

# UC San Diego

## UC San Diego Previously Published Works

### Title

Genetic Network Analysis to Assess the Risk of Human Immunodeficiency Virus Transmission Among Men Who Have Sex With Men Seeking Partners on the Internet

### Permalink

<https://escholarship.org/uc/item/9zz701h4>

### Journal

Clinical Infectious Diseases, 70(5)

### ISSN

1058-4838

### Authors

Martin, Thomas CS  
Chaillon, Antoine  
Graves, Susannah K  
[et al.](#)

### Publication Date

2020-02-14

### DOI

10.1093/cid/ciz278

Peer reviewed

# Genetic Network Analysis to Assess the Risk of Human Immunodeficiency Virus Transmission Among Men Who Have Sex With Men Seeking Partners on the Internet

Thomas C. S. Martin,<sup>1</sup> Antoine Chaillon,<sup>1</sup> Susannah K. Graves,<sup>1</sup> Timothy Lin,<sup>1</sup> Sara Gianella,<sup>1</sup> Davey M. Smith,<sup>1,2</sup> Susan J. Little,<sup>1,a</sup> and Martin Hoenig<sup>1,a</sup>

<sup>1</sup>Division of Infectious Diseases and Global Public Health, University of California, San Diego, and <sup>2</sup>San Diego Veterans Affairs Health System, California

**Background.** Online partner seeking (OPS) among men who have sex with men (MSM) is associated with increased risk behavior including frequency of unprotected anal intercourse, number of partners, and incidence of sexually transmitted infections (STIs). However, the impact on transmission of human immunodeficiency virus (HIV) is uncertain.

**Methods.** MSM diagnosed with acute and early HIV infection were recruited from the Primary Infection Resource Consortium. HIV transmission events in the year following infection were inferred using estimated date of infection combined with genetic network analysis with linked sequences defined as  $\leq 0.015$  sequences/site difference in the HIV type 1 (HIV-1) *pol* coding region. Participants completed a detailed baseline questionnaire including reported methods of meeting sexual partners, including OPS, in the prior 3 months, and regression was performed with inferred transmission as the outcome.

**Results.** From 147 MSM who completed the questionnaire, there were an associated 20 inferred HIV transmissions. No association with OPS was found (odds ratio, 0.64 [95% confidence interval, .24–1.69];  $P = .37$ ), though individuals who reported OPS were more likely to have reported a greater number of partners ( $P = .003$ ) and prior STIs ( $P = .002$ ). Geospatial analysis did not indicate that OPS was associated with increased geographical reach of the user ( $P = .68$ ).

**Conclusions.** Individuals reporting OPS did not have increased odds of inferred HIV-1 transmission in the year following infection using genetic linkage analysis despite apparently increased risk behavior. OPS also did not increase the geographic distance between genetically clustered HIV infections, suggesting that individuals mainly use the internet to meet partners in their local region.

**Keywords.** HIV; transmission network; internet; online partner seeking; MSM.

More than 1 million people live with human immunodeficiency virus (HIV) in the United States and nearly 40 000 new infections occurred in 2017 [1]. Men who have sex with men (MSM) are disproportionately affected by HIV in the United States, accounting for nearly 70% of new cases [1]. Transmission of HIV among MSM has been associated with multiple factors, including high-risk sexual practices (unprotected anal intercourse [UAI], sex with partners of unknown HIV serostatus, rimming, and fisting); use of alcohol, methamphetamine, or poppers during sex; high rate of sexually transmitted infections (STIs); and multiplicity of sexual partners [2, 3]. Demographic factors also play a role in risk of transmission, with younger MSM and black MSM at greater risk of HIV acquisition [4].

Technology has changed the way MSM socialize and seek sex, with use of the internet to meet sexual partners increasing

over the past 2 decades [5–7]. Over this period, online partner seeking (OPS) has evolved from basic hookup websites to sophisticated geospatial social network apps [7]. Several studies have indicated that MSM who use OPS have a greater frequency of UAI, incidence of STIs, and more partners, although there is conflicting evidence regarding whether this translates into increased HIV acquisition [3, 8–15]. OPS may also facilitate serostatus disclosure, serosorting, negotiation regarding condom usage, discussion of sexual practices, and user risk assessment, therefore mitigating or even lowering overall risk [5, 8, 14–18]. One study using a combination of observational data combined with a prospective daily diary suggested that MSM were less likely to have UAI with partners met through the internet compared to when the same individual met partners using other means [15]. The impact of OPS on risk behavior may also change with shifts in how MSM use the internet. One study found that the proportion of bisexual men and MSM meeting their primary partner online increased in the period 2001–2014 [19]. Among those who met their primary partner in 2014, 80% did so online. Other factors involved in HIV transmission such as preexposure prophylaxis (PrEP) usage and their association with OPS remain underexplored. One study in

Received 13 December 2018; editorial decision 26 March 2019; accepted 1 April 2019; published online April 6, 2019.

<sup>a</sup>S. J. L. and M. H. contributed equally to this work.

Correspondence: T. C. S. Martin, Division of Infectious Diseases and Global Public Health, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093 (thm001@ucsd.edu).

Clinical Infectious Diseases® 2020;70(5):925–32

© The Author(s) 2019. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com.

