Growth and Geographic Spread of HIV Transmission Clusters, United States, 2007-2012

Abstract 241

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BACKGROUND

- Transmission network analysis can be used to identify clusters of persons with genetically related viruses
- Clusters of HIV infection that continue to grow likely represent ongoing transmission and are potential points for intervention
- Predicting which clusters are likely to grow could guide the appropriate allocation of limited prevention resources toward ensuring viral suppression and stemming transmission

Objective

To describe temporal growth and geographic spread of clusters

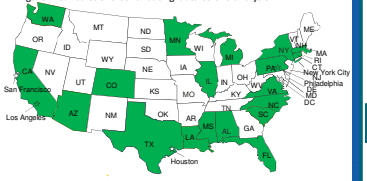
METHODS

Inclusion Criteria

We analyzed HIV-1 *pol* sequences collected in 19 states through the U.S. National HIV Surveillance System and reported during 2001–2013

- Earliest sequence selected when more than one sequence available
- Sequence < 500 nucleotides in length excluded
- Potential contaminants (sequences closely related to HXB2) excluded

Figure 1. Jurisdictions contributing data to this analysis



Sequence and Network Analysis

- Aligned sequences to a reference sequence (HXB2)
- Performed pairwise Tamura-Nei 93 genetic distance calculations for all pairs of sequences
- Constructed an HIV transmission network which included all sequences with distance ≤1.5% from at least one other sequence
- Network constructed on a MacPro computer using software developed by the Viral Evolution Group at University of California, San Diego

Analysis of Cluster Growth and Characteristics

- For clusters of ≥5 persons in 2007, characterized growth through 2012
  - Used multivariable logistic regression to examine potential predictors of various levels of growth, using characteristics of cluster in 2007
- For clusters of ≥30 persons (large clusters) in 2012:
  - Fit sigmoidal curves to estimate growth remaining through 2020
  - Created dot plot of each cluster, plotting transmission category and race/ethnicity of each cluster member by year of diagnosis
- Described geographic spread of 8 large clusters
  - For 3 geographically diverse clusters, conducted Bayesian relaxed molecular clock analysis using BEAST v1.8.1 and displayed phylogenetic trees

RESULTS

Table 1. Characteristics of HIV transmission clusters

	2007	2012
No. of persons with sequences	36,947	70,669
No. of persons who clustered	4,667	21,117
Percentage of persons who clustered	13%	30%
No. of clusters of ≥2 persons	1,520	5,336
Size of largest cluster	65	155
No. of clusters of ≥5 persons in 2007	178	
No. of persons in these 178 clusters	1,492	3,500

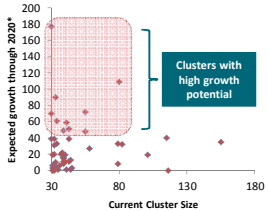
Table 2. Associations of selected factors with various thresholds of cluster growth among 178 clusters

	≥100%	≥200%	≥400%
No. of clusters above threshold	n=77	n=30	n=15
Size in 2007	NS	NS	NS
Growth from 2006 to 2007	P=0.007	NS	P=0.03
Racial/ethnic composition	NS	NS	NS
U.S. census region	NS	NS	NS
Percentage of MSM	P=0.03	NS	NS
Percentage aged 13–19y	NS	NS	NS

MSM: men who have sex with men, including MSM who inject drugs; NS: not significant
As determined by 3 backward elimination logistic regression models, each predicting a given level of growth (≥100%, 200%, or 400%) and containing all listed variables

Higher growth in the previous year and higher percentage of MSM predicted future cluster growth

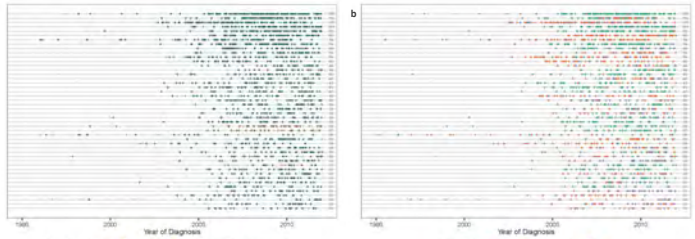
Figure 2. Expected growth remaining through 2020, among clusters with ≥30 persons in 2012



*Calculated by subtracting current size from estimated size in 2020, as determined by fitting a sigmoidal curve to cluster growth.

