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Sex with Older Partners Is Associated with Primary HIV Infection among Men Who Have Sex with Men in North Carolina

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Abstract

Background—Studies from the 1990s suggested sex with older partners was associated with HIV infection. We evaluated the hypothesized association between primary HIV infection (PHI) and having older sexual partners among men who have sex with men (MSM).

Methods—MSM with PHI and HIV-uninfected MSM completed audio computer-assisted self-interviews exploring behaviors involving their three most recent sexual partners prior to enrollment (if uninfected) or diagnosis (if PHI).

Results—Of 74 men reporting any lifetime sex with men, 20 had PHI (27%). Demographics (including age) were similar between groups; 39% were non-white and 74% identified as gay. The mean age of sex partners differed significantly: men with PHI had partners on average 6 years older than themselves, while uninfected men's partners were 4 months their junior ($P<0.001$). After adjusting for race, sex while intoxicated, and having a serodiscordant/serostatus unknown partner, a participant had twice the odds of PHI if his sex partner was 5 years his senior (OR 2.0, 95% CI, 1.2, 3.3).

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Conclusions—Among a sample of young MSM, the odds of HIV infection increased significantly as the age of sexual partners increased. These findings can inform behavioral interventions in communities of at-risk MSM as well as secondary prevention efforts among those already living with HIV.

Keywords

primary HIV infection; men who have sex with men; age mixing; North Carolina

INTRODUCTION

The number of Americans growing older with HIV is increasing. Before the advent of combination antiretroviral therapy (cART), half of patients died within 10 years of their HIV diagnosis.¹ With current antiretrovirals (ARVs), the life expectancy of a 25 year-old infected with HIV is at least another 35 years.² As the size of the population living with HIV increases and the population ages, the number of opportunities for HIV transmission will increase, because of increasing net exposure through sexual contact.

The factors driving selection of sex partners are complex. In one large qualitative study of men who have sex with men (MSM), roughly half of participants cited age of a potential partner as a specific draw, alongside other physical features.³ Among many younger MSM, relationships with older men connote stability, emotional maturity, and mentorship.³ For older men living in an increasingly ageist culture, having a younger partner may provide a sense of power or virility and frame aging in a positive light.³ MSM seeking long-term partnerships seem to narrow their desired age range, while those looking for a partner for casual sex generally have less stringent requirements for partner age.⁴

Near the peak of the domestic HIV epidemic in the 1990s, epidemiologic and modeling studies suggested that selection of older partners in sexual networks was associated with acquiring HIV infection – both among MSM^{5–9} and heterosexuals.^{10–13} This “dissortative” mixing in sexual networks (selecting partners unlike oneself) appeared to fuel HIV transmission.^{5, 14–15} Given increasing trends among young MSM for unprotected anal intercourse with partners of unknown HIV serostatus¹⁶ and frequency of age-mixing with older sex partners among adolescents and young adults,¹⁷ the potential for secondary transmission of HIV from older MSM to younger ones requires re-examination. Among those younger than 25 years old diagnosed with HIV in the state in 2007, 63% were MSM.¹⁸ We performed the present study to determine if having an older sexual partner was a risk factor for acquisition of HIV among MSM in North Carolina (NC).

METHODS

Study Population

Social Networks and Partnerships (SNAP) was a case-control study conducted in central NC from January 2008 to January 2009. SNAP’s goal was to describe the social and sexual networks and transmission risk behavior of young MSM. Recruitment was based on a respondent-driven sampling (RDS) model, in which seed participants could be either HIV-uninfected or have primary HIV infection (PHI, defined below). Participants with PHI were identified through the NC Screening and Tracing of Acute Transmission program^{19, 20} or HIV providers at our facility, and referred for study screening. HIV-uninfected MSM came from Internet and community recruitment (if seeds) or as referrals to the study from other participants. Seed participants were asked to recruit their three most recent sexual partners and three social friends for the study. Each of these first generation participants then recruited three sex partners and three friends, to create a network with two generations of observations tied to

each seed participant (Figure 1A). If the participant's HIV status was unknown, a symptom review for PHI was performed and an OraQuick ADVANCE rapid HIV-1/2 oral fluid antibody test administered (OraSure Technologies, Inc., Bethlehem, PA). Any reactive tests were confirmed with enzyme immunoassay (EIA) and Western blot.

