

Impact of changing donor
demographics on HIV transmission risk: A
ten year analysis of individual donation
NAT screening



SANBS

South African National Blood Service

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Disclaimer



- Race classifications are described as per the South African government classifications and are not meant to be discriminatory nor pejorative.



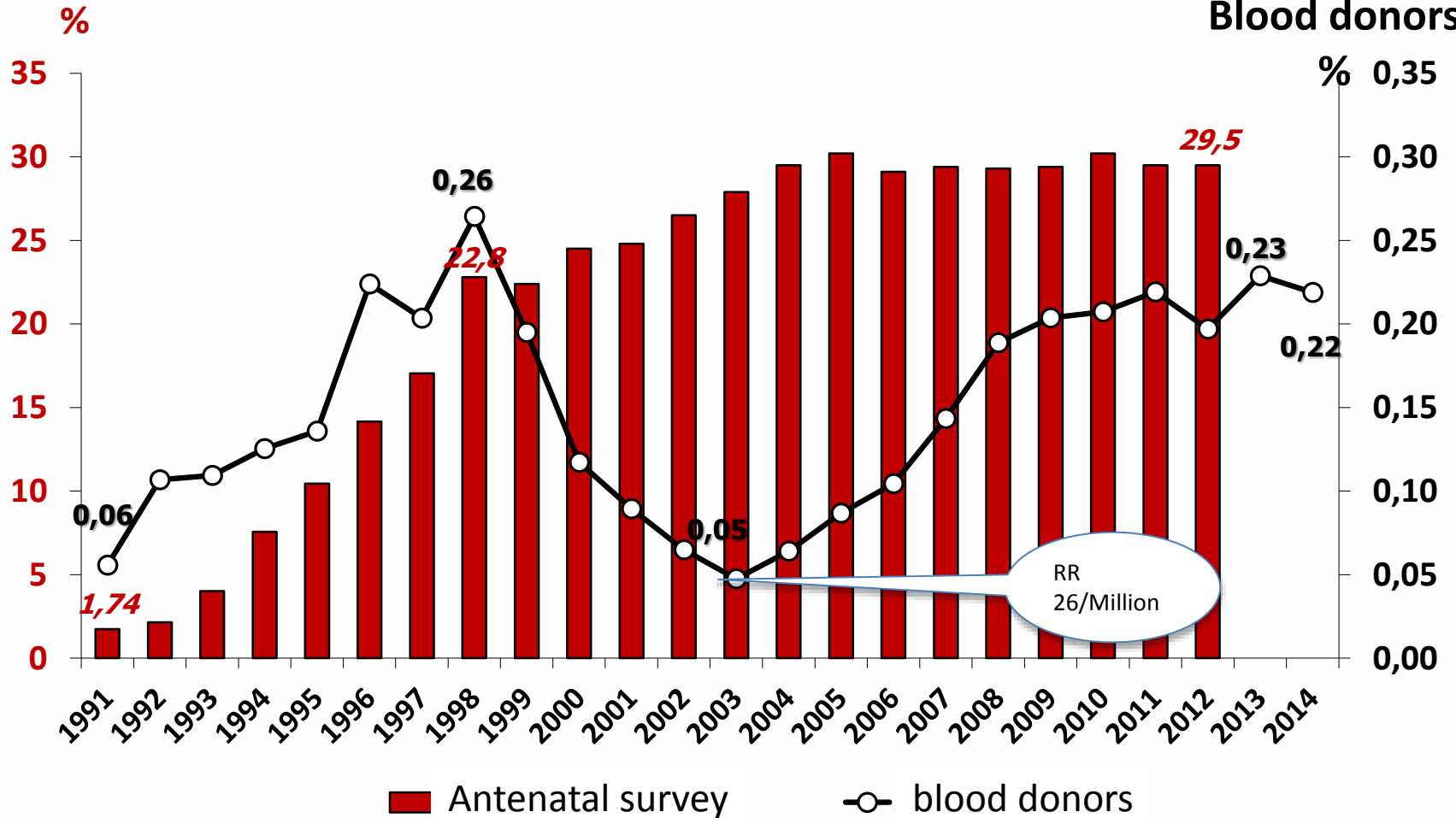
Background on HIV epidemic



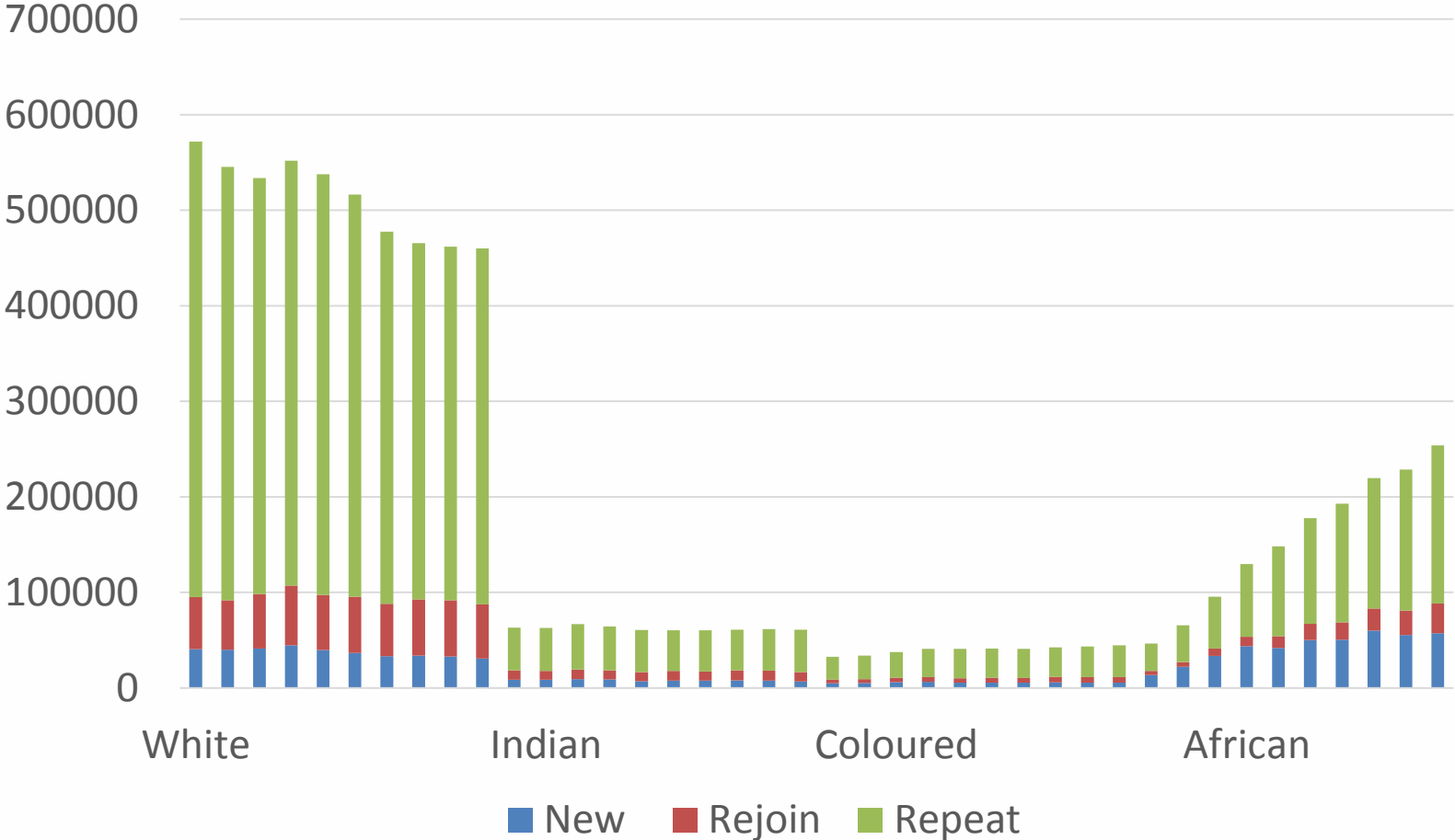
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Antenatal Survey

