

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

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Objective: Young men who have sex with men (MSM) and MSM of color have the highest HIV incidence in the United States. To explore possible explanations for these disparities and known individual risk factors, we analyzed the per contact risk (PCR) of HIV seroconversion in the early highly active antiretroviral therapy era.

Methods: Data from 3 longitudinal studies of MSM (HIV Network for Prevention Trials Vaccine Preparedness Study, EXPLORE behavioral efficacy trial, and VAX004 vaccine efficacy trial) were pooled. The analysis included visits where participants reported unprotected receptive anal intercourse (URA), protected receptive anal intercourse, or unprotected insertive anal intercourse (UIA) with an HIV seropositive, unknown HIV serostatus, or an HIV seronegative partner. We used regression standardization to estimate average PCRs for each type of contact, with bootstrap confidence intervals.

Results: The estimated PCR was highest for URA with an HIV seropositive partner (0.73%; 95% bootstrap confidence interval [BCI]: 0.45% to 0.98%) followed by URA with a partner of unknown HIV serostatus (0.49%; 95% BCI: 0.32% to 0.62%). The estimated PCR for protected receptive anal intercourse and UIA with an HIV seropositive partner was 0.08% (95% BCI: 0.0% to 0.19%) and 0.22% (95% BCI: 0.05% to 0.39%), respectively. Average PCRs for URA and UIA with HIV seropositive partners were higher by 0.14%–0.34% among younger participants and higher by 0.08% for

UIA among Latino participants compared with white participants. Estimated PCRs increased with the increasing number of sexual partners, use of methamphetamines or poppers, and history of sexually transmitted infection.

Conclusions: Susceptibility or partner factors may explain the higher HIV conversion risk for younger MSM, some MSM of color, and those reporting individual risk factors.

Key Words: HIV, MSM, United States, per contact risk

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INTRODUCTION

Overall, new cases of HIV have been stable in the United States at approximately 50,000 per year.¹ There has been a 12% increase in incidence among men who have sex with men (MSM) between 2007 and 2010.² Young MSM are the most heavily impacted group in the United States with a 22% increase in HIV incidence during this period.² In addition to age disparities in HIV incidence, there are significant racial/ethnic disparities. In 2010, black and Latino MSM represented the highest proportion of new HIV diagnoses among all MSM in the United States: 36% and 22%, respectively.² Young black MSM in particular have had the highest increase in HIV incidence between 2006 and 2010.² However, little is known about why this occurs.³ Current data indicate that MSM of color have similar or lower individual risk behaviors, including the number of anal sex partners and substance use, suggesting that differences in racial/ethnic assortativity in partner selection, partner serostatus, and prevalence of nonsuppressed HIV viral load among HIV-positive partners are likely driving the disparities.^{4–6}

An analysis of per contact risk (PCR) of HIV seroconversion, the probability of HIV acquisition per sexual act, may contribute to our understanding of the extent to which disparities by race and age are driven by differences in the infectiousness of partners and/or the susceptibility of individuals or, alternatively, by misclassification of HIV-positive partners as HIV negative or of unknown serostatus.^{7,8} Previous estimates of PCRs for MSM have been based on relatively small samples and used methods that were not designed to assess heterogeneity by race/ethnicity, number of sexual partners, substance use, and history of sexually transmitted infections (STIs), which have been associated with an

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increased risk of HIV seroconversion.^{7,8} In this analysis, we use a new approach designed to accommodate heterogeneity.

We had 2 goals for this analysis. First, we compared the PCR of HIV seroconversion in the pre-highly active antiretroviral therapy (HAART) and early HAART era, to identify the early impact of HAART on PCR. Second, we evaluated whether the PCR of sexual practices with known HIV-positive partners differed by age and race/ethnicity. This analysis removes the lack of knowledge of partner serostatus as a factor in age and race/ethnicity disparities and may point to differences in the infectiousness of partners and/or the susceptibility of individuals to explain these disparities.

METHODS

Participants and Data Collection

We identified 4 existing prospective, longitudinal, HIV prevention cohort studies of MSM in the United States for inclusion in this analysis. The multisite Centers for Disease Control and Prevention Collaborative HIV Seroincidence Study (Jumpstart) was used to model PCR estimates in the pre-HAART era.⁹ This study enrolled 2189 HIV-uninfected MSM from 3 US cities from 1992 to 1994 who were followed for up to 18 months at semiannual intervals until the completion of study in 1995.

