INTEGRATION OF HIV CLUSTER AND EPIDEMIOLOGIC DATA TO INFORM PREVENTION IN CALIFORNIA

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BACKGROUND

- An estimated 156,000 people were living with HIV in California at the end of 2018 and approximately 5,000 people are newly diagnosed each year.
- Transmission network analysis using HIV-1 *pol* sequences provides a systematic approach to identifying recent HIV transmission that represent missed opportunities for public health intervention.
- **Objective:** To examine both individual- and community-level predictors of HIV transmission clusters in California. We used a multilevel regression model, and community-level variables included both community sociodemographics as well as community measures of the HIV care continuum.

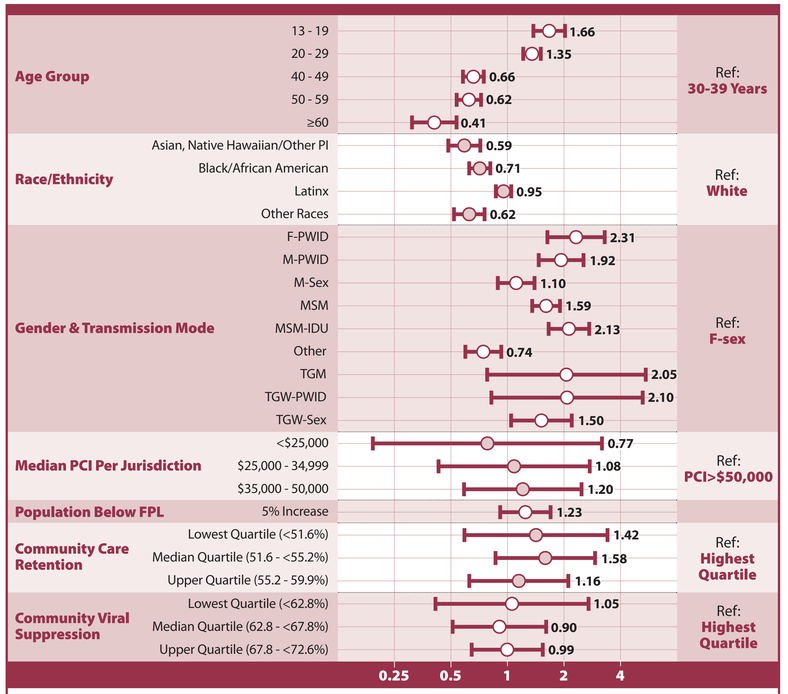
RESULTS

- Of the 61 jurisdictions in CA, 39 had at least 20 HIV diagnoses and accounted for 16,504 (99%) of the 16,657 people diagnosed with HIV from 2016–2018. Individual-level demographic, epidemiologic, and clinical (CD4, VL, and genotypic testing) information is presented in Table 1.
- Among people diagnosed from 2016 to 2018 and included in the study, 18.3% (95% CI: 12.3%-24.2%) had a sequence that clustered with the sequence of at least one other person. The proportions of molecular clustering at or below the 0.5% distance threshold in the state's three largest counties, Los Angeles, San Diego, and Orange Counties, were 22.4% (CI: 19.9%-24.9%; sequence completeness 57.6%), 15.9% (CI: 13.2%-18.6%; sequence completeness 61.1%), and 23.1% (CI: 19.4%-26.7%; sequence completeness 71%) respectively.
- Higher frequency of molecular clustering was associated with younger age (compared to older); and with cis-gendered men who have sex with men, transgender women, and people who inject drugs (compared to cisgender women at sexual risk). Lower frequency of molecular clustering was associated with being Asian/Native Hawaiian/Other Pacific Islander, or Black/African American (compared to White), while Latinx were not significantly different from the comparison group. After multivariable adjustment, higher poverty and a higher proportion of people not retained in care in a jurisdiction showed positive albeit nonsignificant associations with molecular clustering (Figure 1).

Table 1: Demographics, Transmission Risk, and Clinical Characteristics of People With HIV Diagnosed From 2016 – 2018 and Associations With Molecular Clustering

