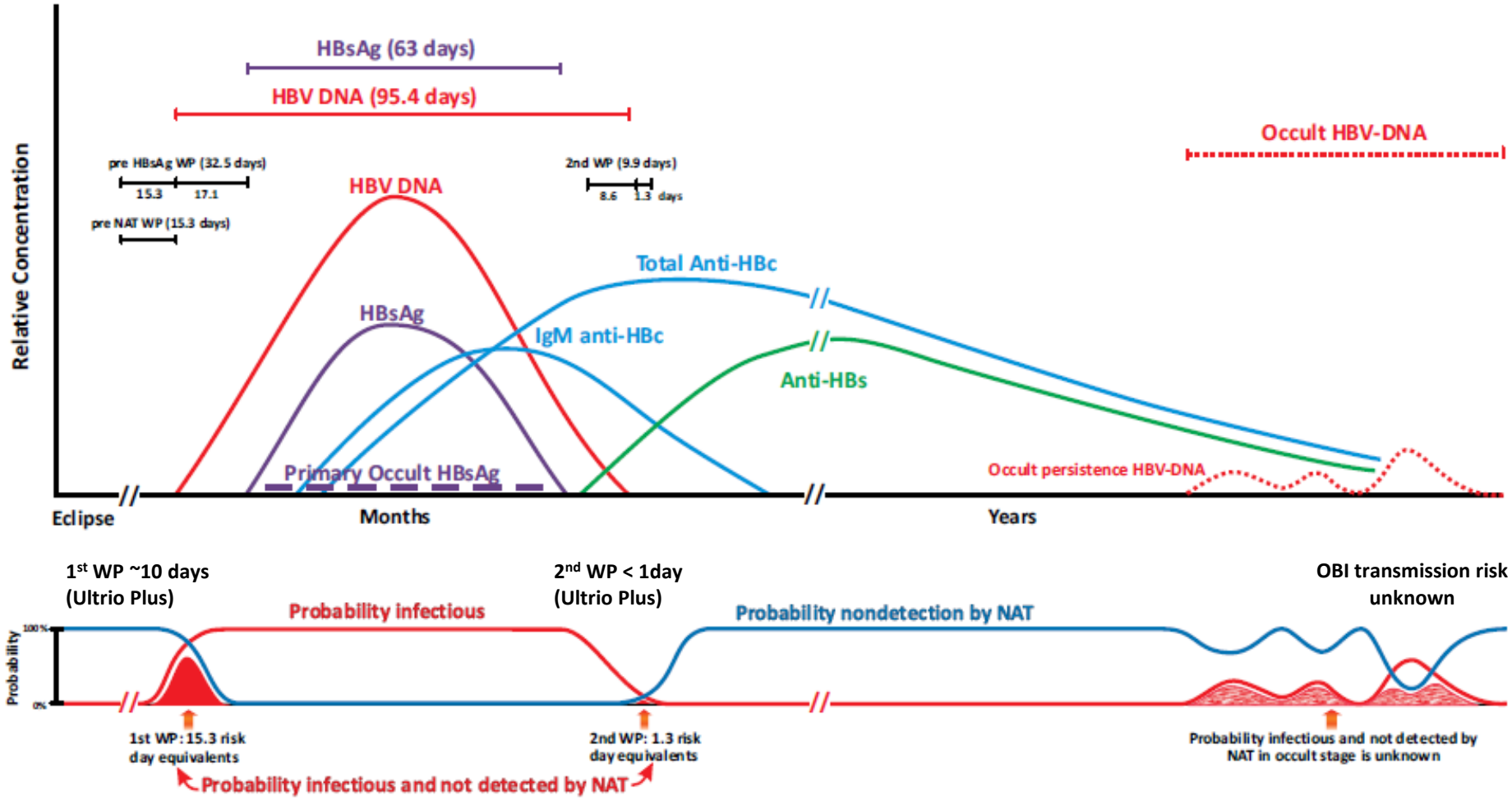
Foundations for evaluating efficacy of HBV testing scenarios



Bruhn et al, Transfusion 2013:53:2399-2412, Bruhn et al Transfusion 2015;55:1195-205, Lelie et al, manuscript in preparation

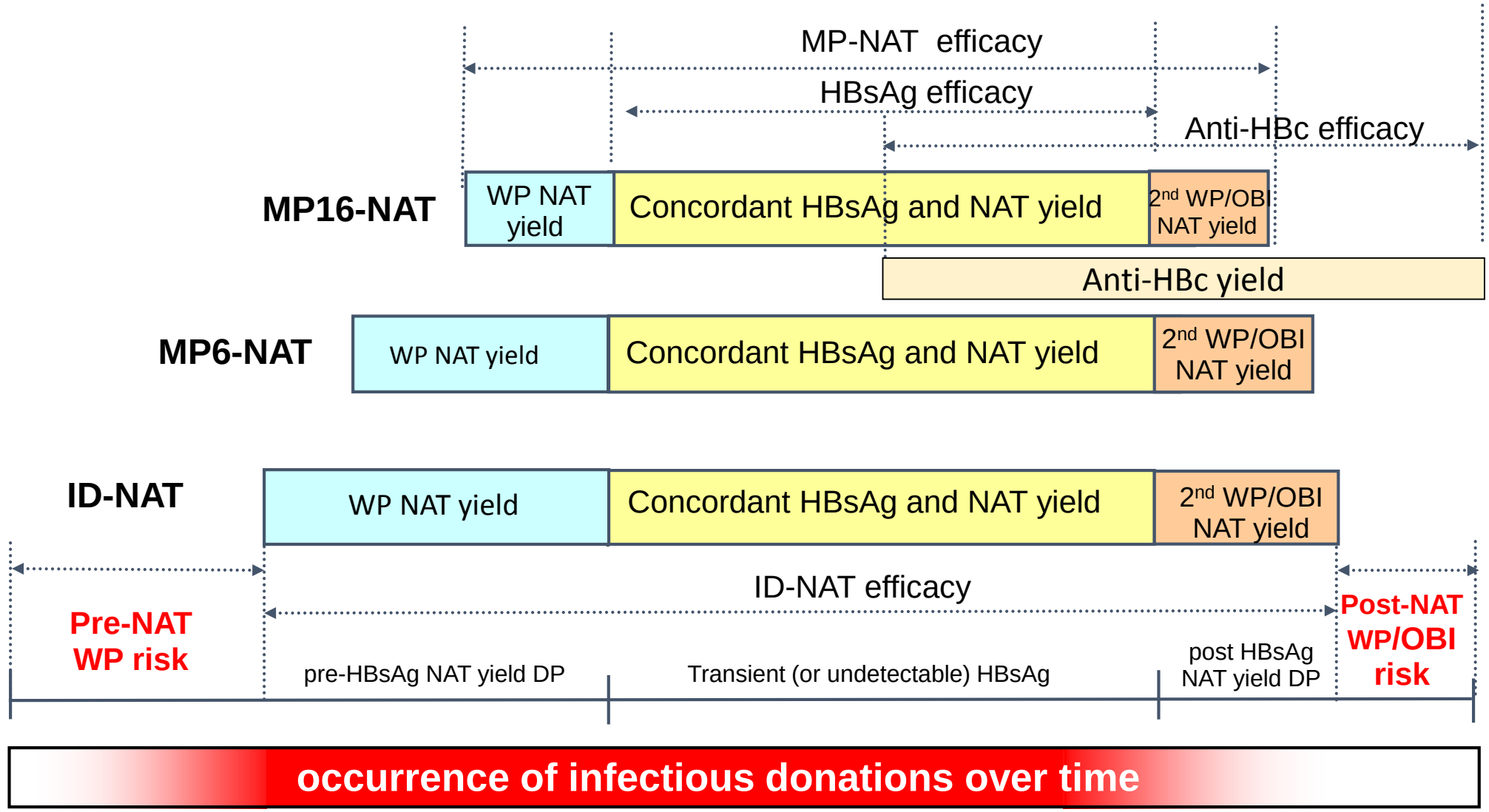
Course of HBV markers and residual transmission risk in ID-NAT



