Comparison of Cross-Sectional Incidence Assay Results from DBS and Plasma

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Background

- Assays have been developed for cross-sectional HIV incidence estimation using plasma samples.
- Large scale surveillance programs are planned using dried blood spot (DBS) specimens for incidence assessment.
- However, limited information exists on the performance of HIV cross-sectional incidence assays using DBS.
- This study compared results obtained from three incidence assays using plasma and DBS samples.

Methods

- 3 assays were evaluated: Maxim HIV-1 Limiting Antigen Avidity EIA (LAg-Avidity), Sedia HIV-1 BED-Capture EIA (BED-CEIA), and CDC optimized BioRad HIV-1/2 Plus O Avidity-based Assay (BioRad Avidity).
- 100 matched HIV positive plasma and DBS samples, with known duration of infection, from the CEPHIA repository were tested.
- All assays were run in duplicate for each sample type.
- Categorical and continuous results were analyzed to determine the degree of variability within and between results for each sample type.
- Bland Altman, R^2 values, and kappa coefficient (κ) were used to assess correlation.

Characteristics of matched DBS and plasma samples

Characteristic	n
Duration of Infection	
>1 year	*75*
<1 year	*25*
**Viral Load*	
>10,000	*31*
400 – 10,000	*21*
<400	*40*
**CD4 Cell Count*	
>500	*58*
200 - 500	*33*
50-199	*2*
<50	*0*
On ART	
No	*76*
Yes	*24*
Country	
Brazil	*25*
United States	*75*

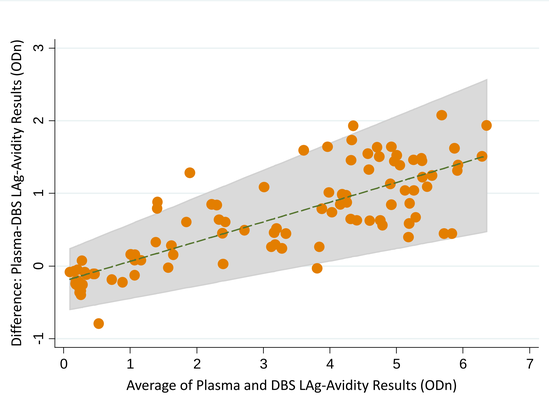
*8 pairs of samples did not have viral loads and 7 did not have CD4 counts

Results

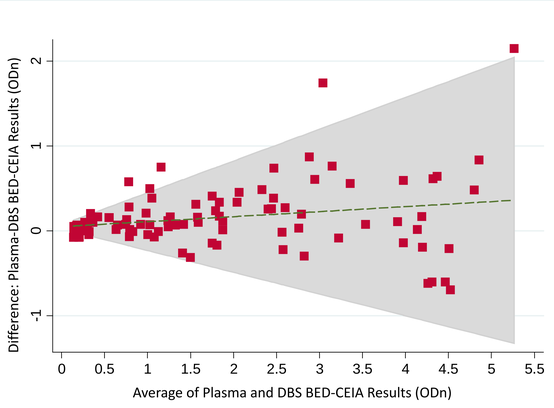
- Intra-assay variability using the same sample type was high for all assays (R^2: 0.96 to 1.00).
- The R^2 values comparing DBS and plasma results for LAg-Avidity, BED-CEIA, and BioRad Avidity were 0.96, 0.93, and 0.84, respectively.

Bland-Altman plots of the results obtained from matched plasma and DBS samples

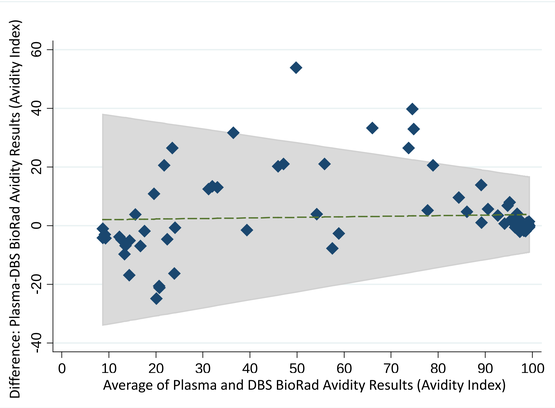
LAg-Avidity



BED-CEIA



BioRad Avidity



Comparison of categorical results obtained from matched plasma and DBS samples run on incidence assays

LAg- Avidity

Duration of Infection

PLASMA	<1 Year	>1 Year	Total
ODn<1.5	13	15	28
ODn>1.5	12	60	72
Total	25	75	100

Concordance = 73%
kappa = 0.31 (p<0.01)

Duration of Infection

DBS	<1 Year	>1 Year	Total
ODn<1.5	14	19	33
ODn>1.5	11	56	67
Total	25	75	100

Concordance = 70%
kappa = 0.28 (p<0.01)

BED-CEIA

Duration of Infection

PLASMA	<1 Year	>1 Year	Total
ODn<0.8	15	17	32
ODn>0.8	10	58	68
Total	25	75	100

Concordance = 73%
kappa = 0.34 (p<0.01)

Duration of Infection

DBS	<1 Year	>1 Year	Total
ODn<0.8	16	21	37
ODn>0.8	9	54	63
Total	25	75	100

Concordance = 70%
kappa = 0.31 (p<0.01)

BioRad Avidity

Duration of Infection

PLASMA	<1 Year	>1 Year	Total
AI<50%	21	11	32
AI>50%	4	64	68
Total	25	75	100

Concordance = 85%
kappa = 0.63 (p<0.01)

Duration of Infection

DBS	<1 Year	>1 Year	Total
AI<50%	18	14	32
AI>50%	4	57	61
Total	22	71	93

Concordance = 81%
kappa = 0.54 (p<0.01)

Summary & Conclusions

- Data generated using DBS and plasma samples was highly correlated.
- However, there is a scalar problem since the assays perform differently across their dynamic ranges.
- DBS samples were more likely to be classified as recent using all three assays, which may lead to over estimation of incidence in surveys using performance criteria derived from plasma samples.
- These results suggest that the performance characteristics of these incidence assays may be different for DBS and plasma.