Blood donors



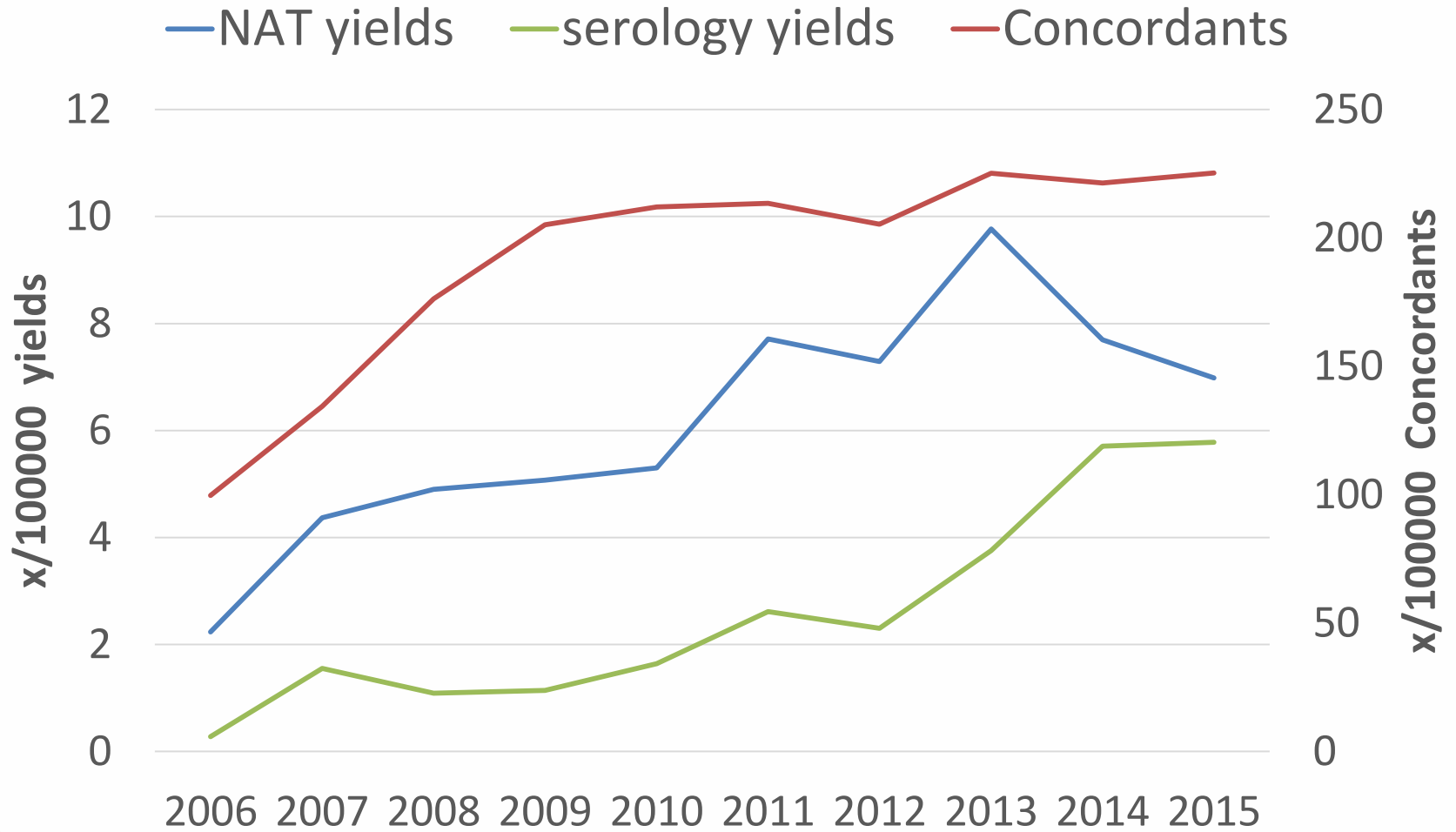
Collections by race and donor type over 10 years