We defined being MSM as a male who had ever had sexual contact with a male partner, rather than identifying same-sex attraction to other men. PHI was defined as either of the following: a negative HIV-1 EIA with detectable HIV RNA or a documented negative EIA within 180 days of a positive EIA and confirmatory Western blot. Twenty MSM with PHI and 54 HIV-uninfected MSM made up our cases and controls, respectively.

Measurements

Participants completed an audio computer-assisted self-interview (ACASI) at their study visit. Demographic information was collected, including age, education level attained and whether they were in a committed relationship. We asked participants to identify their three most recent sexual partners before diagnosis (if PHI) or enrollment (if uninfected), and enter the numerical age for each. If exact age was unknown, participants were asked to provide their best estimate. In the ACASI, we inquired about sex under the influence of drugs or alcohol and use of condoms with each of these partners. Participants also enumerated their number of lifetime HIV tests and lifetime sexual partners, including those met over the Internet.

Statistical Analysis

Participants were categorized as having PHI or being HIV-uninfected; four men with chronic HIV infection were excluded from analysis. (The single participant identified with undiagnosed HIV infection through our screening was also excluded). For each participant, we determined the mean age of his reported sex partners and the age of his oldest sex partner. From each of these values, we subtracted the participant's age to create two variables representing age differences. These differences were considered as continuous variables, yielding positive values for men whose sex partners were older than they and negative values if partners were younger.

We performed bivariate comparisons of individual characteristics with the participant's HIV status using Pearson's χ^2 test or Fisher's exact test for categorical variables and Student's *t* test or the Wilcoxon rank sum test for continuous variables. We determined odds ratios (OR) and 95% confidence intervals (CI) for PHI after adjusting for the effect of individual factors using logistic regression modeling. Factors of interest were not limited solely to those variables with statistical significance in bivariate comparisons. Confounding was assessed by stepwise removal of variables from our regression model and determining their impact on the OR estimate from the fully inclusive model. Statistical significance was defined as $P < 0.05$. All analyses were performed using Stata/IC v.10.1 (Stata Corporation, College Station, TX).

Human Subjects Protection

This study was approved by the Public Health/Nursing Institutional Review Board (IRB) at the University of North Carolina at Chapel Hill. Because of the sensitive nature of the questions asked, we also obtained a federal certificate of confidentiality from the National Institute of Mental Health.

RESULTS

Overall the participants were significantly skewed toward younger ages, with three-quarters of the sample ≤ 25 years old (range 18–48). The median age of the PHI group was 24.5, while that of HIV-uninfected men was 22.5 ($P=0.33$, Table 1). Among those with PHI, 60% were

nonwhite, compared with only 33% of uninfected men ($P=0.03$). Men with PHI reported having significantly more lifetime HIV tests than their counterparts. Sex while under the influence of drugs or alcohol was strongly associated with PHI ($P<0.001$). Compared with HIV-uninfected men, those with PHI were more likely to have performed oral sex without a condom or had unprotected anal sex (either insertive or receptive) with their most recent serodiscordant or serostatus unknown (SD/SU) partner (all $P<0.05$). Sex with a partner known to be HIV-infected was significantly more common among men with PHI ($P=0.01$).

The partners of men in the PHI group were on average 6 years older than partners of the uninfected men (29.8 vs. 23.9, $P<0.001$). The distribution of the differences between sex partner ages and those of the participant is depicted in Figure 2. Regarding the difference between the mean age of sex partners and the age of the participant, HIV-uninfected men more often selected partners very close to their own age (4 months younger), while men with PHI had partners almost 4 years older ($P=0.006$). After adjusting for being nonwhite, having sex while intoxicated, and having sex with a SD/SU partner, this difference corresponded to 2.0 times the odds of PHI if a participant's sex partner was 5 years his senior (95% CI, 1.2, 3.3; Figure 3). We examined the effect of the participant's age by dichotomizing into two groups at the median participant age – those ≤ 23 years old, and >23 . After also adjusting for nonwhite race, sex while intoxicated, and having a SD/SU partner, a man aged 23 or younger had a significant 2.5-fold increase the odds of PHI when his sex partners were 5 years older than him (95% CI, 1.2, 5.4), compared with 2.0 times for participants 24 years and older (95% CI, 0.6, 6.1).

DISCUSSION

This study demonstrates that selection of an older sex partner is significantly associated with PHI among a sample of young MSM in NC. After adjusting for covariates, we noted that having a sex partner five years older doubled the odds of PHI. Our findings expand upon and update the work of modelers of the MSM epidemic in the 1990s, before the advent of cART – in particular, two studies that used egocentric network analysis to assess the association between having an older sex partner and increased HIV risk. Both of these studies reflected the epidemic in the early 1990s, with a gradation of HIV prevalence directly proportional to the age of the men.

