Sociodemographic Factors Associated with HIV Clustering across Botswana Communities

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Abstract # 911

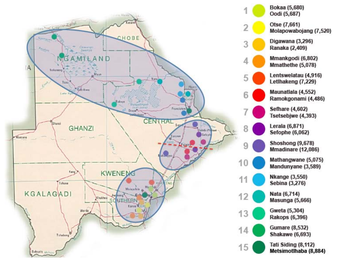
BACKGROUND

- Understanding HIV transmission networks is important for intervention programming. However, factors associated with molecular HIV clusters in southern Africa are not well-studied.
- We sought to identify independent predictors of being part of a molecular HIV cluster using data from HIV-positive persons enrolled in a large community-randomized HIV prevention trial in Botswana.

METHODS

- The Botswana Combination Prevention Project was conducted in 30 communities across Botswana in 2013-2018 (Fig 1)[1]. At study enrollment, near-full length HIV-1 genome sequences were obtained (from RNA or DNA)[2] from HIV-positive persons and analyzed for their phylogenetic relationships at different thresholds of cluster definition.
- We defined an inferred molecular HIV cluster (transmission network) as a phylogenetically distinct viral lineage giving rise to a monophyletic subtree of the overall phylogeny using five thresholds of bootstrap support of splits (bt) and mean pairwise distances (pwd). The following thresholds were used for cluster definition: (1) bt ≥0.80 and no pwd (Figure 2); (2) bt ≥0.80, pwd ≤12.5%; (3) pwd ≥0.90, dt ≤10%; (4) pwd ≥0.95, pwd ≤7.5%; and (5) pwd ≥0.95, dt ≤5%.
- We used modified Poisson generalized estimating equations to obtain risk ratios (RR), corresponding Huber robust SEs and 95% Wald CIs to examine associations between individual participant characteristics and the binary outcome of being part of a cluster. This method takes into account the cluster-randomized design of BCPP, where pair-matched communities were randomly assigned to receive the intervention or standard-of-care. Adjusted models were derived applying backwards selection methods with an exit criteria of p<0.10.

Figure 1. Map of 30 pair-matched communities participating in the BCPP



RESULTS

- Among the 3,596 HIV-positive BCPP participants in the year 1 survey, sequences were obtained on 2,901 (81%). We identified 1,215 (42%) clusters, with cluster sizes 2 – 14. Cluster members were mostly female (71%) with a median (IQR) age of 39 years (32, 47).
- The following factors were associated with being in a cluster:
  - sexually active in the last year but not having any concurrent sexual relationships [adjusted Risk Ratio (aRR):1.21; 95%CI:1.01–1.44[or having concurrent sexual relationships (aRR:1.33; 95%CI:1.16-1.52) as compared to no sexual activity in the last year and
  - not being virally suppressed (aRR:1.11; 95%CI:1.00-1.23), Table 1.

***Figure 2**: Clustering of Near Full-Length HIV-1C sequences (n=2,901; clusters defined as monophyletic subtrees with ≥0.80 bootstrap support and are shown in green; clusters with seroconverters are shown in red)*

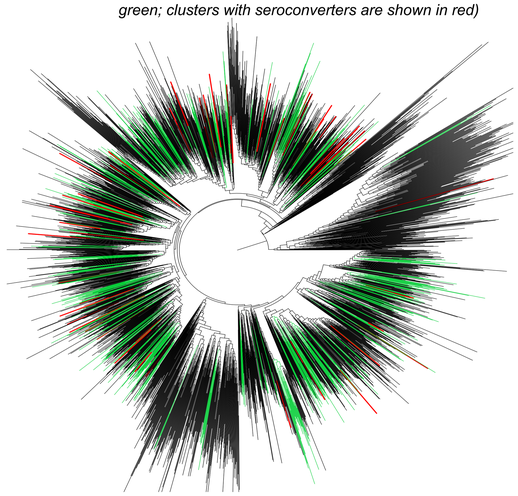
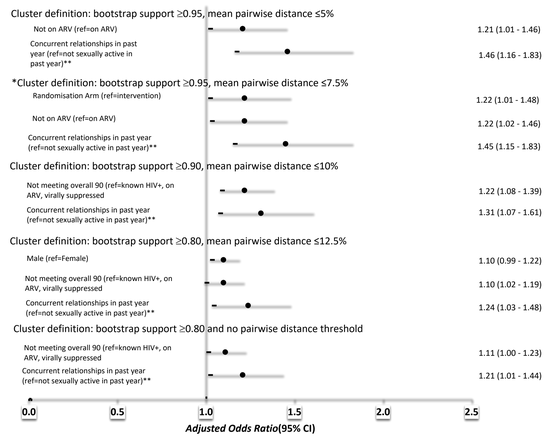


