

Sensitivity of Alinity HIV-Ag/Ab combo assay

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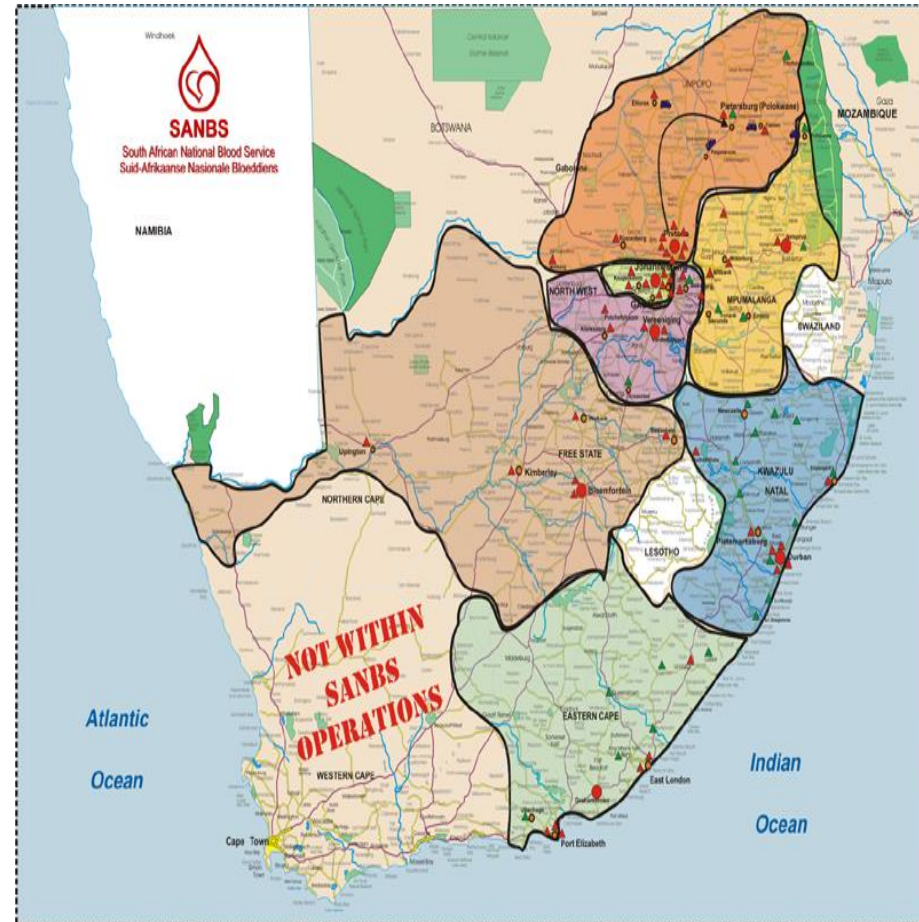
Pre-IPFA-PEI Satellite Workshop

Thirty years post-market performance follow up of NAT and serologic assays for detection of blood borne viruses

May 9th 2023, Hotel NH Bologna de la Gare

South African population and SANBS coverage

- Total Population - 59,39 million in 2021
- HIV Prevalence - 13,1%
- SANBS operates in 8 of 9 provinces in South Africa
- Collects over one million units annually
- 100% voluntary non remunerated donors



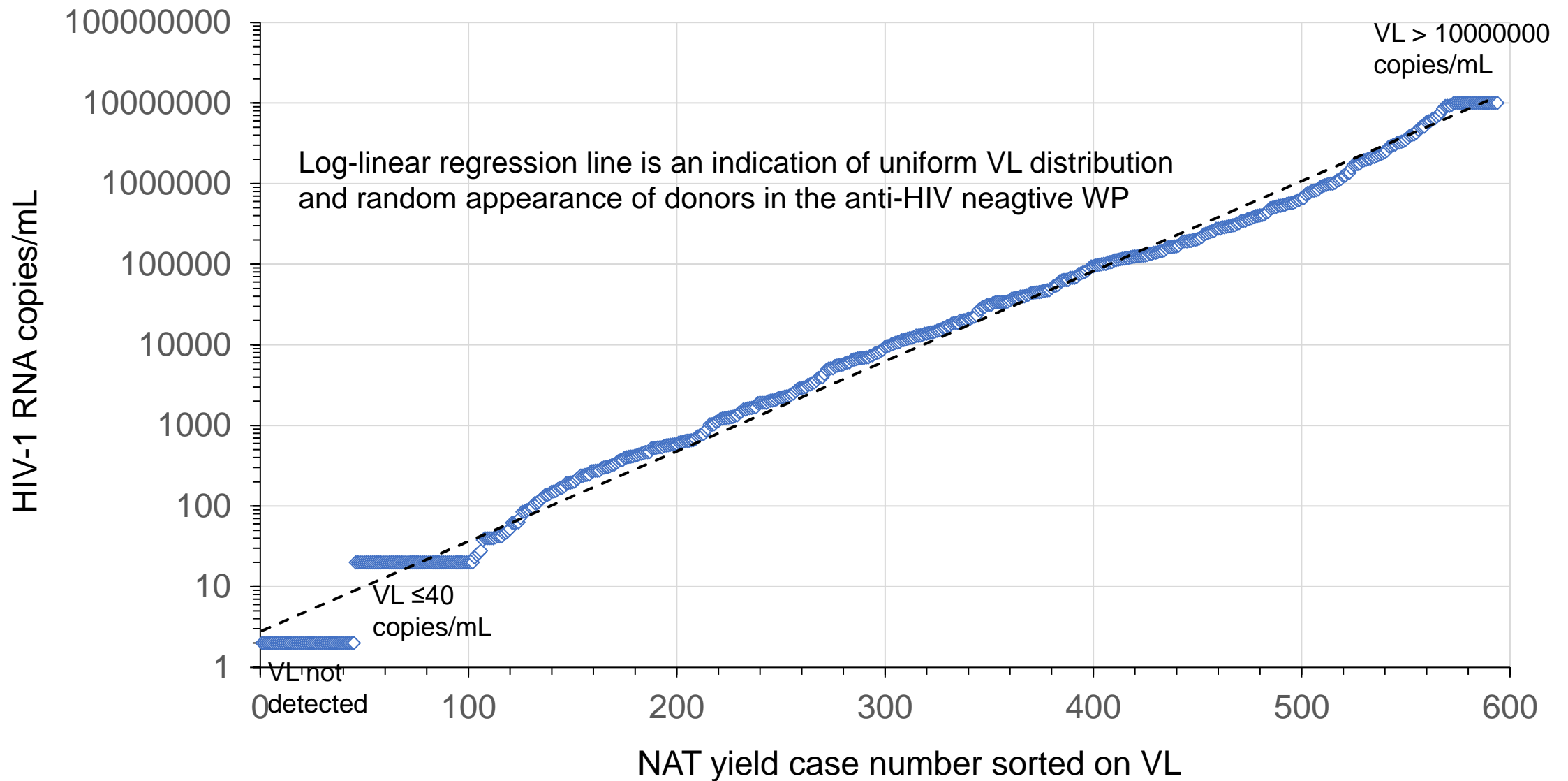
HIV Screening and confirmation testing algorithm

