Geospatial and Phylogenetic Clustering of Acute HIV Infections in Lilongwe, Malawi

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Background

HIV transmission during acute (pre-seroconversion) HIV infection (AHI) contributes disproportionately to population-level HIV incidence[1-3] due to elevated viral loads[4,5] and decreased HIV status awareness.[6,7]

AHI may play a larger role in geographic and demographic subpopulations[8] with greater partner switching and concurrency.[9,10]

Characterizing phylogenetic and geospatial clustering of AHI could inform strategies for detecting AHI and initiating treatment and prevention efforts during this phase.

- Strong geospatial clustering would suggest that spatially focused interventions for AHI detection could be efficient.
- Large phylogenetic clusters or chains consisting predominately of people with AHI would suggest a role for interventions propagated along sexual networks.

Methods

Population: persons presenting to Bwaila STI clinic in Lilongwe, Malawi, and screened for the iKnow study[11] between 2015 and 2019.

- 144 persons with AHI (HIV seronegative, HIV RNA+).
- 30 persons with recent HIV infection based on Sedia HIV-1 Lag-Avidity EIA.
- 652 persons with chronic HIV infection (HIV seropositive, recent-).

Geospatial methods:

- Geolocation of households with an AHI case.
- Geospatial cluster identification with flexible scan statistic (α=0.2) using a 30-meter resolution population denominator.

Phylogenetic methods:

- Maximum likelihood phylogenetic trees from viral samples using the veSEQ-HIV protocol[12], *shiver*[13], genecutter[14], MAFFT[15], and IQ-tree.[16]
- Monophyletic sequences with genetic distances <1.5% were considered phylogenetic clusters.
- For *gag* and *pol* analyses, we excluded sequences with <90% coverage for each gene.

Results

38% of people with AHI resided in <1% of the populated clinic catchment area.

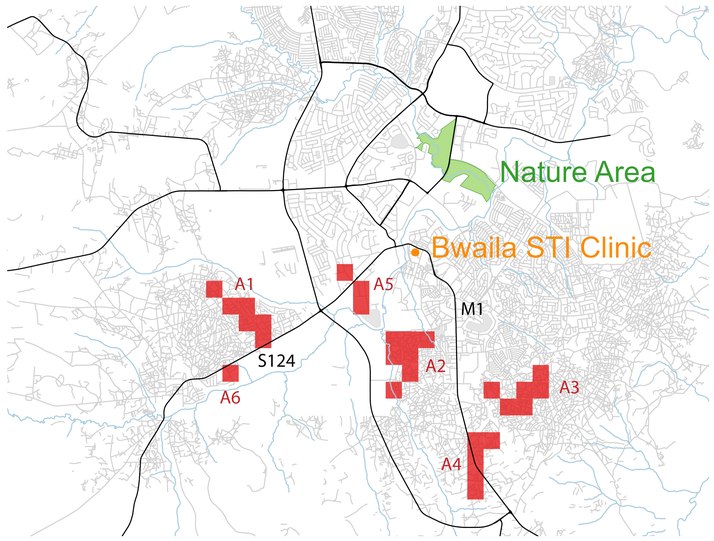


Figure 1: Purely spatial clusters of AHI in Lilongwe, Malawi

We identified eight two-person transmission clusters, but no larger chains.

Table 1: Phylogenetic clusters with sufficient gag or pol data

ID	Type	Genetic Distance (gag)	Genetic Distance (pol)	Ages	Referral Link?	Temporal Distance	Euclidean Distance
AR1	Acute-Recent	0.00%	0.00%	22, 23	No	42 days	Unknown
AC1	Acute-Chronic	0.37%	excluded	20, 21	Yes	23 days	Unknown
AA1	Acute-Acute	excluded	0.44%	27, 29	No	95 days	4.5 km
CC1	Chronic-Chronic	1.26%	excluded	23, 26	No	108 days	Unknown
CC2	Chronic-Chronic	1.42%	0.44%	26, 28	Yes	13 days	Unknown
AC2	Acute-Chronic	0.97%	1.47%	32, 32	Yes	0 days	Unknown
CC3	Chronic-Chronic	0.85%	0.93%	22, 32	No	8 days	Unknown

Table 2: Phylogenetic clusters without sufficient gag or pol data

ID	Pair Type	Region Overlap (# base pairs)	Genetic Distance	Ages	Referral Link?	Temporal Distance	Euclidean Distance
AA2	Acute-Acute	Nef (185), Env (1160)	0.19%	22, 30	No	19 days	0.2 km

Discussion

We observed clear evidence of spatial AHI clustering, suggesting that geographically focused AHI detection, treatment, and transmission prevention interventions could be powerful tools in the pursuit of HIV elimination in this setting.

With no phylogenetic cluster larger than 2 members, there was limited evidence of extensive AHI transmission chains, suggesting that network-based interventions focusing on AHI detection may have a more limited impact on the identification of people with AHI and prevention of transmission during this phase. However, quantification of intervention impact or efficiency was outside the scope of this study.

Low sequencing coverage (~30%) may have obscured transmission clusters but plans for resequencing are in place. We also acknowledge that our reliance on data from an STI clinic population further results in only a partial view of the full HIV transmission network.

Our study in a large population of persons with AHI in an urban setting suggests that geospatial and phylogenetic analysis among STI clinic patients can inform AHI-focused HIV detection, treatment, and prevention efforts radiating along geospatial and/or network lines.

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