THE HIV GENOMIC INCIDENCE ASSAY MEETS FRR AND MDRI PERFORMANCE STANDARDS

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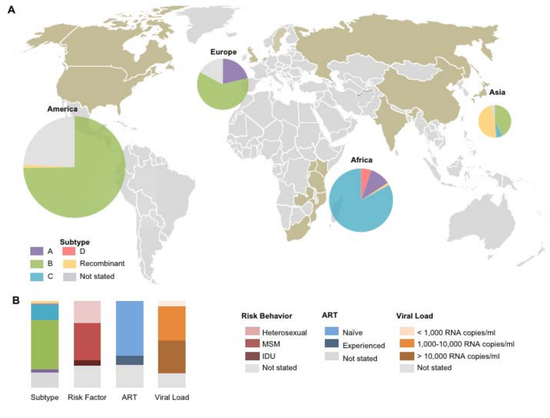
Introduction

HIV incidence is a direct metric of HIV intervention and prevention trial efficacy. Incidence assay performance is evaluated by mean duration of recent infection (MDRI) and false-recent rate (FRR).

i) FRR is the probability that a chronically infected subject is misclassified.
ii) MDRI is the average length of time in which subjects are classified as recently infected.

There is an immediate need for an assay meeting performance standards (MDRI > 1 year and FRR < 1%) to estimate incidence using a single measure.

Meta Analysis Global Cohort

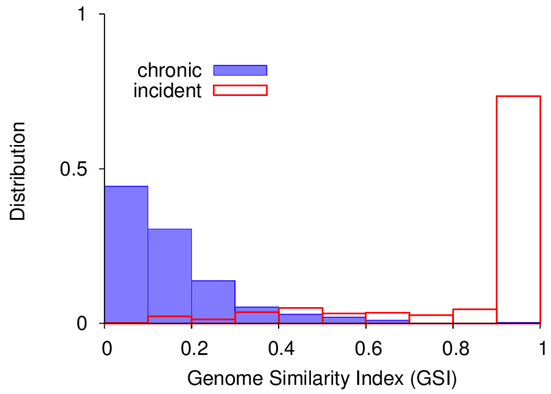


I. 274 chronic specimens > 2 years after documented HIV infection

II. 252 incident specimens < 2 years since infection based on Fiebig laboratory staging

III. 194 serial specimens from 43 subjects whose first sample was obtained < 6 months of infection

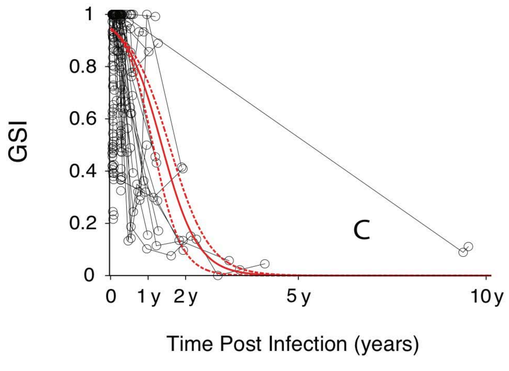
Genomic Biomarker of 305 Chronic & 438 Incident

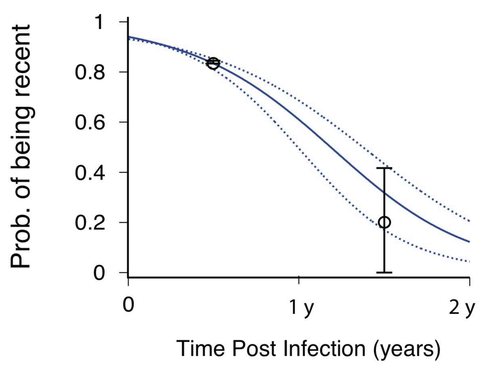


All except one chronic subject had GSI values below 0.67

: **FRR = 0.33% [0% - 0.98%]**

Genomic Biomarker Dynamics : Beta Regression on 438 Incident Specimens





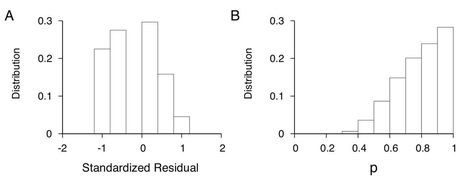
Probability of being recent $P_R(t) = p(GSI > \theta|t) = \int_\theta^1 p(GSI|t)d(GSI) = 1 - I_\theta[\alpha(t), \beta(t)]$,

$MDRI = \int_0^T P_R(t)\,dt = \int_0^T 1 - I_\theta[\alpha(t), \beta(t)]\,dt$,

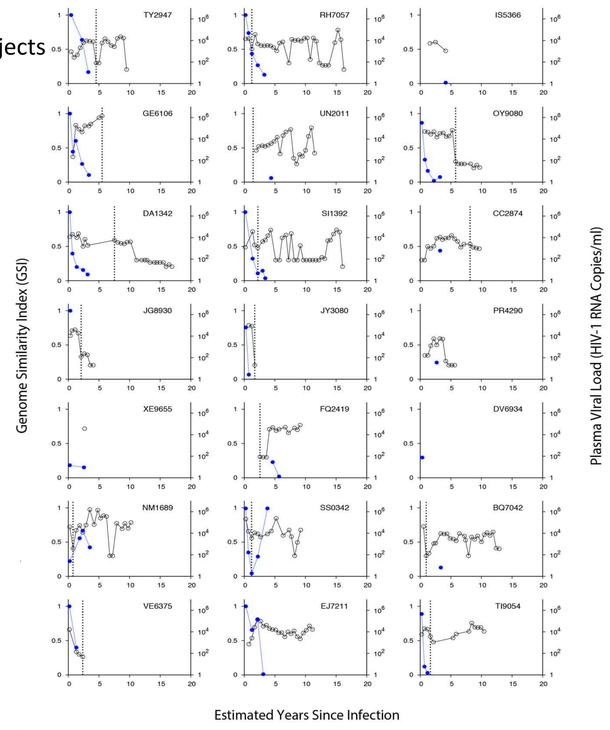
MDRI= 420 [361-467] days

Validation with the Women Interagency HIV Study (WIHS) Cohort

744 Envelope gene segments from 21 WIHS subjects



Both standardized residual test and Anderson-Darling test showed that the WIHS test dataset is statistically consistent with our model biomarker distribution



	Genomic Incidence Assay	LAg	BED
MDRI (days)	427 [361 - 467]	188 [165 – 211]	302 [274 - 331]
FRR (%)	0.33 [0.0 – 0.98]	1.3 [0.3 -3.2]	7.4 [4.8 – 10.9]

The genomic incidence assay is the first assay meeting the current performance standards.

Signatures of HIV gene diversification can allow precise cross-sectional surveillance with a desirable temporal range of incidence detection.

Acknowledgement

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