Data from the HIV Network for Prevention Trials Vaccine Preparedness Study (VPS), the VaxGen VAX004 trial, and the EXPLORE study were combined to model PCR estimates from the early HAART era.¹⁰ VPS enrolled 3275 MSM in 6 US cities from 1995 to 1997, and they were followed every 6 months for 18 months of follow-up until study completion in 1999.^{11,12} The VAX004 trial enrolled 4643 MSM in 57 US sites from 1998 to 1999 as part of a randomized, placebo-controlled, efficacy trial of a recombinant gp120 HIV-1 vaccine, which did not show efficacy in reducing HIV incidence.¹³ Participants were followed at 6-month intervals for 36 months, and the study was completed in 2002. The EXPLORE study enrolled 4295 MSM in 6 US cities from 1999 to 2001 into a randomized clinical trial of a 10-session behavioral intervention, which showed no difference in HIV incidence rates between the control and active arms.¹⁴ Participants were followed every 6 months until study completion in 2003.

Although there was some variability in specific enrollment criteria, all studies enrolled HIV-negative men who reported anal intercourse with at least 1 male partner in the past 12 months. VAX004 was the only cohort study that excluded men who reported injection drug use (IDU) at baseline. Both EXPLORE and VAX004 excluded men who had been in mutually monogamous relationships for the previous year. Participants in all studies were asked to self-identify race/ethnicity at baseline. For the purposes of this analysis, we classified participants into 1 of 4 race/ethnicity categories: black, Latino, white, or other to maintain consistency across cohorts. In the analysis, men who self-identified as both black and Latino contributed to PCR estimates for both groups. Self-reported sexual risk behavioral data were collected through audio computer-assisted self-interview (EXPLORE) or structured interview (Jumpstart, VAX004,

and VPS) and included sexual behaviors in the past 6 months with partners of each HIV serostatus type (negative, positive, or unknown). Sexual behaviors with sexual partners were defined as unprotected receptive anal intercourse (URA), unprotected insertive anal intercourse (UIA), or protected receptive anal intercourse (PRA). Other self-reported behavioral risk data included in this analysis were popper use, methamphetamine use, heavy alcohol use, and STIs (gonorrhea, syphilis, or chlamydia), as each has been found to independently predict HIV infection in MSM. Jumpstart participants who reported IDU at baseline or follow-up were excluded from this analysis because it was associated with HIV seroconversion. However, IDU at baseline and follow-up was not significantly associated with HIV infection in the VPS, VAX004, and EXPLORE cohort studies, and exclusion did not change our findings in sensitivity analysis, so participants who reported IDU were included in the adjusted analysis.

PCR Estimation

Our previous estimates of PCRs were based on a Bernoulli model.^{7,8,15} Under this model, PCRs are assumed constant, and more distal cofactors for seroconversion, including age, race/ethnicity, numbers of partners, substance use, and STI, only affect risk through the number of contacts. However, this model does not accommodate heterogeneity in the PCRs. To do this, we used a pooled logistic model, including the distal cofactors and the numbers of contacts.

Our approach allows heterogeneity in the PCRs in part by flexibly modeling the number of contacts, so that the absolute risk of 5 URA contacts with a positive partner can be more than 20% of the risk of 25 such contacts. In addition, because the logistic model is multiplicative, the absolute risk resulting from sexual contacts increases with the baseline risk determined by the cofactors. For example, the risk resulting from 10 URA contacts with a positive partner is larger for a young man of color who reports multiple partners and methamphetamine use than for an older white man with none of these cofactors.

To obtain estimates of the PCRs, we estimate the absolute increment in risk resulting from each type of contact as the difference between the fitted risk for each participant-visit and the potential risk if no such contacts of the given type had been reported.¹⁶ Then, the PCRs are calculated from the number of contacts and the increment in absolute risk. In a final step, the PCRs are averaged, both overall and within the subgroups defined by age, race/ethnicity, number of partners, substance use, and STI, with bootstrap confidence intervals (BCI). Additional details are provided in the **Supplemental Digital Content** (see **Appendix**, <http://links.lww.com/QAI/A457>).