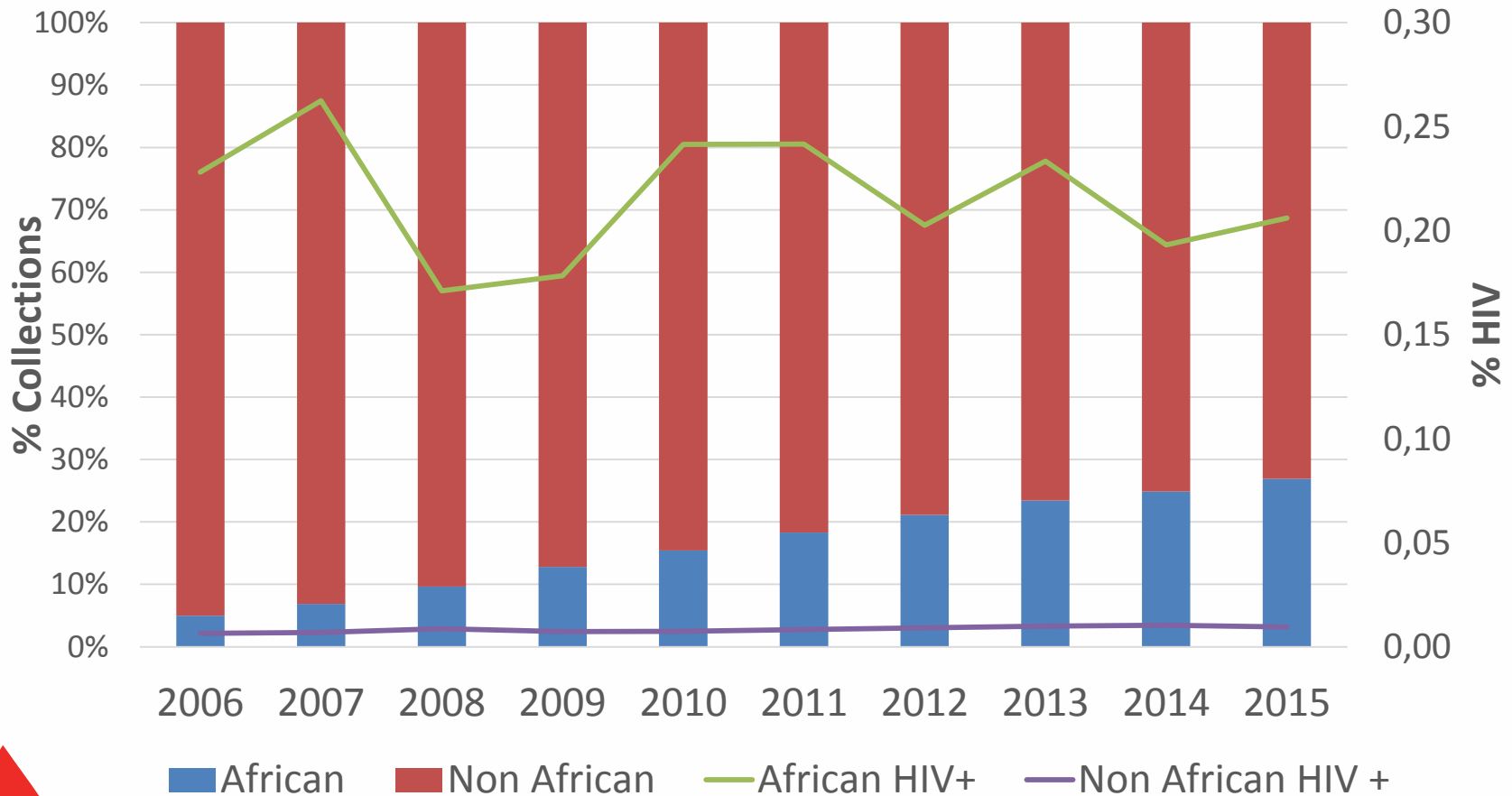
HIV rate



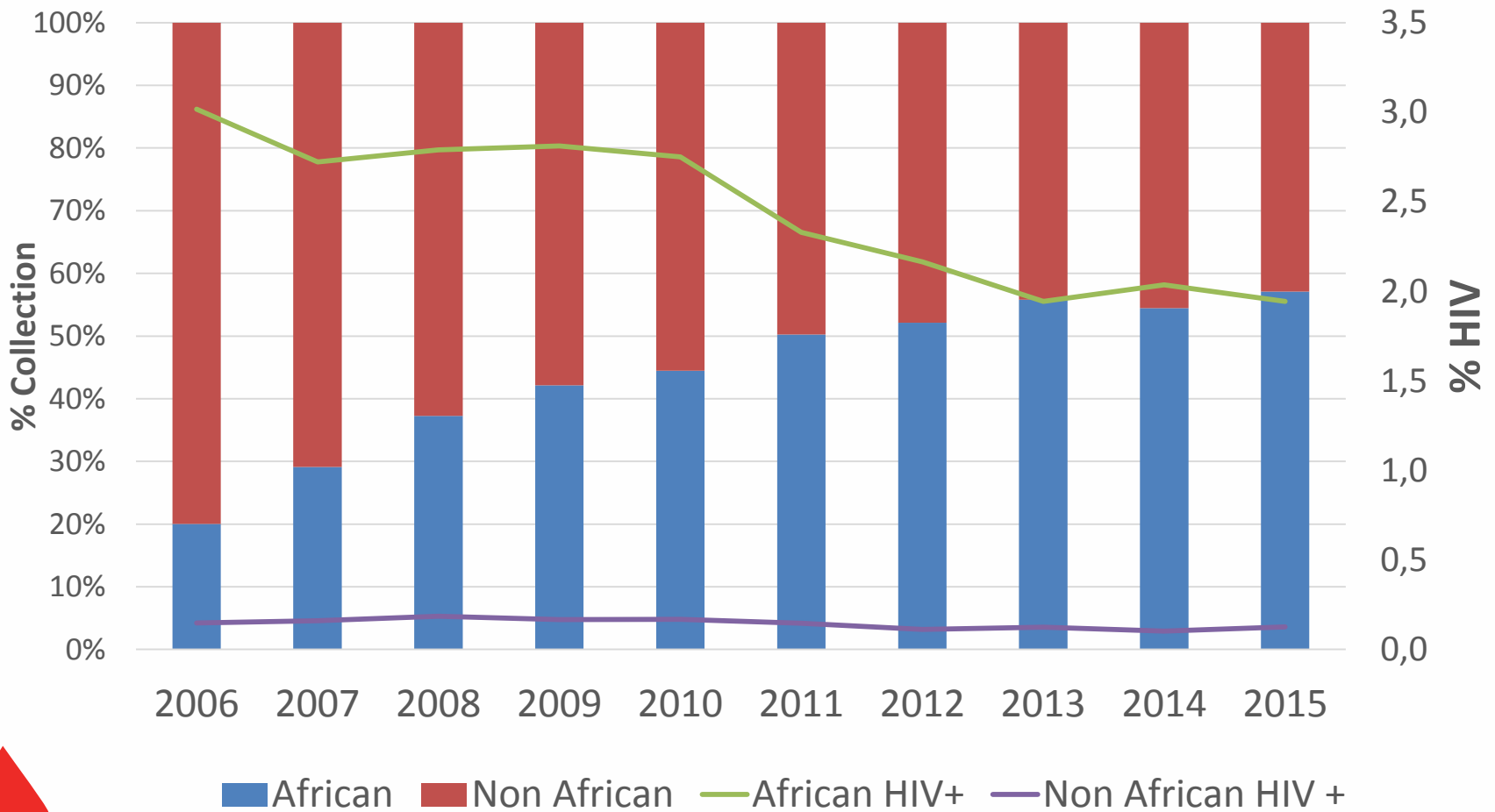
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Collections and HIV rate in repeat donors



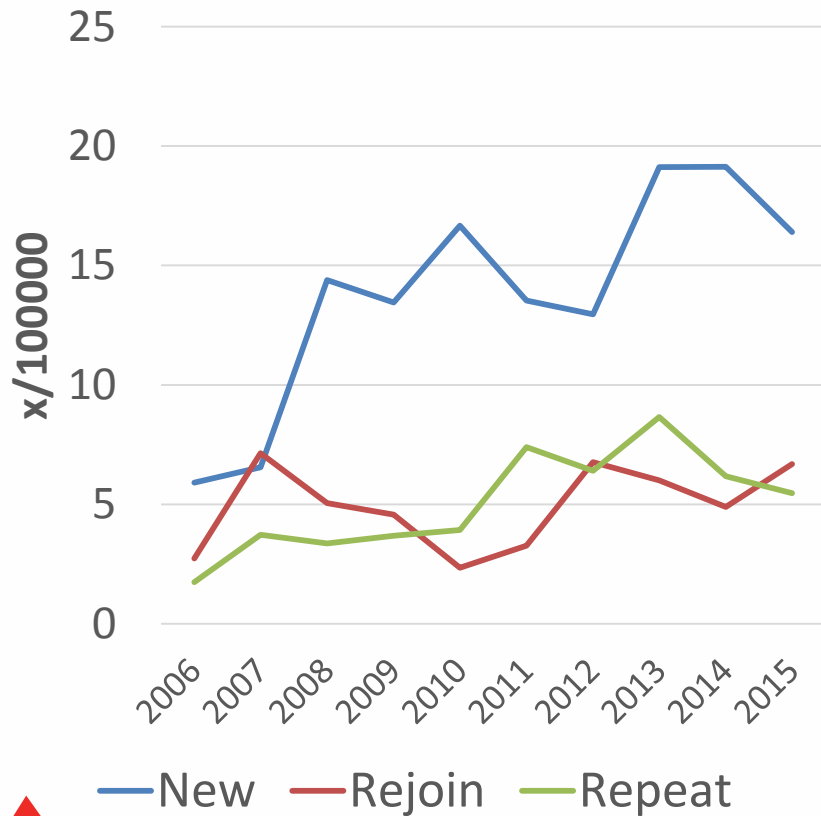
Collections and HIV rate in new donors



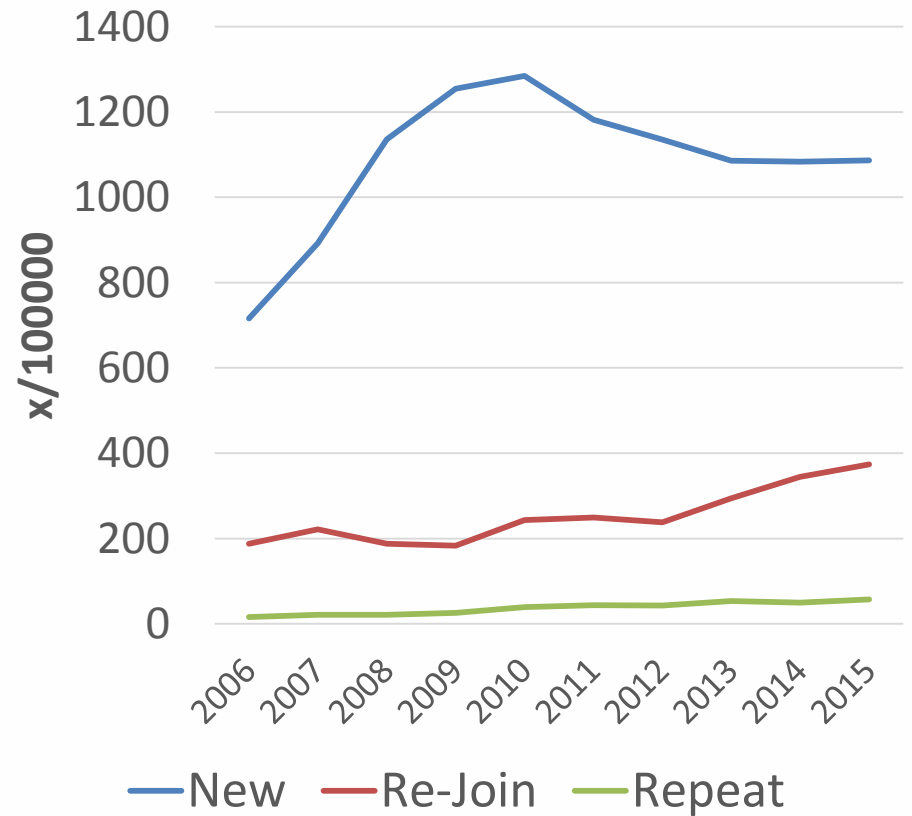
HIV rates by donor type and classification



