Performance of BED-CEIA and Avidity Index Assays in a Sample of ARV-Naïve, Female Sex Workers in Kigali, Rwanda

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Background

Operating characteristics of STARHS assays, including their combined use, are not well described in sub-Saharan Africa.

We assessed the performance, including sensitivity and specificity, of the BED-CEIA (BED) and Avidity Index (AI) assays among female sex workers (FSW) in Kigali, Rwanda.

Methods

800 FSW of unknown HIV status and aged ≥18 years were HIV tested in a cross-sectional survey

- At baseline, HIV-positive participants (N=190) were tested by: BED assay (window=155 days); AI assay (using AxSYM HIV-1/2gO EIA, window=180 days); CD4 cytometry
- HIV-positive participants (N=141) were re-tested by BED and AI ≥12 months later to estimate assay false-recent rates (FRR)
- All women were interviewed for demographic and risk information at baseline and repeat STARHS testing

397 HIV-negative, non-pregnant FSW were enrolled in a prospective HIV seroconversion study

- Incident HIV infections by rapid HIV test, EIA confirmation
- Specimens from seroconverters (N=19) tested by BED and AI for assay sensitivity and specificity

Outcome definitions and statistical methods

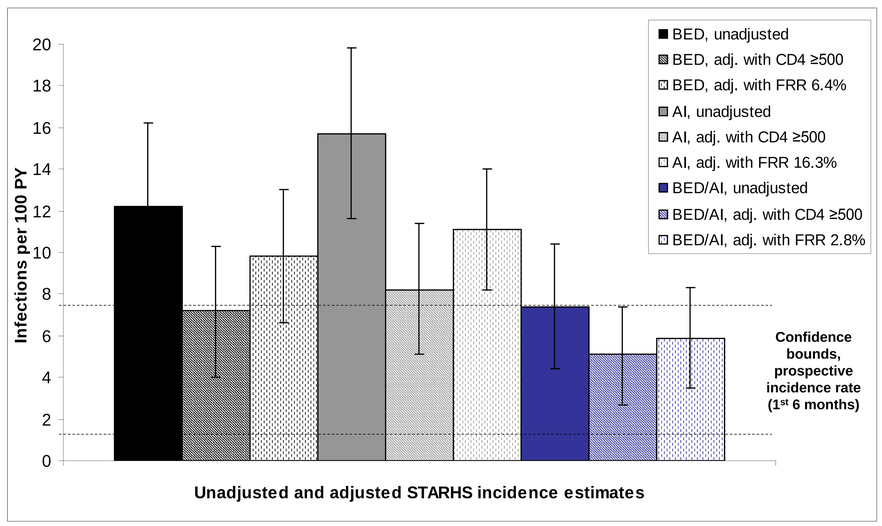
- Sensitivity=proportion of seroconverter specimens collected within the assay window period and classified as "recent infection" (RI)
- Specificity=proportion of seroconverter specimens collected beyond the assay window period and classified as "long-term infection" (LTI)
- FRR=proportion of specimens from HIV+ survey participants with known LTI but classified as RI on repeat STARHS tests
- Proportions and incidence rates with 95% confidence intervals (CI)
  - STARHS-based crude and adjusted (with assay FRR and CD4 data) incidence estimates using formula from Hargrove *et al.* 2008

Results

Cross-sectional survey (N=190 HIV positive)
Recent infection: 19% by BED, 30% by AI; 12% by BED and AI combined
Long-term infection: 81% by BED, 70% by AI, 64% by BED and AI combined

Prospective HIV seroconversion study (N=19 incident HIV infections)
12-month HIV incidence rate: 3.5 per 100 person-years (PY) (CI 1.6, 5.4)
1st 6 months: 4.6/100 PY (CI 1.6, 7.7)
2nd 6 months: 2.2/100 PY (CI 0.1, 4.4)

Comparison of STARHS-based and observed prospective HIV incidence rates



HIV incidence estimates based on STARHS assays (95% CI)