DOI: 10.1093/cid/ciz278

Southern California found that 10% of geospatial network users had reported PrEP use [20].

HIV transmission networks can be inferred from sequencing of the HIV type 1 (HIV-1) *pol* coding region, which is performed routinely for resistance testing among persons newly diagnosed with HIV infection. Combining these data with estimated date of infection (EDI), genetic network analysis can be used to infer transmission events between individuals [21]. Prior studies looking at OPS as a risk for HIV acquisition or transmission are limited and have not shown consistent findings [9, 11]. The use of genetic network methods to infer potential HIV transmission events and correlate with risk behavior may be able to provide further insight. Such network-based linkage data can also be used to investigate the association of OPS with the geospatial characteristics of an identified genetic cluster. Using a transmission network constructed from an acute and early HIV infection cohort in San Diego, California, we evaluated the association of OPS with the risk for inferred transmission of HIV within the first year of infection among MSM.

## METHODS

### Selection and Description of Participants

This study, conducted between May 2009 and September 2017, was designed as a nested cohort study of the Primary Infection Resource Consortium (PIRC), an acute infection screening program from 1996 to the present in San Diego [22]. Individuals were recruited from several HIV testing sites including the Lesbian, Gay, Bisexual, Transgender Center and the Gay Men's Health Clinic; the San Diego County Health Department; the University of California, San Diego (UCSD) AntiViral Research Center; and substance abuse treatment centers. Social marketing included distribution of flyers at gay-oriented venues, printed advertisements in gay-oriented publications, and banner advertisements on websites used for gay dating and hookups [23]. HIV diagnosis details and baseline characteristics of the PIRC cohort have been described previously [21, 24]. For each participant, an EDI is calculated using a stepwise algorithm derived from HIV RNA, Western blot, and enzyme immunoassay results as described previously [24].

This analysis recruited MSM who entered the PIRC cohort with an EDI within 90 days before study entry (ie, acute or early HIV infection). Only participants who completed a computer-assisted self-interview (CASI) including the venue questionnaire (introduced in May 2009) were eligible for the study.

### Data Collection

Baseline demographics, STI history, recent risk behavior, and plasma HIV RNA levels (Amplicor, Roche) were collected from study participants as described previously [22]. MSM enrolled in the study completed a CASI, usually within 30 days of recruitment, including detailed information regarding venues used to meet new sex partners during the prior 3 months.

### Genetic Network–based Transmission Inference

An HIV network was inferred from sequencing of the HIV-1 *pol* coding region with presumed linkage in individuals with  $\leq 0.015$  substitutions per site [25]. The *pol* coding region was used as it provides convenient genetic information that is routinely collected in new HIV diagnoses. Sequence curation, alignment, and network inference were performed using either the HyPhy package or freely available software (<https://github.com/veg/HIV-1Clustering>, <https://github.com/veg/TN93>). Directionality of infection was inferred if the putative “recipient” node EDI was at least 30 days past the date at which the initial sequence partner sequence was isolated [21, 26]. The transmission network score (TNS), a validated methodology using network linkage position to predict future transmission events, was calculated for each participant at time of diagnosis and ranged from 0 to 1 [21].

### Geospatial Linkage

Geospatial dispersal of the clusters was determined by calculating the average spatial distances between reported residences at baseline (centroids of 5-digit zip code) of genetically linked individuals [25]. Correlations of average cluster distances with OPS were performed using the R packages *maptools* and *mapdata*.

### Statistical Analysis

Categorical variables were recorded as present (1) or absent (0). The number of male partners reported in the last 3 months was categorized as  $\geq 5$  or  $< 5$  [27]. Venues for meeting sex partners were grouped as internet and noninternet with subsequent analysis dividing the noninternet group into social meeting venues (venues where the individual cannot have sex) and cruising venues (venues where the individual can have sex) [10]. Participants were grouped depending on the presence of an inferred transmission event in the first year after infection. Univariate regression was performed with transmission as the dependent variable. Independent variables with  $P < .15$  were included in a stepwise manner into a multiple logistic regression. The associations of OPS with included demographic variables were assessed using  $\chi^2$  or Fisher exact tests for categorical variables and *t* test for continuous variables. All statistics were performed using Stata version 12.0 software.

### Ethical Considerations

The UCSD Human Research Protections Program approved the study protocol and consent, and the methods were carried out in accordance with the UCSD Institutional Review Board's approved guidelines and regulations. All study participants provided voluntary, written informed consent before study enrollment.

## RESULTS

Two hundred twenty-six MSM were diagnosed with acute or early HIV infection between May 2009 and September 2017

and were eligible for the study, from which 147 completed the venue questionnaire and were included. Reasons for not completing the questionnaire included (1) that the questionnaire was not offered during temporary interruptions in study funding (2013–2014) and (2) noncompletion of the CASI questionnaires (of which the venue questionnaire was part of) by study participants. Demographics and TNS of the population stratified by OPS are shown in [Table 1](#). Individuals using OPS were more likely to have an education to degree level, report any prior STI, and report  $\geq 5$  partners in the prior 3 months. Individuals identifying as Hispanic were less likely to meet partners using the internet. Reported methods for meeting sexual partners were notable for the high usage of 4 methods: online (68.7%), bar or club (33.3%), friend's residence (29.9%), and bath house sex clubs (15.0%). Other venues reported include gym (8.2%), private properties (8.2%), adult book/video store (7.5%), chat lines (5.4%), and community clubs/organizations/social functions (5.4%). A full list of venues can be found in [Supplementary Table 1](#). The proportion of men that reported meeting partners online increased during the study period ( $P = .04$ ).

