Recency staging of HIV Infections Through Routine Diagnostic Testing

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INTRODUCTION

- HIV recency results on individual patients, obtained at the time of diagnosis (as practiced in some national programmes and being contemplated in other large-scale systems) helps guide psychosocial support strategies, contact tracing, and inclusion in clinical trials.
- However, as recency testing is currently a specialist service using custom recency assays, this implies additional expense and a delay between HIV diagnosis and the delivery of the recency result.
- Previously, the microtitre-based HIV screening and confirmatory assays were only able to give qualitative results which could not be used to stage infection based on the levels of reactivity – at least not without altering either the specimen input or incubation conditions, or disrupting the chemical interactions measured in the test.
- The introduction of high dynamic range (such as chemiluminescent) platforms has opened up the possibility of adding staging interepretations to diagnostic test results, for both clinical and epidemiological applications.
- We explore whether this under-utilized quantitative information (e.g., signal-to-cutoff ratio, S/CO) can immediately stage new diagnoses as recent, or at least support prioritisation, by identifying specimens that should, or need not, be referred for specialised recency testing.

METHODS

- 2500 specimens with good clinical characterisation were tested diagnostically using an Abbott ARCHITECT HIV Ag/Ab Combo Assay (ARCHITECT) and by Sedia ™ HIV-1 Limiting Antigen for HIV recency determination (LAg).
- ART-naive specimens with a well-defined duration of infection were used to represent specimens from new diagnoses.
- We compared the recency classifications based on the two platforms through a number of regressions and correlations.
- To provide a systematic basis for utility in a surveillance application, a hypothetical epidemiological scenario was constructed where:
  - HIV Prevalence is 30% (HIV being detected with individual-level nucleic acid amplification testing)
  - HIV Incidence is 1.5 cases per 100 person-years
  - Treatment Coverage is 80% of infected individuals (with no false results among treated individuals, as long as a supplementary viral load threshold is applied)
  - Mean Duration of Recent Infection (MDRI), estimated for a range of recency discrimination thresholds, is adjusted for sensitivity of the HIV screening algorithm in the hypothetical survey
  - Context-specific Fuzzy Recency Rate (FRR) is calculated by estimating the probability of testing recent as a function of time since infection in the hypothetical population.

RESULTS

- Figure 1. The probability of a specimen being classified as LAg recent (ODn<1.5), as a function of the ARCHITECT platform result (signal-to-cutoff ratio, or S/CO). The probability curve is generated by means of a logistic regression model. Note that at S/CO values below 200 the majority of specimens will yield a LAg normalised optical density (ODn) below 1.5, and at S/CO above 500, almost no specimens will produce a LAg recent classification.
- The Pearson correlation coefficient between LAg and ARCHITECT results is 0.81.
- Figure 2. Mean Duration of Recent Infection, as a function of primary assay result (ODn for LAg and S/CO for ARCHITECT) recency discrimination threshold. This indicates that the notion of recent infection can be robustly defined, over comparable time scales, by tuning a threshold on the two platforms.

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REFERENCES


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