RESULTS

In Jumpstart, 1813 participants, 4168 unique visits, and 52 seroconversions were used to calculate the PCR in the pre-HAART era (Table 1). For the early HAART era, we included 10,760 participants, 42,395 unique visits, and 584 HIV seroconversions from VPS, EXPLORE, and VAX004 (Table 1). The majority of participants from all the cohorts were

TABLE 1. Baseline Demographics, Risk Characteristics, and Cohort Descriptive of Jumpstart, VPS, EXPLORE, and VAX004 Studies

	Cohort				P
	Jumpstart	VPS	EXPLORE	VAX004	
Demographics					
Age, (yr), n (%)					<0.001
<25	370 (20)	419 (18)	715 (18)	517 (11)	
26–30	485 (27)	609 (27)	847 (22)	753 (16)	
>30	958 (53)	1238 (55)	2351 (60)	3311 (72)	
Race/ethnicity, n (%)					<0.001
White	1422 (78)	1730 (76)	2864 (73)	3968 (87)	
Black	102 (6)	132 (6)	283 (7)	154 (3)	
Latino	198 (11)	289 (13)	566 (14)	320 (7)	
Other	91 (5)	115 (5)	200 (5)	139 (3)	
Education, n (%)					<0.001
Less than high school	50 (3)	31 (1)	56 (1)	57 (1)	
High school graduate	808 (45)	841 (37)	1298 (33)	1546 (34)	
College graduate	663 (37)	949 (42)	1717 (44)	1963 (43)	
Graduate degree	291 (16)	445 (20)	841 (22)	1015 (22)	
Risk factor*					
No. sex partners, n (%)					<0.001
0–1	101 (6)	29 (1)	196 (5)	426 (9)	
2–5	611 (34)	865 (38)	974 (25)	1389 (30)	
≥6	1101 (61)	1372 (61)	2743 (70)	2766 (60)	
Unprotected anal sex, n (%)†	1277 (70)	1426 (63)	3406 (87)	3640 (79)	<0.001
HIV+ sex partner, n (%)	335 (18)	477 (21)	1982 (51)	2498 (55)	<0.001
Popper use, n (%)	704 (39)	943 (42)	1942 (50)	2074 (45)	<0.001
Heavy alcohol use, n (%)	331 (18)	523 (23)	549 (14)	816 (18)	<0.001
Amphetamine use, n (%)	337 (19)	362 (16)	989 (25)	816 (18)	<0.001
IDU, ever, n (%)	0 (0)	62 (3)	648 (17)	132 (3)	<0.001
STI, self report (%)	269 (15)	188 (8)	621 (16)	347 (8)	<0.001
Cohort descriptives					
Total participants	1813	2266	3913	4581	—
No. visits	4168	5041	17,657	19,697	
No. seroconversions	52	52	202	330	

* In previous 6 months.

† Insertive or receptive, with HIV positive, unknown serostatus, or negative partner.

older than 30 years, white, reported having more than 6 sexual partners, and having UIA or URA in the 6 months before baseline. A higher proportion of participants reported an HIV seropositive sexual partner in EXPLORE (51%) and VAX004 (55%) compared with VPS (21%) or Jumpstart (18%).

PCR in Pre-HAART and Early HAART Era

Overall, the estimated PCRs were similar in the pre-HAART and early HAART era (Table 2). The estimated PCR of HIV seroconversion for URA with an HIV seropositive partner was similar in the pre-HAART (0.60%; 95% BCI: 0.34% to 1.09%) and early HAART (0.73%; 95% BCI: 0.45% to 0.98%) era (Table 2). URA with partners of unknown HIV serostatus was the second highest estimated PCR during the pre-HAART (0.40%; 95% BCI: 0.26% to 0.59%) and early HAART (0.49%; 95% BCI: 0.32% to 0.62%) era. The estimated PCR was lowest for URA with HIV-negative partners in both the pre-HAART and early

HAART era (0.02%; 95% BCI: 0% to 0.07%; and 0.03%; 95% BCI: 0%–0.11%, respectively).

Despite relatively minor differences between pre-HAART and early HAART cohorts, we limited the remaining analyses to the latter 3 cohorts, to avoid confounding from unmeasured variables in the pre-HAART era. The estimated PCR for URA with an HIV-positive partner was significantly higher than all other types of contacts, except URA with a partner of unknown HIV status (95% BCI for pairwise difference excludes zero) (Table 3). As expected, URA with an unknown serostatus partner was also significantly more risky than PRA with an unknown partner, and either URA or PRA with partners believed to be HIV negative.