Genetic network analysis indicated 87 of 147 participants to be part of a genetic cluster. Overall, there were 20 inferred HIV transmissions in the year following HIV infection. A graphical representation of the PIRC transmission network indicating OPS or no OPS is shown in [Figure 1](#). OPS was not associated with an increased probability of being part of a genetic cluster ( $P = .58$ ) or increased mean distance between clustered individuals ( $P = .68$ ). The average distance between residences of clustered individuals stratified by use of the internet to meet partners is shown in [Figure 2](#), and a graphical representation of

participant distribution and proportion that cluster is shown in [Figure 3](#).

Univariate logistic regression demonstrated that using the internet to meet sexual partners in the prior 3 months was not associated with inferred transmission of HIV in the next year by genetic network analysis (odds ratio [OR], 0.64 [95% confidence interval {CI}, .24–1.69];  $P = .37$ ). Multiple logistic regression was performed for variables with  $P < .15$ , finding a trend for TNS to predict onward transmission (OR, 4.38 [95% CI, .95–20.2];  $P = .06$ ). Results of the regression analysis are shown in [Table 2](#).

## DISCUSSION

In a large HIV genetic linkage analysis among acute and early HIV infections in Southern California, we did not find an association between OPS and inferred transmission of HIV in the year following infection. OPS was, however, associated with increased odds of having a greater number of sexual partners and prior history of STI, though not with reported UAI. OPS did not increase the odds of being part of a genetic linkage cluster and was not associated with increased mean distance between clustered individuals.

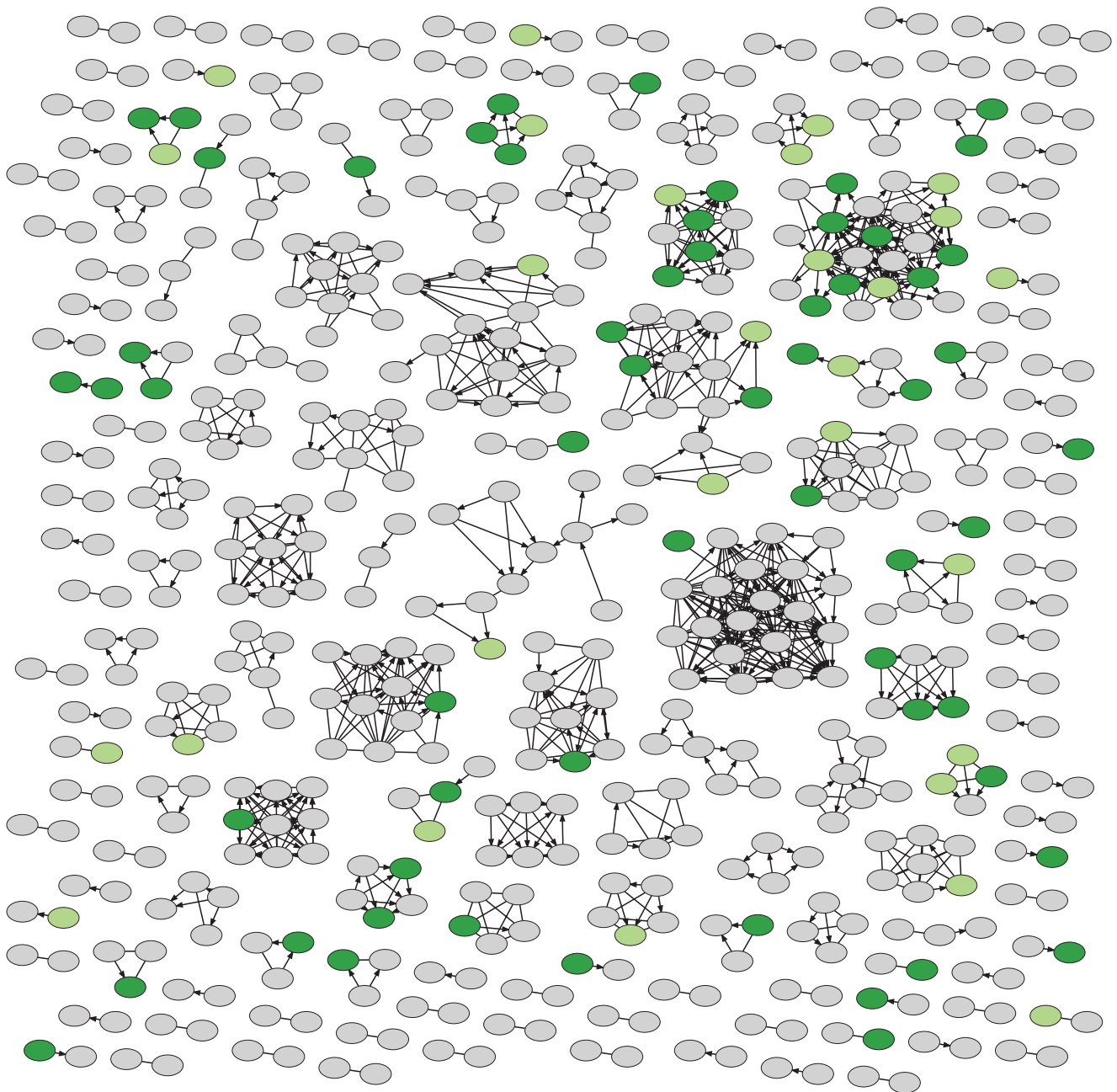
Consistent with prior studies, there was an increasing prevalence of OPS during the study period, with  $>80\%$  of participants meeting partners online in the period 2014–2016 [5]. Despite indications of increased risk behavior among individuals reporting OPS, we did not find increased odds of inferred HIV transmission. This may be related to the limited power in our study (20 inferred transmissions), although findings from prior studies have also not consistently demonstrated increased odds

