EVALUATION OF CROSS-SECTIONAL HIV INCIDENCE TESTING IN THE HPTN 071 (PopART) TRIAL

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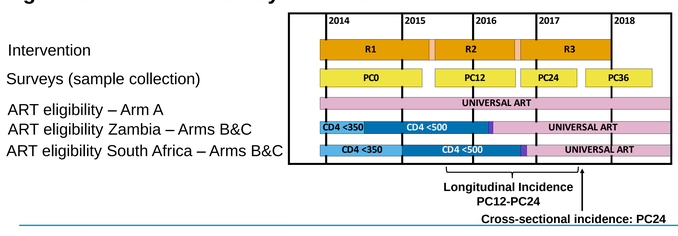
Background

- HIV incidence estimation from cross-sectional surveys is often performed using an algorithm that includes the Limiting Antigen Avidity assay (LAg-Avidity) and HIV viral load (VL) (CDC algorithm, LAg+VL).
- We previously optimized an alternate multi-assay algorithm (MAA) for cross-sectional HIV incidence in subtype C epidemics (MAA-C). The MAA-C algorithm includes the LAg-Avidity assay, a BioRad-Avidity assay, and VL.
- In these testing algorithms, low HIV viral load (VL) is used as a surrogate marker for non-recent infection.
- We compared cross-sectional incidence (CSI) estimates obtained with these two algorithms to observed incidence in the community-randomized HPTN 071 (PopART) trial, where a substantial proportion of HIV+ participants were virally suppressed.
- HPTN 071 (PopART) was conducted in 21 communities in Zambia and South Africa and included three study arms:
  - **Arm A**: prevention interventions + universal antiretroviral treatment (ART)
  - **Arm B**: prevention interventions + ART according to local guidelines
  - **Arm C**: standard of care
- The study enrolled a Population Cohort (PC) of >48,000 adults and followed them for up to three years with four annual surveys (PC0, PC12, PC24, and PC36).

Methods

- We assessed HIV incidence in the PopART PC 1-2 years after study initiation (from PC12 to PC24, for those with samples at both visits, Figure 1).
- The analysis included: 221 persons who seroconverted between PC12 and PC24; 217 persons who seroconverted between PC0 and PC12; 15,845 persons who were HIV negative at PC12 and PC24; 3,500 persons who were HIV+ at PC0 enrollment; and 689 persons who were HIV+ at PC12 enrollment.
- 71% of all persons with prevalent infection and 29% of the seroconverters were virally suppressed at PC24 (VL <400 copies/ml).
- Observed HIV incidence was based on confirmed seroconversion events between PC12 and PC24.
- CSI was estimated at PC24 using Sedia LAg-Avidity, BioRad-Avidity, and VL data. At PC24, 76% of those with prevalent infections and 31% of seroconverters had a VL<1,000 copies/ml.
- The CDC algorithm (LAg+VL) classified infections as recent if they had a LAg-Avidity result <1.5 ODn and an HIV VL >1,000 copies/ml. The mean duration of recent infection (MDRI) for this algorithm is 130 days.
- The MAA-C algorithm classified infections as recent if they had a LAg-Avidity result <2.8 ODn, a BioRad-Avidity Index (AI) <95% and a VL >400 copies/ml. The MDRI for this algorithm is 248 days.
- Incidence estimates and confidence intervals (CIs) were generated with the ABIE v3 Incidence Calculator by CEPHIA (Kasssanjee, et al. ARHR 2014; 30:45-49).

Figure 1. HPTN 071 – Study Timeline



A widely-used LAg+VL algorithm and an algorithm optimized for incidence estimation in clade C epidemics (MAA-C) accurately estimated HIV incidence in a cohort that had a high rate of viral suppression (76% of prevalent infections and 31% of incident infections <1,000 copies/mL)

Observed incidence:	1.34 (95% CI: 1.17 - 1.53)
LAg+VL	1.37 (95% CI: 0.95 - 1.80)
MAA-C	1.26 (95% CI: 0.95 - 1.57)

<1/2 of those infected <1 year were classified as recent infections using the cross-sectional algorithms (45% for MAA-C, 27% for LAg+VL)