Covariate Effects on HIV Seroconversion in VPS, EXPLORE, and VAX004

Next, we evaluated factors associated with HIV infection in the 3 early HAART longitudinal cohorts. Participants

TABLE 2. Per Contact Risks in Pre-HAART Era (Jumpstart) and Early HAART Era (VPS, EXPLORE, and VAX004 Cohort Studies)

Partner Serostatus	Contact Type	Cohort	
		Jumpstart* PCR (95% BCI)	VPS, EXPLORE, VAX004 PCR (95% BCI)
HIV positive	URA	0.60 (0.34 to 1.09)	0.73 (0.45 to 0.98)
	PRA	0.04 (0.00 to 0.15)	0.08 (0.00 to 0.19)
	UIA	0.14 (0.04 to 0.29)	0.22 (0.05 to 0.39)
Unknown serostatus	URA	0.40 (0.26 to 0.59)	0.49 (0.32 to 0.62)
	PRA	0.08 (0.01 to 0.16)	0.11 (0.02 to 0.20)
HIV negative	URA	0.02 (0.00 to 0.07)	0.03 (0.00 to 0.11)
	PRA	0.09 (0.04 to 0.16)	0.12 (0.06 to 0.18)

* Estimates based on model omitting covariates (see statistical methods).

in VAX004 had higher odds of HIV seroconversion compared with VPS [odds ratio (OR), 1.72; $P = 0.001$] (Table 4). In combined cohort analysis, younger (<25 years) participants were at a higher risk than older (>30 years) participants (OR, 1.31; $P = 0.03$). Furthermore, black participants were at a greater risk compared with white participants (OR, 1.78; $P = 0.002$), whereas Latino participants had a trend toward higher risk (OR, 1.26; $P = 0.08$). Having greater than 1 sexual partner, any self-reported use of methamphetamines or poppers, heavy alcohol use, or history of STI in the previous 6 months were also associated with an increased risk.

Demographic and Risk Factor Disparities in PCR of HIV Seroconversion

In evaluating the differences by age, race/ethnicity, number of partners, substance use, and STI, we focused on the PCR for unprotected anal intercourse with known HIV seropositive partners, to eliminate the knowledge of partner serostatus in these risk estimates. The PCR for URA with HIV seropositive partners was significantly higher for MSM younger than 25 years (0.98%) and between 25 and 30 years olds (0.87%) compared with MSM older than 30 years (0.64%) ($P < 0.05$) (Fig. 1A). MSM younger than 25 years had the highest PCR, despite a lower mean number of

reported contacts (7.1 vs. 10.3). Similarly, the PCR for UIA with HIV seropositive partners was significantly higher for younger MSM (<25 years and 25–30 years) compared with MSM older than 30 years (0.35% and 0.33% vs. 0.19%; $P < 0.05$) (Fig. 1A).

Similarly, some MSM of color had higher PCRs with HIV-positive contacts (Fig. 1B). We found weak evidence that PCR for URA with HIV seropositive contacts was higher for black (1.04%) and participants classified as other (1.06%) than for white participants (0.71%; $P > 0.05$) (Fig. 1B). Among Latino participants, there is stronger evidence for an elevated PCR for UIA with HIV seropositive contacts compared with white participants (0.29% vs. 0.21%; $P < 0.05$). Black participants reported the lowest mean number of contacts compared with all other racial groups, for both URA (3.1) and UIA (5.0). In contrast, the number of contacts and PCRs for URA or UIA with HIV seropositive partners were similar in Latino and white MSM.

The PCRs were significantly higher for those who reported more than 1 HIV-positive partner (Fig. 1C), with those reporting URA with more than 5 partners having the highest PCR. Those reporting methamphetamine or popper use, or a STI had significantly higher PCRs for URA and UIA with HIV seropositive partners compared with those who did not report these risk factors (Fig. 1D).

DISCUSSION

Our analysis of HIV seroconversion in 4 large cohorts of high-risk MSM in the United States suggests that the PCR of 7 types of sexual contact was similar during the pre-HAART and early HAART era. However, our new modeling approach, designed to accommodate heterogeneity, did identify substantial age and racial/ethnic disparities in the early HAART era and differences in PCRs by the numbers of sexual partners, STIs, and use of substances other than alcohol. These data support that susceptibility or partner factors may explain the higher HIV incidence among younger MSM, MSM of color, and those reporting multiple sexual partners, popper or methamphetamine use, or an STI.