**Table 1. Baseline Characteristics of the 147 Men Who Have Sex With Men With Acute or Early Human Immunodeficiency Virus Infection, Stratified by Reported Online Partner Seeking in the Prior 3 Months**

Baseline Characteristics	OPS (n = 101)	No OPS (n = 46)	P Value
Mean age, y	34.7	31.6	.94
Race/ethnicity			
White	80 (79.2)	30 (65.2)	.07
African American	7 (6.9)	5 (10.9)	.42
Asian	9 (8.9)	2 (4.3)	.50
Hispanic	25 (25.0)	19 (41.3)	<b>.05</b>
Other	7 (6.9)	6 (13.0)	.23
Household income $> \$2000/\text{mo}$	49 (51.0)	15 (35.7)	.10
Education to bachelor's degree or higher	44 (50)	9 (28.1)	<b>.03</b>
Any reported prior STI	79 (85.9)	26 (56.5)	<b>.002</b>
Any reported prior stimulant drug use	49 (48.5)	20 (43.5)	.57
Unprotected anal intercourse	83 (83.0)	36 (85.7)	.69
$\geq 5$ sexual partners	46 (45.5)	9 (19.6)	<b>.003</b>
Mean HIV viral load at recruitment, $\log_{10}$	4.94	4.91	.57
Clustered individual	59 (58.4)	28 (60.1)	.67
Mean TNS	0.25	0.27	.38

Data are presented as no. (%) unless otherwise indicated.  $P$  value  $\leq .05$  in bold.

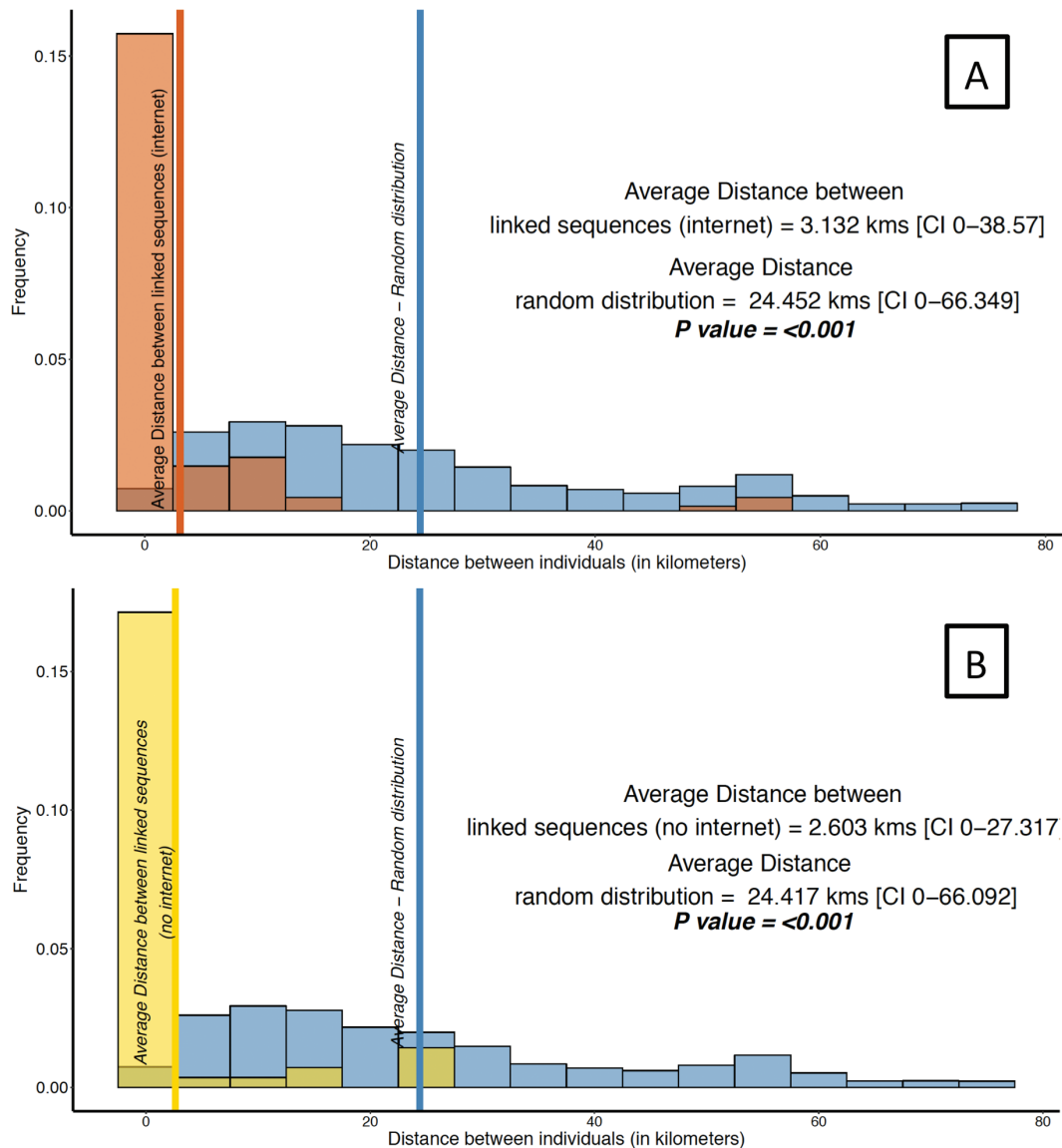
Abbreviations: HIV, human immunodeficiency virus; OPS, online partner seeking; STI, sexually transmitted infection; TNS, transmission network score.