- All blood donations are screened in parallel using serology assays and ID-NAT
 - Anti-HIV, Abbott PRISM - until 2018
 - HIV- Ag/Ab Combo assay- Abbott Alinity since 2019
 - ID NAT- Ultrio Plus/Elite, Grifols- since 2005
- Extensive confirmation algorithm; donations classified as:
 - HIV negative
 - HIV concordant
 - HIV NAT yield
 - HIV serology yield
- Viral loads (Abbott m2000) done on all HIV NAT yields
- Innogenetics p-24 Ag ELISA done on HIV NAT yields during the PRISM screening period

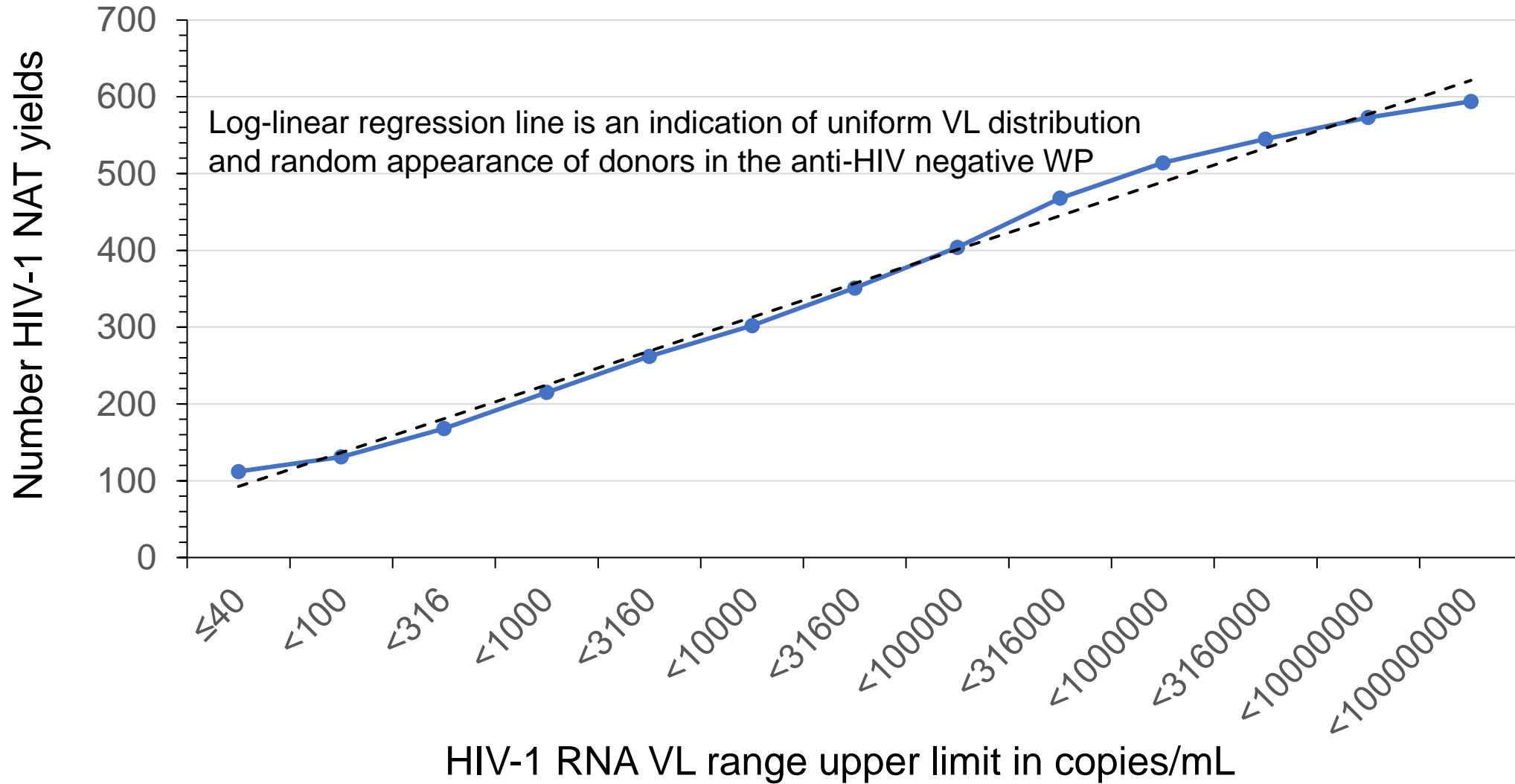
Studies and evaluation panels

Study objective	HIV-1 samples	Collection Period	n
Viral load (VL) distribution	PRISM anti-HIV negative WP-NAT yields	2005-2017	594
Sensitivity of Innogetics p24-Ag ELISA	PRISM Anti-HIV negative WP-NAT yields	2005-2017	571
Comparison of sensitivity of Innogenetics p24-Ag ELISA and Alinity HIV-Ag/Ab combo assay	PRISM Anti-HIV negative WP NAT yields (selection)	2010-2017	159
Determine cut off crossing point in Alinity and Innogenetics assays	PRISM Anti-HIV negative (selection)	2010-2017	145
Determine cut off crossing point in Alinity assay	HIV-1 subtype B standard (Tissue culture, inactivated)	1996	4 x 8
Comparison of HIV-RNA VL distribution (Abbott m2000) in three-year PRISM and Alinity screening periods	<ul style="list-style-type: none"> • PRISM neg WP-NAT yields • Alinity neg WP NAT yields 	2015-2017 2019-2021	179 155
Comparison of sensitivity of anti-HIV detection in PRISM and Alinity	Concordant HIV-NAT and serology reactive samples	2015-2017 2019-2021	4846 3935
Comparison of sensitivity of anti-HIV detection in PRISM and Alinity	HIV-RNA negative serology yields	2015-2017 2019-2021	239 569