The first estimates of PCR for MSM in the pre-HAART era reported a PCR of URA with an HIV-positive partner of 0.82%.⁷ A more recent analysis of PCR from Australia in the

TABLE 3. Absolute Differences in PCR for HIV Seroconversion With HIV-Positive Partners, Partners of Unknown HIV Serostatus, and HIV-Negative Partners From Early HAART Era Cohorts (Vaccine Preparedness Study, EXPLORE, and VAX004)

Partner's HIV Serostatus	Contact Type	PCR	HIV Positive		HIV Unknown		HIV Negative	
			PRA 0.08	UIA 0.22	URA 0.49	PRA 0.11	URA 0.03	PRA 0.12
HIV positive	URA	0.73	0.66*	0.51*	0.24	0.62*	0.70*	0.61*
	PRA	0.08	—	-0.15	-0.41*	-0.04	0.04	-0.05
	UIA	0.22	—	—	-0.27*	0.11	0.19	0.10
HIV unknown	URA	0.49	—	—	—	0.38*	0.46*	0.37*
	PRA	0.11	—	—	—	—	0.08	-0.01
HIV negative	URA	0.03	—	—	—	—	—	-0.09

* 95% BCI for pairwise difference excludes 0.

TABLE 4. Bivariable Factors Associated With HIV Seroconversion Among MSM in Longitudinal Cohorts in the Early HAART Era (Vaccine Preparedness Study, EXPLORE, and VAX004)

Variable	Visits	Seroconversions	Rate	OR (95% BCI)*	P
Cohort					
VPS	5041	52	1.03	Ref	
EXPLORE	17,657	202	1.14	0.87 (0.63 to 1.20)	0.39
VAX004	19,697	330	1.68	1.72 (1.27 to 2.33)	0.001
Age					
<25	6227	103	1.65	1.31 (1.03 to 1.66)	0.03
26–30	8572	129	1.50	1.11 (0.90 to 1.38)	0.32
>30	27,596	352	1.28	Ref	
Race/ethnicity					
White	34,271	454	1.32	Ref	
Black	1970	33	1.68	1.78 (1.23 to 2.56)	0.002
Latino	4416	70	1.59	1.26 (0.97 to 1.64)	0.08
Other	1738	27	1.55	1.16 (0.80 to 1.68)	0.45
Sex partners					
0–1	7095	47	0.66	Ref	
2–5	15,632	152	0.97	1.46 (1.04 to 2.04)	0.03
>5	19,668	385	1.96	1.88 (1.34 to 2.63)	<0.001
Risk factors†					
Methamphetamines‡	5187	170	3.28	1.67 (1.36 to 2.06)	<0.001
Poppers‡	13,797	303	2.20	1.42 (1.19 to 1.71)	<0.001
Alcohol§	3536	69	1.95	1.33 (1.03 to 1.73)	0.03
STI	1437	49	3.41	1.62 (1.18 to 2.23)	0.003
Past IDU	3210	54	1.68	1.25 (0.90 to 1.74)	0.18
Current IDU	1384	33	2.38	1.19 (0.78 to 1.80)	0.43

* All estimates are adjusted for numbers of unprotected and protected anal intercourse.

† In the previous 6 months.

‡ Any use (yes vs. no).

§ Heavy use defined as 4 drinks per day or consumed an amount of alcohol equal to >5drinks per occasion (yes vs. no).

|| Self-report of gonorrhea, syphilis, or chlamydia (yes vs. no).

early HAART era (2001–2004) reported similar PCR estimates for unprotected anal intercourse: 1.43% with ejaculation and 0.65% without ejaculation.⁸ A likely explanation for our finding of similar PCR estimates in the pre-HAART and early HAART era is the relatively low proportion of HIV-positive MSM with a suppressed HIV viral load. Based on current estimates, approximately 80% of those with HIV are aware of their infection, but less than 30% have a suppressed HIV viral load.¹⁷ Given the evolution in HIV testing and treatment recommendations, it is likely that rates of HIV viral load suppression were even lower when these cohort studies were conducted.^{18,19}

There are several possible explanations for the finding of higher PCRs among young MSM. One is that younger MSM are less able than older MSM to negotiate safer sex with partners.²⁰ For example, younger MSM may not have the skills or knowledge to navigate other risk reduction strategies with HIV-positive partners (such as withdrawal before ejaculation), which may have a lower HIV risk.⁸ Survivor bias is another possible explanation for our findings. Because all of the participants had to be HIV negative at enrollment, the older MSM were likely able to remain HIV uninfected for longer than the younger MSM, potentially reflecting a reduced average susceptibility to HIV infection.²¹ Furthermore, we did

not measure additional partner characteristics that may have been protective. For example, older MSM may also have older HIV-positive partners who are often engaged in care and have lower HIV viral loads compared with younger HIV-positive MSM.²² Finally, although there is evidence of increased biologic susceptibility for young women, there are no current studies to suggest a biological basis to explain these disparities for young MSM.²³

