Power Analysis of PEPFAR's Recency Surveillance Strategy: Practical Limitations of Hotspot Identification

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Background

Since 2019, PEPFAR introduced routine recency testing to identify hotspots of new and on-going HIV transmissions geographically, by age cohort, and among key population groups. Four years into programmatic implementation, coverage remains limited in many countries and questions have been raised about the utility and practicality of the program.

Methods

We conducted a power analysis to determine minimum sample sizes (new HIV diagnoses / recency assays conducted) required in a geographic or population-based sub-sample to reliably detect recency rate increases of 25% to 200% of baseline at a power level of 90% and varying p-values of .05-.2. We varied our assumptions of acceptable Type 1 error (p-value) to account for recency testing as surveillance rather than hypothesis testing.

Stage 1: Unadjusted power analysis;
Stage 2: Adjusted for RITA reclassification rates of recency assays
Stage 3: As per Stage 1 but adjusted for recency assay/biomarker sensitivity and RITA specificity
Stage 4: As per Stage 2 but adjusted for recency assay/biomarker sensitivity and RITA specificity

Assumptions:

Baseline Recency Rate: 7.28% (based on Eswatini recency average data)
Recent Infection Testing Algorithm (RITA) reclassification rate: 41%
RTRI Sensitivity for recent infection: 50%
RITA Specificity: 95%

Results

Results for all stages are shown in tables 1 - 4. The low sensitivity of LAg-based recency assays has a substantial effect on the size of the sub-population (individuals newly diagnosed for HIV/unique recency assays conducted) required to reliably detect recent infection hotspots. Reliable detection of even a 100% increase over baseline in recent infections at a p-value of 0.2 still requires more than 700 new HIV diagnoses in the sub-population/geographic region being assessed.

Figures 1 & 2 show quarterly and annual numbers of new HIV diagnoses per facility for 2022 in PEPFAR priority districts. New HIV diagnoses for the vast majority of PEPFAR supported facilities are insufficient for any reliable detection of recent infection outbreaks (quarterly mean facility: 21, median: 9; annual mean facility: 75, median: 31). Even at district level, new HIV diagnoses remain low for identifying hotspots (N=880, quarter mean diagnoses: 426, median: 196, annual mean: 1,700, median: 778).

Figure 1: Quarterly # of New HIV Diagnoses per Facility (FY2022) (N=61,759 Facility Quarters)

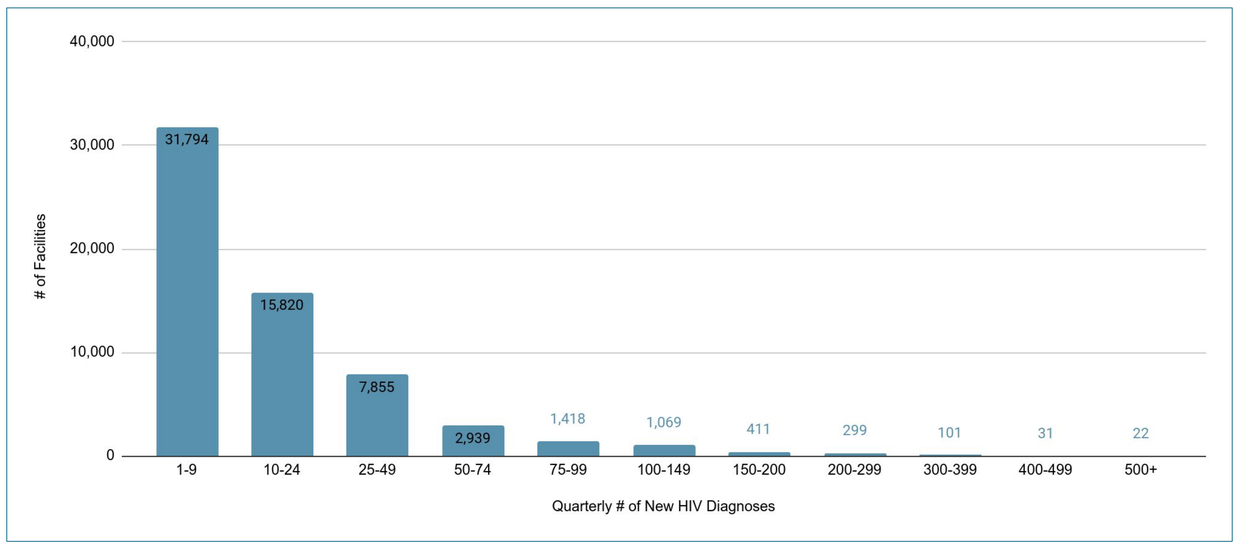
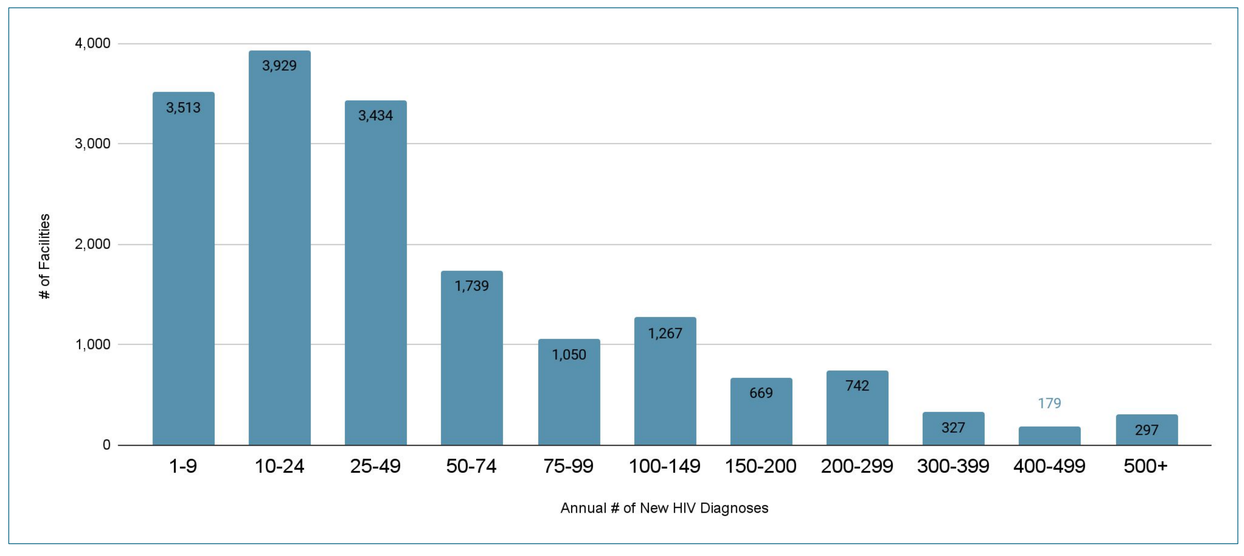


