Statewide Real-Time Integration of Molecular and Contact Tracing Data to Disrupt HIV Transmission

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CROI 2024
March 3-6, 2024
Denver, Colorado

BACKGROUND

- Public health needs tools beyond contact tracing to disrupt HIV transmission.
- Molecular cluster analysis has proven useful in outbreak investigation, but its value in routine public health prevention efforts remains untested.
- We hypothesized that routinely re-interviewing newly HIV-diagnosed persons whose sequences cluster molecularly, would motivate them, and enhance identification of partners, new HIV cases, and people at high risk for acquiring HIV, beyond standard contact tracing.

METHODS

- To address the hypothesis, we:
  1. Built an academic-governmental partnership in the State of Rhode Island (RI);
  2. Established and were guided by an ethics framework;
  3. Maximized statewide representation of HIV-1 *pol* sequences identified in our jurisdiction;
  4. Developed an automated bioinformatics pipeline to aggregate de-identified data across academic and public health systems, and used an ensemble of molecular clustering methods for cluster analyses; and
  5. Conducted a 2-year prospective statewide study (Jan 2021 - Dec 2022) in which we attempted to re-interview all newly HIV-diagnosed persons in the state whose HIV sequences had clustered, and assess the impact of informing them of that fact.

RESULTS

Interview and Clustering Results

- Of 100 newly diagnosed persons in RI during the study (**Table 1**), 52 were part of molecular clusters (red branches in **Figure 1**).
- In initial interviews, 19/52 named any partner. Of 139 partners named, 14 could be contacted, leading to one newly determined HIV status, and one PrEP referral.
- Re-interviews were feasible for 18/52 (35%), revealing an important gap (**Table 2**). Only 1/18 provided potentially new information beyond first interviews and the study was stopped early for futility.
- Of the remaining 34/52, 14/52 (27%) had a 'combined' interview (because clustering was known at the time of a delayed initial interview), and 20/52 (38%) did not have a re-interview (**Table 2**).

Other Results

- Substantially higher clustering was seen with phylogenetic versus distance-only methods. High (89%) phylogenetic concordance existed within the phylogenetic ensemble (**Table 3**).
- Sequencing 118 of RI persons with missing sequences resulted in 11 new clusters, 14/118 joined known clusters, 9/118 formed new clusters and 8 previously-unclustered persons joined clusters.

Re-interviewing newly HIV-diagnosed persons found in molecular clusters in Rhode Island during 2021-2022 did not improve public health contact tracing.

Figure 1: Phylogenetic Relationships Between Genotyped HIV-1 cases in Rhode Island

