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# Reconciling Named Partner and Genetic Partner HIV-1 Transmission Networks in New York City

Joel O. Wertheim[1], Sergei L. Kosakovsky Pond[1], Konrad Scheffler[1], Davey M. Smith[1,2], Sanjay R. Mehta[1], Sharmila Shah[3], Lisa A. Forgione[3], and Lucia V. Torian[3]

[1] University of California, San Diego, [2] Veterans Affairs San Diego Healthcare System, [3] NYC Department of Health and Mental Hygiene

Contact Information:
220 Dickinson St.
San Diego, CA 92103
jwertheim@ucsd.edu
(619) 543-5069

## Background

- HIV transmission largely occurs along links in the social network connecting risk-sharing partners: injection drug use or sexual contacts
- The HIV transmission network is a subset of all of these risk exposure interactions
- Critical to the development of an HIV intervention strategy is identification of true transmission partners
- Absent a gold standard for HIV surveillance, named partners infected with genetically highly similar viruses may be closest we get to identifying true transmission partners

## NYC Field Services Unit

- New York City Department of Health and Mental Hygiene (DOHMH) interviews persons with newly diagnosed HIV infection (index cases) and elicits named partners, who are notified of exposure and offered HIV testing
- When resistance testing is ordered by a physician with whom the case or positive partner has initiated care, the viral nucleotide sequence is reported to surveillance
- 756 index cases named 586 unique partners that were HIV positive and had a *pol* sequences reported to DOHMH between 2006 and 2012

**Use partner naming and phylogenetics to guide choice of genetic distance cutoff for inferring genetic transmission network**

## Phylogenetic Analysis

- Align all 1342 *pol* sequences to HXB2 reference
- Construct maximum likelihood phylogenetic tree in RAxML v.8
- Determine if index case and named partner are "phylo-linked": closest relatives in the phylogeny ignoring other partners named by index case or named partner

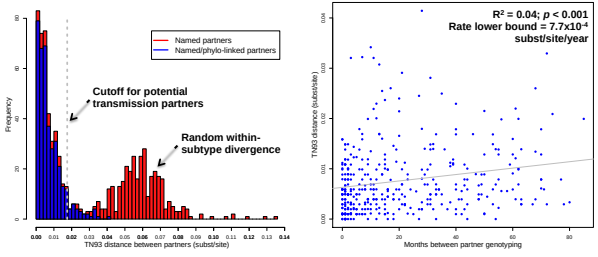



**Figure 1.** Genetic distance (TN93) separating index cases and named partners (A) Histogram depicting TN93 genetic distance between named partners. Index cases whose named partners are phylo-linked. Dashed gray line indicates 0.0175 expected substitutions/site TN93 distance cutoff. (B) Genetic distance separating phylo-linked named partners and time between viral genotyping. Slope is consistent with HIV-1 substitution rate.

**Use genetic network to determine if index case and named partner are genetically linked**

## Network Construction

Named-Partner Network: Connect all index cases to their named partners to form clusters

Genetic Network: Connect all nodes separated by ≤1.75% substitutions/site to form clusters

A. Genetic data on named-partner network

B. Naming data on genetic network

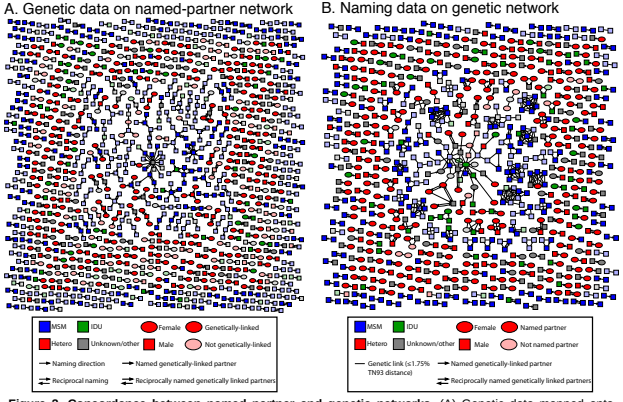



**Figure 2. Concordance between named partner and genetic networks.** (A) Genetic data mapped onto named partner network. Edges indicate partner naming. (B) Partner naming data mapped onto genetic network. Edges indicate genetic linkage (≤0.0175 expected substitutions/site).