**Figure 1.** Transmission network from Primary Infection Resource Consortium (PIRC), with linkages shown between nodes (individuals) with viral genotypes  $\leq 0.015$  substitutions/site [21]. Use of the internet to meet sexual partners is shown by dark green, and those who did not use the internet to meet sexual partners are shown in light green. Gray nodes represent individuals who are part of the PIRC who were recruited prior to the introduction of the venue questionnaire, had an estimated date of infection  $>90$  days prior, or who did not complete the venue questionnaire during the study period.

of OPS among MSM diagnosed with HIV [9, 11, 28–30]. Two previous case-control studies have focused on OPS associations with new HIV diagnoses with one study among black MSM finding an association with sexual networking apps (adjusted OR, 2.15), whereas the other study, among MSM in California, did not find increased odds of geosocial networking apps use in those newly diagnosed with HIV (adjusted OR, 0.72;  $P = .10$ ) [9, 11].

One explanation for the inconsistency of association may be related to per-sexual-act risk modification among individuals using OPS through increased serostatus disclosure and serosorting, increased discussion regarding condom usage, discussion of sexual practices, or perhaps increased PrEP use [8, 14, 31–33]. PrEP use prevalence among a sample of young MSM using geosocial network apps was previously estimated at 10% with greater uptake among wealthier participants ( $> \$10\,000$

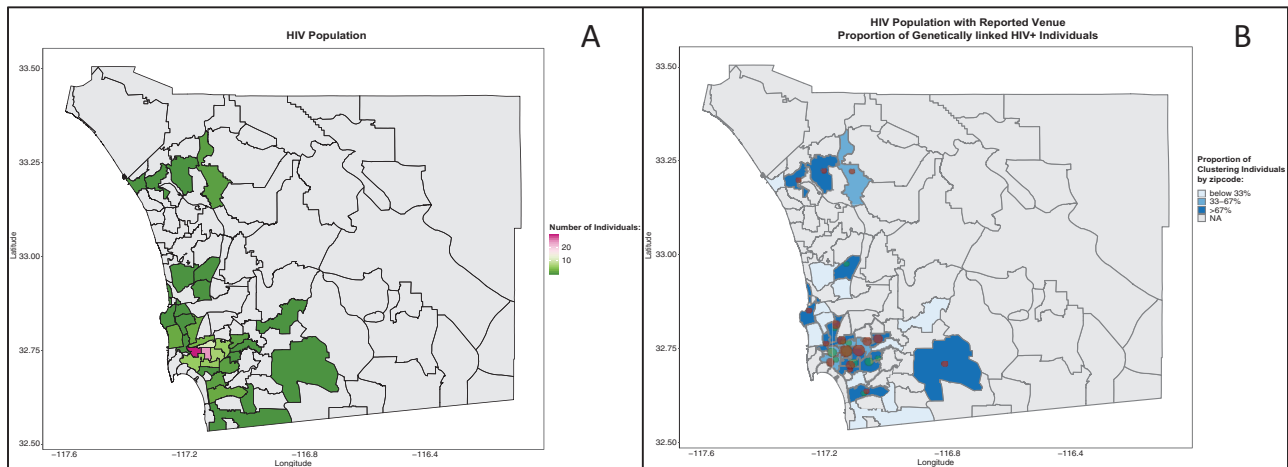


**Figure 2.** Mean geographical distance with 95% confidence intervals between individuals who have genetically related human immunodeficiency virus infection ( $\leq 0.015$  substitutions/site) and individuals using online partner seeking (OPS) (A) or those who reported no OPS (B). P values refer to the difference in mean geographical distance of clustered individuals (orange/yellow bars) compared to the average distance between random selection of sequences (blue bars). Abbreviation: CI, confidence interval.

annually) and those at greater sexual risk of HIV acquisition [20]. It is possible that participants using OPS could have increased PrEP usage, which could moderate any increased risk behavior. This would simultaneously explain higher rates of STI infection among those using OPS without increasing risk of HIV infection.