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

Lengths of window periods and detection periods based on Ultrio assay versions are currently being revised

Efficacy of HBV Screening Assays

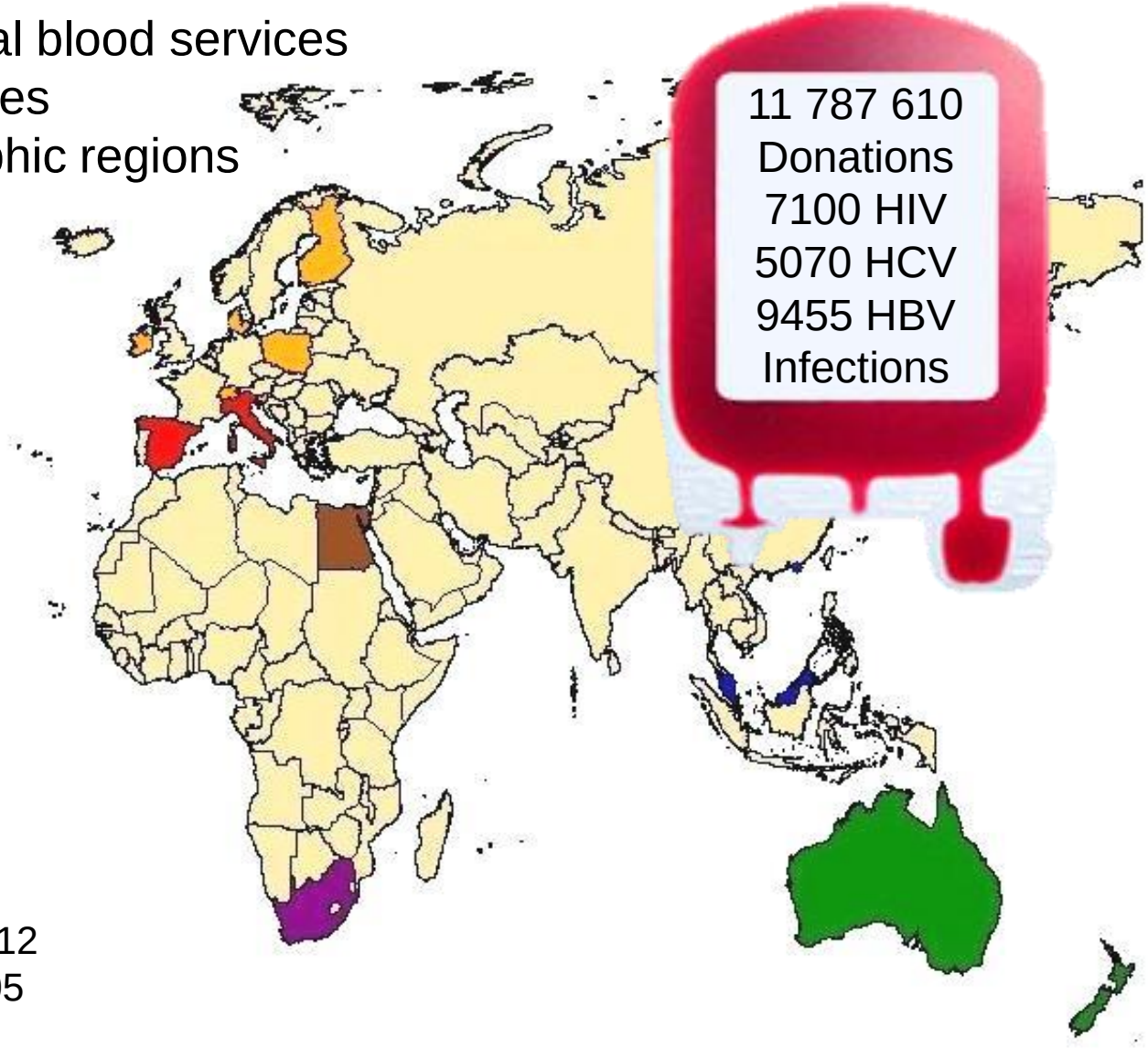


Lelie et al, manuscript in preparation

International ID-NAT Survey 2005-2011

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

22 national blood services
15 countries
6 geographic regions



Bruhn et al. Transfusion 2013:53:2399-2412
Bruhn et al Transfusion 2015:55:1195-1205
Lelie N et al. Transfusion 2017:57:24-35

HBV infections (n=9455) per category in international survey among ID-NAT (Ultrio) users

Infection stage	Pattern HBV markers					First time	Lapsed	Repeat
	HBV-DNA	HBs Ag	anti-HBc	IgM-anti-HBc	anti-HBs	n (%)	n (%)	n (%)
Pre-HBsAg WP	+	-	-	-		39 (0.47%)	20 (5.2%)	77 (10.8%)
Acute occult	+	-	-	-		2 (0.02%)	3 (0.79%)	5 (0.70%)
A-HBs breaktrh	+	-	-	-	+	5 (0.06%)	4 (1.05%)	13 (1.83%)
HBsAg+/DNA+	+	+				7523 (90.0%)	218 (57.2%)	275 (38.7%)
Post- HBsAg WP	+	-	+	+		28 (0.33%)	7 (1.84%)	20 (2.81%)
HBsAg+/DNA-	-	+	+			579 (6.9%)	19 (5.0%)	12 (1.69%)
OBI anti-HBs-	+	-	+	-	-	82 (0.98%)	52 (13.6%)	141 (19.8%)
OBI anti-HBs+	+	-	+	-	+	85 (1.02%)	50 (13.1%)	145 (20.4%)
OBI anti-HBs only	+	-	-	-	+	10 (0.12%)	5 (1.31%)	11 (1.55%)
OBI no marker	+	-	±	-	-	1 (0.01%)		1 (0.14%)
Unclassified	+	-				9 (0.11%)	3 (0.79%)	11 (1.55%)
Total infections						**8363 (100%)**	**381 (100%)**	**711 (100%)**