Morris, *et al.* investigated the effect of selecting older sex partners on the odds of HIV infection using data from the Longitudinal AIDS Impact Project in New York City (NYC).⁵ Seven waves of interviews were conducted with a closed cohort of MSM in NYC from 1985–1991. Comparing the partnerships of 71 young HIV-uninfected men with ten HIV-infected counterparts, the results were striking. Among those participants who reported unprotected receptive anal sex, the seroprevalence was zero if all sex partners were less than 25 years old, and 44% among those with at least one sex partner over 25. For unprotected sex with an insertive partner, the prevalence leapt from zero when no partners were over 25 years old to 15% when at least one sex partner was older than 25. Service and Blower used empirical data collected in 1993 as part of a longitudinal study of HIV transmission among MSM in San Francisco to develop and test a predictive mathematical model estimating the likelihood of seroconversion within the cohort.⁶ Seropositive men had a greater probability of having more than one sex partner over age 30, when compared with HIV-uninfected men – in both the 18–24 age range (59% vs. 22%) and the 25–29 range (42% vs. 70%). When the inputs to the model were changed from men having no sex partners over 30 to all partners over 30, the seroprevalence jumped four- to five-fold. Thus, assortative age mixing seemed to be protective against HIV infection by limiting exposure to earlier “waves” of MSM with high HIV prevalence.^{8, 9} Finally, Bingham, *et al.* analyzed Los Angeles' data from the Young Men's Survey in 1999–2000. Nearly 35% of MSM reported “mostly” having sex partners more than

5 years their senior – and their odds of HIV infection were 3.5 times greater than men with partners closer to their own age (95% CI, 1.6, 7.8).⁷

Taken together, these studies and our work examine three distinct periods of the domestic HIV epidemic among MSM. Consider the CDC's recent back-calculation estimates of HIV incidence, which showed the peak of infections among MSM in 1984–85, a nadir in 1991–93, and a steady increase since then to over 30,000 new cases estimated for 2003–2006.²¹ Morris, *et al.*'s initial data spanned 1985 to 1991; Service and Blower's study sampled men in 1993; Bingham, *et al.* looked at the epidemic in 1999–2000; and our data are from 2007–08. The late 1980s were characterized by a community-driven response to HIV among MSM. At least some of the decline in incidence can be attributed to the death of a substantial number of those infected. The early 1990s saw the impact of the first therapies, the height of the public health response, and the beginning of the reversal in HIV/AIDS-related mortality that has continued to the present. Despite the different prevailing approaches to HIV management in each period, age mixing represented a heightened risk for transmission. Is it possible that the potential impact of age mixing has simply been underestimated all of this time? Issues like sexual concurrency,^{22, 23} Internet sex-seeking,^{24–26} and having sex while intoxicated^{26–28} are all associated with incident HIV infection, yet our screening methods remain almost exclusively focused on the traditional risk factors established at the start of the epidemic, like injection drug use or unprotected intercourse.^{29, 30} Through behavioral surveillance among MSM with PHI and a better understanding of individual-level, “non-traditional” risks leading to their HIV infection, we have the potential to provide more tailored, contemporary prevention messages to high-risk populations. Addressing factors perceived as being less influential than traditional risks could, in aggregate, help to reduce the incidence of HIV. A compelling case can be made that age mixing, along with other “non-traditional” risk factors, ought to take a position alongside traditional factors at the forefront of behavioral surveillance.

Our most significant limitations center on the age of sex partners reported by participants. These men may not have accurately estimated the age of sex partners. Those with PHI might also introduce a differential recall bias regarding the age of sexual partners, having given more thought to risk behaviors following their HIV diagnosis. A single partner much older than the other two reported partners could skew the mean age upward, and would exaggerate the estimated effect of age on odds of PHI. However, when we examined the odds ratios in models using the oldest sex partner age and the mean age of partners, the point estimates were essentially unchanged (data not shown). The SNAP study was designed to determine the feasibility of using a RDS model to recruit and evaluate a cohort of MSM at high risk for HIV infection. This approach was an attractive option given its proven ability to sample at-risk hidden populations like illicit drug users,^{31, 32} sex workers,^{33–35} and transgendered people.^{33, 36} The extended “reach” of this design overcomes many of the issues of sampling bias that inherently limit studies employing venue-based or facility-based sampling methods, thus improving external validity.³⁷ However, because of poor recruitment from seeds living long distances from the study site, our controls may reflect a somewhat different base population than that from which the cases came. Because SNAP was intended to demonstrate our capacity to utilize participants as recruiters, we did not structure the study to include sufficient waves to reach network equilibrium (the point at which bias from non-random selection of seed participants is overcome).³⁸

