HIV Transmission Clusters Offer Clues to HIV Risk in Young Black MSM

Mark Mascolini

Phylogenetic analysis of young black men who have sex with men (MSM) in Chicago confirmed high connectivity to HIV transmission clusters and permitted scrutiny of factors that favored high cluster connectivity and thus high risk of acquiring HIV [1]. The three factors predicting high connectivity were self-reported bisexual (versus gay) identity, depression, and any marijuana use.

Researchers have long used phylogenetic analysis to delineate sexual networks of people with HIV infection. University of Chicago researchers and colleagues explored using phylogenetic analysis to identify young black MSM with high connectivity to HIV transmission clusters and to pinpoint factors favoring high or low connectivity. Such an analysis, the researchers proposed, can help prioritize HIV prevention interventions for HIV-negative men and thus control HIV outbreaks.

As in other parts of the United States, young black MSM in Chicago run a greater risk of HIV infection than other high-risk groups and help drive continuing spread of the virus. Across the United States, the Chicago team noted, 2 of 3 new HIV diagnoses involve MSM, 1 of 2 involves black MSM, 1 of 4 involves Hispanic MSM, and 1 of 11 involves white MSM. Research on young black MSM identifies three characteristics of their involvement in transmission clusters: (1) They are more likely to be members of HIV transmission clusters [2]. (2) They are more likely to be members of larger transmission clusters. (3) They tend to be members of segregated networks that have higher HIV rates.

The Chicago team planned this analysis (1) to describe local HIV phylogenetic transmission networks and (2) to assess factors associated with HIV phylogenetic transmission cluster size in young black MSM. The analysis focused on young black MSM in uConnect, an ongoing longitudinal study with a survey-based design and blood spot collection. Men are eligible for the study if they identify themselves as African American or black, are born male, are 16 to 29 years old, report oral or anal sex in the past 24 months, and live in Chicago.

The researchers analyzed HIV-1 pol sequences from viral samples of participants and identified transmission between men if their pol sequences were 1.5% or less genetically distant from each other. The research team defined clusters as 1 or more ties to another sequence. They used logistic regression analysis to assess membership in a phylogenetic cluster and Poisson regression to assess numbers of ties to other individuals.

The study group averaged 23.7 years in age (range 16 to 29) and averaged 4.4 sex partners (range 0 to 35). About three quarters of men (76%) identified themselves as homosexual, 55% had condomless sex in the past 12 months, 82% used marijuana, and 28% used any other recreational drug. While 58% of men had health insurance and 58% had some college education, 52% were unemployed, and 53% were ever incarcerated.
Wave 1 of uConnect recruitment included 216 men (35% of the sample) diagnosed with HIV infection. The phylogenetic analysis focused on 54 pol sequences, 53 of them from men with viral suppression. Of the 54 HIV sequences, 42 (78%) had a genetic tie to 1 or more persons. Genetic ties per sequence averaged 4.4 and ranged from 0 to 20. The analysis identified 7 HIV clusters.

Poisson regression analysis singled out four factors independently associated with a high degree of connectivity to HIV clusters among young black MSM, at the following relative risks (RR) and 99.99% confidence intervals (CI):

-- Bisexual versus gay sexual identity: HR 5.55 (99.99% CI 1.56 to 19.81)
-- Depressive symptoms versus none: HR 2.51 (99.99% CI 1.18 to 5.34)
-- Light recreational marijuana use versus never: HR 3.27 (99.99% CI 1.01 to 10.62)
-- Heavy recreational marijuana use versus never: HR 3.10 (99.99% CI 1.05 to 19.23)

Three factors were independently associated with a low degree of connectivity in the clusters:

-- Current insurance: HR 0.22 (99.99% CI 0.11 to 0.44)
-- In a relationship versus single: HR 0.38 (99.99% CI 0.18 to 0.84)
-- Use of one or more recreational drugs besides marijuana versus never: HR 0.21 (99.99% CI 0.05 to 0.91)

The investigators proposed that HIV prevention efforts tailored to these risk factors may help reduce HIV transmission among young black MSM. In particular, they called for greater access to mental health services and youth-focused drug use prevention programs.

