Viral load criteria and threshold optimization to improve HIV incidence assay characteristics

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Abstract

Objective: Assays for classifying HIV infections as ‘recent’ or ‘nonrecent’ for incidence surveillance fail to simultaneously achieve large mean durations of ‘recent’ infection (MDRIs) and low ‘false-recent’ rates (FRRs), particularly in virally suppressed persons. The potential for optimizing recent infection testing algorithms (RITAs), by introducing viral load criteria and tuning thresholds used to dichotomize quantitative measures, is explored.


Methods: MDRIs were estimated using regression, and FRRs as observed ‘recent’ proportions, in various specimen sets. Context-specific FRRs were estimated for hypothetical scenarios. FRRs were made directly comparable by constructing RITAs with the same MDRI through the tuning of thresholds. RITA utility was summarized by the precision of incidence estimation.

Results: All assays produce high FRRs among treated patients and elite controllers (10–80%). Viral load testing reduces FRRs, but diminishes MDRIs. Context-specific FRRs vary substantially by scenario – BioRad Avidity and Limiting Antigen provided the lowest FRRs and highest incidence precision in scenarios considered.

Conclusion: The introduction of a low viral load threshold provides crucial improvements in RITAs. However, it does not eliminate nonzero FRRs, and MDRIs must be consistently estimated. The tuning of thresholds is essential for comparing and optimizing the use of assays. The translation of directly measured FRRs into context-specific FRRs critically affects their magnitudes and our understanding of the utility of assays.