In summary, young MSM in NC who select older sex partners have significantly greater odds of acquiring HIV infection, even after controlling for specific high-risk behaviors. Our findings and earlier empirical data support the application of an individualized approach to counseling when talking to young MSM about their sexual risk behavior. Provision of safe sex messages should include both traditional and non-traditional risk factors, directed at all age groups of sexually active individuals. Young men who have older sexual partners should be informed of

the comparatively increased risk that such partnerships pose for HIV infection. In parallel, older MSM living with HIV and engaged in care should receive secondary prevention messages encouraging disclosure of their status to partners, maintenance of safer sex behavior, and that antiretroviral treatment alone isn't enough to prevent transmission. Delivery methods like social marketing campaigns and new media could be important and novel ways of reaching a greater audience.

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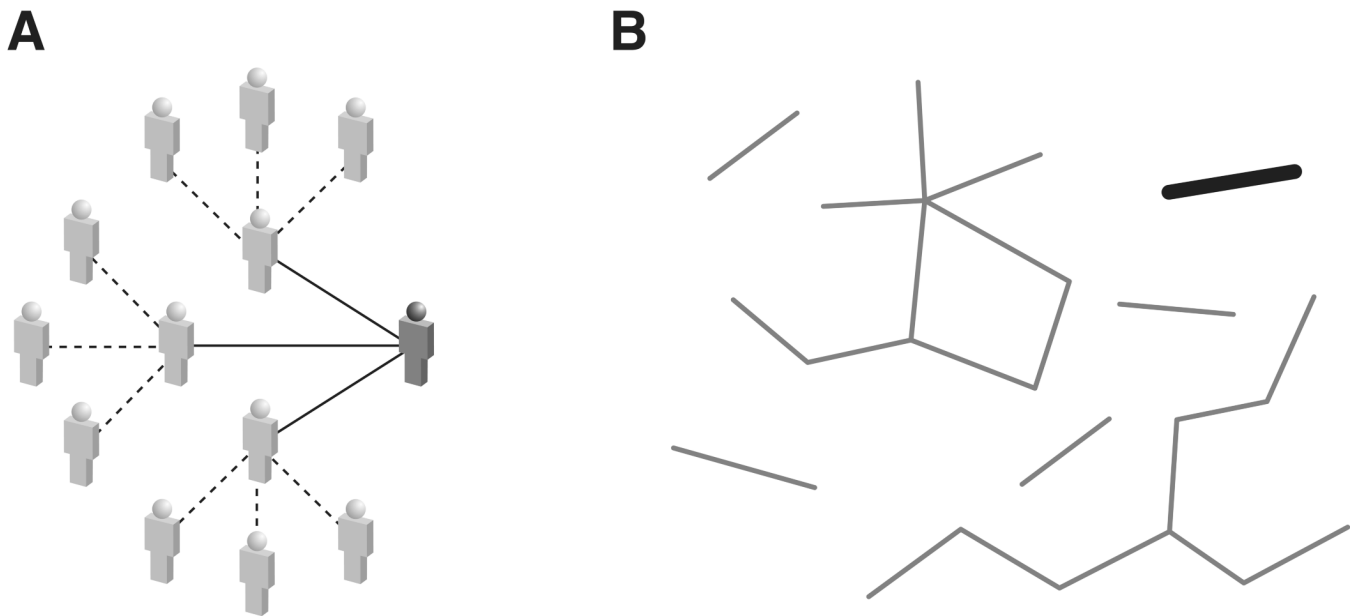


Figure 1. Respondent-driven sampling and structure of the SNAP sexual network

(A) Each seed participant (dark gray) recruited three sexual partners (solid lines), who in turn recruited three sexual partners of their own – creating two generations for the study. (B) The two largest components of the sexual network had 9 participants each; one had a three-core (the closed, four-vertex “loop” of the upper component). Of five dyads, only one involved men with PHI (thick black line). Not shown are 18 PHI and 25 HIV-uninfected participants who did not recruit any eligible participants.