Another possible explanation for the lack of association between OPS and inferred HIV transmission in our study was the lack of differentiation between different modalities of OPS. More recently performed cross-sectional studies have delineated between hookup websites, social networking sites, and geosocial network apps [9, 11, 28]. From the studies that looked specifically at geosocial network apps, one found increased odds of

gonorrhea/chlamydia infection and the other increased odds of new HIV infection [9, 11]. In our study, due to the lack of specificity in our venue questionnaire, any increase in risk of HIV transmission among those using geosocial network apps may have been counteracted or diluted by those using other OPS modalities. Future studies looking at the impact of OPS will need to design questionnaires that clearly delineate between these different modalities to enable targeted risk-reduction programs. In addition, questionnaires should clarify the user intentions such as for seeking casual sex partners, regular sex partners, or friendship. They should also incorporate questions targeted to serostatus disclosure habits, discussion of sexual preferences including condom use, and PrEP usage. Prospective studies



**Figure 3.** A, Number of study participants by zip code in San Diego County, California. B, Proportion of participants (by zip code) who were found to be part of a genetic cluster. The number of individuals who were part of a genetic cluster is shown by a red dot (reported online partner seeking [OPS]) or green dot (no reported OPS). Size of dot is representative of the number of individuals.

could periodically update the modalities/websites that are in use among participants and correlate with public health HIV seroconversion data. This could avoid questionnaires becoming obsolete as trends in internet use change during study periods. Contemporaneous detailed data on internet modality use would also facilitate public health messages or sexual health screening messages. Larger multicenter studies with greater focus on these risk aspects are needed to definitively assess the risk of HIV acquisition/transmission.

Despite the potential for the internet to increase the geographic sexual network range of OPS users, we found that OPS did not increase the probability of being part of a geographically distant cluster. This in turn suggests that OPS was used mainly to meet partners in an individual's local area. Future work in this area could look at different internet modalities and providers for OPS to see if these locate to specific genetic clusters, geographic areas, or clusters with high TNS score. If such a finding were made, it might

**Table 2. Univariate Logistic Regression With Dependent Variable Outcome of Inferred Transmission of Human Immunodeficiency Virus by Network Linkage**

Variable	Univariate Logistic Regression, OR (95% CI)	PValue	Multiple Logistic Regression, OR (95% CI)	PValue
Age	0.96 (.91–1.01)	.14	0.99 (.93–1.04)	.62
Hispanic	1.2 (.47–3.47)	.63	...	
White	0.57 (.21–1.57)	.28	...	
African American	2.31 (.57–9.40)	.24	...	
Venues used to meet partners in prior 3 mo				
Internet	0.64 (.24–1.69)	.37	...	
Cruising venues	0.97 (.35–2.70)	.95	...	
Social venues	0.83 (.31–2.22)	.31	...	
Stimulant drug use in prior 3 mo	0.56 (.21–1.51)	.25	...	
≥5 sexual partners in prior 3 mo	0.37 (.12–1.18)	.09	0.49 (.14–1.70)	.26
Any history of STI	1.04 (.32–3.42)	.95	...	
UAI in prior 3 mo	1.04 (.28–3.89)	.96	...	
Degree-level education or higher	0.73 (.25–2.15)	.57	...	
Household income >\$2000/mo	0.44 (.16–1.23)	.12	0.47 (.15–1.43)	.18
Log <sub>10</sub> HIV viral load	0.98 (.67–1.42)	.91	...	
TNS	3.53 (.89–14.5)	.08	4.38 (.95–20.2)	.06

Multiple logistic regression performed on variables with  $P < .15$ .

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; STI, sexually transmitted infection; TNS, transmission network score; UAI, unprotected anal intercourse.

in turn be used for specific targeted interventions to reduce the ongoing spread of a specific genetic cluster.

Hispanic participants were less likely to report OPS in our study, consistent with prior studies performed in Southern California [11]. Potentially this could be related to lower educational attainment (OR of education to degree level, 0.37 [95% CI, .16–.84];  $P = .02$ ) or to cultural stigma. It is notable that while the rate of new diagnoses among white MSM is falling, among Hispanic and black MSM it continues to rise; simultaneously, the rate of PrEP uptake among Hispanics is reduced [1, 34].

The internet has great potential to improve public health access to MSM, deliver safe sex messages, and encourage PrEP uptake and testing. However, this could be further enhanced by social networks/hookup sites improving access to their platforms for public health bodies [35]. Given evidence that MSM meeting partners online are more likely to disclose serostatus and serosort, the potential to enhance this behavior could bring about significant benefits. For example, one study modeling the impact of serosorting among MSM indicated a near 50% reduction in HIV prevalence compared to if no serosorting occurred, while another indicated that post-HIV behavioral change reduced overall HIV prevalence by about 10% [36, 37].