Results

LAg+VL results

- 535/4627 LAg-Avidity <1.5 ODn
- 3390/4627 VL <1,000 copies/ml
- 73 with LAg-Avidity <1.5 ODn and VL >1,000 copies/ml

➢ 60/221 infected <1 year were classified as recent
➢ 6/3500 infected >2 years were classified as recent

MAA-C results

- 1295/4627 LAg-Avidity <2.8 ODn
- 1508/4607 BioRad <95% AI
- 3290/4627 VL <400 copies/ml
- 136 with LAg-Avidity <2.8 ODn and BioRad <95% AI and VL >400 copies/ml

➢ 100/221 infected <1 year were classified as recent
➢ 18/3500 infected >2 years were classified as recent

Cross-Sectional vs. Longitudinal Incidence in the full cohort

Observed incidence:	1.34 (95% CI: 1.17 - 1.53)
LAg+VL	1.37 (95% CI: 0.95 - 1.80)
MAA-C	1.26 (95% CI: 0.95 - 1.57)

Figure 2. Cross-Sectional vs. Longitudinal Incidence in Study Sub-groups

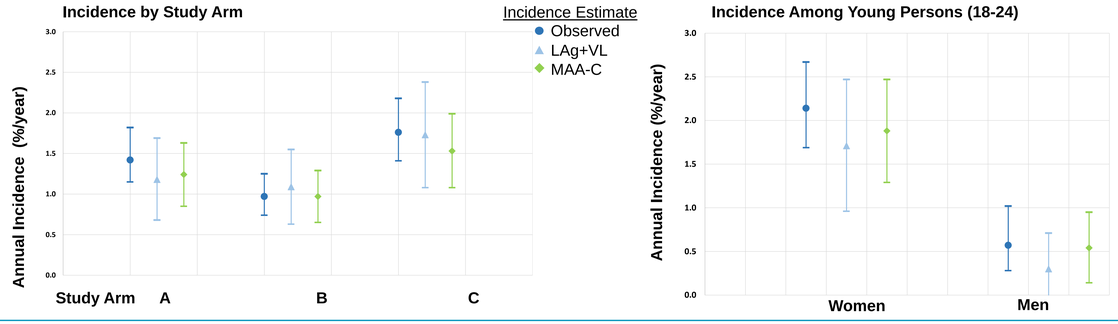
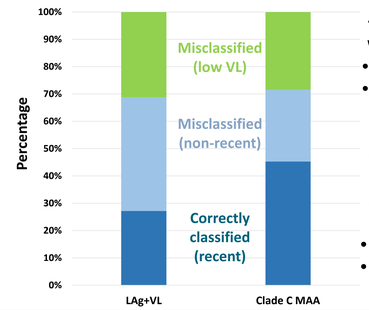


Table 1. Participant Demographics

	Arm A	Arm B	Arm C	Overall
# Participants	6727 (33%)	7534 (37%)	6212 (30%)	20472
Zambia	3912 (33%)	4304 (36%)	3658 (31%)	11874
South Africa	2812 (33%)	3230 (37%)	2556 (30%)	8598
Male	1685 (31%)	1928 (36%)	1742 (33%)	5355
Female	5039 (33%)	5606 (37%)	4472 (30%)	15117
18-24	1951 (33%)	2142 (37%)	1775 (30%)	5868
25+	4773 (33%)	5392 (37%)	4439 (30%)	14604

Figure 3. Classification of seroconverters infected <1 year (PC12-24)



<50% of the 221 seroconverters were classified as recently infected:
- 27% (60/221) by LAg+VL
- 45% (100/221) by MAA-C

Many of the seroconverters were classified as having non-recent infection because they were virally suppressed within 1 year of infection:
- 31% (69/221) <1,000 copies/ml
- 29% (63/221) <400 copies/ml

Conclusions

- Both the LAg+VL and MAA-C algorithms yielded accurate point estimates of incidence, despite high rates of viral suppression
- The MAA-C estimates had smaller CIs than the LAg+VL estimates, and were closer to observed incidence in most of the smaller, subgroup analyses
- A higher portion of those infected <1 year were classified as recently infected using the MAA-C algorithm; however, both algorithms classified >1/2 of the seroconverters as non-recent infections
- We suspect the high proportion of low VLs amongst the recently infected individuals may be due to ART use and should be further investigated

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