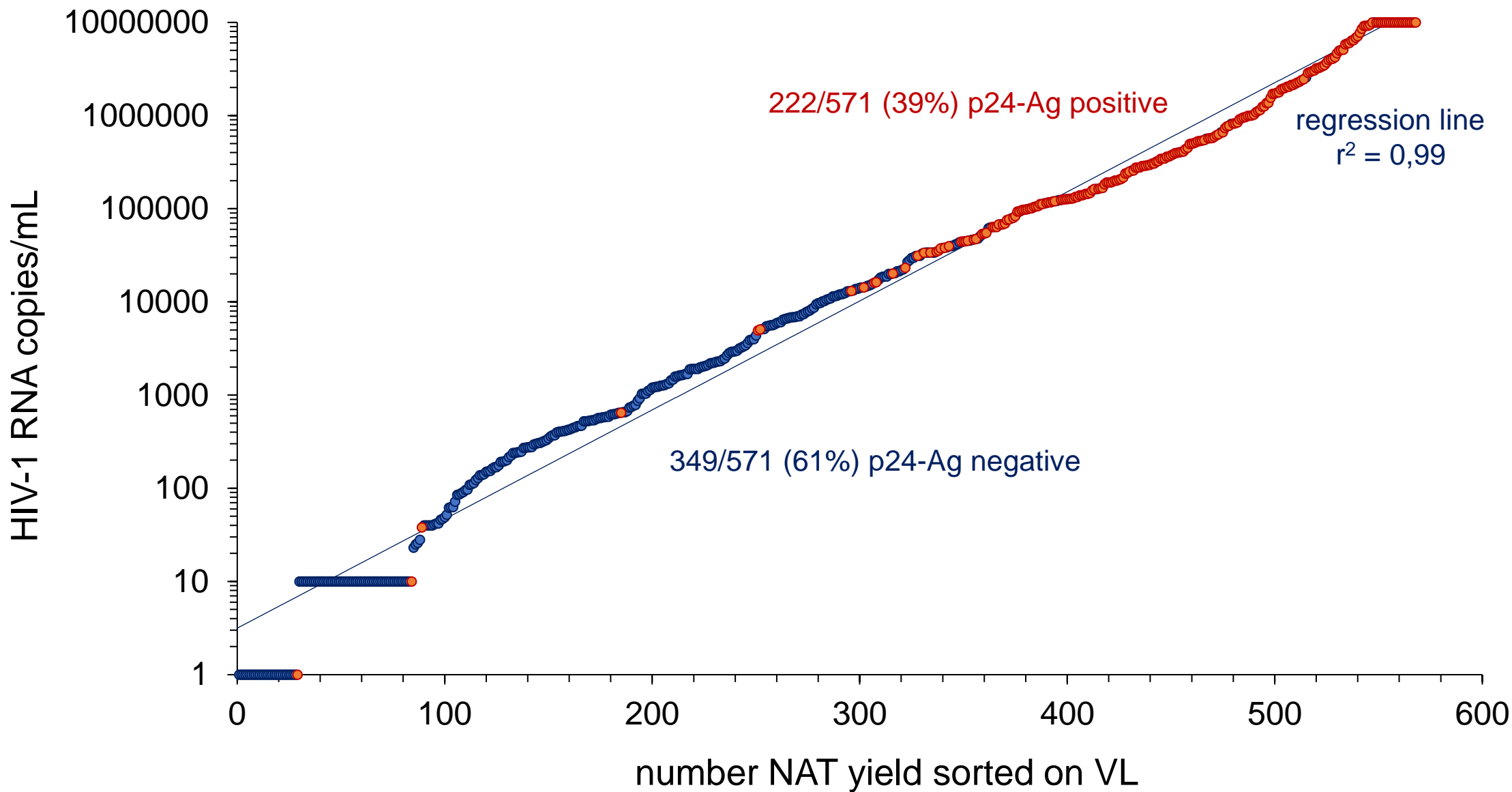
VL distribution in 594 PRISM anti-HIV nonreactive WP NAT yields (2005-2017)



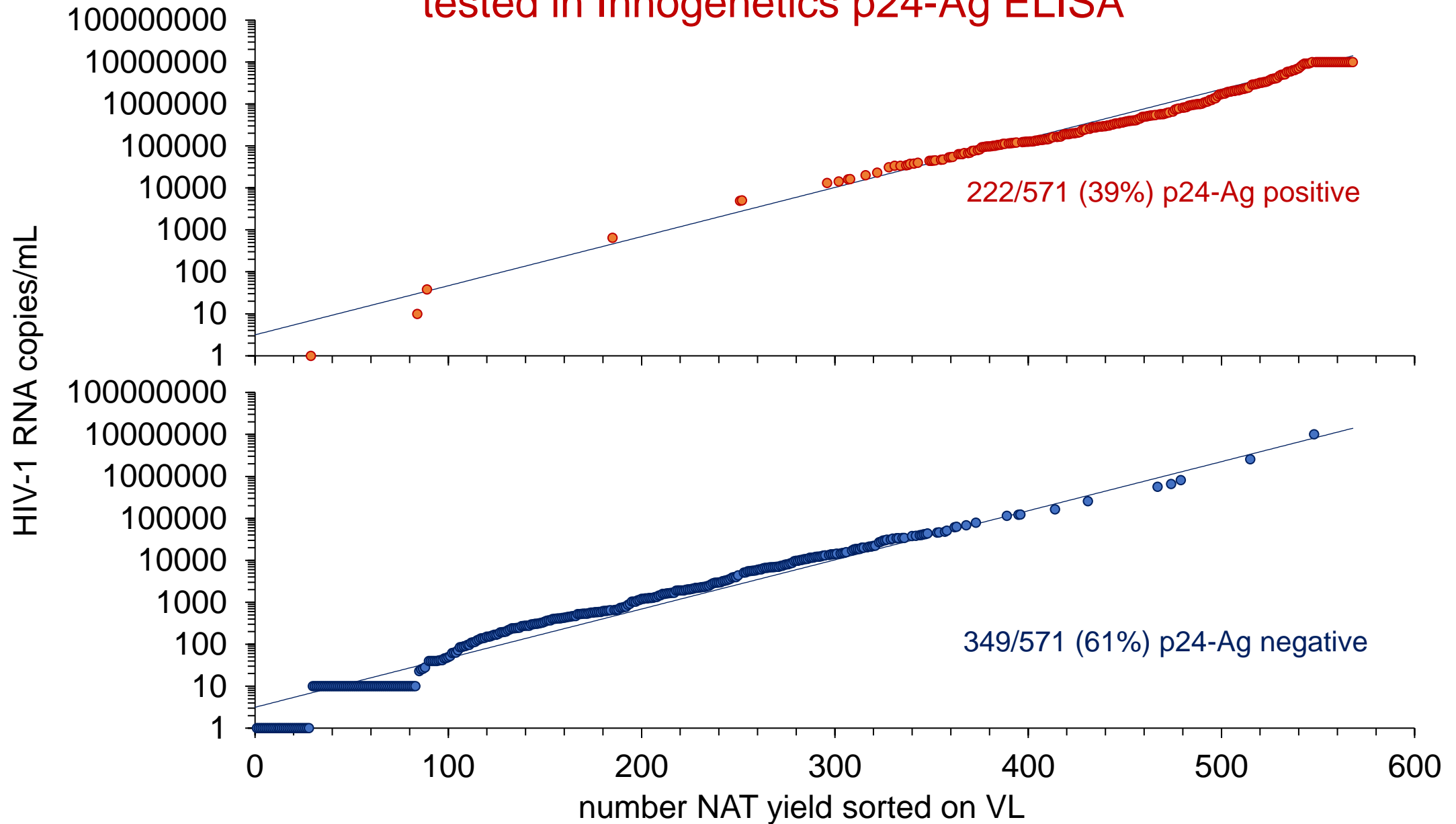
Cumulative VL distribution in 594 anti-HIV nonreactive WP NAT yields