Lelie N et al. Transfusion 2017:57:24-35

Detection rates for different HBV infection categories in sequential Ultrio and Ultrio Plus screening periods of one year

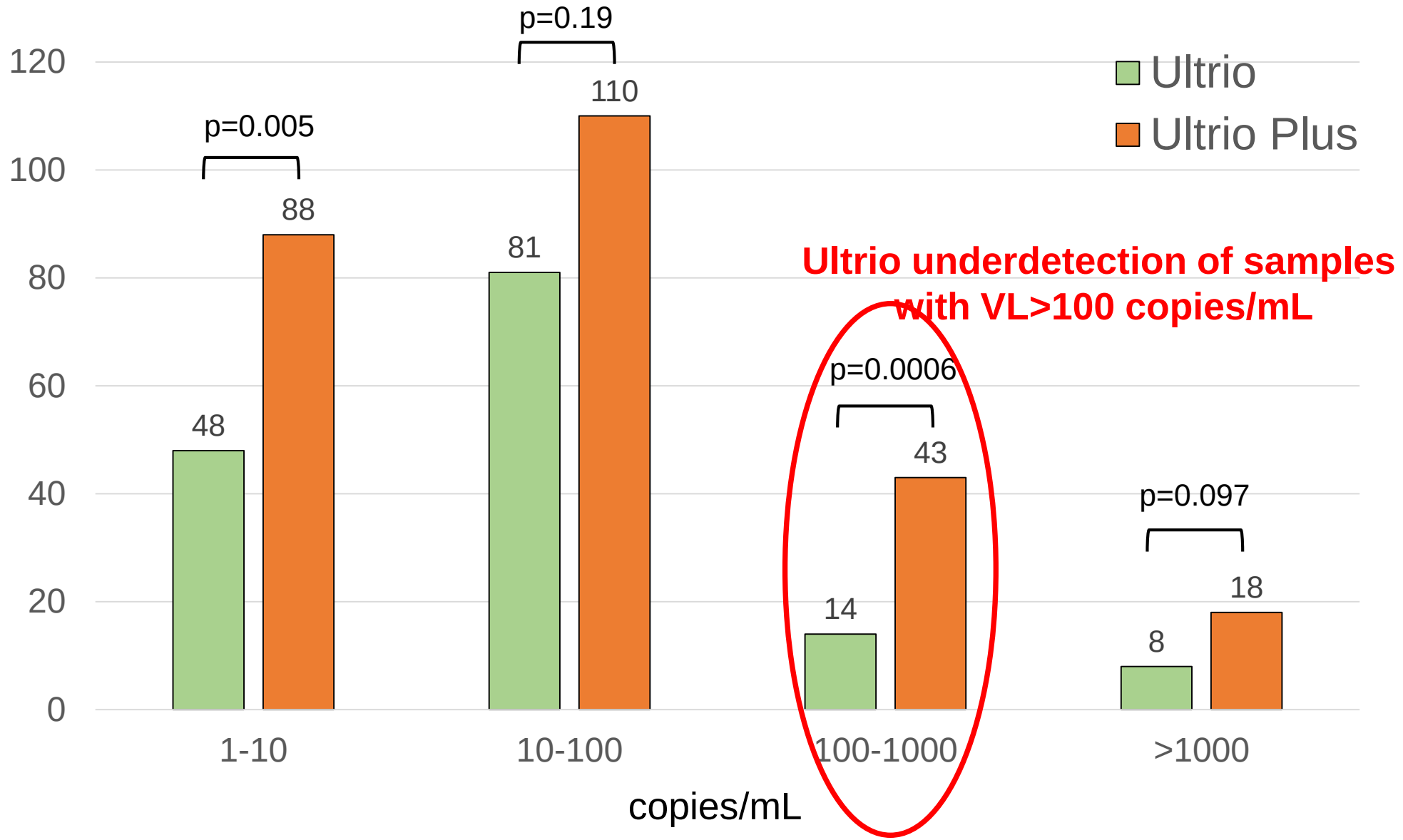
	Ultrio	Ultrio Plus	factor[$]	p value
number donations	775 444	789 948		
HBV-NAT yield	151 (1:5204)	259 (1:3 050)	1.72	<0.00001
pre-HBsAg WP^	47 (1:16 499)	80 (1:9 874)	1.70[§]	0.005
post-HBsAg WP	10 (1:77 544)	17 (1:46 468)	1.67	0.19
OBI	94 (1:8249)	162 (1:46 468)	1.72	0.00004
HBsAg positive	820 (1:946)	841 (1:939)	1.03	0.89
HBsAg+/DNA+	744 (1:1042)	809 (1:976)	1.07	0.0598
HBsAg+/DNA-	38 (1:20 406)	16 (1: 49 372)	0.42	0.002
All HBV infections	971 (1:799)	1100 (1:718)	1.11	0.016

[$] Ratio of Ultrio Plus to Ultrio detection

^ included possible WP NAT yields of which infection stage was not fully confirmed by follow up testing.

§ 2.1 fold increase if possible anti-HBs breakthrough infections with very low VL (that could also represent chronic 'anti-HBs only OBIs') were excluded # Vermeulen et al. manuscript in press