References
Discussion

• **Associated with larger transmission clusters:**
  • Self-reported sexual identity as bisexual
  • Depressive symptoms
  • Any marijuana use

• **Associated with smaller transmission clusters:**
  • Having health insurance
  • Having a main partner

• **Intensifying HIV prevention efforts to persons reporting these factors may reduce transmission among YBMSM**
HIV Phylogenetics Inform Prevention Among Young Black Men Who Have Sex With Men in Chicago

Ethan Morgan, Epidemiology PhD Candidate
Department of Public Health Sciences, University of Chicago
The Chicago Center for HIV Elimination
Background

- HIV infection rates in the United States vary widely by race and ethnicity
  - Overall, 15.0 cases/100,000 persons\(^1\)
  - 55.9 cases/100,000 persons among blacks\(^1\)

- HIV infection among MSM
  - 2 in 3 of new HIV diagnoses\(^2\)
  - 1 in 2 for black MSM, 1 in 4 for Hispanic MSM, and 1 in 11 for white MSM\(^2\)

\(^1\)Centers for Disease Control and Prevention, 2014
\(^2\)Centers for Disease Control and Prevention, 2016

Background

- Inferring HIV phylogenetic networks increasingly utilized to understand HIV transmission
  - Highlights differences in subtypes\(^1\), over time\(^2\), and by presence of drug resistance\(^3\)
  - Used to assess differences across geographic regions\(^4\)
  - Identify characteristics of clustered individuals\(^5\)
  - Can be used to prioritize interventions and control outbreaks\(^6\)

\(^1\)Chalmet et al., BMC Infect Dis, 2010
\(^2\)Hué et al., Proc Natl Acad Sci USA, 2015
\(^3\)Yerly et al, AIDS, 2009
Background

• Young black MSM and transmission clusters
  • Young black MSM are more likely to be members of transmission clusters\(^1\)
  • Young black MSM are likely to be in larger transmission clusters\(^2\)
  • Black MSM tend to be insular (more assortative mixing)\(^3\), have networks that are segregated, and have higher rates of HIV\(^4\)
  • More detailed research is required to disrupt YBMSM transmission clusters

1Lubelchek et al, JAIDS, 2015
2Morgan et al, Under Review, 2016
3Oster et al, AIDS, 2009
4Centers for Disease Control and Prevention, 2016

Aim

1. **Describe** local, inferred HIV phylogenetic transmission networks

2. **Assess** factors which are associated with HIV phylogenetic transmission cluster size among YBMSM
Dataset

- **uConnect**
  - Longitudinal study on young Black MSM
    - 2013-2016, 3 waves, 9 months between waves
    - Largest single-site study of black MSM
    - Respondent driven sampling
    - Survey-based design and blood spot collection
  - Eligibility criteria:
    1. Identify as African American or black
    2. Born male
    3. Between the ages of 16-29
    4. Reported oral/anal sex within past 24 months
    5. Reside in Chicago

1Morgan et al., AIDS Behav, 2015
Figure 1. Map of Chicago by region. uConnect recruited from South side of Chicago (N = 618).
Methods

• Genetic analyses
  - HIV-1 genetic sequences were obtained from the pol region
  - Aligned to HXB2 reference sequence using MUSCLE multiple sequence alignment¹
  - Pairwise genetic distance was determined using Tamura-Nei 93 model with 50% partial deletion²
  - Transmission events identified between persons whose pol sequences were ≤1.5% genetically distant (≤0.015 nucleotide substitutions per site)³,⁴
  - Clusters defined as ≥1 tie to another sequence³

¹Edgar, Nucleic Acids Res, 2004
²Tamura et al., Mol Biol Evol, 1993
³Oster et al, AIDS, 2009
⁴Lubelchek et al, J AIDS, 2015