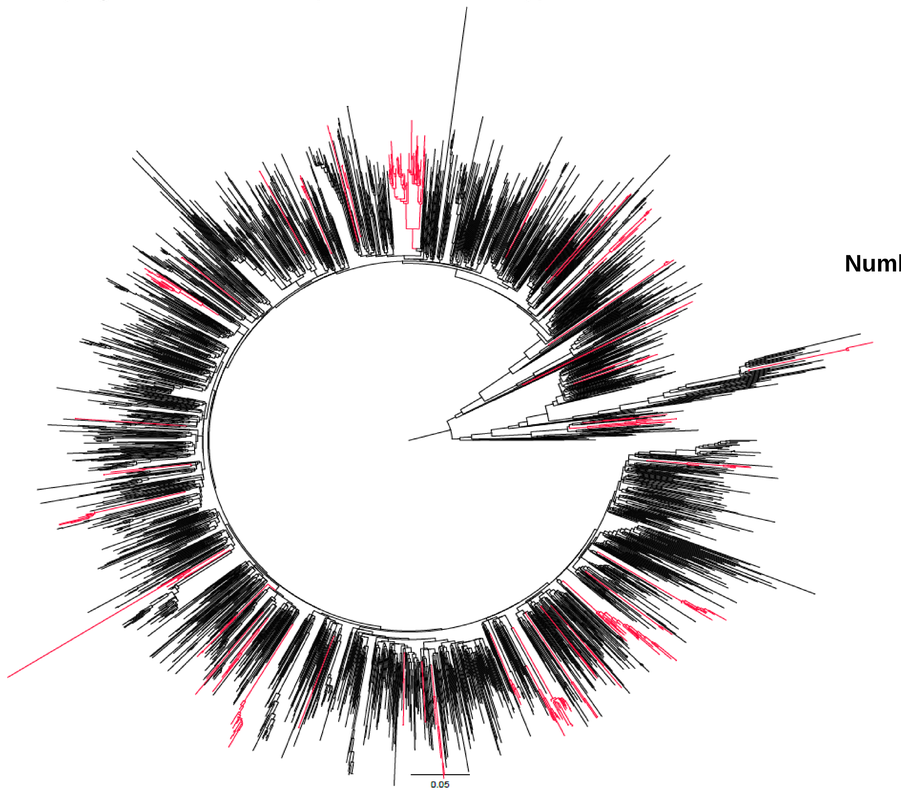

Table 1: New HIV Diagnoses in RI in '21-'22

		All (N=100)	Cluster (N=52)	Not in a cluster (N=48)
Gender	Female	18 (18%)	8 (15%)	10 (21%)
	Male	80 (80%)	43 (83%)	37 (77%)
	Transgender	2 (2%)	1 (2%)	1 (2%)
Age at Diagnosis; Mean (SD)		39 (14)	39 (13)	39 (15)
Men Who have Sex with Men		57 (57%)	34 (65%)	23 (48%)
Persons who Inject Drugs		3 (3%)	2 (4%)	1 (2%)
Ethnicity	Non-Hispanic	75 (75%)	40 (77%)	35 (73%)
	Hispanic	24 (24%)	12 (23%)	12 (25%)
Race	Asian	1 (1%)	0 (0%)	1 (2%)
	Black	26 (26%)	14 (27%)	12 (25%)
	Other	5 (5%)	3 (6%)	2 (4%)
	White	56 (56%)	31 (60%)	25 (52%)
Country of Birth	Not USA	37 (37%)	16 (31%)	21 (44%)
	USA	51 (51%)	32 (62%)	19 (40%)
Subtype	B	83 (83%)	45 (87%)	38 (79%)
	Non-B	17 (17%)	7 (14%)	10 (21%)
CD4 count at Diagnosis; Mean (SD)		352 (278)	401 (288)	294 (259)
Log VL at Diagnosis; Mean (SD)		4.8 (1.0)	5.0 (0.7)	4.6 (1.3)
Days to 1st interview; Mean (SD)		41 (26)	47 (32)	36 (16)

Table 2: Re-interview Outcomes in RI in '21-'22

	2021	2022	Total
Reinterview Yield			
Potentially new information	1 (2%)	0 (0%)	1 (2%)
No other information	10 (19%)	7 (14%)	17 (33%)
Total new diagnoses who cluster	11 (21%)	7 (14%)	18 (35%)
Reason Reinterview Not Conducted			
Combined interview	8 (15%)	6 (12%)	14 (27%)
Unable to locate for only reinterview	2 (2%)	6 (12%)	8 (15%)
Unable to locate for both interviews	0 (0%)	1 (2%)	1 (2%)
Refused	2 (4%)	4 (8%)	6 (12%)
Out of jurisdiction	1 (2%)	1 (2%)	2 (4%)
Sensitive	0 (0%)	3 (6%)	3 (6%)
Total new diagnoses who cluster	13 (25%)	21 (40%)	34 (65%)
Grand Total New Diagnoses Who Cluster	24 (46%)	28 (54%)	**52 (100%)**

Table 3:
Number of Persons Who Cluster by Phylogeny and Distance Methods

Clustering Method	HIV TRACE	RaxML	IQTree	FastTree	FastTree Alrt	MEGA	Any Phylo
HIV TRACE 1.5%	22	22	22	22	22	22	22
RaxML		51	43	45	41	47	51
IQTree			44	41	42	42	44
FastTree				46	39	43	42
FastTree Alrt					42	40	42
MEGA						47	47
Any phylogenetic							52

CONCLUSIONS

- In RI, re-interviewing newly diagnosed persons whose HIV sequences clustered with other statewide HIV sequences did not improve the yield of contact tracing.
- Building a strong academic-public health partnership, statewide epidemic representation, and a comprehensive set of cluster inference tools has prepared us to study other uses of routine, near-real-time use of cluster analyses in public health interventions to disrupt HIV transmission.