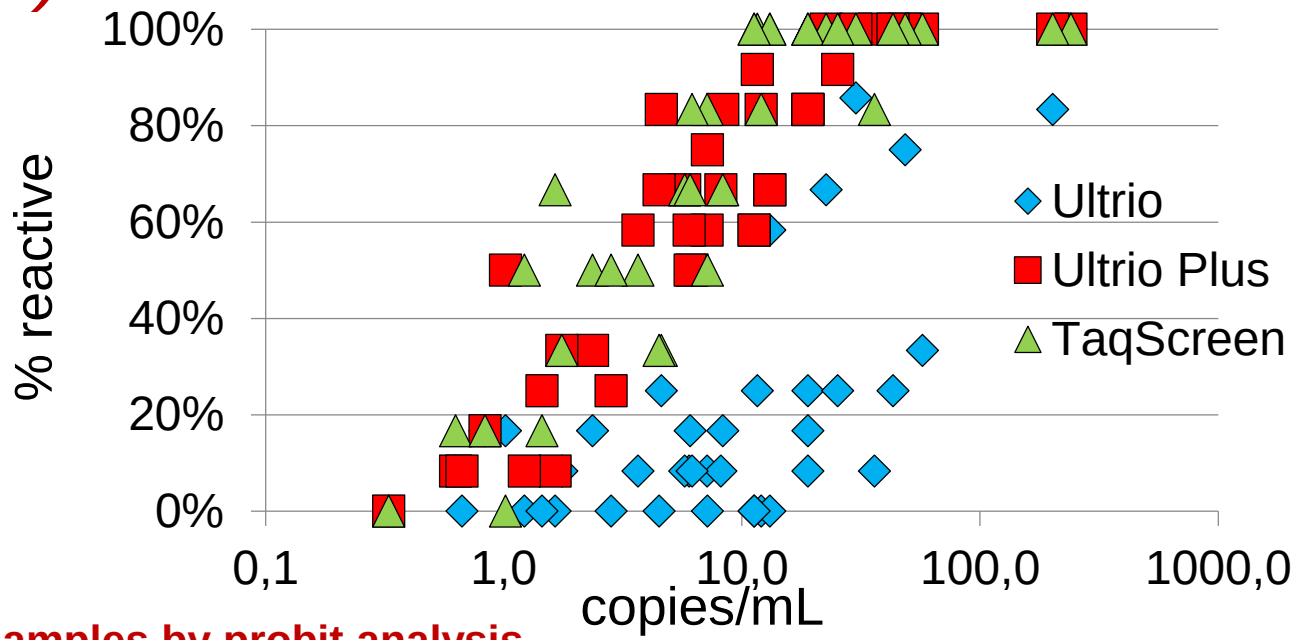
Viral load distribution in HBV-NAT yields from sequential Ultrio and Ultrio Plus screening periods of one year



Estimation of LODs of NAT methods on South African HBV yield samples *(predominantly genotype A1)*

Data previously published by Vermeulen et al (Transfusion 2013;53:2459-2466).

Proportion NAT reactive on HBsAg positive/ Ultrio nonreactive samples or 1:8 dilutions

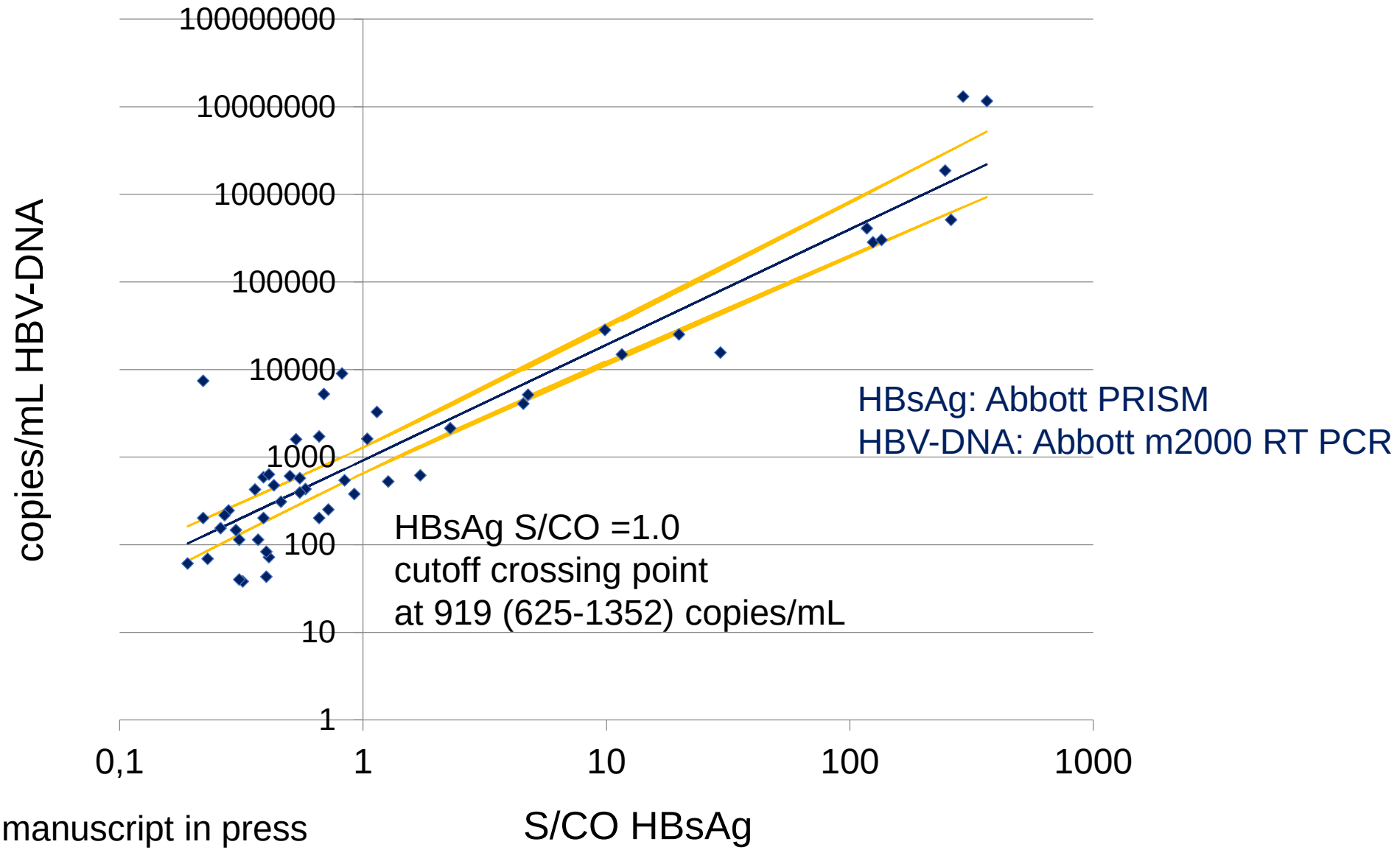


Estimation of LODs on Ultrio and HBsAg yield samples by probit analysis

HBV yield category	n samples	LOD (copies/mL) Ultrio		LOD (copies/mL) Ultrio Plus		LOD (copies/mL) TaqScreen	
		50% (CI)	95% (CI)	50% (CI)	95% (CI)	50% (CI)	95% (CI)
HBsAg positive/ Ultrio nonreactive	**32**	**375 (156-1267)**	**1248 (564-3974)**	**4.0 (2.8-5.6)**	**34.8 (26.8-139)**	**2.5 (1.4-4.1)**	**37.9 (20.6-89.2)**
HBsAg negative/ Ultrio reactive	107	10.6 (9.2-12.3)	120 (94.8-157)	4.3 (3.7-5.0)	48.7 (39.3-62.2)	4.6 (3.6-5.9)	51.7 (38.3-71.7)
Geometric mean values on both HBV yield categories		**63.0 (37.9-124.8)**	**387 (231-790)**	**4.1 (3.2-5.3)**	**41.2 (32.4-93.0)**	**3.4 (2.2-4.9)**	**44.3 (28.1-80.0)**