Our study is the first to use genetic networks to evaluate associations between OPS and HIV transmission. We show the utility of the TNS for identifying individuals/clusters at higher risk of transmission through their genomic linkage at diagnosis, and strategies to target these clusters are needed. Limitations of our study include the small number of inferred transmission events that occurred during the study period (20 transmissions), which limits the power of the study. Given the elevated odds of prior STIs among OPS users, it remains possible that in a larger and more detailed study, risk factors for HIV acquisition or transmission related to OPS would be identified. We did not collect specific details about individuals' internet usage such as use of apps or social networking platforms, as the study was designed before their widespread use. This, unfortunately, limited our ability to draw conclusions regarding aspects of OPS that place individuals at greater risk for HIV transmission. Finally, our study was limited to one area in the United States (Southern California) and therefore may not be generalizable to other populations.

Internet use as a factor in sexual behavior is increasing, and our understanding of its role in the transmission of infectious diseases including HIV is important. Our study provides some insight to the role of the internet in HIV transmission, although further work is needed to look in greater depth into the impact of differing modalities and platforms on sexual risk and PrEP uptake among HIV-negative individuals using OPS and HIV acquisition. Involvement of social networks and geospatial applications in developing interventions and education for users will be needed to further reduce risk behavior. Given the proportion of MSM using online sites to

meet sexual partners, the impact of interventions online is potentially large.

## Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

## Notes

**Acknowledgments.** The authors thank Joel Wertheim for his contributions to an earlier version of this analysis.

**Financial support.** This work was supported in part by the National Institutes of Health (grant numbers 5T32AI007384-28, T32AI007384-24, AI036214, MH113477, AI106039, AI106039, and MH100974).

**Potential conflicts of interest.** M. H. has received grant funding from Gilead Sciences, Inc. S. J. L. has served as a member of a data monitoring committee for a GlaxoSmithKline-sponsored clinical trial, and has received research grants awarded to her institution and antiretroviral medications provided by Gilead Sciences, Inc. All other authors report no potential conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

## References

- Centers for Disease Control and Prevention (CDC). HIV surveillance report. Atlanta, GA: CDC, 2017:29.
- Scott HM, Vittinghoff E, Irvin R, et al. Age, race/ethnicity, and behavioral risk factors associated with per contact risk of HIV infection among men who have sex with men in the United States. *J Acquir Immune Defic Syndr* 2014; 65:115–21.
- Macdonald N, Elam G, Hickson F, et al. Factors associated with HIV seroconversion in gay men in England at the start of the 21st century. *Sex Transm Infect* 2008; 84:8–13.
- Hoeningl M, Chaillon A, Morris SR, Little SJ. HIV infection rates and risk behavior among young men undergoing community-based testing in San Diego. *Sci Rep* 2016; 6:25927.
- Paz-Bailey G, Hoots BE, Xia M, Finlayson T, Prejean J, Purcell DW; NHBS Study Group. Trends in internet use among men who have sex with men in the United States. *J Acquir Immune Defic Syndr* 2017; 75(Suppl 3):288–95.
- Bolding G, Davis M, Hart G, Sherr L, Elford J. Where young MSM meet their first sexual partner: the role of the internet. *AIDS Behav* 2007; 11:522–6.
- Grov C, Breslow AS, Newcomb ME, Rosenberger JG, Bauermeister JA. Gay and bisexual men's use of the internet: research from the 1990s through 2013. *J Sex Res* 2014; 51:390–409.
- Cruess DG, Burnham KE, Finitis DJ, et al. Online partner seeking and sexual risk among HIV+ gay and bisexual men: a dialectical perspective. *Arch Sex Behav* 2017; 46:1079–87.
- Eaton LA, Maksud JL, Gamarel KE, Siembida EJ, Driffin DD, Baldwin R. Online sex partner meeting venues as a risk factor for testing HIV positive among a community-based sample of black men who have sex with men. *Sex Transm Dis* 2016; 43:360–4.
- Gama A, Abecasis A, Pingarilho M, et al. Cruising venues as a context for HIV risky behavior among men who have sex with men. *Arch Sex Behav* 2017; 46:1061–8.
- Beymer MR, Weiss RE, Bolan RK, et al. Sex on demand: geosocial networking phone apps and risk of sexually transmitted infections among a cross-sectional sample of men who have sex with men in Los Angeles County. *Sex Transm Infect* 2014; 90:567–72.
- Kerr ZY, Pollack LM, Woods WJ, Blair J, Binson D. Use of multiple sex venues and prevalence of HIV risk behavior: identifying high-risk men who have sex with men. *Arch Sex Behav* 2015; 44:443–51.
- Yang Z, Zhang S, Dong Z, Jin M, Han J. Prevalence of unprotected anal intercourse in men who have sex with men recruited online versus offline: a meta-analysis. *BMC Public Health* 2014; 14:508.
- Lewnard JA, Berrang-Ford L. Internet-based partner selection and risk for unprotected anal intercourse in sexual encounters among men who have sex with men: a meta-analysis of observational studies. *Sex Transm Infect* 2014; 90:290–6.