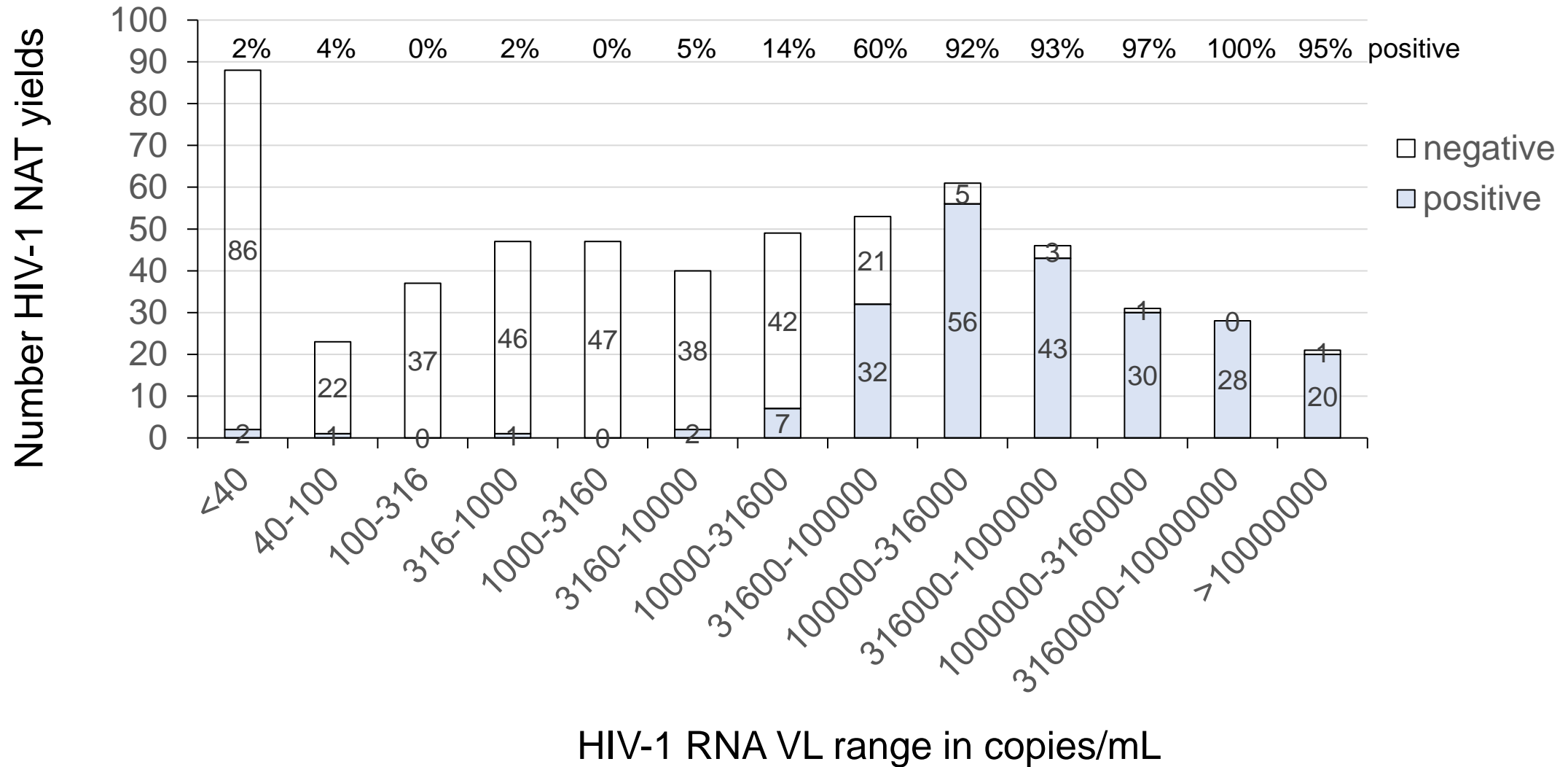
VL distribution in 571 anti-HIV PRISM nonreactive WP NAT yields (2005-2017) tested in Innogenetics p24-Ag ELISA



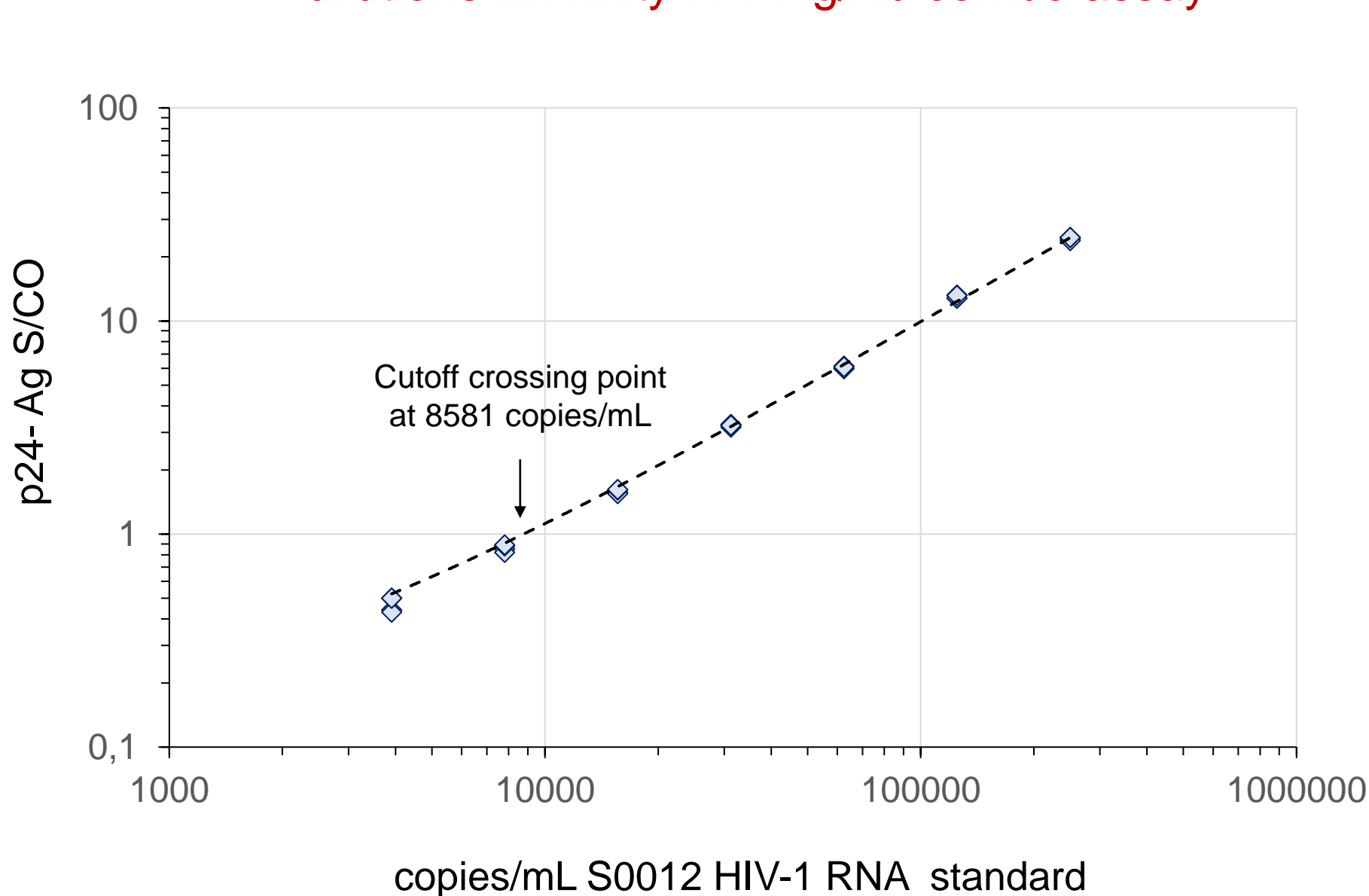
VL distribution in 571 anti-HIV PRISM nonreactive WP NAT yields (2005-2017) tested in Innogenetics p24-Ag ELISA