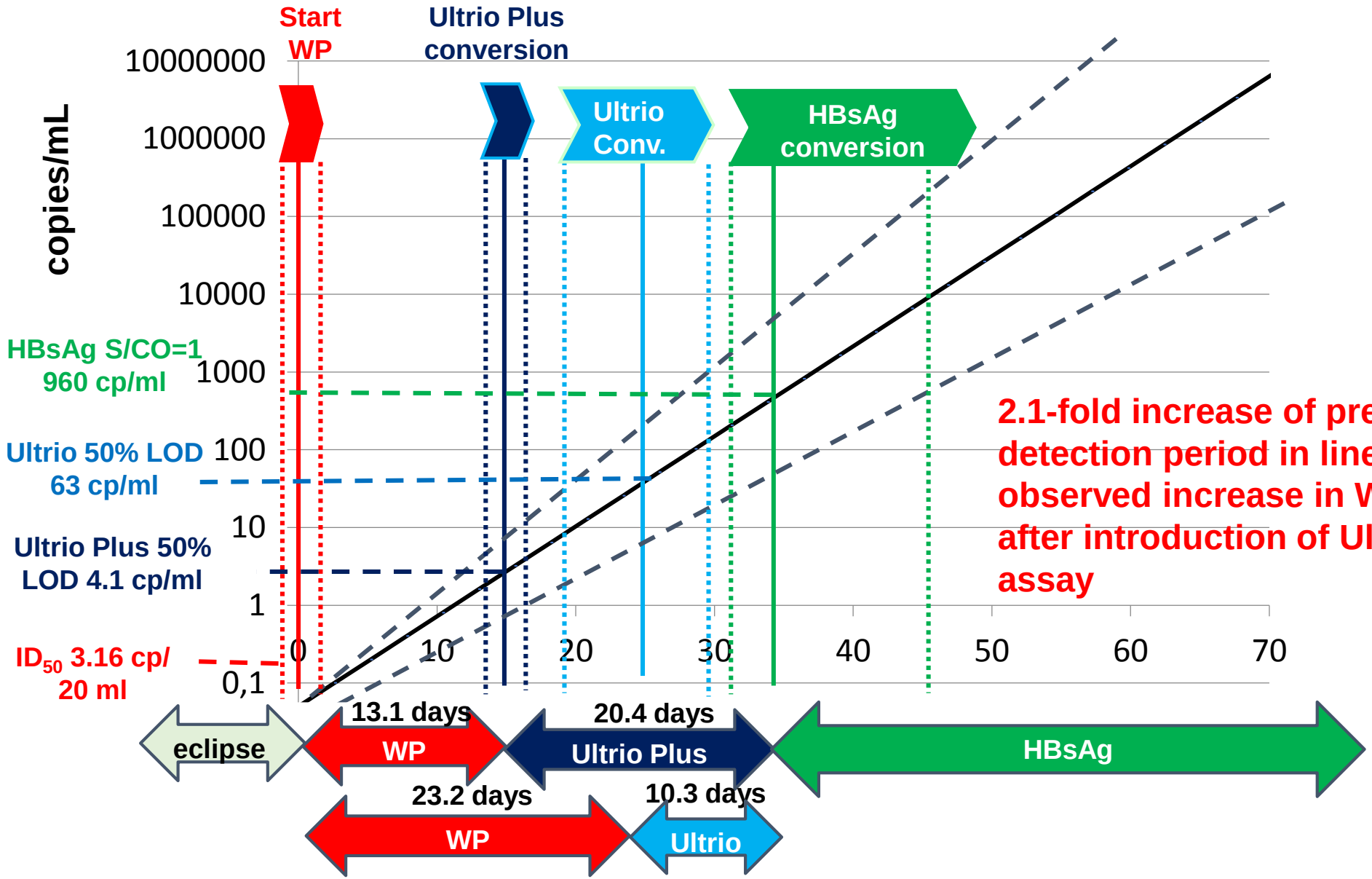
LODs used for modelling

Correlation of Log HBV-DNA and Log S/CO HBsAg in South African anti-HBc negative HBV ramp up samples