**Genetic data provide evidence for transmission along 50% (388/771) of edges in named partner network; genetic data are incompatible with transmission along remaining edges**

**Partner naming provides evidence for transmission along 53% (388/735) of edges in genetic network**

**Table 1. Logistic regression analysis of index case being genetically-linked to at least one of their named partners.**

| Demographic | Category | Index cases | Named ≥ 1 genetically linked partner, n (%) | Did not name a genetically linked partner, n (%) | Odds Ratio[1] | 95% confidence interval | *p*-value |
|---|---|---|---|---|---|---|---|
| Total | - | 756 | 449 (59%) | 307 (41%) | - | - | - |
| Risk | Hetero (F) | 215 | 166 (77%) | 49 (23%) | 1 | - | - |
| | Hetero (M) | 92 | 71 (77%) | 21 (23%) | 1.07 | 0.59–1.97 | 0.819 |
| | MSM | 339 | 143 (42%) | 196 (58%) | 0.21 | 0.14–0.32 | <0.001 |
| | IDU (F) | 15 | 8 (53%) | 7 (47%) | 0.35 | 0.12–1.05 | 0.061 |
| | IDU (M) | 35 | 15 (43%) | 20 (23%) | 0.20 | 0.09–0.43 | <0.001 |
| | Other/Unknown | 60 | 46 (77%) | 14 (23%) | 1.13 | 0.56–2.26 | 0.731 |

Hetero, heterosexual; MSM, men who have sex with men; IDU, injecting drug user
[1]Model adjusted odds ratio including country of race, birth, subtype, stage at diagnosis, AIDS status in 2013, and age at diagnosis

**MSM and male IDUs are less likely to be genetically linked to at least one named partner than heterosexual females**

**Table 2. Index case genetically linked (TN93 distance ≤1.75%) to reciprocally named partners (n=189 partner pairs).**

| Demographic | Category | Index cases | Named ≥ 1 genetically linked partner, n (%) | Did not name a genetically linked partner, n (%) |
|---|---|---|---|---|
| Total | - | 189 | 149 (79%) | 40 (21%) |
| Risk | Hetero (F) | 51 | 46 (90%) | 5 (10%) |
| | Hetero (M) | 28 | 24 (86%) | 4 (14%) |
| | MSM | 78 | 50 (64%) | 28 (36%) |
| | IDU (F) | 6 | 5 (83%) | 1 (17%) |
| | IDU (M) | 4 | 3 (75%) | 1 (25%) |
| | Other/Unknown | 22 | 21 (95%) | 1 (5%) |

Hetero, heterosexual; MSM, men who have sex with men; IDU, injecting drug user

**Reciprocally named partners are more likely to be genetically linked for all risk factors: model adjusted odds ratio = 3.72 (95% CI: 2.43–5.72).**

## Comparing Named Partner and Genetic Networks

- At least half the connections in named-partner network did not lead to transmission
- Genetic sequences help filter out many spurious connections implied by partner naming
- Lack of naming information does not contradict the genetic data; it merely suggests an absence of epidemiological evidence supporting transmission
- More than half of genetic links supported by epidemiological data, and much of remaining half of the genetic links may represent transmission events
- Genetic data are more informative for inferring transmission partners

## Conclusions

- **Genetic data analysis can augment partner tracing by identifying previously unknown parts of the transmission network (i.e. unnamed partners)**
- **Half of named partners are likely not transmission partners**
- **MSM and IDU are less likely than heterosexuals to be genetically linked to a named partner**
- **Index cases who did not identify a genetically linked partner represent candidates for further interview by DOHMH**

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