Sensitivity of Innogenetics p24-Ag ELISA in 571 PRISM anti-HIV nonreactive WP NAT yields divided over half-log different VL ranges (2005-2017)



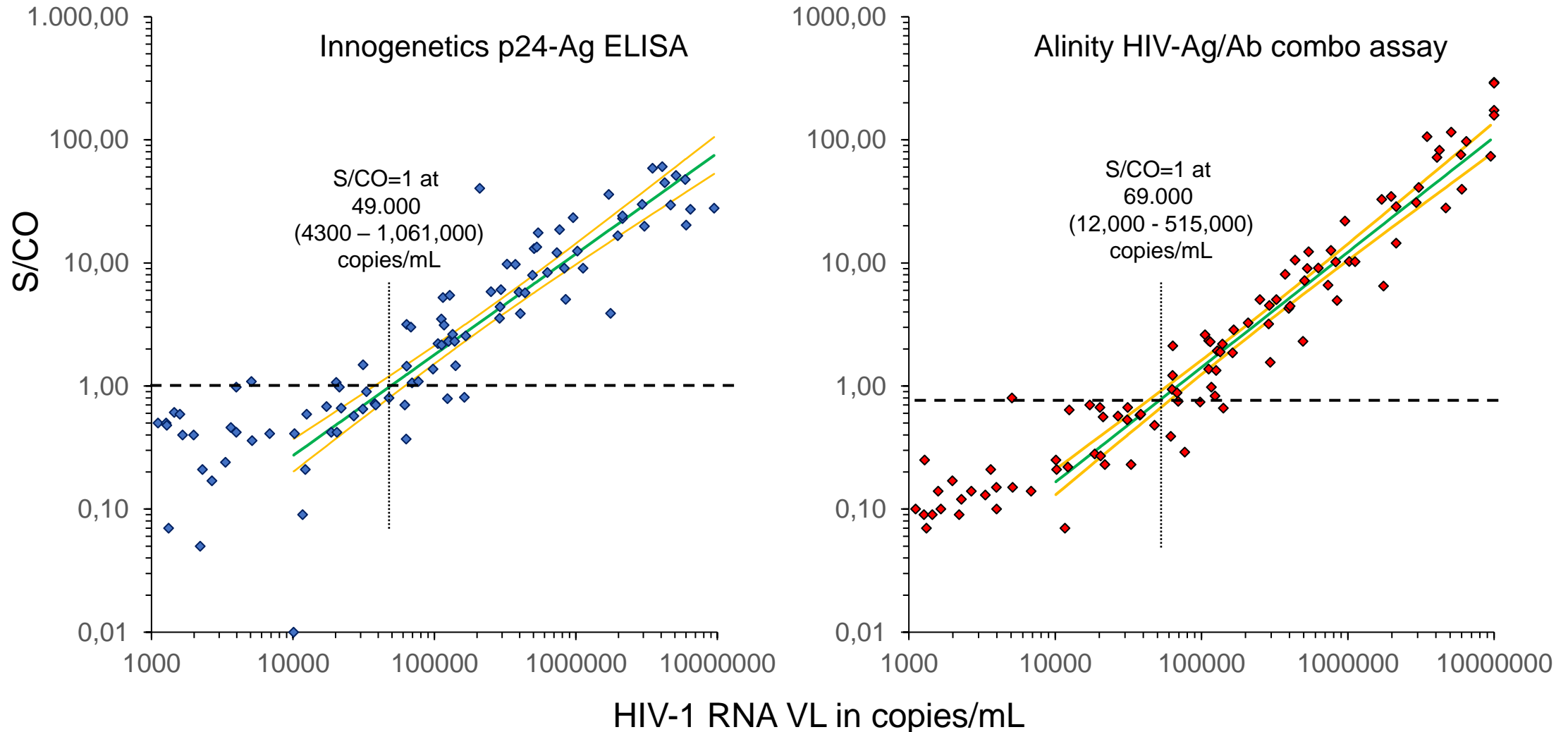
Correlation between VL and p24 Ag S/CO value on HIV-1 subtype B standard[^] dilutions in Alinity HIV-Ag/Ab combo assay



HIV-1 RNA copies/mL	p24-Ag S/CO
250000	24,21
250000	23,87
250000	24,69
250000	24,69
125000	12,81
125000	13,25
125000	12,78
125000	13,16
62500	5,99
62500	5,99
62500	6,14
62500	6,09
31250	3,18
31250	3,27
31250	3,24
31250	3,24
15625	1,57
15625	1,55
15625	1,61
15625	1,62
7813	0,85
7813	0,82
7813	0,88
7813	0,89
3906	0,44
3906	0,43
3906	0,5
3906	0,5