Methods

• Statistical analyses
  - Chi-square and Student’s T-test
  - Unadjusted and adjusted weighted zero-inflated Poisson regression
    • Outcome (two-stage regression):
      1. Membership in a phylogenetic cluster
         • Logistic regression
      2. Number of ties to other individuals
         • Poisson regression
Results

• **Demographic data**
  - Age, mean: 23.7 years (range: 16-29)
  - Number of sexual partners, mean: 4.4 partners (range: 0-35)
  - *Majority of sample:*
    - Some college education, 57.9%
    - Unemployed, 51.9%
    - Have health insurance, 58.3%
    - Ever incarcerated, 53.2%
    - Identify as homosexual, 76.4%
    - Any condomless sex in the past 12 months, 55.1%
    - Drug use: marijuana, 81.9%; any other drug use, 28.2%

• uConnect (Wave 1) contained 216 HIV-diagnosed persons (34.6% of sample)

• We analyzed 54 HIV *pol* sequences (25.0% of HIV+ persons)
  - 53 (24.5%) virally suppressed
  - 37 (17.1%) declined laboratory collection
  - 72 (33.3%) below detectable limit

• Of 54 HIV sequences, 42 had a tie to genomes from ≥1 other person (77.8% of analyzed sequences)

• **Ties:**
  - Mean, total: 4.4 (range 0-20)
  - Mean, clustered only: 5.6 (range: 1-20)
    - Number of clusters: 7
Figure 1. Inferred HIV transmission network among YBMSM (n = 42, 77.8% of sequences) in Chicago. Nodes represent an individual. Edge connection between nodes represents an inferred potential transmission between individuals as assessed via phylogenetic analyses of the pol region with a maximum genetic distance of 0.015 nucleotide substitutions per site (n = 54).
Table 3. Adjusted zero-inflated Poisson regression model of selected characteristics with both membership in a cluster\(^1\) and degree of connectivity within a cluster\(^1\) among HIV diagnosed YBMSM, uConnect (N = 216 persons)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Degree of Connectivity(^2)</th>
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<tbody>
<tr>
<td><strong>Demographics</strong></td>
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<tr>
<td>Age</td>
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<tr>
<td>16-19</td>
<td>Ref</td>
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<td>20-24</td>
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<tr>
<td>25-29</td>
<td>0.69</td>
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<td>Ref</td>
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<tr>
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<td>5.55**</td>
</tr>
<tr>
<td>Other</td>
<td>3.10</td>
</tr>
</tbody>
</table>

**Mental Health\(^4\)**

Depressive symptoms
- Not depressed: Ref
- Depressed: 2.51\(^{**}\) 1.18-5.34

**Drug and alcohol use\(^5\)**

Recreational marijuana use
- Never: Ref
- Light use: 3.27\(^{*}\) 1.01-10.62
- Heavy use: 3.10\(^{*}\) 1.05-19.23

**Other drug use\(^6\)**

- Never: Ref
- 1 or more drugs: 0.21\(^{*}\) 0.05-0.91

**Binge drinking\(^7\)**

- Never: Ref
- < 5 times: 0.38 0.12-1.20
- 5 or more times: 1.80 0.92-3.54

**Network measures**

**Number of sex partners**: 1.08 0.99-1.18

Abbreviations: YBMSM = young black men who have sex with men, IRR = incidence rate ratio, CI = confidence interval

\(^1\) Cluster was defined as having ≥2 connected persons whose pol sequences were <1.5% genetically distant

\(^2\) Using Poisson regression; logistic models are not shown

\(^3\) Self-reported via the Brief Symptom Inventory 18 questions survey

\(^4\) In the past 12 months

\(^5\) Includes the use of ecstasy, molly/E, poppers, crack/cocaine, heroin, psychedelics, methamphetamines, prescription drugs

\(^6\) Defined as consuming ≥1 or more drinks in one sitting in the past 30 days

\(^{*}\) p <0.0045; \(^{**}\) p <0.001
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