NAT yield rate



HIV concordants



Number (%) of HIV infection category

	New	Rejoin	Repeat	Inter-don interval days (p)#	Total SANBS
NAT yields*	137 (1.3)	44 (1.9)	301 (12.0)	101 (p<0.05)	482 (3.1)
Serology* Yields	186 (1.7)	17 (0.7)	3 (0.1)	781 (p<0.05)	206 (1.3)
Concordant	10545 (97.0)	2285 (97.4)	2208 (87.9)	231	15038 (95.6)
Total	10868 (100)	2346 (100)	2512 (100)		15726 (100)

*p value <0.005 when comparing proportion of repeat and rejoin donors with new donors

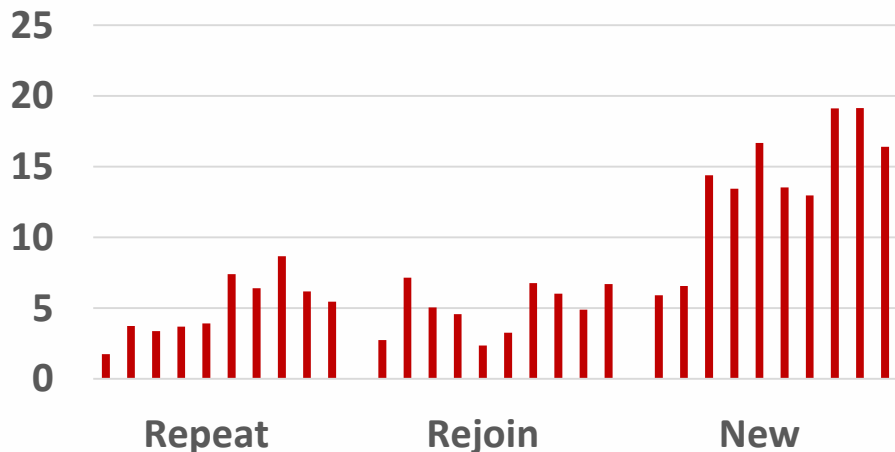
p value < 0.05 when comparing interdonation intervals of NAT and serology yields with concordants (student t test)

