Comparison of Recency Assays to Estimate HIV Incidence in the SIENA (Estimating HIV Incidence Among AGYW) Study in Uganda

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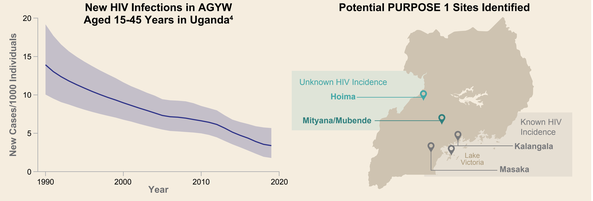
Introduction

- Accurate estimates of background HIV incidence (bHIV) are critical to site selection and evaluation of efficacy in next-generation pre-exposure prophylaxis (PrEP) studies with counterfactual designs[1]
- HIV-1 recent infection testing algorithms (RITAs) use recency assays to estimate population-level HIV incidence and are currently being employed in PrEP studies to estimate bHIV[2,3]
  - Incorporating a viral load (VL) cutoff in the RITA improves the ability of recency assays to support bHIV calculation[3]
- The PURPOSE 1 study (NCT04994509) is using the novel counterfactual bHIV design and requires a high bHIV (> 3.5/100 person-years [PY])
  - This trial is evaluating the efficacy and safety of lenacapavir and emtricitabine/tenofovir alafenamide for PrEP in adolescent girls and young women (AGYW) in South Africa and Uganda
  - The primary endpoint will compare HIV incidence in each active study arm (lenacapavir and emtricitabine/tenofovir alafenamide) to bHIV in the screened population
- The SIENA study was conducted to determine the bHIV among AGYW in and around central and midwestern Uganda in regions with sociodemographic factors associated with higher HIV incidence (eg, marital/relationship status, education level, financial independence, and available occupations)

Figure 1. HIV Incidence and Potential PURPOSE 1 Sites in Uganda



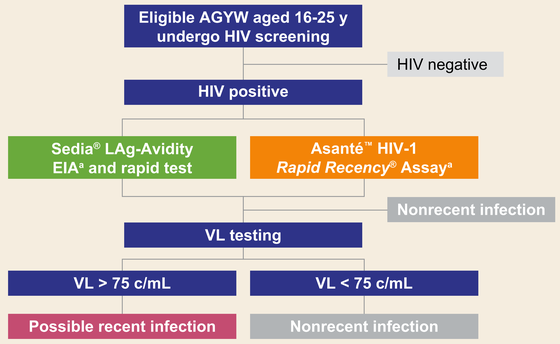
- In Uganda, HIV incidence has decreased at the national level; however, micro-epidemics still occur in key populations and high-risk communities
- 4 potential sites were identified, including 2 (Mityana/Mubende and Hoima regions) that have sociodemographic characteristics suggesting increasing HIV incidence, but with no recent data on bHIV
- Mityana/Mubende was confirmed as a PURPOSE 1 site due to a bHIV of 23.2/100 PY (95% confidence interval [CI] 13.1, 41.2)[5]

Objectives

- To compare recency assay platforms by assessing their suitability, performance, and reliability for estimating bHIV in future PrEP studies, and the effect of VL cutoff on assay performance

Methods

Figure 2. SIENA Study RITA



[a]Sedia Biosciences Corporation, Beaverton, OR. EIA = enzyme immunoassay; LAg = limiting antigen.

- Eligibility criteria: female sex, aged 16-25 years, unknown HIV status, and no HIV testing in past 3 months
- A cross-section of AGYW were recruited from HIV testing sites and known areas of commercial sex activity, eg, bars, nightclubs, lodges, gold mines, factories, farmlands, islands, and fishing communities
- HIV diagnosis and confirmation via Alere Determine™ HIV-1/2 (Abbott Laboratories, Abbott Park, IL) and OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test (OraSure Technologies, Bethlehem, PA)

Table 1. Recency Assay Characteristics[6]

	Platform	Method	Cutoff	Cutoff Time, y	MDRI, d	FRR, %	VL Cutoff, c/mL
LAg-EIA	Sedia LAg-Avidity EIA	Ab avidity, EIA	1.5 ODn	1	166.8	6.5	75
Asanté	Asanté HIV-1 *Rapid Recency* Assay	Ab avidity, lateral flow immunoassay, interpreted with electronic reader	2.5 LT/R	1	129.3	5.1	75

Ab = antibody; Ag = antigen; FRR = false recency rate; LAg = limiting antigen; LT/R = long-term/recent band intensity; MDRI = mean duration of recent infection; ODn = normalized optical density.