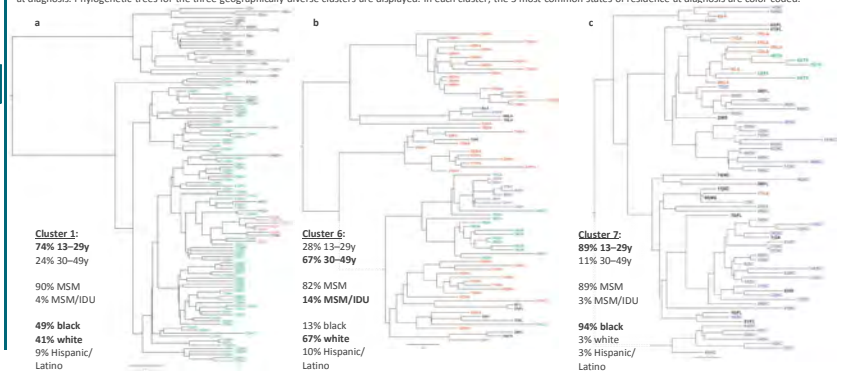
Predicting which clusters have substantial growth remaining can identify targets for intervention

Figures 3a and 3b. Transmission category and race/ethnicity of persons in large clusters. Each cluster with ≥30 persons in 2012 is represented on a horizontal line, with cluster size noted at right. Each dot represents one person in that cluster, plotted by year of HIV diagnosis.



Composition of clusters varies by transmission category and particularly race/ethnicity.

Figure 4a, 4b, and 4c. Geographic spread of large clusters. Five of the 8 largest clusters (size=79–155 in 2012) consisted nearly exclusively (>90%) of persons living in the same state at diagnosis. Phylogenetic trees for the three geographically diverse clusters are displayed. In each cluster, the 3 most common states of residence at diagnosis are color-coded.



Although most large clusters are geographically limited, these three clusters show important geographic diversity, with spread into new locations

LIMITATIONS

- Possible bias due to limited number of participating areas and differences in completeness of reporting by geography and time
- Bulk sequencing may miss minority strains and thus connections
- Partners represent potential partners
  - Cannot definitively draw a direct transmission link between any two persons or establish direction of transmission
  - Can still gain insight into transmission dynamics from numerous potentially indirect links
- Geographic measure used was state of residence at diagnosis
  - May not reflect geographic moves or travel before or after diagnosis
- The sigmoidal growth model is limited to a unimodal growth rate model and may not capture other types of growth

DISCUSSION

- We found substantial growth of clusters over a 5-year period
  - Best predictors of growth were previous year's growth and the percentage of MSM
- Describing demographic and risk characteristics of clusters may help to tailor the approach to prevention
  - Racial/ethnic composition did not drive cluster growth, but may impact selection of prevention modalities
- Fitting sigmoidal curves to large clusters identifies those (typically not the largest ones) with substantial growth remaining
  - This growth may represent persons who are not yet diagnosed or additional transmissions that have not yet occurred
  - Local areas could prioritize members of these clusters with partner services and interventions aimed at improving ART use and viral suppression
- Geographic diversity in some clusters indicates that collaboration between jurisdictions may be important to stemming the spread of HIV
  - Surveillance at the national level is useful for identifying multi-state clusters
- These data suggest that monitoring the growth and composition of clusters can help to identify prevention priorities

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See also: abstract 120 (Wertheim) on drug-resistant clusters

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