Time from Earliest Detection of HIV Infection by Individual Donation Nucleic Acid Testing to Detection by Serological Screening in South African Blood Donors

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Background

- It is critical for the quantification of residual risk of transfusion transmissible infections to have accurate estimates of the window periods of screening assays.
- The South African National Blood Service (SANBS) screened all donations during the study period (2005 to 2015) for HIV with individual donation nucleic acid testing (ID-NAT) and serology, using
  1. Procelix Ultrio Plus multiplexed (HIV, HBV and HCV) NAT assay and positive donations with the Ultrio Plus HIV-1 discriminatory assay on the Tigris platform, and
  2. The ABBOTT PRISM HIV O Plus third-generation chemiluminescent serological assay.
- We used SANBS repeat donor data from 2005 to 2015 to estimate the delay between earliest detection using ID-NAT and earliest detection using serology.
- Further providing the first direct estimate of the diagnostic delay of the PRISM assay.

Methods

- The average duration of the NAT-yield state (i.e. Ultrio+/PRISM-) was estimated using a novel approach based on interpreting the number of NAT-yield cases as a pseudo-Poisson process.
- The inter-donation intervals (IDIs) of all HIV-positive donations were interpreted as 'inverse exposure time'.
- We derived a formula that provides an estimate of the average duration of the NAT-only positive state, based on
  - the number of NAT-yield cases
  - divided by the sum of inverse of IDIs for all donations detected as HIV-positive.
  - 95% confidence intervals were obtained using the properties of the Poisson and Chi-square distributions.

Methods (2)

$$\mu = \frac{n}{\sum_{i=1}^{N} \frac{1}{IDI_i}}$$

with n the number of NAT-yield cases, N the number of donations from repeat donors detected as HIV-positive and IDI_i the time since previous donation of the i^{th} donor.

Study population

We used data from: 2,504 HIV-positive donations from repeat donors with median IDI of 160 days (IQR: 91-245) of which 300 were NAT-yield cases.

Figure 1: Inter-donation intervals of PRISM-positive repeat donors

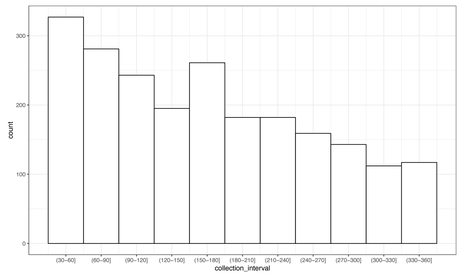
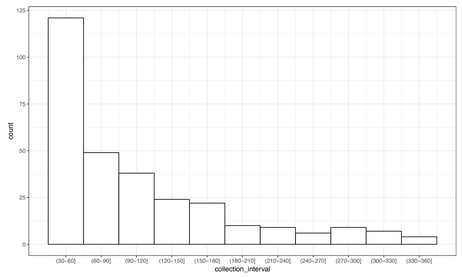


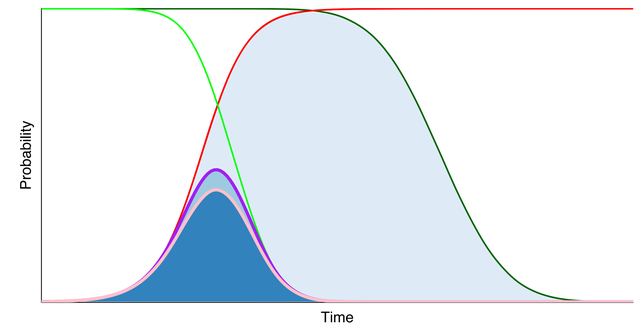
Figure 2: Inter-donation intervals of NAT-yield donors



Results

- We found an average duration of the ID-NAT-positive/PRISM-negative state of 15.03 days (95% CI: 13.37-16.83 days).
- Using an accepted viral load growth model and the 50% limit of detection (LoD) of the Ultrio Plus assay (N. Lelie, personal communication), this suggests a total average delay from first detectability on a NAT assay with a 50% LoD of 1 RNA copy/mL to PRISM seroconversion of 15.69 days.

Figure 3: Residual risk



The red line represents the probability of infectiousness. The light green line shows the probability of non-detection on ID-NAT and the dark green line the probability of non-detection on PRISM. The light blue shaded area represents residual risk with serological screening alone. The darker blue under the purple curve is the residual risk using a naïve model that does not take correlation between infectiousness and detectability into account, and the dark blue under the pink curve is the fully conditioned residual risk taking into account correlation.

Conclusion

- Compared to serology alone, SANBS's use of ID-NAT screening eliminated 15 days from the infectious window period – the bulk of the residual risk.

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