RECONSTRUCTION AND ESTIMATION OF DIRECTED HIV-1 TRANSMISSION USING DEEP SEQUENCES

0928

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BACKGROUND

- Key populations with elevated HIV-1 incidence and/or prevalence have been identified across sub-Saharan Africa, yet their contribution to disease spread remains unclear
- In Uganda, the fisherfolk (FF) (incidence rate of 6/100 person years at risk)[1] and women at high risk of HIV-1 infection (WHR) (3/100 PYAR)[2] are considered important key populations for controlling HIV spread
- Studies[3,4] based on phylogenetic analyses have shown that FF communities of Lake Victoria are not driving the nearby HIV epidemic
- The study objective was to assess the contribution of key populations and certain socio-demographic factors to the HIV-1 epidemic in the general population (GP) based on an independent data set
- We set out to test the hypothesis that key populations are sources of viral transmission

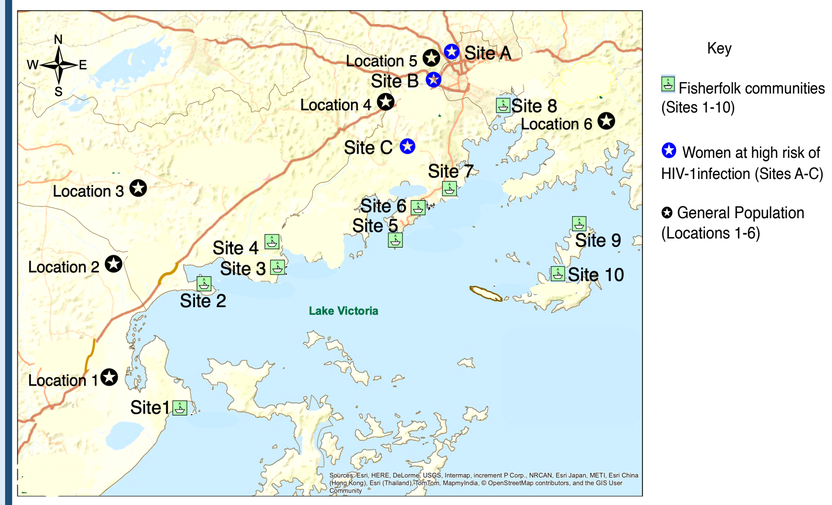
METHODS

- Study participants were recruited in community health facilities (CHF) or during Voluntary Counseling & Testing (VCT) (Table 1), resulting in a convenience sample of HIV positives living in the study area (Figure 1)
- 2,531 study participants who were ART naive and who had plasma viral load >1,000 copies/ml were deep-sequenced
- Directed transmission networks were reconstructed from HIV-1 deep sequence phylogenies using Phyloscanner v1.8.0 and the Phyloflows R package, v1.1.0 was used to quantify HIV-1 transmission flows while adjusting for sampling heterogeneity

Table 1. Study population and number of sequenced individuals

Population and gender	HIV-positive participants	Deep sequenced
Total	**6185**	**2531**
Fisherfolk	**2185**	**895**
Men	1103 (50.5%)	468 (52.3%)
Women	1082 (49.5%)	427 (47.7%)
General population	**3200**	**1309**
Men	1578 (49.3%)	636 (48.6%)
women	1622 (50.7%)	673 (51.4%)
Women at high risk and male clients	**800**	**327**
Men	80 (10.0%)	26 (8.0%)
Women	720 (90.0%)	301 (92.0%)

Figure 1. Map showing the study sites



- Individuals approached in CHF or during VCT campaigns were eligible to participate if they had an HIV-1 positive status and were at least 18 years old (FF communities 1-8) or 14 years (FF communities 9-10)

RESULT: Table 3. Phylogenetically estimated sources of HIV-1 acquisition

	Estimated sources of infection among study participants, based on data excluding same-sex pairs* (mean, 95% credibility interval of posterior density)	
	FF	GP
Recipient		
FF	70.4% (56.2%-81.9%)	29.6 (18.1%-43.8%)
GP	19.8% (10.0%-33.2%)	80.2% (66.8%-90.0%)

* Estimated transmission probabilities from a source to recipient location; shown are the mean and corresponding 95% credibility interval of posterior density. Rows sum to 100%.

- A substantial number of viral introductions into FF communities were found
- 80.2% and 70.4% are lower & upper bound estimates of infection sources

RESULT: Table 4. Phylogenetically estimated HIV-1 transmission flows by gender

Aggregated HIV-1 transmission flows by gender		
Gender (Transmitter)	**Gender (Recipient)**	**Transmission flows (%)**
Female	Male	32% (21.9%-43.4%)
Male	Female	68% (56.6%-78.1%)

- HIV-1 transmissions originated predominantly from men (68.0%, 95% CrI 56.6%-78.1%)

RESULT: Table 2. HIV-1 Transmission Flows

Sources	Recipients	Phylogenetically strongly supported transmission pairs including same-sex pairs (count, proportion)	Phylogenetically strongly supported transmission pairs excluding same-sex pairs (count, proportion)	Estimated transmission flows among study participants, based on data including same-sex pairs (mean, 95% credibility interval of posterior density)	Estimated transmission flows among study participants, based on data excluding same-sex pairs (mean, 95% credibility interval of posterior density)	Estimated transmission flow ratios, based on data excluding same-sex pairs (mean, 95% credibility interval of posterior density)
FF	FF	33 (31.4%)	33 (44.6%)	35.8% (26.2%-46.1%)	45.5% (34.1%-57.0%)	--
FF	GP	9 (8.6%)	9 (12.1%)	9.9% (4.7%-16.8%)	12.7% (6.1%-21.3%)	--
FF	WHR	2 (1.9%)	1 (1.4%)	--	--	--
GP	FF	14 (13.3%)	14 (18.9%)	15.3% (8.7%-23.3%)	19.5% (11.4%-29.3%)	1.56 (0.68 – 3.72)
GP	GP	36 (34.3%)	16 (21.6%)	39.0% (29.0%-49.4%)	22.3% (13.4%-32.7%)	--
WHR	GP	1 (1.0%)	1 (1.4%)	--	--	--
WHR	WHR	10 (9.5%)	0 (0%)	--	--	--

CONCLUSIONS

- **More transmissions** observed from **the GP to FF communities than vice versa**, flow ratio of 1.56 (95% CrI 0.68-3.72)
- The primary limitation to the generalization of these results is that a convenience sample was used. The FF population was surveyed more intensely than the GP however, the flow ratio is not affected by disproportionate survey intensity
- Therefore, study provides further evidence that **fishing communities are net recipients** of HIV-1 transmission flow
- One pair involved a WHR and male participant, suggesting that improved population sampling is needed to assess the role of WHR to the transmission dynamics
- **Men** contributed disproportionally to HIV-1 transmission flow (68.0%, 95% CrI 56.6%-78.1%) regardless of age, suggesting that prevention efforts need to better aid men to engage with and stay in care

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