	Diagnoses & Column %		Clustering in a Transmission Network			
			N	%	Rate Ratio (95% CI)	
ALL	**16,504**		**3,040**	**18.4**		
Age at Diagnosis (Years)						
13 - 19	546	3.3	148	27.1	**1.65**	**(1.35, 2.02)**
20 - 29	6,014	36.4	1,440	23.9	**1.40**	**(1.27, 1.54)**
30 - 39	4,538	27.5	834	18.4	Ref	1
40 - 49	2,811	17	347	12.3	**0.63**	**(0.55, 0.72)**
50 - 59	1,869	11.3	217	11.6	**0.58**	**(0.50, 0.68)**
≥60	726	4.4	54	7.4	**0.36**	**(0.27, 0.48)**
Race/Ethnicity						
American Indian/Alaska Native	49	0.3	9	18.4	0.91	(0.44, 1.89)
Asian	1,038	6.3	121	11.7	**0.54**	**(0.44, 0.66)**
Black/African American	2,835	17.2	439	15.5	**0.74**	**(0.66, 0.85)**
Latinx	7,068	42.8	1,502	21.3	1.10	(1.00, 1.21)
Mutliple races	448	2.7	86	19.2	0.97	(0.75, 1.24)
Native Hawaiian/Other Pacific Islander	44	0.3	16	36.4	**2.32**	**(1.25, 4.31)**
Unknown races	1,006	6.1	74	7.4	**0.32**	**(0.25, 0.41)**
White	4,016	24.3	793	19.7	Ref	1
Gender & Transmission Risk						
Cisgender women who inject drugs	198	1.2	49	24.7	**2.41**	**(1.67, 3.47)**
Cisgender women at sexual risk	1,250	7.6	150	12	Ref	1
Cisgender men who inject drugs	458	2.8	97	21.2	**1.97**	**(1.49, 2.61)**
Cisgender men at sexual risk	1,377	8.3	180	13.1	1.10	(0.87, 1.39)
Cisgender men who have sex w/ men (MSM)	9,697	58.8	2,078	21.4	**2.00**	**(1.68, 2.39)**
MSM who inject drugs	547	3.3	134	24.5	**2.38**	**(1.84, 3.08)**
Other	2,714	16.4	295	10.9	0.89	(0.73, 1.10)
Transgender men	22	0.1	6	27.3	**2.75**	**(1.06, 7.14)**
Transgender women who inject drugs	24	0.1	6	25	2.44	(0.96, 6.25)
Transgender women at sexual risk	217	1.3	45	20.7	**1.92**	**(1.33, 2.78)**
Clinical Status at Diagnosis						
HIV only	12,836	77.8	2,508	19.5	Ref	1
AIDS diagnosed after HIV dx	1,053	6.4	190	18	0.91	(0.77, 1.07)
AIDS and HIV dx concurrent	2,593	15.7	339	13.1	**0.62**	**(0.55, 0.70)**
First CD4 Count After Diagnosis						
>500 CD4 cells/µl	5,495	33.3	1,174	21.4	0.89	(0.81, 0.97)
200 - 500 CD4 cells/µl	5,836	35.4	1,366	23.4	Ref	1
<200 CD4 cells/µl	3,183	19.3	457	14.4	**0.55**	**(0.49, 0.62)**
Unknown	1,990	12.1	43	2.2	**0.07**	**(0.05, 0.10)**

Figure 1: Adjusted Odds Ratios for HIV Molecular Clustering According to Selected Individual- and Population-Level Characteristics, California, 2016-2018



Abbreviations: M-PWID, cisgender men who inject drugs; M-Sex, cisgender men at sexual risk; MSM, cisgender men who have sex with men; MSM-IDU, MSM who inject drugs; TGM, transgender men; TGW, transgender women; PCI, per capita income; FPL, federal poverty level

METHODS

Molecular Network Analysis

- HIV-1 *pol* sequences reported to the state's HIV surveillance system were analyzed with HIV-Trace (www.hivtrace.org) among people diagnosed from 2016-2018 (55.6% sequence completeness).
- Molecular transmission clusters were defined and identified as two or more sequences that linked within a pairwise genetic distance of 0.005 substitutions/site.

Multilevel Regression Analysis

- Mixed-effects logistic regression accounted for individual characteristics and jurisdiction-level (city or county) random intercept and fixed effects (outcome is membership in a cluster); model specified as:

$$\log\left(\frac{\mu_{ij}}{1-\mu_{ij}}\right) = \beta_0 + \sum_{p=1}^{P}\beta_p x_{pij} + \sum_{q=1}^{Q}\gamma_q z_{qi} + \alpha_i$$

  - μ_{ij} - Probability of membership in a recent transmission cluster for the j^{th} case in the i^{th} jurisdiction
  - β_p - Slope for the p^{th} individual-level covariate χ_{ij} including age, race/ethnicity, birth gender and transmission mode
  - α_i - Intercept deviation for the i^{th} jurisdiction and is normally distributed with zero mean
  - γ_q - Slope for the q^{th} jurisdiction-level covariate Z_{qi} consisting of care continuum outcomes and U.S. Census-based sociodemographic measures including population density, median per capita income, % below high school education, % population below FPL, unemployment and housing vacancy rates
- Community care retention is defined as the proportion of people living with HIV in a jurisdiction that have two or more CD4, viral load (VL), or genotype test results that are at least 90 days apart in a 12 month time period. Community viral suppression is defined as the proportion of people living with HIV in a jurisdiction that have a VL result of < 200 copies/ml during the calendar year for the most recent VL result.
- To ensure model convergence and reliability of parameter estimates, only jurisdictions with at least 20 new diagnoses during the study period were included in the analysis.

LIMITATIONS

- Molecular transmission cluster analyses are subject to sampling bias as not all people recently diagnosed with HIV-1 have a reported *pol* sequence.
- Individuals diagnosed with early-stage infection might reflect elevated diagnosis rates rather than exceptional transmission rates.

CONCLUSION

- We examined associations between HIV molecular clustering and both individual and community level factors in a multilevel regression model. This clustering analysis approach can be informative in terms of guiding interventions and providing community-level information about the impact of prevention strategies.
- We observed higher frequencies of molecular clustering in relation to several individual level characteristics including age, race/ethnicity, gender, and transmission category.
- The socioeconomic characteristics by county were not associated with frequencies of molecular clustering, potentially reflecting the geographic dispersion of linked transmissions.

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