15. Mustanski BS. Are sexual partners met online associated with HIV/STI risk behaviours? Retrospective and daily diary data in conflict. *AIDS Care* **2007**; 19:822–7.
16. Grov C. HIV risk and substance use in men who have sex with men surveyed in bathhouses, bars/clubs, and on Craigslist.org: venue of recruitment matters. *AIDS Behav* **2012**; 16:807–17.
17. Grov C, Rendina HJ, Ventuneac A, Parsons JT. Partners met via sex parties present significantly greater odds for condomless anal sex among MSM: an event-level analysis of venues where male partners are met. *J Acquir Immune Defic Syndr* **2014**; 67:564–8.
18. Bolding G, Davis M, Hart G, Sherr L, Eford J. Gay men who look for sex on the internet: is there more HIV/STI risk with online partners? *AIDS* **2005**; 19:961–8.
19. Prestage G, Bavinton B, Grierson J, et al. Online dating among Australian gay and bisexual men: romance or hooking up? *AIDS Behav* **2015**; 19:1905–13.
20. Holloway IW, Dougherty R, Gildner J, et al. Brief report: PrEP uptake, adherence, and discontinuation among California YMSM using geosocial networking applications. *J Acquir Immune Defic Syndr* **2017**; 74:15–20.
21. Little SJ, Kosakovsky Pond SL, Anderson CM, et al. Using HIV networks to inform real time prevention interventions. *PLoS One* **2014**; 9:e98443.
22. Lin TC, Gianella S, Tenenbaum T, Little SJ, Hoenigl M. A simple symptom score for acute human immunodeficiency virus infection in a San Diego community-based screening program. *Clin Infect Dis* **2018**; 67:105–11.
23. Morris SR, Little SJ, Cunningham T, Garfein RS, Richman DD, Smith DM. Evaluation of an HIV nucleic acid testing program with automated internet and voicemail systems to deliver results. *Ann Intern Med* **2010**; 152:778–85.
24. Le T, Wright EJ, Smith DM, et al. Enhanced CD4+ T-cell recovery with earlier HIV-1 antiretroviral therapy. *N Engl J Med* **2013**; 368:218–30.
25. Stecher M, Hoenigl M, Eis-Hübinger AM, et al. Hotspots of transmission driving the local human immunodeficiency virus epidemic in the Cologne-Bonn region, Germany [manuscript published online ahead of print 29 August 2018]. *Clin Infect Dis* **2019**;68:1539–46.
26. Kosakovsky Pond SL, Weaver S, Leigh Brown AJ, Wertheim JO. HIV-TRACE (TRANmission cluster engine): a tool for large scale molecular epidemiology of HIV-1 and other rapidly evolving pathogens. *Mol Biol Evol* **2018**; 35:1812–9.
27. Hoenigl M, Weibel N, Mehta SR, et al. Development and validation of the San Diego early test score to predict acute and early HIV infection risk in men who have sex with men. *Clin Infect Dis* **2015**; 61:468–75.
28. Broaddus MR, DiFranceisco WJ, Kelly JA, St Lawrence JS, Amirkhanian YA, Dickson-Gomez JD. Social media use and high-risk sexual behavior among black men who have sex with men: a three-city study. *AIDS Behav* **2015**; 19(Suppl 2):90–7.
29. Grov C, Golub SA, Parsons JT. HIV status differences in venues where highly sexually active gay and bisexual men meet sex partners: results from a pilot study. *AIDS Educ Prev* **2010**; 22:496–508.
30. Jenness SM, Neaigus A, Hagan H, Wendel T, Gelpi-Acosta C, Murrill CS. Reconsidering the internet as an HIV/STD risk for men who have sex with men. *AIDS Behav* **2010**; 14:1353–61.
31. Horvath KJ, Oakes JM, Rosser BR. Sexual negotiation and HIV serodisclosure among men who have sex with men with their online and offline partners. *J Urban Health* **2008**; 85:744–58.
32. Chiasson MA, Hirshfield S, Remien RH, Humberstone M, Wong T, Wolitski RJ. A comparison of on-line and off-line sexual risk in men who have sex with men: an event-based on-line survey. *J Acquir Immune Defic Syndr* **2007**; 44:235–43.
33. Carballo-Diéguez A, Miner M, Dolezal C, Rosser BR, Jacoby S. Sexual negotiation, HIV-status disclosure, and sexual risk behavior among Latino men who use the internet to seek sex with other men. *Arch Sex Behav* **2006**; 35:473–81.
34. Harawa N, McBride S, Leibowitz A, Pulsipher C, Holloway I. Examining PrEP uptake among Medi-Cal beneficiaries in California: differences by age, gender, race/ethnicity and geographic region. *Southern California HIV/AIDS Policy Research Center*, **2018**. Available at: [www.chprc.org](http://www.chprc.org)
35. Chan PA, Towey C, Poceta J, et al. Online hookup sites for meeting sexual partners among men who have sex with men in Rhode Island, 2013: a call for public health action. *Public Health Rep* **2016**; 131:264–71.
36. Cassels S, Menza TW, Goodreau SM, Golden MR. HIV serosorting as a harm reduction strategy: evidence from Seattle, Washington. *AIDS* **2009**; 23:2497–506.
37. Khanna AS, Goodreau SM, Gorbach PM, Daar E, Little SJ. Modeling the impact of post-diagnosis behavior change on HIV prevalence in Southern California men who have sex with men (MSM). *AIDS Behav* **2014**; 18:1523–31.