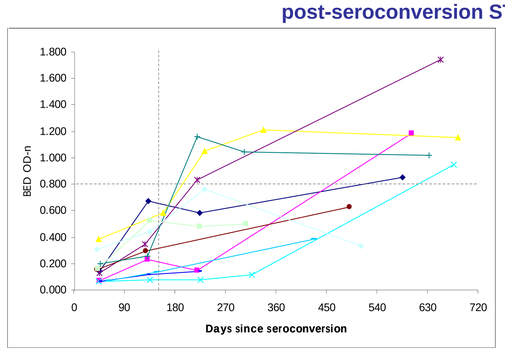
BED, Unadjusted	12.2 (8.2, 16.2)
AI, Unadjusted	15.7 (11.6, 19.8)
BED/AI combined, Unadjusted	7.4 (4.4, 10.4)
BED, Adjusted with CD4[1]	7.2 (4.0, 10.3)
AI, Adjusted with CD4[1]	8.2 (5.1, 11.4)
BED/AI combined, Adjusted with CD4[1]	5.1 (2.8, 7.5)
BED, Adjusted with FRR[2] (6.4%)	9.8 (6.6, 13.0)
AI, Adjusted with FRR[2] (16.3%)	11.1 (8.2, 14.0)
BED/AI combined, Adjusted with FRR[2] (2.8%)	5.9 (3.5, 8.3)

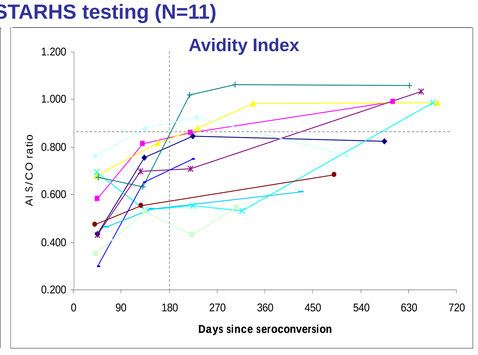
1. Individuals with CD4<500 cell/μl excluded
2. Using study-specific FRR and statistical adjustment formula from Hargrove *et al.* 2008

Selected characteristics of cross-sectional survey participants with known LTI but false recent classification on repeat STARHS testing ≥12 months after HIV diagnosis (N=141)

Characteristics	BED-CEIA Assay			Avidity Index method		
	False-recent result (n=9)	Correctly classified as LTI (n=132)	*P value*	False-recent result (n=23)	Correctly classified as LTI (n=118)	*P value*
Median age in years (IQR)	26.0 (13)	27.0 (9)	0.75	33.0 (15)	27.0 (8)	0.29
Have HIV positive sex partner, %	11	8	0.53	9	4	0.69
Lifetime HIV testing history, %:						
Never tested	22	52	0.01	48	50	0.02
Once	44	30		13	34	
Twice	0	14		17	12	
3-5 times	22	5		17	3	
≥6 times	11	1		5	1	
≥1 AIDS symptom in last 6 months, %	33	43	0.73	22	19	0.77
Median baseline CD4 cells/μl	447	461	0.77	590	444	<0.01
Classified as RI by baseline STARHS test during cross-sectional survey, %	100	0	<0.0001	65	17	<0.0001
Median no. days between baseline and repeat STARHS test	692	623	0.69	593	641	0.42

STARHS assay results over time among prospective study HIV seroconverters with post-seroconversion STARHS testing (N=11)





STARHS assay sensitivity and specificity

Short-term sensitivity and specificity, based on serial specimens from 19 prospective seroconverters:

- BED: Sens=100% (CI 88-100%), Spec=43% (CI 27-61%)
- AI: Sens=92% (CI 74-98%), Spec=43% (CI 27-61%)
- BED/AI combined: Sens=91% (CI 72-97%), Spec=55% (CI 33-67%)

Longer-term specificity, based on repeat STARHS testing of HIV+ survey participants (1-FRR):

- BED: 93.6%
- AI: 83.7%
- BED/AI combined: 97.2%

Conclusions

Adjusted incidence estimates based on a combined BED/AI algorithm were similar to observed HIV incidence in the 1st 6 months of the cohort, when incidence was highest.

- Excluding individuals with CD4<500 cells/μl from incident cases brought STARHS-based estimates closest to observed incidence.

Testing assay 'false-recent' was associated with being classified as RI at baseline and frequent HIV testing history (BED and AI), and higher baseline median CD4 count (AI)

Assay specificity in panel specimens around the time of seroconversion was low, but improved markedly with time since seroconversion

- Specificity would be expected to be substantially higher in population-based testing where a larger proportion of individuals have LTI.

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