We also found evidence that Latino MSM had a higher PCR for UIA with HIV seropositive partners, and inconclusive evidence that black MSM and MSM classified as other had a higher PCRs than white MSM for URA and UIA with HIV seropositive partners. If real, partner-level factors may help to explain this disparity.^{4,5,24} Specifically, MSM of color report more assortive mixing by race, and HIV seropositive black MSM are less likely to have suppressed HIV viral load.^{25,26} Nonetheless, the overall rate of HIV viral suppression was likely low in the early HAART era, suggesting that unmeasured partner-level factors, including STIs, may drive these disparities.^{22,27,28} Reporting bias could contribute, but we believe that this is unlikely given the patterns in the total number of partners of each type and mean number of contacts. For this to hold, MSM of color would have to systematically and differentially underreport unprotected contacts

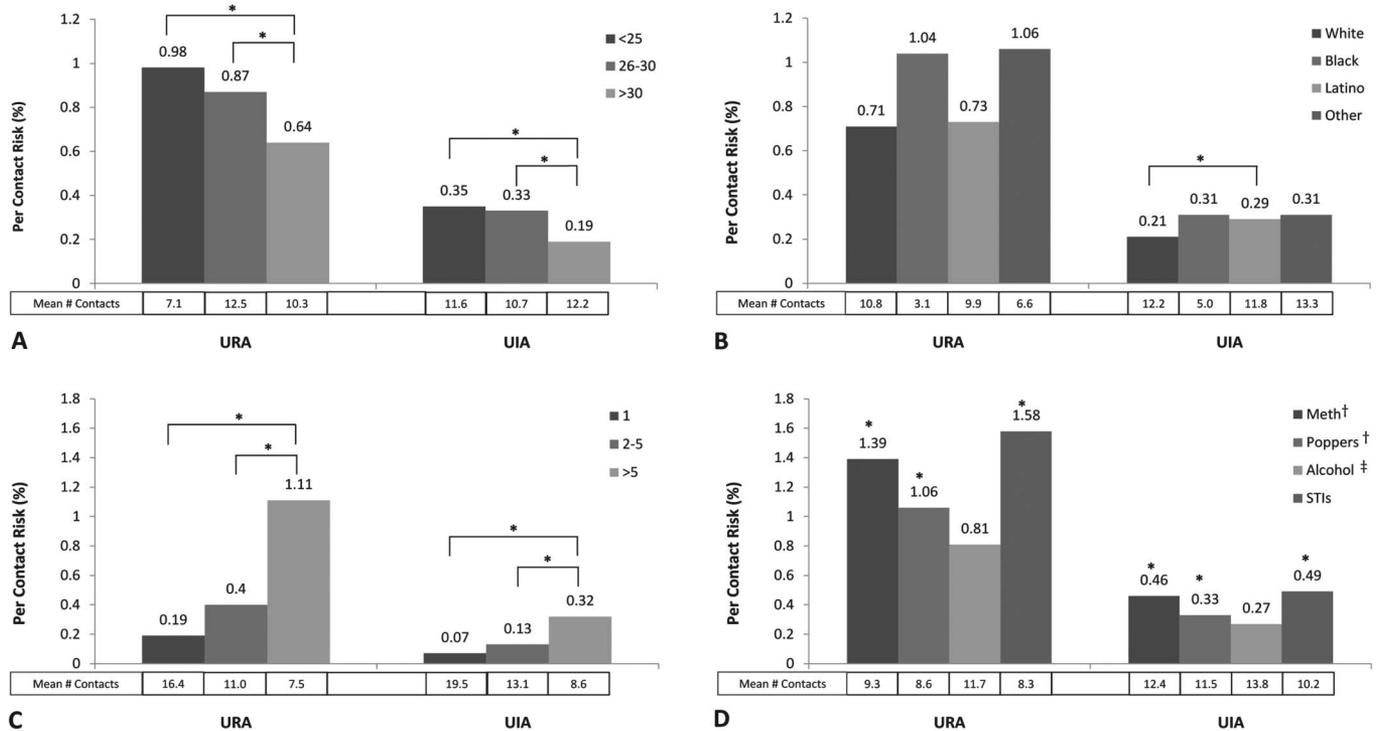


FIGURE 1. PCR of unprotected anal intercourse and mean number of reported contacts with a HIV seropositive partner stratified by age (A), race/ethnicity (B), the number of sexual partners (C), and other risk factors (D). PCR estimates for the controls not reporting the other risk factors in (D) were uniformly lower than for the exposed (data not shown). 95% BCI for difference from reference group excludes 0; †, any use; ‡, heavy use.