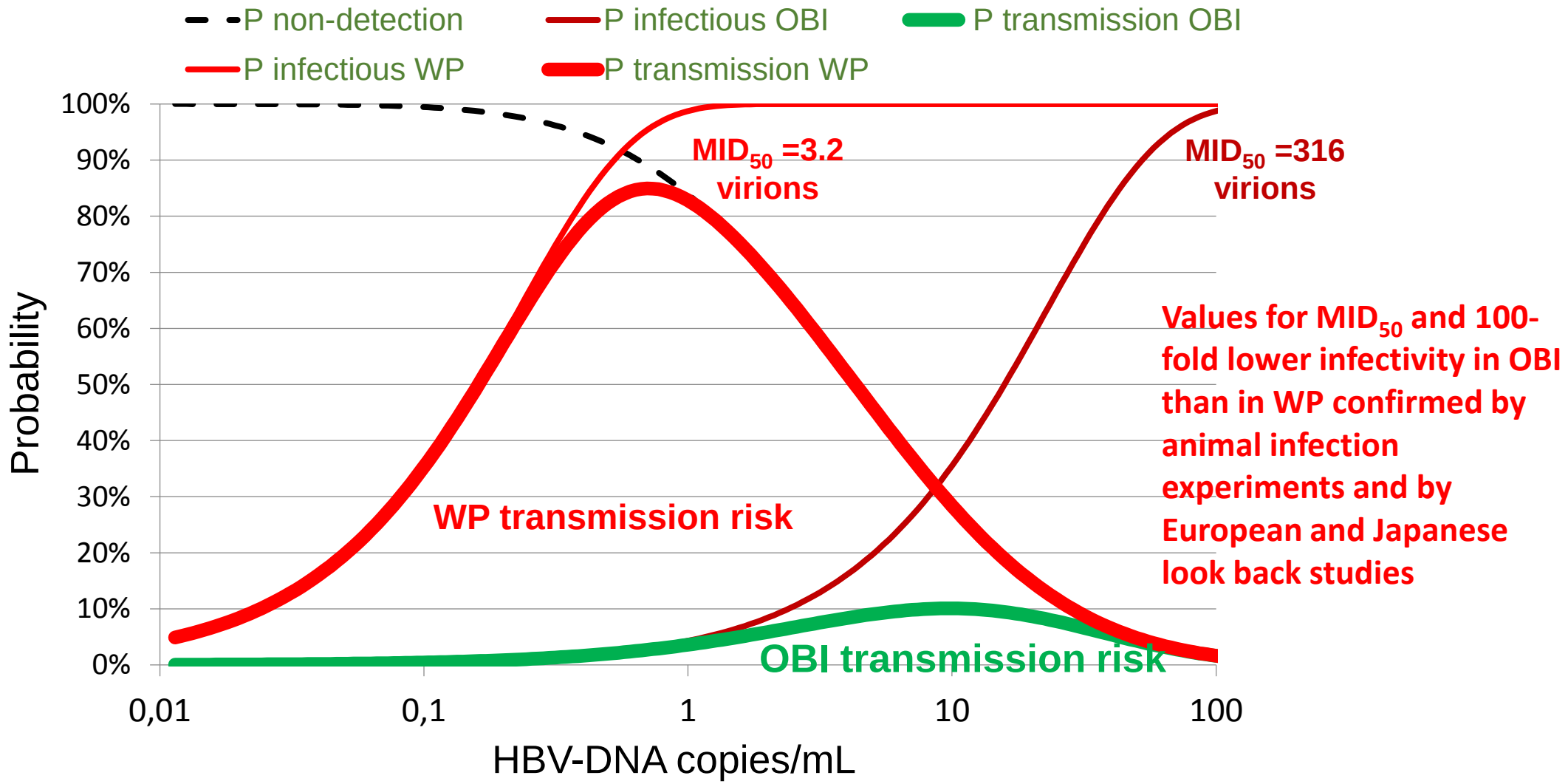
Vermeulen et al. manuscript in press

Reassessement of window periods of HBV screening assays used in ratio modelling



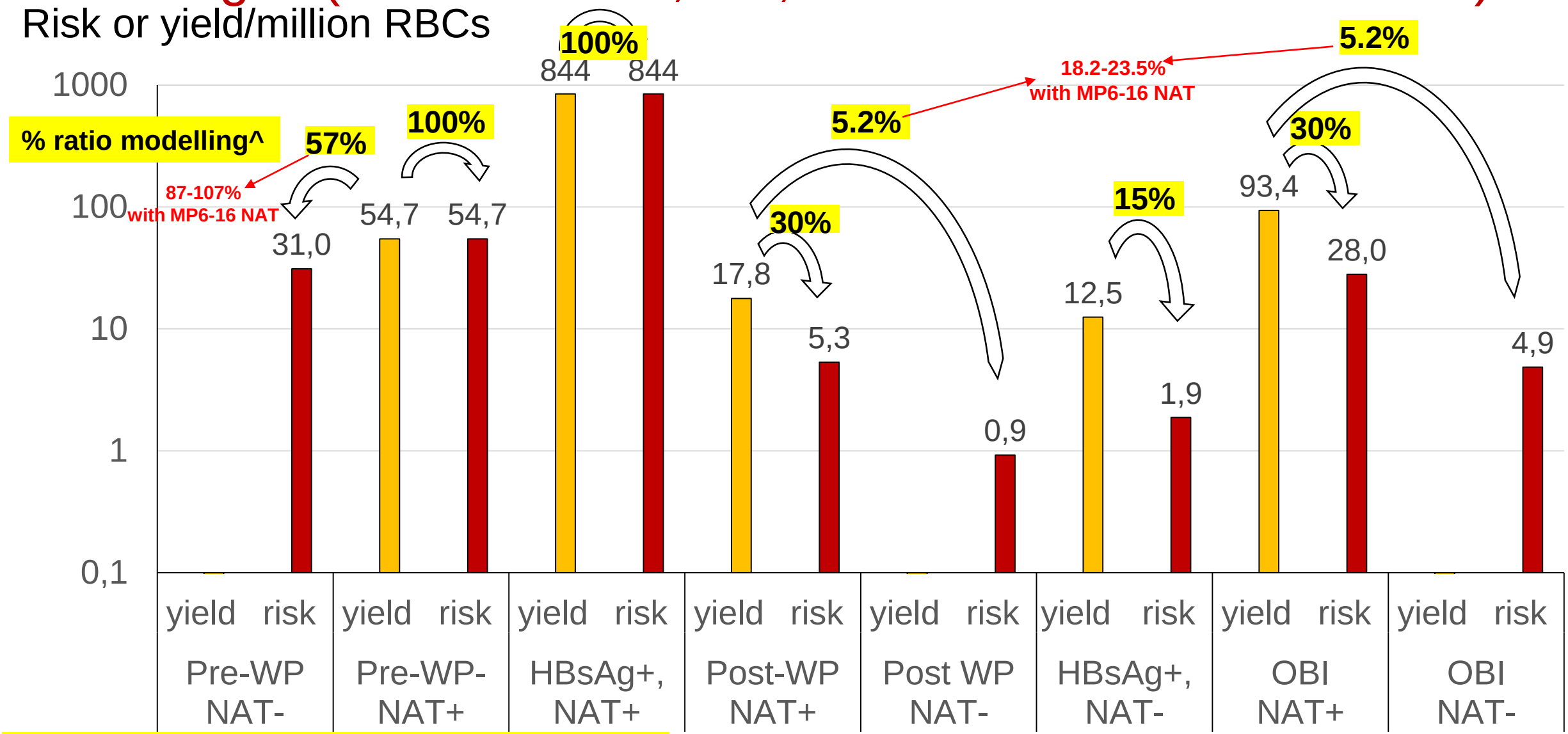
2.1-fold increase of pre-HBsAg NAT detection period in line with observed increase in WP NAT yields after introduction of Ultrio Plus assay

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



Weusten J et al, Transfusion 2011;51:203-15. Weusten et al. Transfusion 2017;57:841-849.

