Context-Specific Performance of Recency Assays in South Africa and Uganda: an In Silico Simulation Approach

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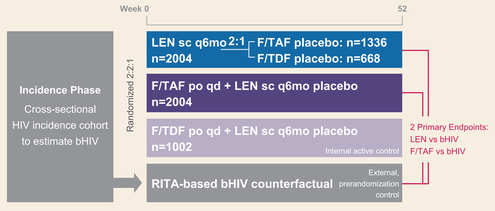
Introduction

- Recency assays use measurements of HIV antibody (Ab) avidity or quantity to determine whether individuals acquired HIV recently
- When incorporated into a recent infection testing algorithm (RITA), recency assays can be used to estimate population-level HIV incidence rates[1,2]
- Key factors affecting RITA performance include:
  - Epidemiologic context, such as regional prevalence, proportion diagnosed, and HIV serotype distribution
  - Assay threshold: enzyme immunoassay (EIA) optical density cutoff defining recent infection
  - Median duration of infection (MDRI): average time postinfection that individuals are classified as recently infected
  - False recency rate (FRR): frequency of false positive recent results
- RITAs have been proposed as a novel method to determine counterfactual (ie, background) HIV incidence rates in HIV prevention studies[3]
- Currently, several HIV pre-exposure prophylaxis (PrEP) studies are using RITA-based incidence rates as an endpoint component (ClinicalTrials.gov NCT04994509, NCT04925752, NCT04652700, and NCT04644029)
- One such study is PURPOSE 1 (ClinicalTrials.gov NCT04994509), which is evaluating lenacapavir (LEN) and emtricitabine/tenofovir alafenamide (F/TAF) for PrEP in cisgender adolescent girls and young women in South Africa and Uganda (Figure 1)

Figure 1. PURPOSE 1 Study Design



bHIV, background HIV incidence; F/TDF, emtricitabine/tenofovir disoproxil fumarate; PY, person-years.

Objective

- To use in silico simulations to study the context-specific performance of 4 RITAs incorporating 4 different recency assays based on the PURPOSE 1 study

Methods

Table 1. Recency Assay Characteristics

Recency Assay	LAg	ARCHITECT	Bio-Rad	Asanté
Platform	Sedia® HIV-1 LAg-Avidity EIA*	ARCHITECT® Ag/Ab Combo†	GS HIV-1/HIV-2 PLUS 0 EIA‡	Asanté™ HIV-1 Rapid Recency® Assay*
Method	Ab avidity, EIA	Ag/Ab chemiluminescent immunoassay	Ab avidity, EIA	Ab avidity, lateral flow immunoassay interpreted with electronic reader
Unit of measurement	Normalized optical density	Signal-to-cutoff ratio	Avidity index, %	LT/R band intensity

*Sedia Biosciences Corporation, Beaverton, Oregon, USA; †Abbott Laboratories, Abbott Park, Illinois, USA; ‡Bio-Rad Laboratories, Inc., Hercules, California, USA. Ag, antigen; LAg, limiting antigen; LT/R, long-term/recent.

