Can Molecular HIV Surveillance Identify Groups to Prioritize for Prevention?

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BACKGROUND

- Studying HIV transmission networks provides insight into the spread of HIV and opportunities for intervention
- Because mutation causes strains of HIV to diverge fairly quickly, two persons with genetically similar HIV sequences are likely to be epidemiologically linked
- Genetic data can be used to infer HIV transmission networks
- Persons that are highly connected in the transmission network may be of particular interest for prevention
- The findings from this type of molecular analysis can be triangulated with other data to identify groups for intensive prevention efforts

Objective

To describe persons with many potential transmission connections

METHODS

Inclusion Criteria

We analyzed HIV-1 *pol* sequences collected through the Molecular HIV Surveillance component of the U.S. National HIV Surveillance System (NHSS) during 2001–2012 (4–18 participating areas, depending on year)

- Aged ≥13y
- One sequence per person (longest and highest quality)
- Sequence length ≥ 500 nucleotides

We excluded potential contaminants (sequences ≤2.0% genetic distance from HXB2)

Analysis

Sequence and Network Analysis

- Aligned sequences to a reference sequence (HXB2)
- Performed pairwise Tamura-Nei 93 genetic distance calculations among all sequences
- Distance ≤1.5% considered evidence of possible linkage
- Constructed an HIV transmission network which included all sequences that had a possible linkage to at least one other sequence
- Transmission network constructed on a MacPro computer using a suite of software developed by the Viral Evolution Group at University of California, San Diego

Analysis of Persons with Many Links

- For persons whose sequence linked to ≥4 other sequences (i.e., the top quartile of those with any links), analyzed:
  - Demographics (sex, age, race/ethnicity)
  - Transmission category, hierarchical (missing data were imputed)
    - Male-male sex
    - Male-male sex and injection drug use
    - Injection drug use (stratified by sex)
    - Heterosexual contact (stratified by sex)
- Created a logistic regression model to determine whether these associations persisted
  - Model included sex, age, race/ethnicity, and transmission category

RESULTS

Network characteristics

- 12,910 (31%) sequences had ≥1 link
  - Formed 3,584 distinct clusters
- Cluster size
  - Range: 2–85 sequences
  - Interquartile range: 2–9 sequences

Figure 1. Number of potential transmission links

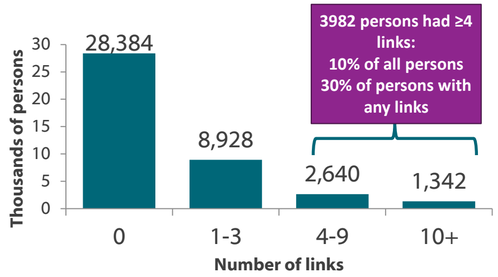


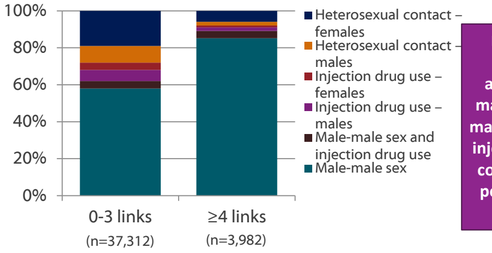
Table 1. Characteristics of persons with HIV-1 sequences

	Total		0-3 potential links		≥4 potential links		Model P-value**
	n	Col %	n	Row %	n	Row %	
Total	41294	100	37312	90	3982	10	
Sex							0.7
Male	32,276	78	28574	89	3702	11	
Female	9018	22	8738	97	280	3	
Race/ethnicity							<0.0001
Asian/Native Hawaiian or Other Pacific Islander	778	2	705	91	73	9	
Black/African American	19493	47	17878	92	1615	8	
Hispanic/Latino	9247	22	8413	91	834	9	
White	10731	26	9367	87	1364	13	
Other*	1045	3	949	91	96	9	
Age group							<0.0001
13-19 years	2282	6	1796	79	486	21	
20-29 years	13951	34	11916	85	2035	15	
30-39 years	11507	28	10611	92	896	8	
40-49 years	8733	21	8318	95	415	5	
50-59 years	3749	9	3619	97	130	3	
≥60 years	1072	3	1052	98	20	2	
Transmission category							<0.0001
Male-male sex	25141	61	21733	86	3408	14	
Male-male sex and injection drug use	1621	4	1478	91	143	9	
Injection drug use – males	2220	5	2158	97	61	3	
Injection drug use – females	1692	4	1639	97	53	3	
Heterosexual contact – males	3259	8	3170	97	89	3	
Heterosexual contact – females	7306	18	7079	97	227	3	

*Includes American Indian/Alaska Native and multiple races
*From multivariable model including all listed variables.

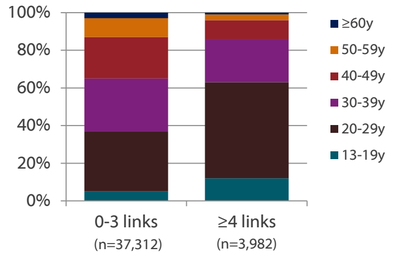
A higher percentage of young persons, persons with infection attributable to male-male sex, and whites had ≥4 links

Figure 2. Number of potential transmission links, by transmission category



Persons with infection attributable to male-male sex or male-male sex and injection drug use comprise 90% of persons with ≥4 links

Figure 3. Number of potential transmission links, by age



Persons aged 13-29 comprised 63% of persons with ≥4 links

LIMITATIONS

- Possible selection/sampling bias due to limited number of participating areas and differences in completeness of reporting
- Sequence results are from bulk sequencing
  - May miss some minority strains, and thus potential connections
- Partners represent potential partners
  - Cannot definitively draw a direct epidemiologic link between any two persons or establish direction of transmission
  - Can still gain insight on transmission dynamics from numerous potentially indirect links

DISCUSSION

- Groups overrepresented among persons with many potential links
  - Persons with infection attributable to male-male sex
  - Young persons
  - Whites
- Suggests that these groups are disproportionately involved in networks associated with HIV transmission
- This finding corroborates other analyses demonstrating high HIV incidence among men who have sex with men and young persons

RECOMMENDATIONS

- Efforts to interrupt HIV transmission and reduce incidence must reach highly connected groups
- Implementation of intensive and other effective interventions should prioritize men who have sex with men and young persons
- Additional work should explore potential geographic and temporal differences in these findings

ACKNOWLEDGEMENTS

- Local and state health department staff participating in Variant, Atypical, and Resistant HIV Surveillance (VARHS) or Molecular HIV Surveillance (MHS)
- Other present and past members of the CDC Incidence and Viral Resistance Team, including Magan Pearson, Richard Kline, Buzz Prejean, Rebecca Ziebell, and Danka Pieniazek

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