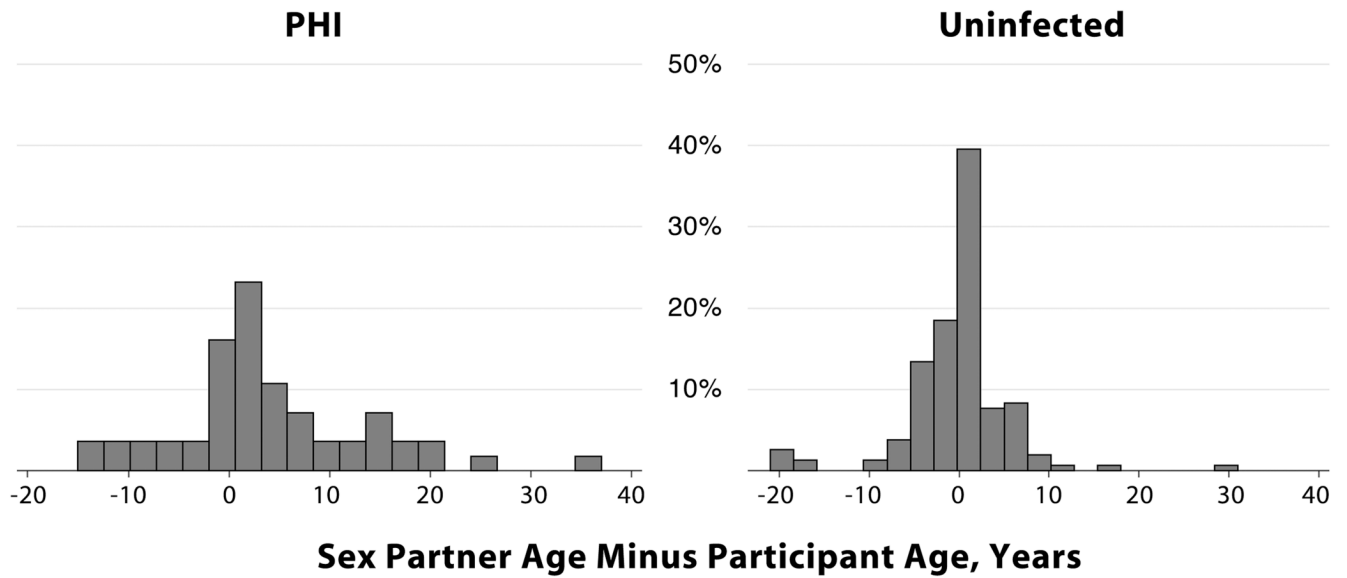


Figure 2. Distribution of differences between ages of individual sex partners and their associated seed participant

Depicted are 60 sex partners of MSM with primary HIV infection (PHI) and 162 partners of HIV-uninfected participants. We noted a broader distribution of ages among partners of the MSM with PHI, while HIV-uninfected participants more often had partners very close to their own age.

