1002 Performance Validation of the Sedia™ HIV-1 Limiting Antigen (LAg)-Avidity EIA in South African Blood Donors

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Background

- **Tests for 'recent' HIV infection have significant application** in major population-level incidence (and incidence trend) estimation projects.
- **Design and validation** of such tests **depends crucially** on robust estimation of a Mean Duration of Recent Infection (MDRI), which is usually based **on data with repeated observations of seroconverting subjects enrolled in studies with other primary goals**, rendering the production of such estimates particularly difficult and expensive.

Methods

- The MDRI of a test is estimated by fitting a statistical model for the **probability of testing recent as a function of time since infection**.
- In the usual context of seroconverter cohorts, this is applied to **multiple observations on a single subject, anchored to a 'point estimate' of infection time**, based on interval censoring applied to diagnostic test data.
- **The midpoints of a seroconversion interval provides a weak infection time estimate** when linked to a single HIV-positive observation at the time of a first positive donation from a previously-negative blood donor.
- We **adapted previously-described methodology in order to use single HIV positive observations in estimating MDRI**, even with very imprecise infection time estimates, by averaging over (unobserved) possible infection times.
- We **estimated a locally-appropriate MDRI for the well-described Sedia LAg-Avidity recency test**, at a range of discriminatory thresholds, using data from the South African National Blood Service.
- **Data were obtained from 2,973 seroconverting repeat blood donors**, with a median inter-donation interval of 357 days. Reproducibility of the MDRI estimates was assessed using subject-level bootstrapping (10,000 iterations).

Results

- **Figure 1 shows the fitted probability of obtaining a 'recent' LAg-Avidity result** (at a discriminatory ODn threshold of 1.5), as a function of time since detectability of infection, assuming a highly-sensitive Nucleic Acid Test (NAT) with a detection threshold of 1 copy viral RNA per ml of plasma.
- Figure 2 shows the **MDRI estimates from a range of fitted curves such as in Figure 1, generated for a range of ODn thresholds** for recent/non-recent discrimination.
- **Table 1 elaborates on Figure 2 by demonstrating the impact of the screening test used to identify HIV positive subjects who are to be classified as recently infected or not, for a range of ODn thresholds.** Values from Figure 2 are in the first results column, while the second column refers to the screening sensitivity in fact deployed operationally at SANBS and hence used to identify the HIV-positive specimens in this study. The third column considers the use of the Abbott PRISM HIV O Plus as a screening test.

Table 1: LAg MDRI by recency discrimination threshold

Screening test:	ID-NAT (1c/ml)	ID-NAT (12c/ml)	PRISM HIV O Plus
Threshold *ODn <*	MDRI (95% CI) *days*	MDRI (95% CI) *days*	MDRI (95% CI) *days*
1.00	119 (111-134)	116 (108-131)	103 (94-117)
1.25	160 (141-186)	156 (138-183)	143 (124-170)
1.50	195 (168-222)	192 (165-219)	179 (151-205)
1.75	236 (201-266)	233 (198-263)	219 (185-250)
2.00	263 (230-289)	260 (227-285)	247 (214-272)

Figure 1: Probability of recent result by time since infection (ODn < 1.5)

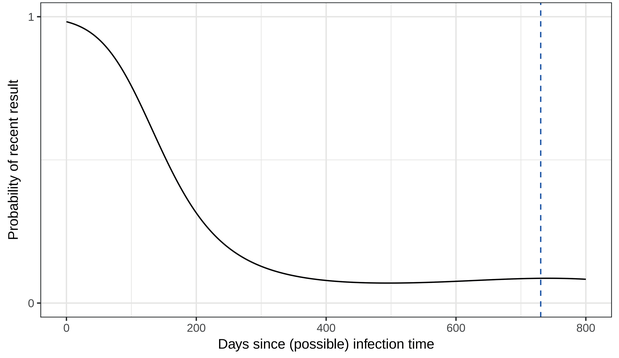
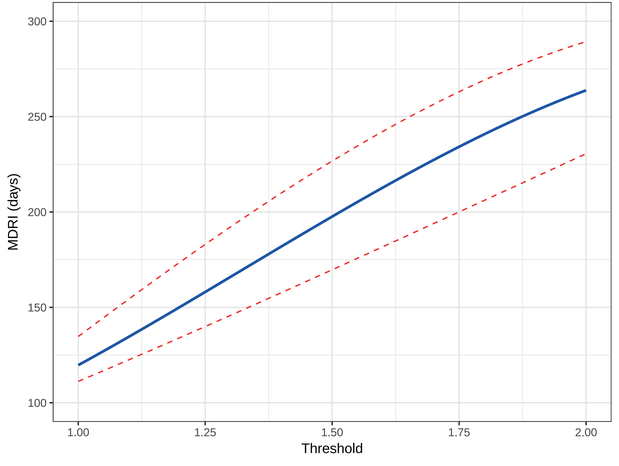


Figure 2: LAg-Avidity MDRI by ODn recency discrimination threshold



Conclusions

- The Sedia LAg-Avidity assay's performance in South African blood donors (overwhelmingly subtype C infections) is **statistically indistinguishable to its previously-described performance** in a multi-origin subtype C panel.
- Specimens from **seroconverting repeat blood donors are a potentially rich, and currently underutilised, source of data on early pathogenesis and early infection biomarkers**, as long as appropriate averaging is performed over uncertain infection times.
- For example, **these results provide context-specific test characteristic estimates** for use in incidence surveillance in first-time blood donors.

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