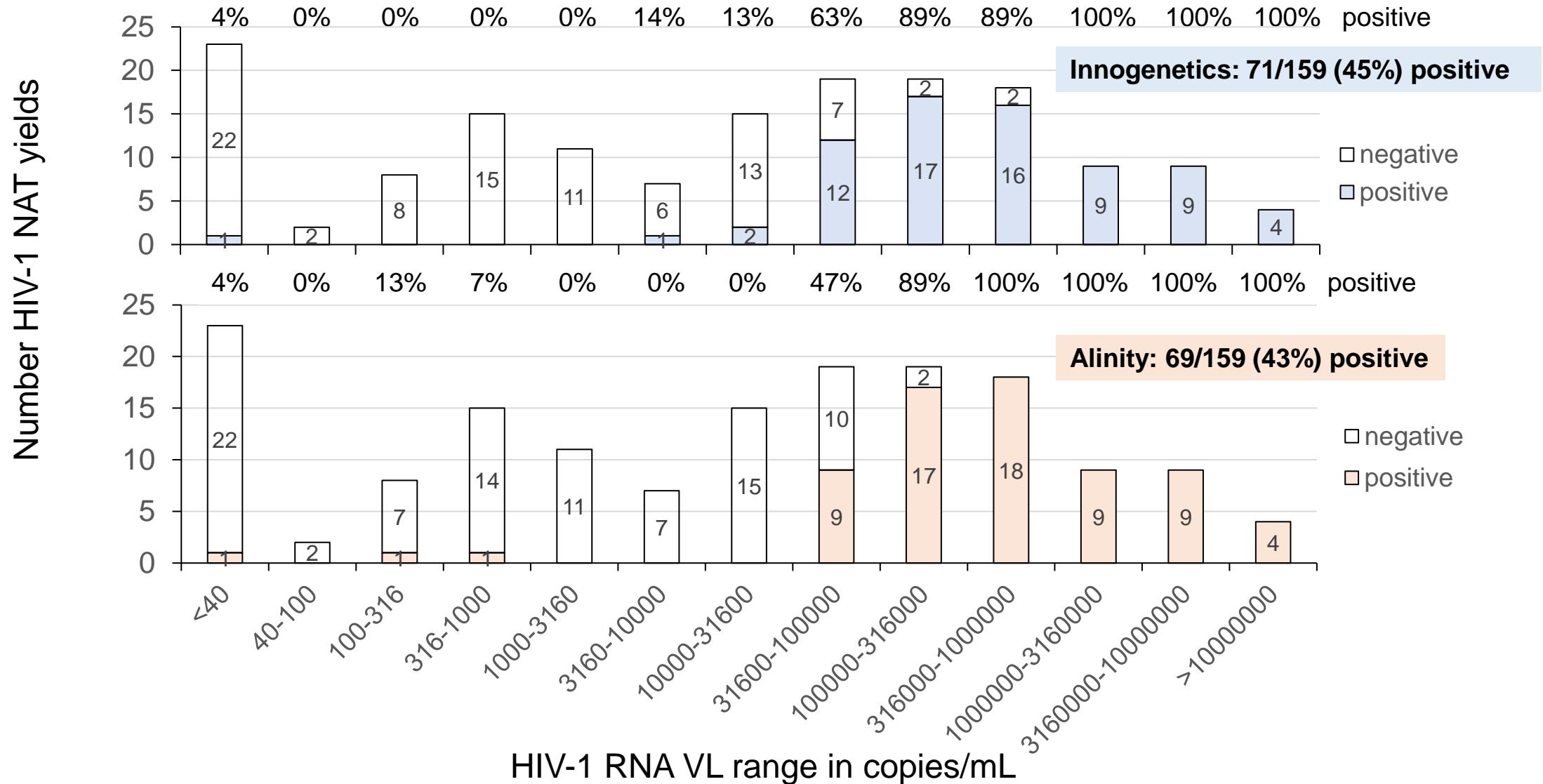
[^] S0012 HIV-RNA subtype B standard was first solvent detergent inactivated to obtain inactivated S0224 standard that was then used for preparing dilution series

Correlation between VL and p24-Ag S/CO value in 77 (of 145) anti-HIV negative WP NAT yields with Innogenetics p24-Ag ELISA and Alinity HIV-Ag/Ab combo assay (archived samples 2010-2017)

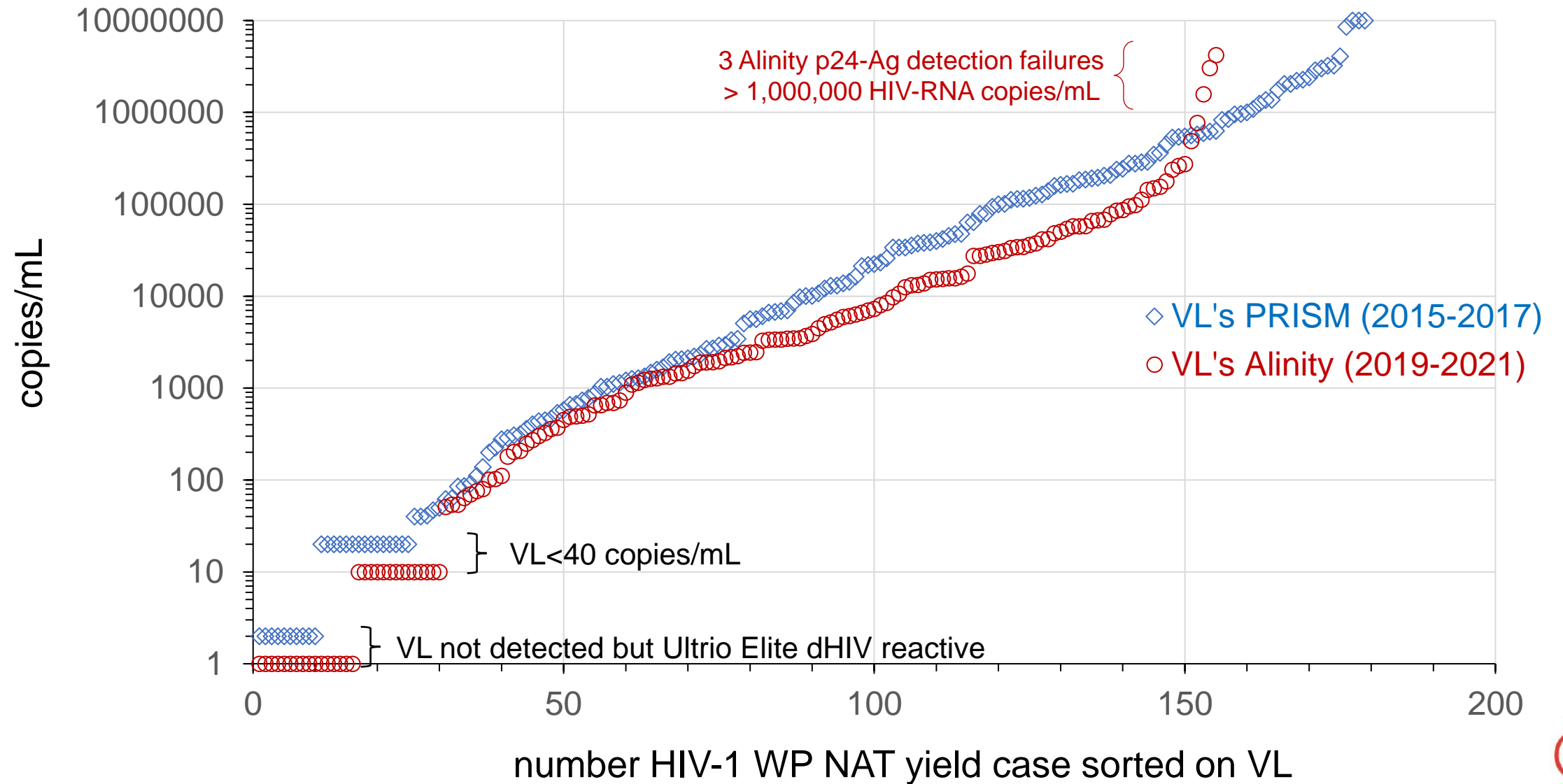


Regression analysis was performed on 77 of 145 WP NAT yield samples in VL range between 10000 and 10000000 copies/mL (64 samples with VL < 10000 copies/mL and 4 samples with VL ≥ 10000000 were excluded from the analysis)