Estimation of HBV transmission risk in different HBV infection stages (modeled on 3,571,315 South African donations)



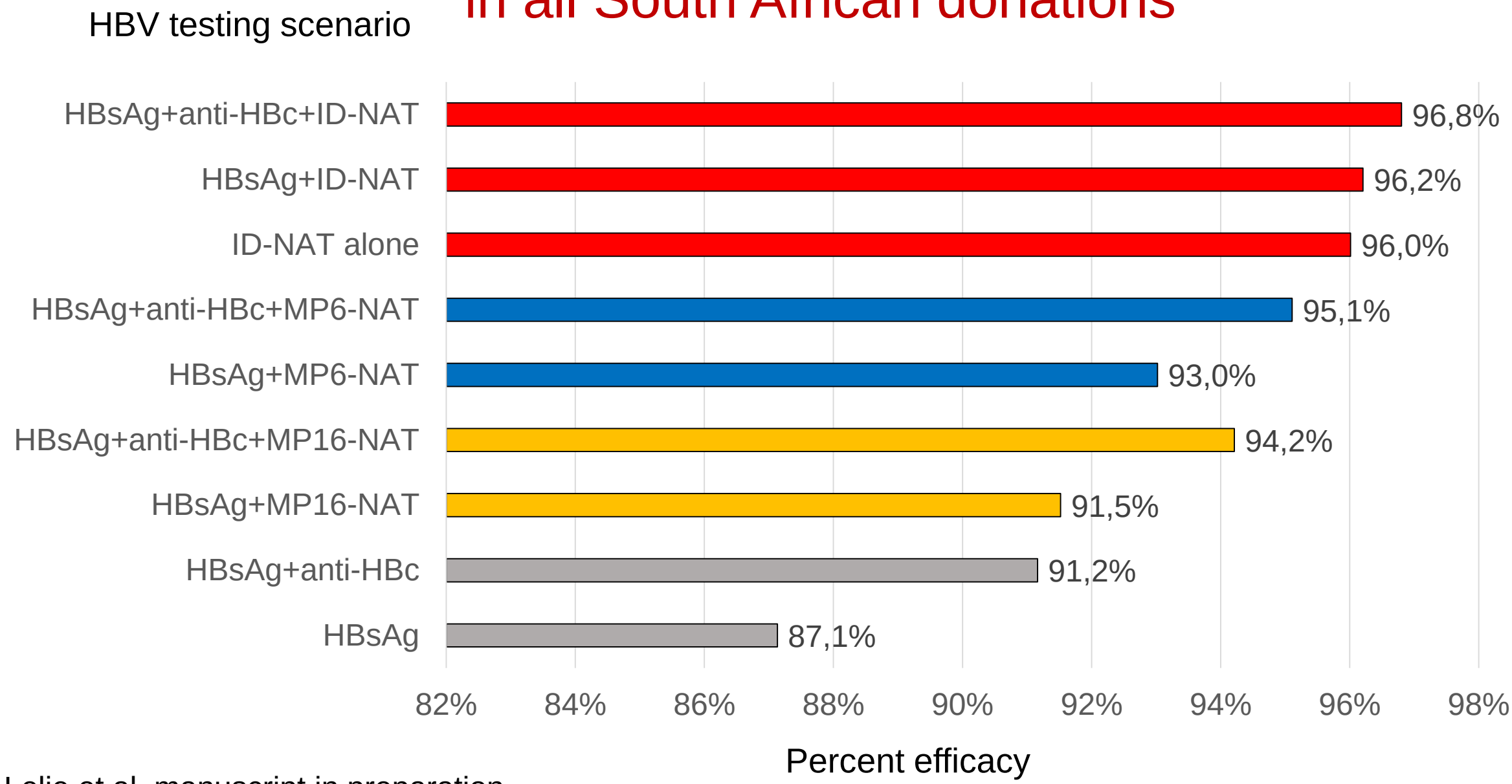
^Busch et al, Transfusion 2013;53:2477; Weusten J et al, Transfusion 2011;51:203; Weusten et al. Transfusion 2017;57:841

Residual HBV transmission risk/million RBCs based on South African screening data (2005-2009)

screening scenario	First time	Lapsed	Repeat	Lapsed + Repeat	All
no screening	7851.56	502.34	158.89	197.55	970.85
HBsAg	382.23	173.08	86.24	96.01	124.93
HBsAg+anti-HBc	191.97	117.94	68.26	73.85	85.79
HBsAg+MP16-NAT^	252.96	114.18	54.51	63.24	82.32
HBsAg+anti-HBc+MP16-NAT^	125.93	77.37	44.78	48.45	56.19
HBsAg+MP6-NAT#	204.72	93.85	47.11	52.37	67.74
HBsAg+anti-HBc+MP6-NAT#	106.35	65.34	37.81	40.91	47.50
ID-NAT alone^	116.13	50.83	27.36	30.00	38.70
HBsAg+ID-NAT^	97.58	50.83	27.36	30.00	36.82
HBsAg+anti-HBc+ID-NAT^	69.47	42.68	24.70	26.73	31.04

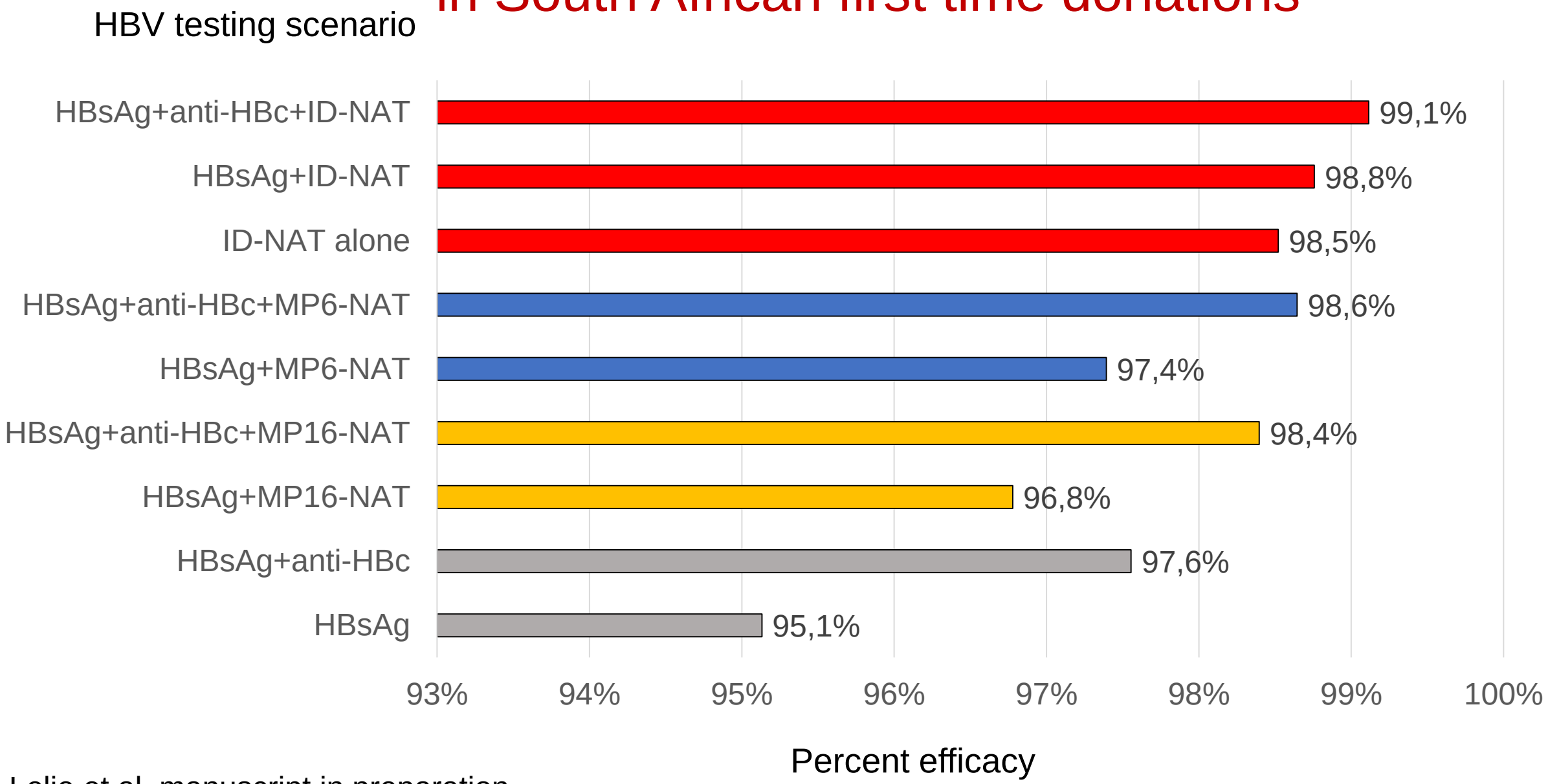
^ Ultrio Plus with 95% and 50% LOD of 41.2 and 4.1 copies/mL
#TaqScreen 1.0 with 95% and 50% LOD of 44.2 and 3.4 copies/mL
LODs reported by Vermeulen et al (Transfusion 2013;53:2459-2466)