Risk factors

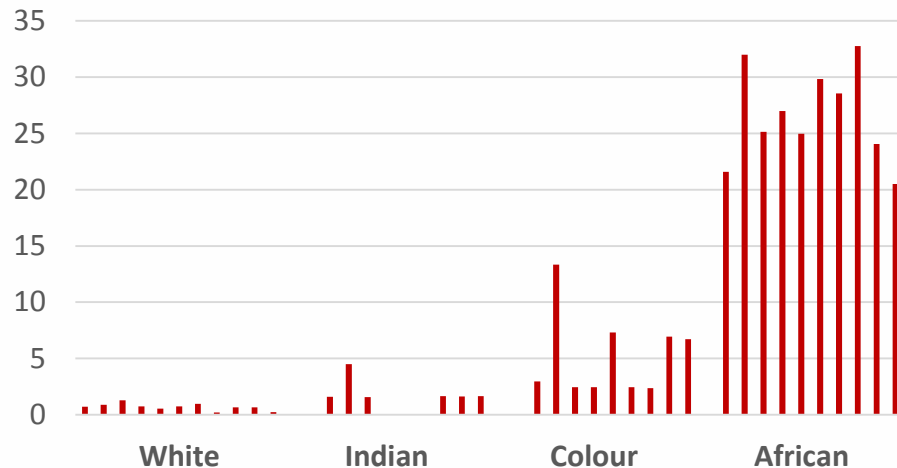
NAT yield/100 000



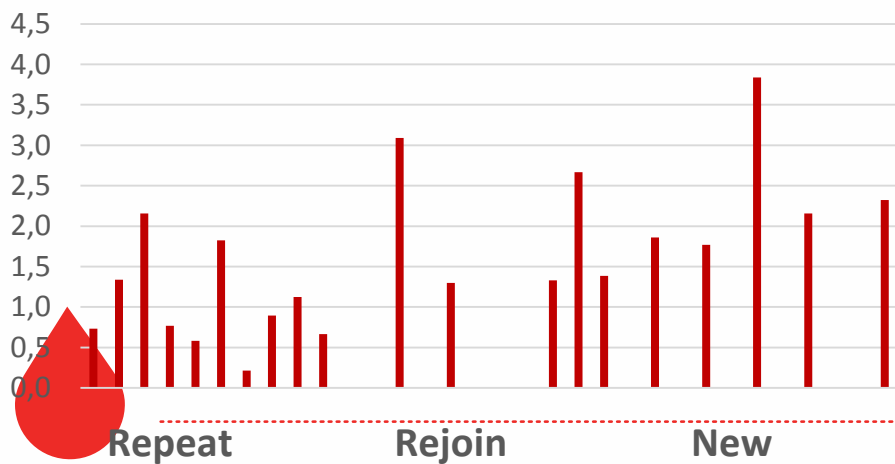
Donor Type



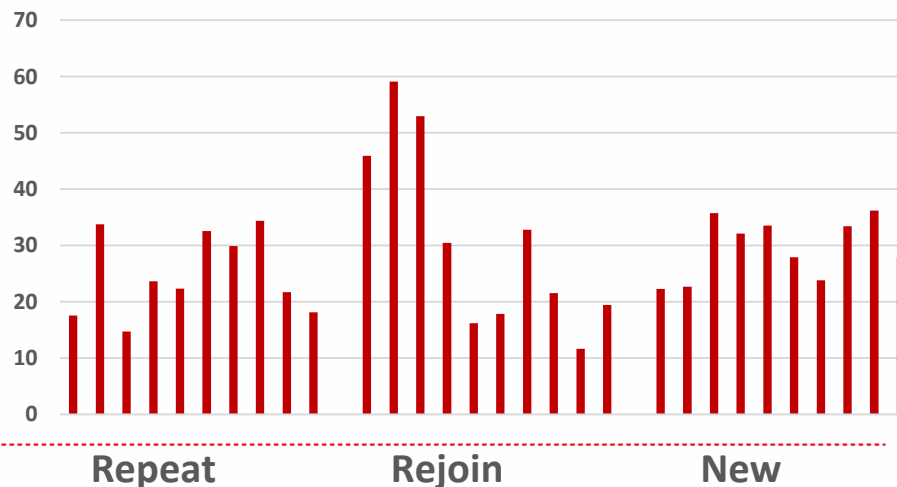
Ethnicity



Non African



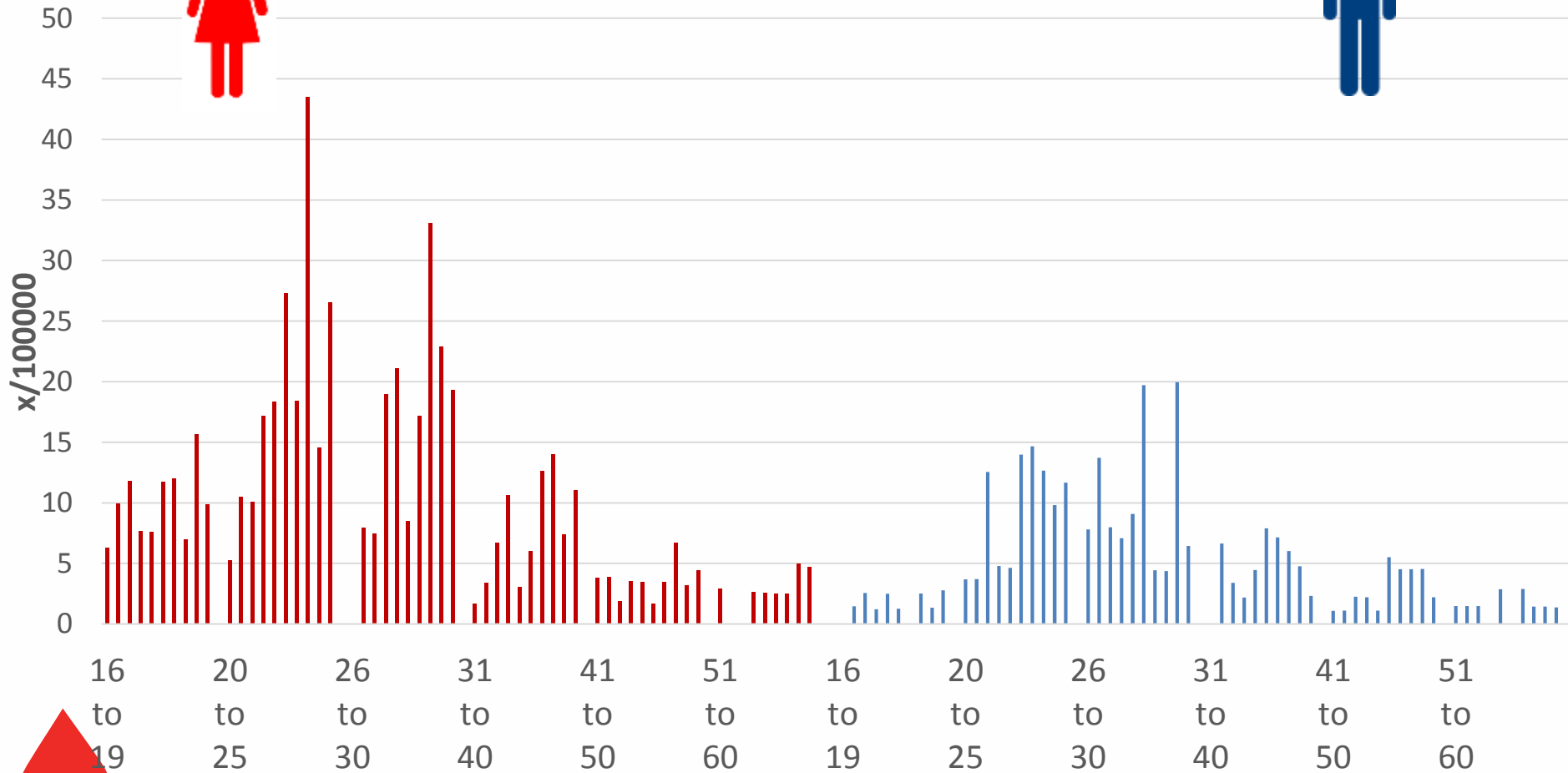
African



HIV NAT yield/100 000 by age and gender



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% HIV by ethnicity and donor type



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Category	Race	Donor type			p value (new vs repeat)
		New	Rejoin	Repeat	
HIV positives	White	0.084	0.052	0.005	<0.005
	Indian	0.138	0.087	0.010	<0.005
	Coloured	0.573	0.354	0.047	<0.005
	African	2.335	1.143	0.214	<0.005
Total		1.122	0.263	0.042	<0.005
NAT yields	White	0.0005	0.0009	0.0007	0.98
	Indian	0.0025	0.0000	0.0016	0.9
	Coloured	0.0036	0.0040	0.0051	0.88
	African	0.0304	0.0240	0.0253	0.1
Total		0.0142	0.0050	0.0050	<0.005

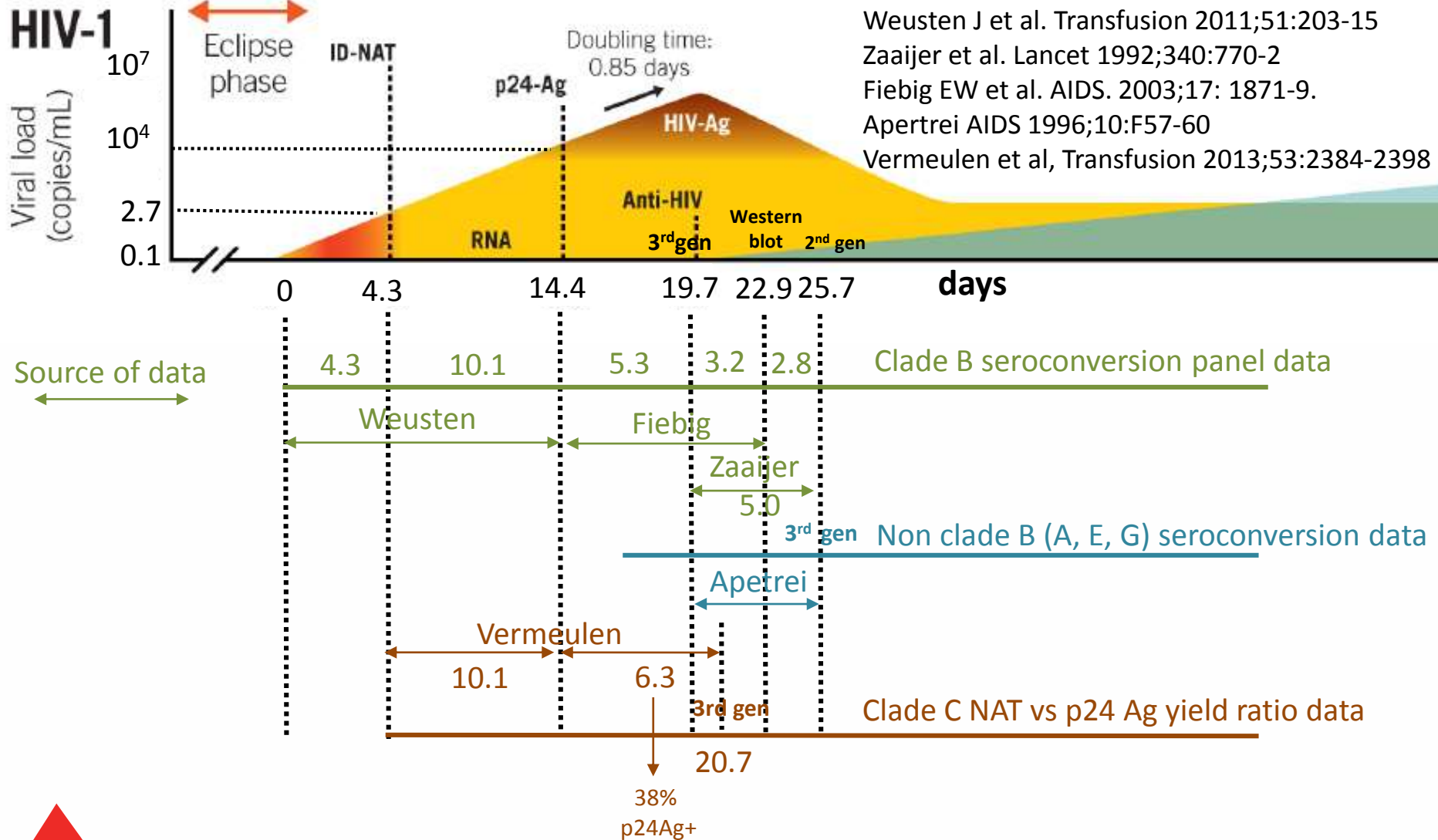


p24 antigen reactivity (%) of NAT yields



	Negative	Positive	Total
2006	8 (53)	7 (47)	15
2007	11 (38)	18 (62)	29
2008	24 (73)	9 (27)	33
2009	26 (68)	12 (32)	38
2010	28 (68)	13 (32)	41
2011	39 (63)	23 (37)	62
2012	30 (55)	25 (45)	55
2013	50 (67)	25 (33)	75
2014	37 (63)	22 (37)	59
2015	32 (53)	24 (43)	56
Total	285 (62)	178 (38)	463

Early dynamics of HIV markers and estimates of lengths of WPs



Weusten J et al. Transfusion 2011;51:203-15
 Zaaier et al. Lancet 1992;340:770-2
 Fiebig EW et al. AIDS. 2003;17: 1871-9.
 Apetrei AIDS 1996;10:F57-60
 Vermeulen et al, Transfusion 2013;53:2384-2398