Figure 2: Annual # of New HIV Diagnoses per Facility (FY2022) (N=17,139 Facilities)



Conclusion

Current LAg-avidity based recency assays lack the sensitivity and specificity characteristics necessary to reliably detect hotspots and sub-populations with even large increases in the rate of recent infections. Based on the number of new infections currently being diagnosed at facility or district level, only the most substantial outliers are likely to be reliably detected, and these are most likely to already be well understood phenomena (i.e. urban areas, youth, and key populations). As countries approach epidemic control, the number of new diagnoses are also expected to decline such that recency testing will become less statistically viable.

Recency testing is more likely to consume resources that provide little additional unique information and provide limited insights in how to adjust programming to prevent infections going forward.

Table 1: Sub-Population/Geographic New HIV Diagnoses Required to Detect Recency Rate Increases

P-Value	RTRI Recency Rate Increase							
	25% (1.8%)	50% (3.6%)	75% (5.5%)	100% (7.3%)	125% (9.1%)	150% (10.1%)	175% (12.7%)	200% (14.6%)
.05	2,141	535	238	134	86	59	44	33
.10	1,745	436	194	109	70	48	36	27
.15	1,509	377	168	94	60	42	31	24
.20	1,339	335	149	84	54	37	27	21

Table 2: Sub-Population/Geographic New HIV Diagnoses Required to Detect Recency Rate Increases Adjusted for Reclassification Rate

P-Value	RTRI Recency Rate Increase							
	25% (1.1%)	50% (2.1%)	75% (3.2%)	100% (4.3%)	125% (5.4%)	150% (6.4%)	175% (7.5%)	200% (8.6%)
.05	3,746	937	417	235	150	105	77	59
.10	3,054	764	340	191	123	85	63	48
.15	2,640	660	294	165	106	74	54	42
.20	2,343	586	261	147	94	66	48	37

Table 3: Sub-Population/Geographic New HIV Diagnoses Required to Detect Recency Rate Increases Adjusted for Assay Sensitivity/Specificity

P-Value	RTRI Recency Rate Increase							
	25% (1.8%)	50% (3.6%)	75% (5.5%)	100% (7.3%)	125% (9.1%)	150% (10.1%)	175% (12.7%)	200% (14.6%)
.05	10,574	2,644	1,175	661	423	294	216	166
.10	8,618	2,155	958	539	345	240	176	135
.15	7,452	1,863	828	466	299	207	153	117
.20	6,612	1,653	735	414	265	184	135	104

Table 4: Sub-Population/Geographic New HIV Diagnoses Required to Detect Recency Rate Increases Adjusted for Assay Sensitivity/Specificity and Reclassification Rate

P-Value	RTRI Recency Rate Increase							
	25% (1.1%)	50% (2.1%)	75% (3.2%)	100% (4.3%)	125% (5.4%)	150% (6.4%)	175% (7.5%)	200% (8.6%)
.05	14,999	4,625	2,056	1,157	740	514	378	290
.10	15,077	3,770	1,676	943	604	419	308	236
.15	13,036	3,259	1,449	815	522	363	267	204
.20	11,566	2,892	1,286	723	463	322	237	181

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