with HIV seropositive compared with unknown serostatus or negative partners, which is not supported by the literature.⁵

These data also provide new insight into the increasing risk of HIV acquisition with multiple sexual partners and other risk behaviors. The lower PCR for men reporting URA or UIA with 1 HIV seropositive partner likely reflects 2 factors, both unmeasured: first, viral suppression may be more common among monogamous partners; and second, the likelihood of contact with at least 1 highly infectious partner increases with the number of HIV seropositive partners because of the heterogeneity in infectiousness.²⁹ Furthermore, the use of methamphetamines, poppers, and self-reported STI was also associated with higher PCR. Ulcerative and non-ulcerative STIs are associated with an increased risk through increasing susceptibility through mucosal breakdown and inflammation.³⁰ The PCRs for poppers and methamphetamines are also high, suggesting that they may also increase the susceptibility to HIV infection, although through less well-elucidated mechanisms.

There are several important limitations to this study. The longitudinal cohorts analyzed in this study occurred early in the HAART era and may not be reflective of later changes in HIV treatment. However, the current estimates are that only approximately 27% of MSM in the United States are on HAART and virally suppressed, so even in 2012, the majority of HIV-positive MSM in the United States are not virally suppressed.²² Misclassification bias for HIV seronegative partners in the absence of an HIV disclosure discussion is

also an important consideration. Our PCR estimate analysis focused on the highest risk sexual behavior for HIV transmission, URA, and UIA with HIV-positive partners, to minimize this bias. Despite the large sample size, there were relatively few visits and HIV seroconversions among black MSM compared with other MSM. Many contact- and partner-specific factors that may explain heterogeneity in PCRs were not measured. Finally, although the new models fit the data better than Bernoulli models, they are nonetheless complicated, and we cannot rule out bias in our PCR estimates, including subgroup-specific PCRs and the differences between them.

PCR of HIV seroconversion represents a novel method to evaluate possible explanations for drivers of HIV incidence. We identified higher PCR of HIV seroconversion among younger MSM, some MSM of color and those who reported the use of poppers, methamphetamines, and a history of an STI in the United States, supporting that susceptibility or partner characteristics are important in understanding why these disparities exist. The mechanisms for the increased HIV incidence and the individual and partner characteristics, beyond individual risk behavior, that drive these disparities warrant further exploration.