Residual risk methodology



- **Incidence rate-WP risk day equivalent model¹**

- No Repeat donations
- No. Seroconverting donors
- Harmonic mean of interdonation interval
- $MID_{50} = 1$
- 95% LOD = 18.4 copies/mL*
- 50% LOD = 2.7 copies/mL*
- 2 copies/virion
- NAT WP 4.3 days

$$RR = \frac{R \text{ Days}}{T \text{ between}} \times \frac{N \text{ seroconverting repeat}}{N \text{ repeat donations}}$$

- **NAT Yield WP ratio model^{1,2}**

- No of NAT yields
- No of donations
- NAT WP = 4.3 days
- NAT+ Ab- = 15.4 days (clade B)
- NAT+ Ab- = 16.4 days (clade C)
- NAT+,p24Ag- = 10.1 days
- NAT+, p24 Ag+=6.3 days

$$RR = \frac{WP \text{ NAT } (T1)}{(WP \text{ HIV Ab} - WP \text{ NAT})(T2)} \times \frac{(NNAT \text{ yields})}{N \text{ all donations}}$$

1. Weusten Transfusion 2011;51:203-15
2. Busch Transfusion 2005;45:254-64



Comparison of models to determine residual risk per million



	Lengths of WP used	WP Incidence rate-risk day equivalent model			WP ratio model
		Repeat	Lapsed	Repeat + Lapsed	Repeat + Lapsed
Pre-NAT WP	Clade B	14.58	13.77	14.52	14.15
Pre-NAT WP	Clade C	14.58	13.77	14.52	13.29
Pre-p24 Ag WP	Clade C	48.68	45.99	48.64	49.01