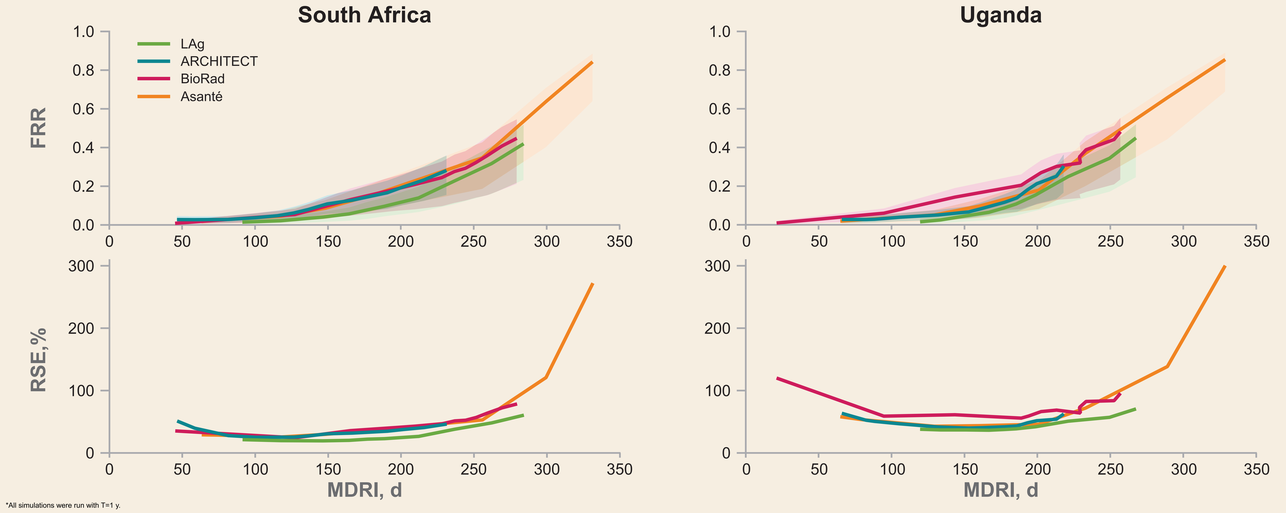
Table 2. Epidemiologic Context Assumptions

	South Africa	Uganda
Screened, n	7260	1238
HIV subtype distribution, %	C: 100	A: 46, D: 53, C: 2
HIV incidence/100 PY	3.8	3.8
HIV prevalence, %	12	9
Diagnosed, %	64	53

- We conducted simulations using public assay calibration data to examine the relationship between FRR, MDRI, and incidence rate estimate precision (relative standard error [RSE]) for 4 recency assay platforms, with context assumptions based on South Africa and Uganda (Tables 1 and 2)
  - We examined the relationship between MDRI, FRR, and RSE at varying assay thresholds for each assay algorithm and epidemiologic context (Figure 2)
  - We determined the assay threshold corresponding to the optimal incidence rate estimate precision for each assay algorithm and epidemiologic context (Table 3)
- MDRI estimates were weighted averages of subtype-specific MDRIs and context-specific FRR estimation accounted for the distribution times since infection in the population
- To minimize bias in MDRI and FRR estimates resulting from frequent testing and early diagnosis and treatment, time cutoffs (T) of 1 and 1.5 y (not shown) were used, and the proportion diagnosed was considered in FRR estimates

Results

Figure 2. Assay Performance Characteristics*



*All simulations were run with T=1 y.

- Increasing assay threshold resulted in increased MDRI, but also led to large increases in FRR and diminished precision, especially when MDRI was >200 d

Table 3. Optimal Assay Thresholds for Maximal Precision

	South Africa		Uganda	
Recency Platform	Optimal Threshold	RSE on Incidence Estimate, %	Optimal Threshold	RSE on Incidence Estimate, %
LAg	1.25	19.5	1.5	36.5
ARCHITECT	125	25.2	175	39.9
Bio-Rad	10	24.5	20	55.8
Asanté	2.5	25.6	2.5	42.9

Conclusions:

- Increasing assay thresholds resulted in higher MDRIs, but also FRRs; this was slightly less pronounced with the LAg assay
- MDRI–FRR tradeoff and bHIV estimate precision were generally similar across platforms
  - LAg-based RITAs demonstrated lower minimal RSEs in both South African and Ugandan contexts
- Although performance characteristics favored the LAg assay, threshold optimization is important and the precision achievable with each assay is likely sufficient for this application
- Important future directions include the development of improved methods to account for the impact of frequent HIV testing and early HIV diagnosis/treatment on RITA performance

References: **1.** Duong TY, et al. AIDS Res Hum Retroviruses 2019;35:896-905; **2.** Kassanjee R, et al. Epidemiology 2012;23:721-8; **3.** Parkin N, et al. IAS 2021, abstr 2322. **Acknowledgments:** We extend our thanks to the participants, their families, all participating investigators and staff, and the Global Community Advisory/Accountability Group members. This study was funded by Gilead Sciences, Inc.