REFERENCES

1. CDC. *HIV Surveillance Report, 2009*. Department of Health and Human Services; 2011. Accessed July 7, 2012.

2. CDC. Estimated HIV incidence in the United States, 2007-2010. *HIV Surveill Suppl Rep*. 2012;17.
3. Buchbinder SP, Vittinghoff E, Heagerty PJ, et al. Sexual risk, nitrite inhalant use, and lack of circumcision associated with HIV seroconversion in men who have sex with men in the United States. *J Acquir Immune Defic Syndr*. 2005;39:82-89.
4. Millett GA, Flores SA, Peterson JL, et al. Explaining disparities in HIV infection among black and white men who have sex with men: a meta-analysis of HIV risk behaviors. *AIDS*. 2007;21:2083-2091.
5. Millett GA, Peterson JL, Flores SA, et al. Comparisons of disparities and risks of HIV infection in black and other men who have sex with men in Canada, UK, and USA: a meta-analysis. *Lancet*. 2012;380:341-348.
6. Millett GA, Peterson JL, Wolitski RJ, et al. Greater risk for HIV infection of black men who have sex with men: a critical literature review. *Am J Public Health*. 2006;96:1007-1019.
7. Vittinghoff E, Douglas J, Judson F, et al. Per-contact risk of human immunodeficiency virus transmission between male sexual partners. *Am J Epidemiol*. 1999;150:306-311.
8. Jin F, Jansson J, Law M, et al. Per-contact probability of HIV transmission in homosexual men in Sydney in the era of HAART. *AIDS*. 2010;24:907-913.
9. Buchbinder SP, Douglas JM, McKirnan DJ, et al. Feasibility of human immunodeficiency virus vaccine trials in homosexual men in the United States: risk behavior, seroincidence, and willingness to participate. *J Infect Dis*. 1996;174:954-961.
10. Vallabhaneni S, Li X, Vittinghoff E, et al. Seroadaptive practices: association with HIV acquisition among HIV-negative men who have sex with men. *PLoS One*. 2012;7:e45718.
11. Seage GR, Holte SE, Metzger D, et al. Are US populations appropriate for trials of human immunodeficiency virus vaccine? The HIVNET Vaccine Preparedness Study. *Am J Epidemiol*. 2001;153:619-627.
12. Flynn NM, Forthal DN, Harro CD, et al. Placebo-controlled phase 3 trial of a recombinant glycoprotein 120 vaccine to prevent HIV-1 infection. *J Infect Dis*. 2005;191:654-665.
13. Bartholow BN, Goli V, Ackers M, et al. Demographic and behavioral contextual risk groups among men who have sex with men participating in a phase 3 HIV vaccine efficacy trial: implications for HIV prevention and behavioral/biomedical intervention trials. *J Acquir Immune Defic Syndr*. 2006;43:594-602.
14. Koblin B, Chesney M, Coates T, et al. Effects of a behavioural intervention to reduce acquisition of HIV infection among men who have sex with men: the EXPLORE randomised controlled study. *Lancet*. 2004;364:41-50.
15. Wilson DP, Law MG, Grulich AE, et al. Relation between HIV viral load and infectiousness: a model-based analysis. *Lancet*. 2008;372:314-320.
16. Vittinghoff E, Glidden D, Shiboski S, et al. *Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models*. 2nd ed. New York, NY: Springer; 2012.
17. Gardner EM, McLees MP, Steiner JF, et al. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis*. 2011;52:793-800.
18. Dybul M, Fauci AS, Bartlett JG, et al; Panel on Clinical Practices for Treatment of HIV. Guidelines for using antiretroviral agents among HIV-infected adults and adolescents. *Ann Intern Med*. 2002;137(5 pt 2): 381-433.
19. Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents*. Washington D.C.: U.S. Department of Health and Human Services. Available at <http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>. Accessed January 6, 2013.
20. Agwu A, Ellen J. Rising rates of HIV infection among young US men who have sex with men. *Pediatr Infect Dis J*. 2009;28:633-634.
21. Lederman MM, Alter G, Daskalakis DC, et al. Determinants of protection among HIV exposed seronegative persons: an overview. *J Infect Dis*. 2010;202(suppl 3):S333-S338.
22. CDC. *HIV in the United States: The Stages of Care CDC Fact Sheet*. 2012. Available at <http://www.cdc.gov/nchstp/newsroom/docs/2012/Stages-of-careFactSheet-508.pdf>. Accessed January 6, 2013.
23. Yi TJ, Shannon B, Prodder J, et al. Genital immunology and HIV susceptibility in young women. *Am J Reprod Immunol*. 2013;69(suppl 1):74-79.
24. CDC. Disparities in diagnosis of HIV infection between Blacks/African Americans and other racial/ethnic populations—37 States, 2005-2008. *MMWR Morb Mortal Wkly Rep*. 2011;60:93-98.
25. Berry M, Raymond HF, McFarland W. Same race and older partner selection may explain higher HIV prevalence among black men who have sex with men. *AIDS*. 2007;21:2349-2350.
26. Raymond HF, McFarland W. Racial mixing and HIV risk among men who have sex with men. *AIDS Behav*. 2009;13:630-637.
27. Hall HI, Byers RH, Ling Q, et al. Racial/ethnic and age disparities in HIV prevalence and disease progression among men who have sex with men in the United States. *Am J Public Health* 2007;97:1060-1066.
28. Adimora AA, Schoenbach VJ. Social context, sexual networks, and racial disparities in rates of sexually transmitted infections. *J Infect Dis*. 2005;191(suppl 1):S115-S122.
29. Kalichman SC, Eaton L, Cherry C. Sexually transmitted infections and infectiousness beliefs among people living with HIV/AIDS: implications for HIV treatment as prevention. *HIV Med*. 2010;11:502-509.
30. Galvin SR, Cohen MS. The role of sexually transmitted diseases in HIV transmission. *Nat Rev Microbiol*. 2004;2:33-42.