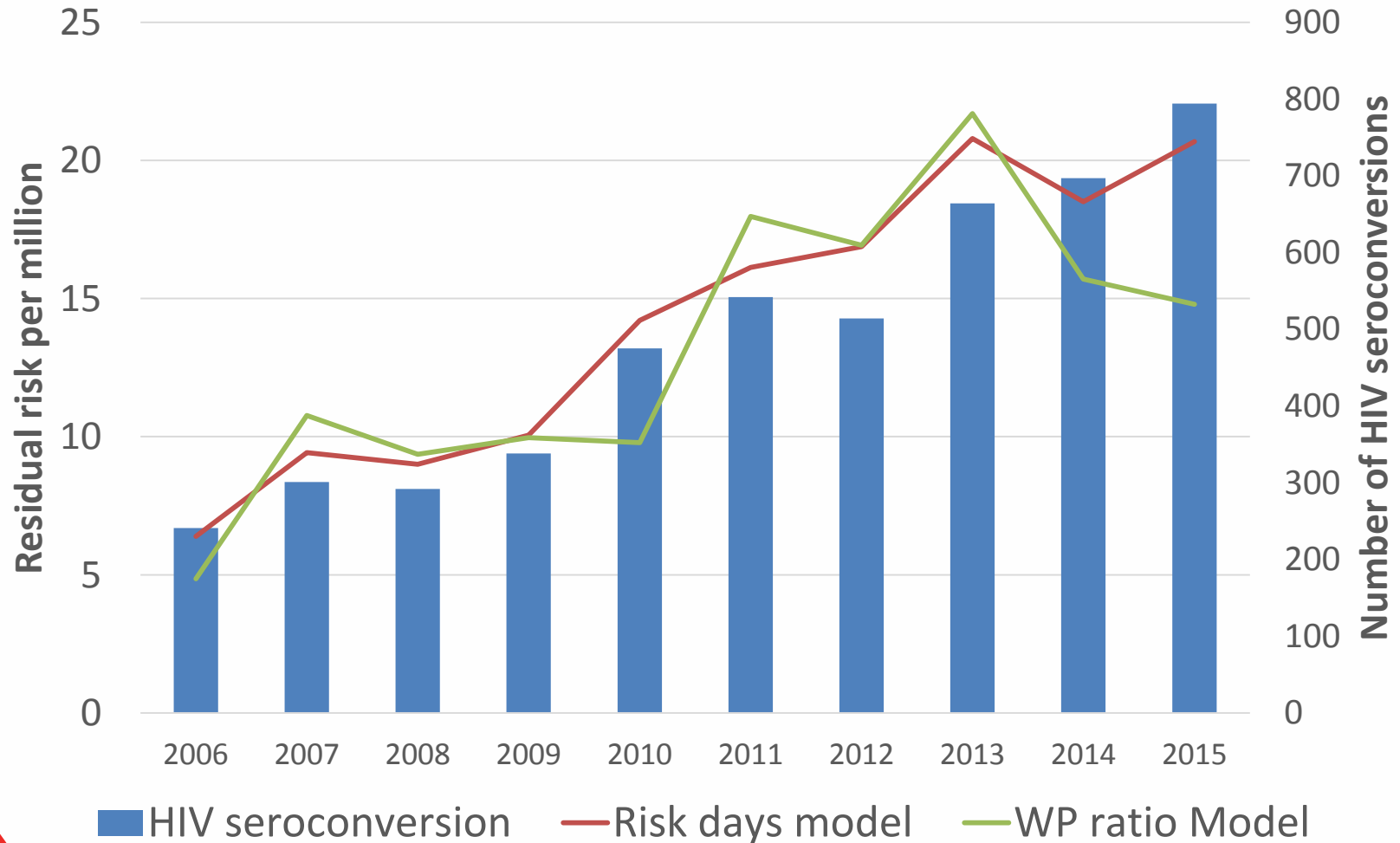


MID₅₀ = 1 virion

Trend of residual HIV transmission risk

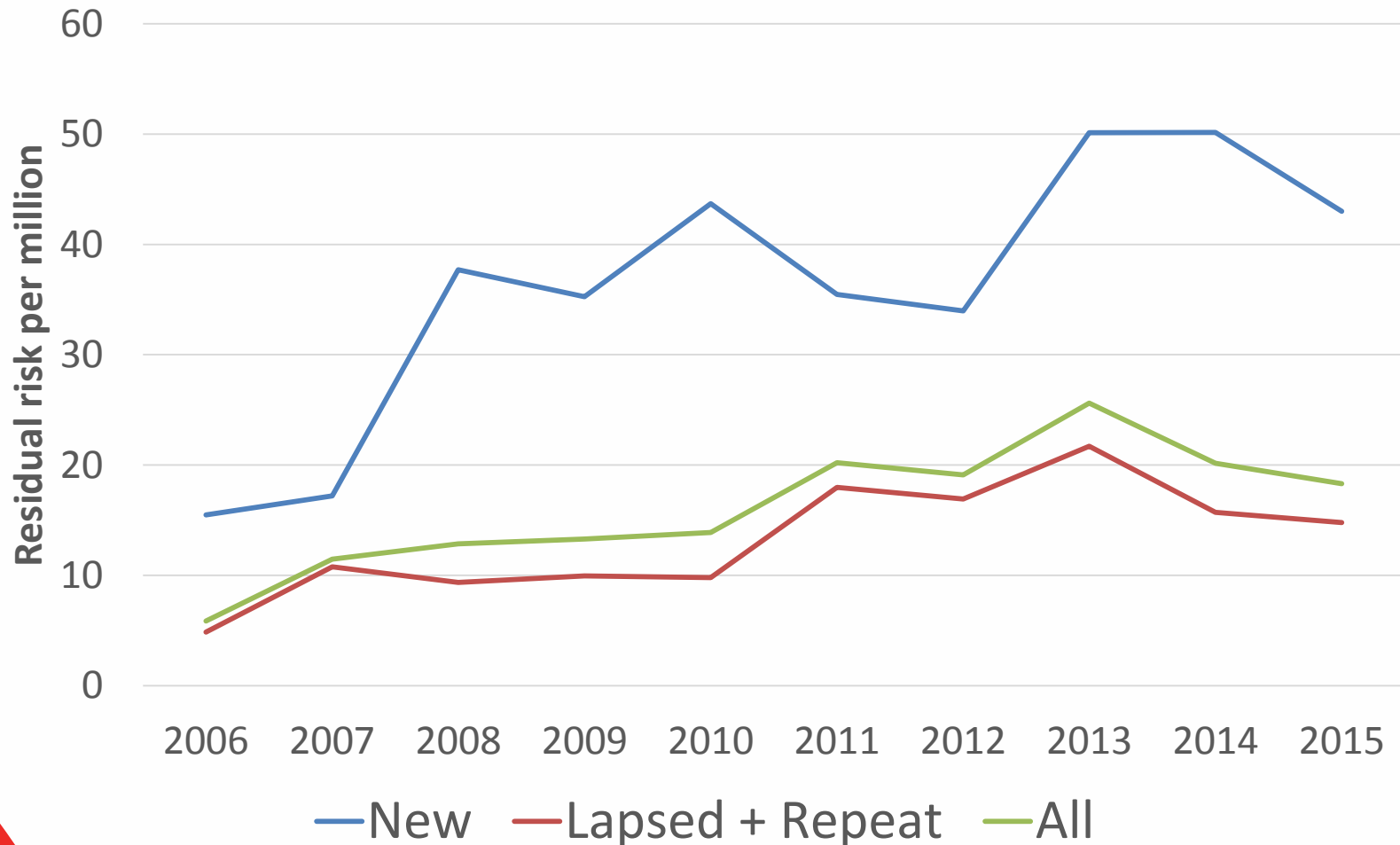


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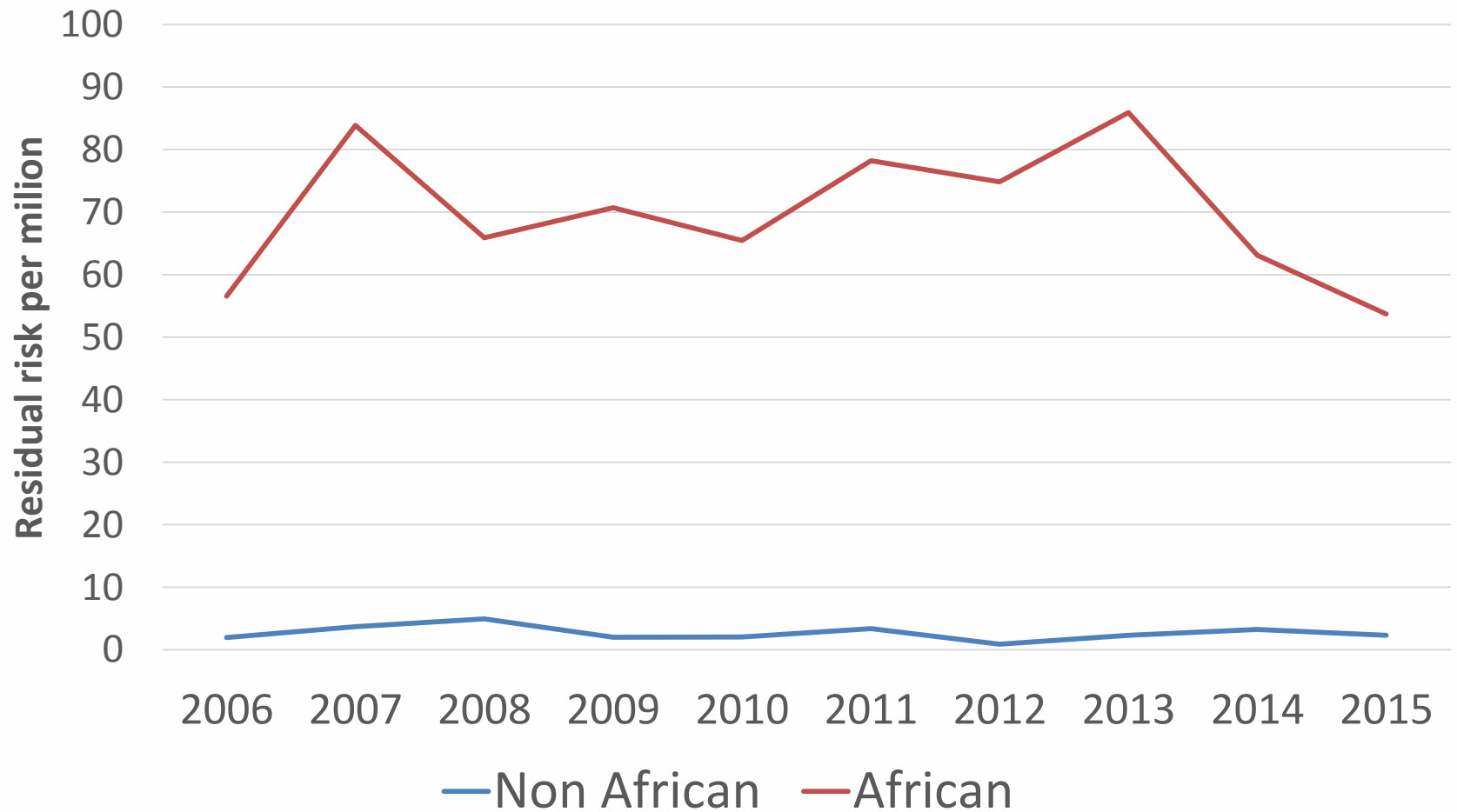
(MID₅₀ = 1 virion, Clade C parameters)

Trend residual HIV transmission risk by donor type



(WP ratio model, $MID_{50}=1$ virion, Clade C parameters)

Trend residual HIV transmission risk by race



WP ratio model, MID₅₀ = 1 virion, Clade C parameters)

Residual HIV transmission risk by donor type and ethnicity



		African	Non African	All
RR x:Million (MID ₅₀ =1)	New	79.7	3.1	38.1
	Repeat & Lapsed	65.9	2.7	13.3
	All	69.7	2.7	16.2
RR 1:x	New	1:12,548	1:323,438	1:26,264
	Repeat & Lapsed	1:15,174	1:370,342	1:75,407
	All	1:14,349	1:371,776	1:61,557



WP ratio model, MID₅₀ =1 virion, Clade C parameters)

HIV ID-NAT breakthrough infection



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	Donor		Recipient
	Transfused unit	Index donation	Recipient
Date Bled	19/09/2014	04/12/2014	14/02/2015
Unit number	26001167	26198447	
Transfused date	28/09/2014		Started ARV 28/01/2015
Prism HIV S/CO	0.56	54.13	
NAT S/CO	0.65	11.96	
Viral load			936 copies/ml
CD4			578