Efficacy of HBV testing scenarios in all South African donations



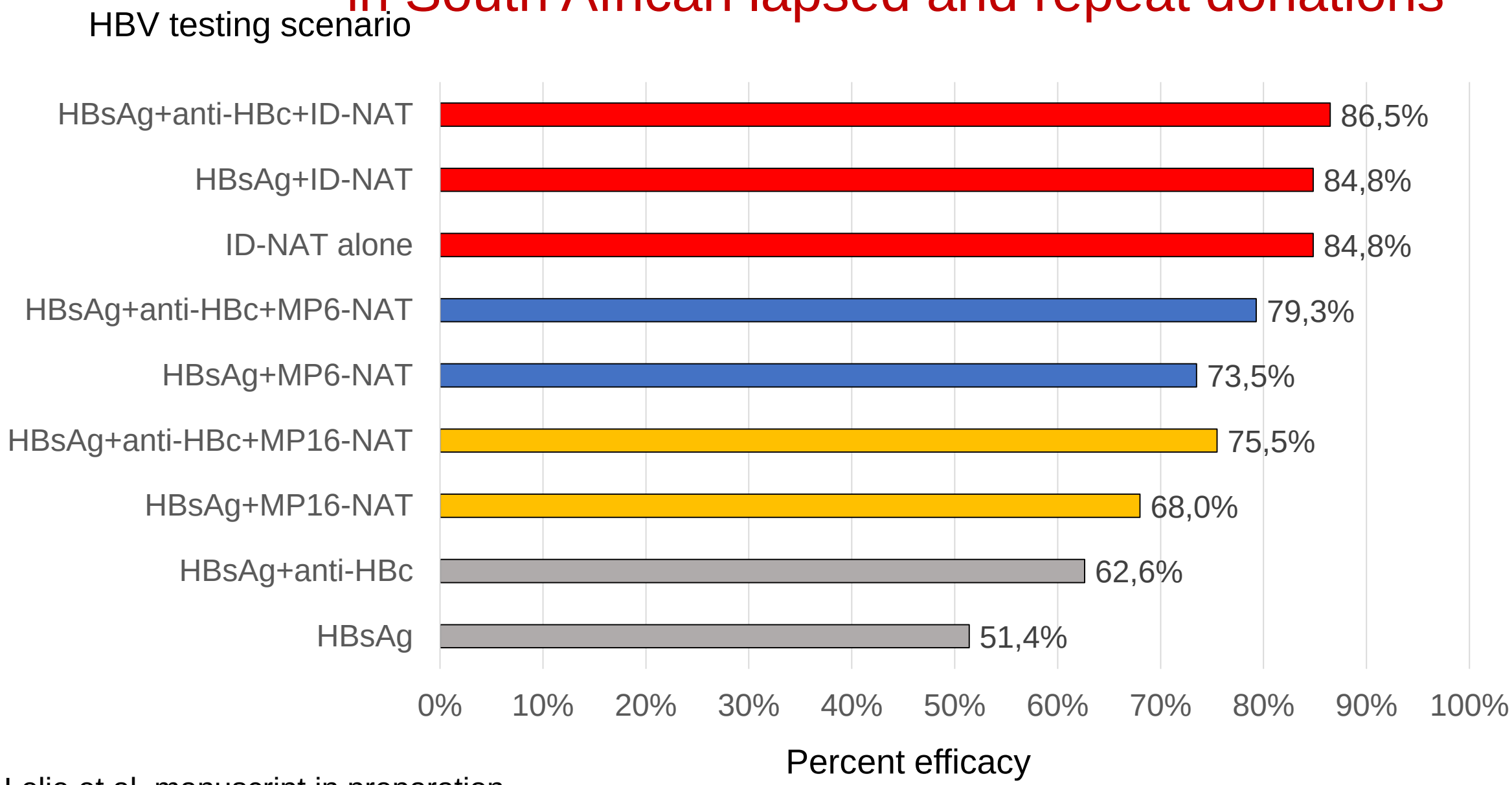
Lelie et al, manuscript in preparation

Efficacy of HBV testing scenarios in in South African first time donations



Lelie et al, manuscript in preparation

Efficacy of HBV testing scenarios in South African lapsed and repeat donations



Lelie et al, manuscript in preparation

Conclusions and discussion

- ID-NAT alone reaches higher efficacy in removing HBV transmission risk than MP-NAT in combination with HBsAg and anti-HBc testing
  - in all South African donations, and particularly in repeat donations
  - but comparable efficacy was found in first time donors
- Efficacy of HBV testing scenarios is mainly a function of assay sensitivity and is not so much influenced by the regional prevalence and incidence (data not shown)
- Risk and efficacy estimates are influenced by:
  - 100-fold higher MID_{50} in OBI than in WP (316 versus 3.16 copies)
  - Relative contribution of HBV WP versus OBI transmission risk in regional donor population
    - Proportion first time (unscreened) and repeat donors (pre-screened)
  - LODs of NAT methods in regional samples/genotypes and MP sizes
  - Proportion OBI donations neutralized by anti-HBs
  - Plasma volume in blood component
    - Possibility of infectious HBV attached to RBCs, platelets or leucocytes has so far not been addressed by infectivity models