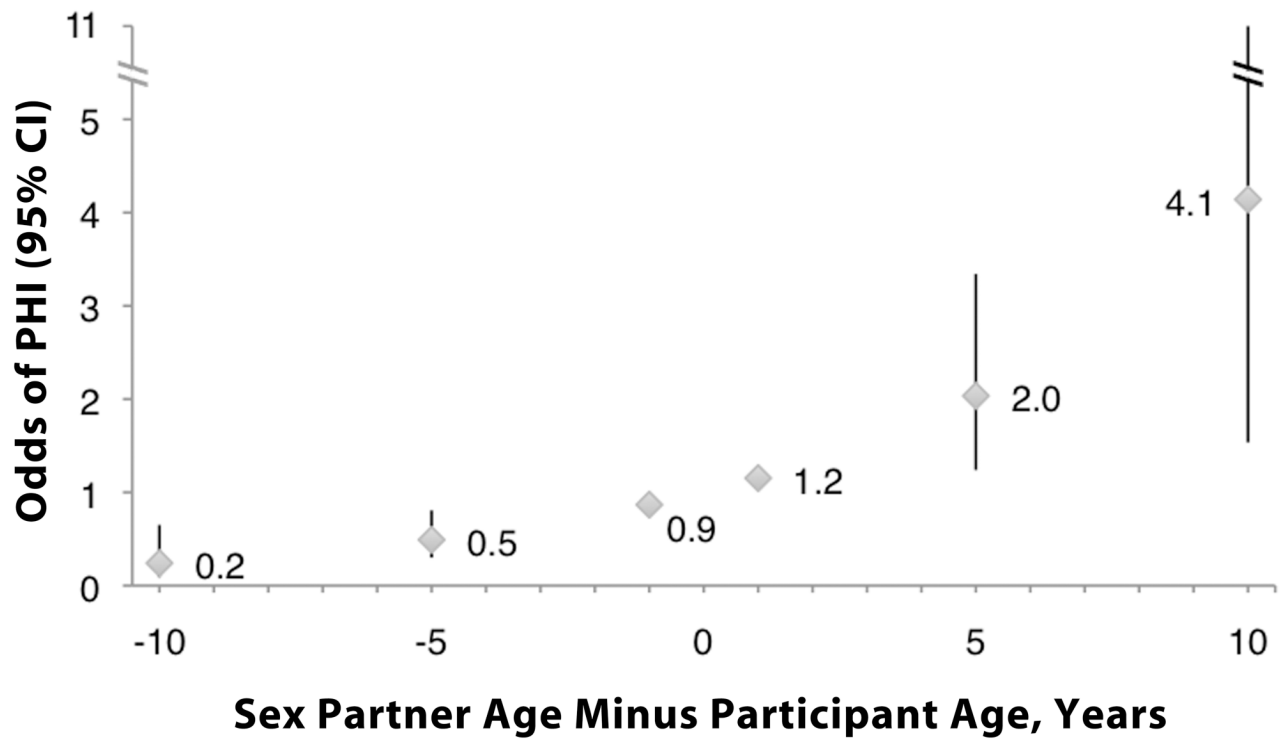


Figure 3. Odds of primary HIV infection (PHI) increase as sex partner age increases
After adjusting for nonwhite race, sex while intoxicated, and having a serodiscordant or serostatus unknown (SD/SU) partner, having sex with a partner 5 years older than the participant doubled the odds of PHI (OR 2.2, 95% CI, 1.2, 3.3), while a partner 10 years older quadrupled the odds (OR 4.1, 95% CI, 1.5, 11).

Table 1

Characteristics of Participants in SNAP, by HIV Status*

Characteristic	PHI (n=20)	Uninfected (n=54)	P †
Age in years, median (IQR)	24.5 (20.5–27.5)	22.5 (21–25)	0.33
Race/Ethnicity, %			
Caucasian/White	40	69	
Black	35	20	
Latino/Hispanic	15	5	0.46
Asian/Pacific Islander	0	2	
Native American	5	0	
Mixed	5	4	
College graduate, %	30	33	0.82
In committed relationship, %	15	28	0.12
Lifetime sex partners, median (IQR)	15 (8–40)	14 (7–35)	0.36
Lifetime online sex partners, median (IQR)	9 (4–20)	6 (2–17)	0.44
Lifetime HIV tests, median (IQR)	5 (3–9)	3 (2–5)	0.02
Lifetime STIs, median (IQR)	1 (1–2)	1 (0–1)	0.16
Sex under influence of drugs or alcohol, %	75	31	<0.001
Had group sex with partner(s), %	25	20	0.86
Partner(s) having concurrent sex, %	60	51	0.62
Internet sex-seeking ≥4 days/week, %	30	15	0.13
No condom with last SD/SU, where participant was:			
Insertive partner for anal sex	15	0	<0.001
Receptive partner for anal sex	45	5	<0.001
Giving oral sex	70	38	0.02
Receiving oral sex	65	47	0.17
Had sex partner(s) with known HIV, %	45	16	0.01
Sex partner age, mean (SD)	29.8 (8.4)	23.9 (6.2)	<0.001

* Abbreviations: PHI, primary HIV infection; IQR, interquartile range; STIs, sexually transmitted infections; SD/SU, serodiscordant/serostatus unknown; SD, standard deviation

† Pearson's χ^2 test was used for nominal and categorical variables; Wilcoxon rank-sum test was used to compare medians; and Student's *t* test was used to compare means.

Table 2

Results of multivariable logistic regression model for primary HIV infection among 20 MSM with PHI and 54 MSM without PHI.

Characteristic	Adjusted Odds Ratio (95%CI)	P
Difference between participant age and mean age of sex partners	1.15 (1.04, 1.27)	0.005
Partner with discordant or unknown serostatus	7.95 (1.39, 45.7)	0.02
Sex while intoxicated	4.70 (0.99, 22.4)	0.052
Nonwhite race	5.90 (1.24, 28.1)	0.026