Lookback investigation

HIV-1 Subtype C

100% boot strap in phylogenetic sequencing

Observed risk 1:7.7 million

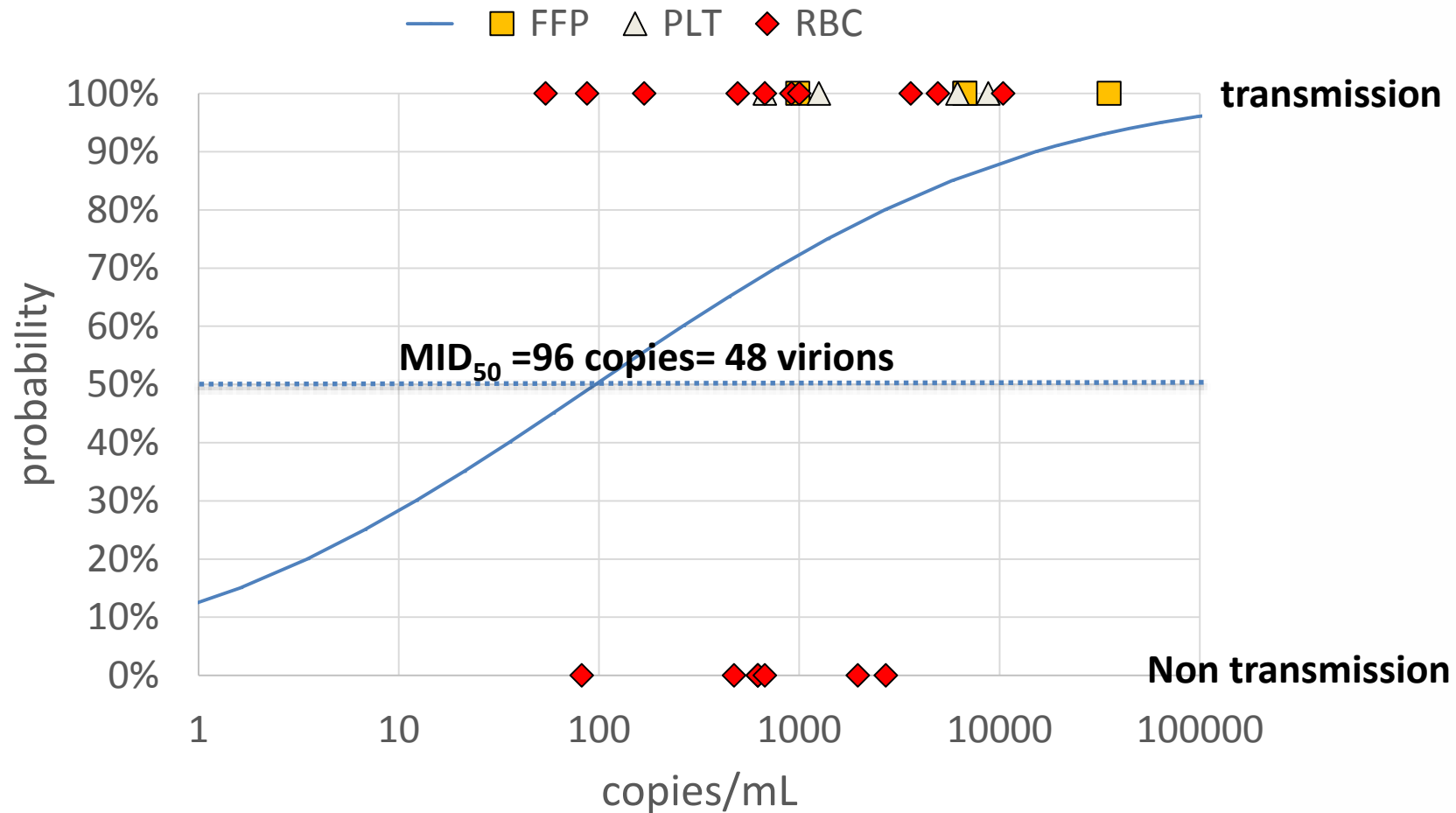


HIV NAT breakthrough cases



Test Failure Break-Through Cases												
Country	Blood Product	Storage time days	Screening Assay	50% LOD cps/mL	95% LOD cps/mL	Pool size	Cps/mL estimate	Viral load method	Approx plasma mL	Estimated copies transfused	Recipient Infected	Reference
Germany	RBC		In-house			96	6400	TaqMan	20	128,000	Yes	Schmidt M et al. Transfusion 2009;49:1836-1844
Germany	RBC		In-house	4.2	22.1	96	12800	TaqMan	20	256,000	Yes	Chudy M et al. Transfusion.1537-2995.2011.03281.x
Viral Load Below Detectable Level												
Germany	PLT		In-house			24	0	TaqMan	240	0	No	Kalus U et al. , Transfusion 2009;49:435-439
Germany	RBC		Gfe Blut			96	23.6		20	472	No	Muller B. Transfusion. 2013;53:2422-30
France	RBC		Nuclisens-Ampliscreen	1.9	15.5	24	45.6	50% LOD	20	912	Yes	Najjiouallah F et al. J Med Virol 2004;73:347-349
USA	FFP		Duplex	2.1	15.6	16	33.6	50% LOD	200	6720	Yes	Phelps R et al. Transfusion 2004;44:929-933
USA	RBC		Duplex	2.1	15.6	16	33.6	50% LOD	20	672	Yes	Phelps R et al. Transfusion 2004;44:929-933
USA	FFP		Duplex	2.1	15.6	16	33.6	50% LOD	200	6720	Yes	Stramer S et al. Transfusion 2003;43:Supplement :40-41A
USA	RBC		Duplex	2.1	15.6	16	33.6	50% LOD	20	672	No	Stramer S et al. Transfusion 2003;43:Supplement :40-41A
USA	RBC		In-house			24	180	NGI ^b	20	3600	Yes	Delwart ELet al. Vox Sang 2004;86:171-177
Singapore	PLT		No NAT				50	Probit	25	1250	Yes	Ling AE et al. JAMA 2000; 28:4:210-214
Singapore	RBC		No NAT				50	Probit	20	1000	Yes	Ling AE et al. JAMA 2000; 28:4:210-214
S. Africa	RBC		No NAT				31	Probit	20	620	No	Ferriera MCet al. Transfusion 2006;46:156-157
S. Africa	PLT		No NAT				31	Probit	20	620	Yes	Ferriera MCet al. Transfusion 2006;46:156-157
Italy	RBC		No NAT				98	TaqMan	20	1960	No	Zanetti et al. Transfusion 2007;47:1328-1329
Denmark	PLT		In-house			96	246	Abbott RT	25	6150	Yes	Harritshoj Let al. Transfusion 2008;48:2026-28
Denmark	RBC		In-house			96	246	Abbott RT	25	4920	Yes	Harritshoj Let al. Transfusion 2008;48:2026-28
Japan	RBC		AmpliNAT	10.4	43.6	50	520	50% LOD	20	10400	Yes	Satake M et al. Journal of Hematology 2004;80:306-10
USA	RBC		Duplex	2.1	15.6	16	33.6	50% LOD	20	672	Yes	Laffoon et al, MMWR 2010;59:1335-6
Greece	RBC		No NAT	2.1	15.6	4	8.4	50% LOD	20	168	Yes	Hatzakis et al. (personal communication, 2006)
Spain	RBC	28	Ampliscreen	4.3	22.1	44	135	Ampl Monitor	20	2700	No	Alvarez et al. Transfusion 2016;56:831–836
Spain	PLT	2	Ampliscreen	4.3	22.1	44	135	Ampl Monitor	65	8775	Yes	Alvarez et al. Transfusion 2016;56:831–836
Spain	FFP-MB		Ampliscreen	4.3	22.1	44	135	Amp Mon	261	35235	Yes	Alvarez et al. Transfusion 2016;56:831–836
Japan	RBC		TaqScreen	4.1	28.0	20	4.1	50% LOD	20	82	No	Shinohar N. Transfusion 2014;54:2361-2
Japan	FFP		TaqScreen	4.1	28.0	20	4.1	50% LOD	240	984	Yes	Shinohar N. Transfusion 2014;54:2361-2
Brazil	RBC	11	in house		22.6	24	4.4	probit	20	87	Yes	Salles NA. Transfusion 2013;53:2593-5
Thailand	RBC		TaqScreen	4.1	28.0	6	24.6	50% LOD	20	492	Yes	Rujirojindakul P. Vox Sang 2015:109 Suppl 1 226 P-408 (abstract)
SANBS	RBC		Ultrio Plus	2.7	18.4	1	2.7	50% LOD	20	54	Yes	Vermeulen M personal communication

HIV transmissibility in NAT breakthrough cases



Impact of MID_{50} on overall residual HIV transmission risk



MID_{50}	x/million	1:x
1	16	1:61,557
3.16	11.17	1:90,909
31.6	3.26	1:306,748
316	0.49	1:2,040,816
Observed rate	0.13	1:7,692,307

Possible reasons for lower observed rate:

- 50% mortality rate
- 18% adult population already infected
- Poor ability to contact patients post discharge



Conclusions



- Yield ratio and incidence rate models were comparable when using same WP (risk day) estimates
- No difference in residual risk between repeat and lapsed blood donors
- No difference in NAT yield rate and in residual risk in new, repeat or lapsed donors within African donors (and within non African donors)
- Difference and trends in NAT yield rate and residual risk depends on donor demographics
- Estimated residual risk is >10 fold than observed rate
- The implementation of ID-NAT has enabled SANBS to increase the African donor base and maintain the RR 18/million window period donations compared to 26/million in 2005 (Pre-NAT)

Thank you