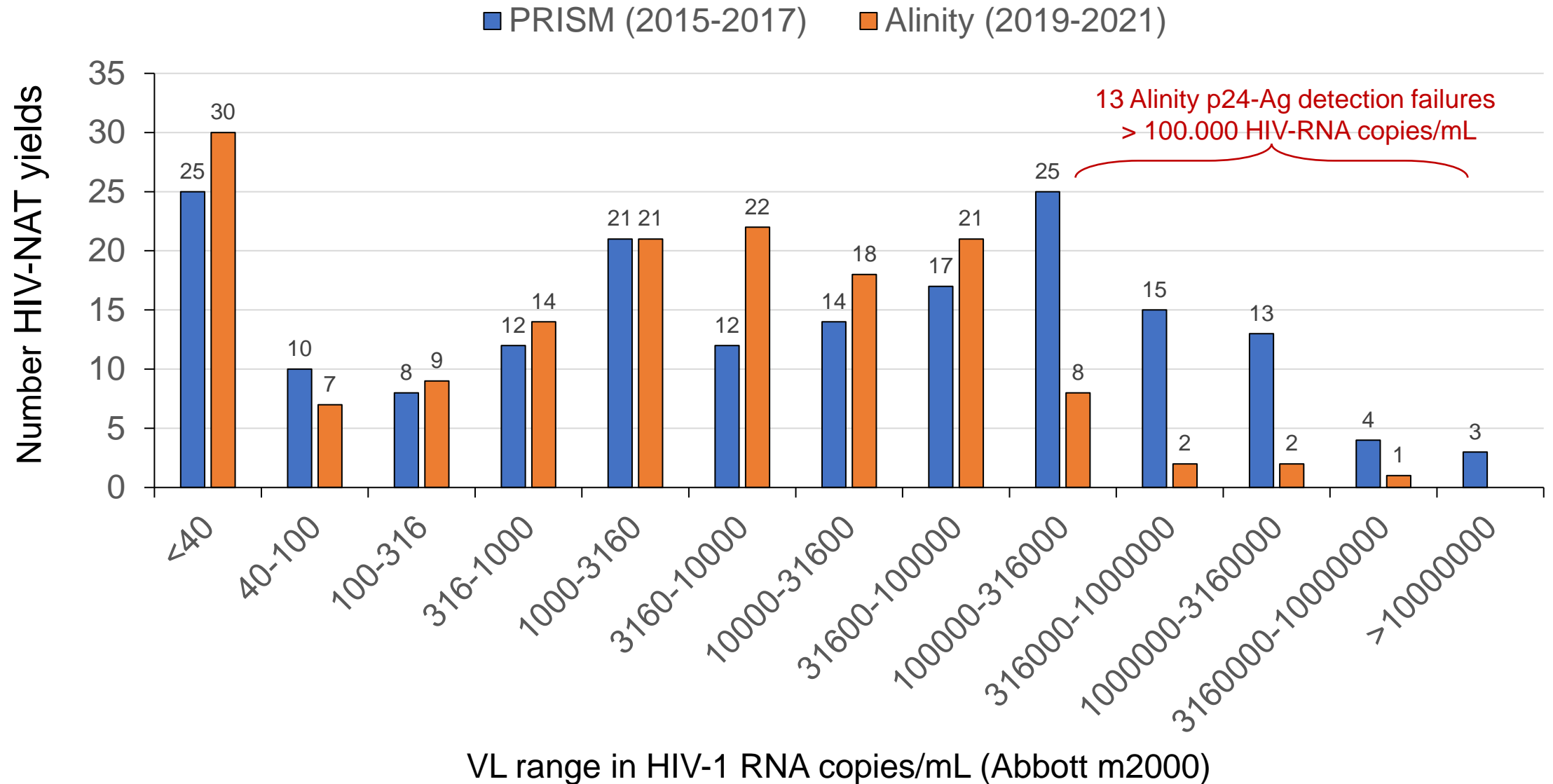
Sensitivity of Innogenetics p24-Ag ELISA and Alinity HIV-Ag/Ab combo assay in 159 PRISM anti-HIV nonreactive WP NAT yields divided over half-log different VL ranges (selected samples 2010-2017)



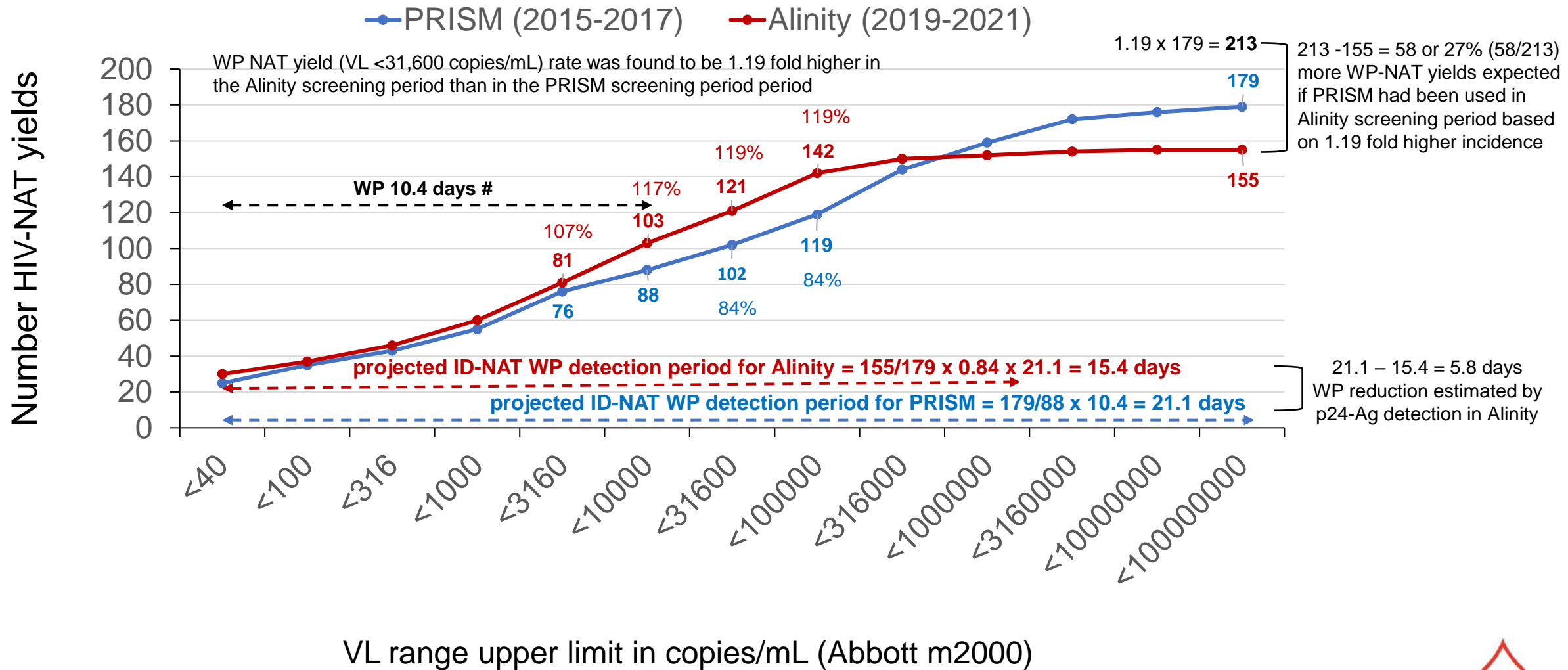
VL distribution in HIV-1 WP NAT yields during three-year screening periods of PRISM anti-HIV and Alinity HIV-Ag/Ab combo assay