- Positive samples analyzed for recent infection using the Sedia LAg-Avidity EIA and Asanté HIV-1 *Rapid Recency* Assay
- VL determined by COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test, v2.0 (Roche Diagnostics, Indianapolis, IN)
- bHIV and 95% CI calculated using previously determined MDRI and FRR specific to the study population, based on Gao et al[7]
- Participants diagnosed with HIV referred to appropriate sites for treatment

Results

Table 2. Participant Characteristics

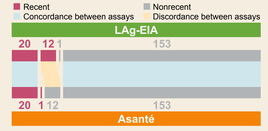
		Total: N = 742
Median age, y (range)		21 (16-26)
Secondary education or higher, n (%)		359 (48)
Living with partner/cohabiting, n (%)		109 (15)
Median time living in community, y (Q1, Q3)		1.2 (0.5, 5.5)
Median age at 1st sex encounter, y (Q1, Q3)		16 (14, 17)
Median mo since last HIV test (Q1, Q3)		8 (5, 15)
Sex partners in past 3 mo, n (%)[a]	0	0
	1	73 (10)
	≥ 2	630 (90)
Median number of vaginal sex encounters in past 3 mo (Q1, Q3)		100 (24, 100)
Condom use in past 3 mo, n (%)	Never	241 (32)
	Rarely	250 (34)
	Sometimes	195 (26)
	Often	47 (6)
New sex partner in past 3 mo, n (%)		518 (70)
Concerned about having HIV, n (%)	Somehow worried	321 (56)
	Very worried	222 (39)
Partner provided financial/material support, n (%)[b]		473 (91)
Primary occupation, n %	Commercial sex worker, bar/lodge/hotel attendant	479 (65)
	Other	263 (35)

[a]39 participants in Mityana/Mubende group reported number of sex partners not known; Mityana/Mubende %s calculated from n = 332; total %s calculated from n = 703; [b]105 participants in Hoima and 120 in Mityana/Mubende groups reported not applicable or missing data; Hoima %s calculated from n = 266; Mityana/Mubende %s calculated from n = 251; total %s calculated from n = 517. Q = quartile.

- Of 742 AGYW screened, 191 were diagnosed with HIV, of whom 44 (23%) had VL < 75 c/mL
- 53% of participants had HIV subtype A, 23% subtype D, and 18% subtype A/D

Figure 3. Correlations Between Assays

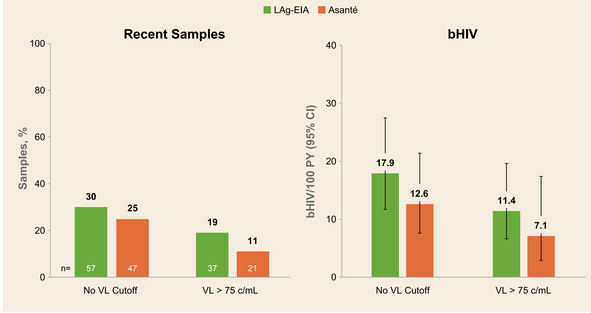
Infections	Asanté: Recent	Asanté: Nonrecent	Total
LAg-EIA: Recent	20	12	32
LAg-EIA: Nonrecent	1	153	154
Total	21	165	186



5 infections called recent by LAg-EIA were considered HIV negative by Asanté assay and results were excluded by assay protocol.

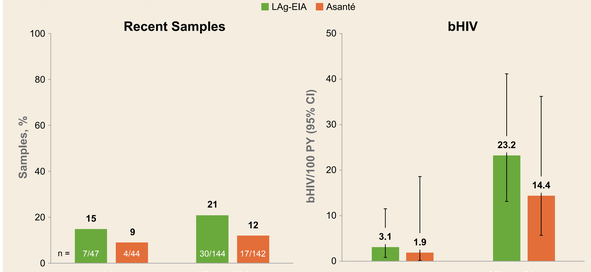
- LAg-EIA and Asanté assay results were significantly correlated (φ = 0.7376)

Figure 4. RITA Results by Assay



- The 2 assays identified 47-57 recent samples without a VL cutoff and 21-37 recent samples using the VL cutoff < 75 c/mL

Figure 5. RITA Results by Site
VL > 75 c/mL



Conclusions

- In the SIENA study, 23% (44/191) of samples were found to have a VL < 75 c/mL, suggesting widespread antiretroviral therapy use or elite controller status[8,9]
- Using a RITA with a VL cutoff < 75 c/mL led to decreases in calculated HIV incidence by both assays, but still demonstrated a high HIV incidence in AGYW in the study's setting
- Overall, the LAg-EIA and Asanté recency assays identified high levels of recent infections, resulting in high estimates of bHIV in Uganda consistent with results seen evaluating other Ugandan HIV micro-epidemics
- These analyses support using these recency assays in the RITA to estimate bHIV in future PrEP studies
- The results demonstrate extremely high prevalence and incidence of HIV in AGYW in central and midwestern Uganda, highlighting the need for expanded HIV prevention options in these areas

References: **1.** Parkin N, et al. IAS 2021, poster 2322; **2.** Duong YT, et al. *AIDS Res Hum Retroviruses.* 2019;35:896-905; **3.** Kassanjee R, et al. *Epidemiology.* 2012;23:721-8; **4.** Institute for Health Metrics and Evaluation. GBD 2019: 2022. http://vizhub.healthdata.org/gbd-compare; **5.** Matovu Kiweewa F, et al. AIDS 2022, poster EPC114; **6.** Grebe E, et al. EACS 2021, poster PE6/19; **7.** Gao F, et al. *Stat Commun Infect Dis.* 2021;13:2020000; **8.** Chang LW, et al. *Lancet HIV.* 2016;3:e368-96; **9.** Musumari PM, et al. *PLOS One.* 2021;16:e0249465.
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