***Figure 3**: Sensitivity analyses for factors associated with cluster membership for selected definitions of cluster: bootstrap support (bt) and TN93 distance threshold (dt)*



*Income also significant; **sexually active but not concurrent" compared to "not sexually active" is also significant

***Table 1**: Univariable Models plus Selected Multivariable Model for Cluster Definition at ≥0.80 bootstrap support and no distance threshold (n=2901 sequences)*

Predictors		Univariable Models RR (95% CI)	p-value	Selected Adjusted Model RR (95% CI)	p-value
Randomization Arm (ref=Intervention)	Standard of Care	1.05(0.95, 1.15)	0.379		
Age (ref=55-64 years)	16-24 years	1.03(0.85, 1.25)	0.750		
	25-34 years	1.14(0.97, 1.34)	0.102		
	35-44 years	1.05(0.88, 1.25)	0.579		
	45-54 years	0.94(0.81, 1.09)	0.424		
Gender (ref=F)	M	1.10(1.01, 1.19)	**0.031**		
Education, highest level attained (ref=Non-formal/Primary)	Higher than second	1.02(0.90, 1.17)	0.721		
	Secondary	1.09(1.00, 1.20)	**0.061**		
Ever married (ref=Yes)	No	1.02(0.92, 1.14)	0.676		
Currently employed (ref=Yes)	No	1.02(0.92, 1.13)	0.717		
Income, past 1 month (ref=1000-4999 pula ($96 to $477))	1-999 pula (<$96)	1.11(1.01, 1.23)	**0.029**		
	>4999 pula (>$477)	1.05(0.87, 1.27)	0.620		
	None	1.04(0.95, 1.13)	0.387		
Sexually active, past 12 months (ref=No)	Yes	1.22(1.04, 1.44)	**0.014**		
Transactional sex, past 12 months (ref=0. Not sexually active in last year)	1. Sexually active but no transactional sex	1.19(1.02, 1.39)	**0.023**		
	2. Sexually active and transactional sex	1.40(1.15, 1.70)	**<.001**		
Intergenerational sex (ref=0. Not sexually active in last year)	1. Partner similar age	1.19(1.03, 1.38)	**0.015**		
	2. Partner older or younger	1.22(1.03, 1.44)	**0.024**		
Inconsistent condom use (ref=0. Not sexually active in last year)	1. Sexually active + no report of inconsistent condom	1.21(1.04, 1.41)	**0.012**		
	2. Sexually active + inconsistent condom use	1.20(1.01, 1.41)	**0.038**		
Concurrency, past 12 months (ref=0. Not sexually active in last year)	1. No concurrency in the last year	1.18(1.00, 1.39)	**0.056**	1.21(1.01, 1.44)	**0.034**
	2. Concurrent relationships in last year	1.30(1.14, 1.48)	**<.001**	1.33(1.16, 1.52)	**<.001**
On ARV (ref=Yes)	No	1.07(0.96, 1.20)	0.207		
First 90 (knowledge of HIV+ status) (ref=Yes)	No	1.07(0.92, 1.25)	0.355		
Overall 90 (known HIV+, on ART, virally suppressed) (ref=Yes)	No	1.11(1.00, 1.23)	**0.044**	1.11(1.00, 1.23)	**0.047**

RESULTS

- In sensitivity analyses examining factors associated with membership in a cluster with a seroconverter identified being employed (aRR:2.25; 95%CI:1.42-3.56), highest education of secondary (as compared with non-formal or primary) (aRR:1.56; 95%CI:1.12-2.17) and lack of knowledge of HIV status (aRR:1.57; 95%CI:1.05-2.36).
- In sensitivity analyses, being in multiple concurrent relationships in the past year or being sexually active without concurrency (compared to not being sexually active) was an independent predictor of cluster membership across all definitions of cluster thresholds (Fig 3). Individuals that were not virally suppressed (compared to those that knew their status, were on ARVs and were virally suppressed) or not on ARV (versus being on ARVs) were also independent predictors of some definitions of cluster membership (Fig 3).
- Most strict thresholds (bootstrap support ≥0.95, mean pairwise distance ≤7.5% & ≤5%) identified not being on ART significantly associated with being in a transmission cluster (Fig 3)

CONCLUSION

- Molecular epidemiology can be applied to characterize HIV transmission networks. Clustering was associated with having any concurrent partnerships, lack of viral suppression and not being on ART.
- Being employed, none or non-formal highest education level and knowledge of HIV status were associated with NOT being in a cluster with a seroconverter.
- These findings reinforce the importance of enhanced targeted HIV testing programs and scale-up of ART to increase viral suppression in persons living with HIV.

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