VL distribution in HIV-1 WP NAT yields during three-year screening periods of PRISM anti-HIV and Alinity HIV-Ag/Ab combo assay



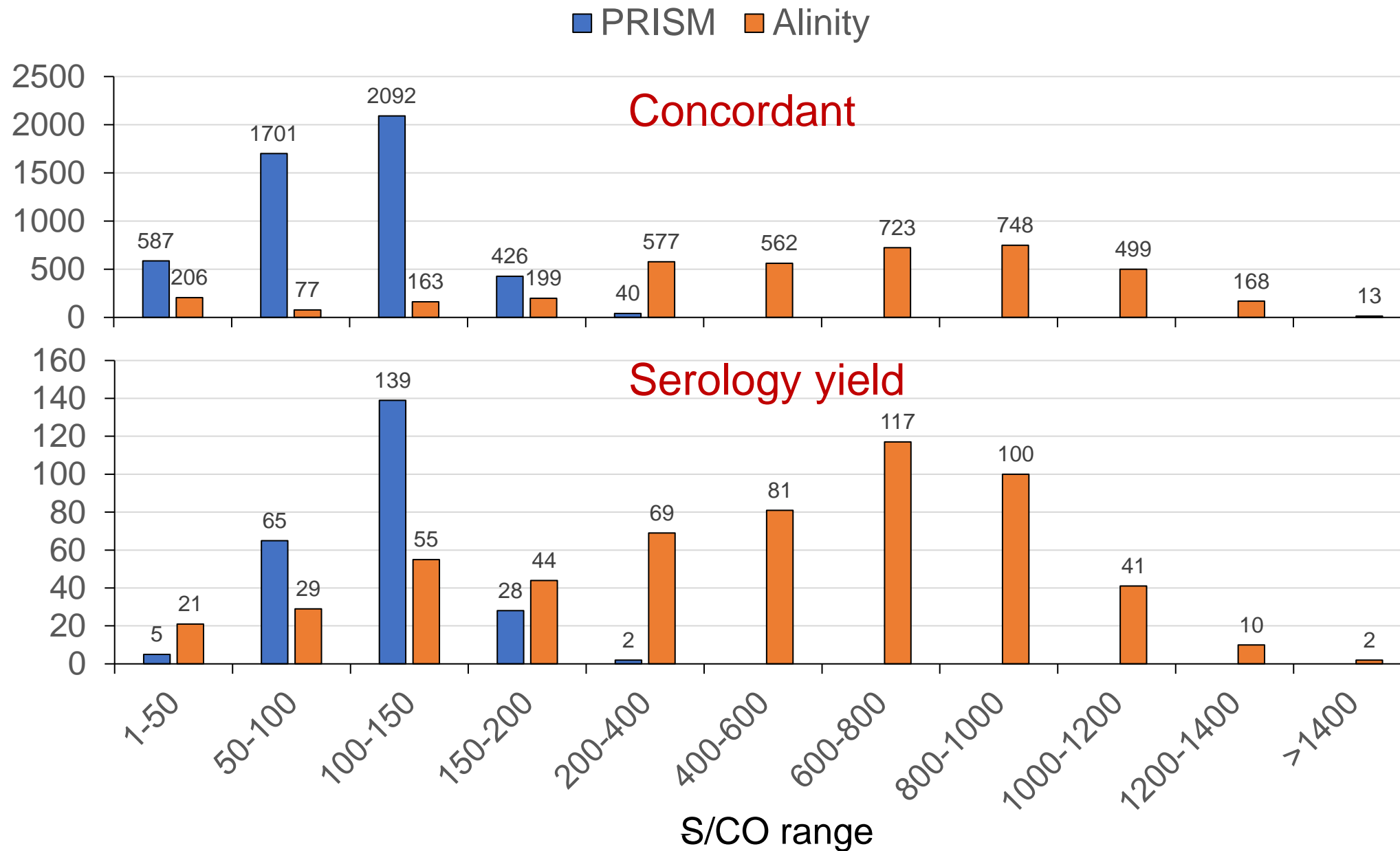
Cumulative VL distribution in WP HIV-1 NAT yields during three-year screening periods of PRISM anti-HIV and Alinity HIV-Ag/Ab combo assay



pre-ID-NAT WP <10,000 copies/mL determined using Weusten WP model with doubling time of 0.85 days and Ultrio Elite 50% and 95% LOD of 2.1 and 10.4 copies/mL respectively on HIV-1 subtype C standard requantified in copies/mL by Abbott m2000 assay (Coleman et al. Transfusion 2020)



Distribution of anti-HIV S/CO values in PRISM and Alinity tests



Distribution of S/CO values on HIV serology yield donations

Unit_Number	S/CO	Prism	Assay S/CO	Alinity	Unit_Number	S/CO
30080719	0.25	5 (2%)	1-50	21 (4%)	32068526	0.09
26914809	14.23	65 (27%)	50-100	29 (5%)	32906699	1.22
27361969	35.52	139 (58%)	100-150	55 (10%)	33243997	5.44
27927735	36.76	28 (12%)	150-200	44 (8%)	34510414	9.16
26473090	42.92	2 (1%)	200-400	69 (12%)	32029451	12.85
		0 (0%)	400-600	81 (14%)	35166299	12.86
		0 (0%)	600-800	117 (21%)	34798551	13.00
		0 (0%)	800-1000	100 (18%)	37124414	15.69
		0 (0%)	1000-1200	41 (7%)	33082167	16.16
		0 (0%)	1200-1400	10 (2%)	32450209	22.01
		0 (0%)	>1400	2 (0%)	33349842	22.61
					32745191	24.21
					32987254	28.50
					34722226	33.75
					32559831	34.83
					32015377	38.73
					32886447	38.84
					31929413	39.62
					33230621	43.02
					31915682	43.97
					32588681	49.59

Conclusions and discussion

- Some high VL WP NAT yield samples were not detected by the Alinity HIV-Ag/Ab combo assay and the Innogenetics p24-Ag ELISA.
- It was estimated that the Alinity HIV p24 antigen assay component offers a WP reduction of ~5.8 days by detecting ~27% of WP samples based on modeling VL distribution data observed during three year-screening periods of the PRISM and Alinity assay respectively.
- Analytical sensitivity of p24 antigen detection by the Alinity combo assay was 8-fold lower on HIV-1 (subtype C) WP NAT yield samples than on a widely used HIV-1 subtype B standard according to quantification in HIV-RNA copies/mL by the Abbott m2000 assay.
- Anti-HIV S/CO ratios in ID-NAT nonreactive 'serology yield' samples obtained during three-year screening periods were ~10-fold higher in Alinity than in PRISM assay, but it is unclear how this affects the clinical sensitivity of anti-HIV detection in samples with low antibody levels (which may be false reactive).