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Sara Herbst Date

No Evidence of Risk Compensation on Pre-Exposure Prophylaxis (PrEP) for HIV Prevention in a Longitudinal Analysis of Men Who Have Sex with Men (MSM) in South Africa

By

Sara E. Herbst
MPH

Global Epidemiology

_____

Aaron J. Siegler, PhD
Committee Chair

_____

Jeb Jones, PhD, MPH, MS
Committee Member

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By

Sara E. Herbst

Bachelor of Arts, Psychology
University of Minnesota – Twin Cities
2011

Thesis Committee Chair: Aaron J. Siegler, PhD

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ABSTRACT

No Evidence of Risk Compensation on Pre-Exposure Prophylaxis (PrEP) for HIV Prevention in a Longitudinal Analysis of Men Who Have Sex with Men (MSM) in South Africa

By Sara E. Herbst

Objective: To assess evidence of changes in sexual risk behavior associated with pre-exposure prophylaxis (PrEP) among a cohort of men who have sex with men (MSM) in South Africa.
Design: This analysis uses data from a longitudinal, prospective cohort pilot study that sought to assess the feasibility of providing a tailored combination HIV prevention package to MSM in South Africa. Conducted in two cities, participants in the pilot were able to initiate PrEP as part of the intervention package at either month 1 or month 4 if clinically and behaviorally eligible.
Methods: Of the 202 MSM prospectively enrolled, 167 were HIV-negative and retained for follow-up. Using computer-assisted self-interview (CASI), sexual risk behaviors were assessed at baseline and post-enrollment at months 3, 6, and 12. We analyzed the longitudinal data to estimate the association between PrEP use and sexual behaviors using logistic regression and Generalized Estimating Equations (GEEs) adjusted for age, income, marital status, and partner's HIV status.
Results: Among all participants during follow-up we observed decreases in reported condomless sex and the total number of sexual partners. Persons who initiated PrEP reported lower levels of unprotected sex relative to those who did not initiate PrEP. A non-significant trend was observed for lower numbers of reported sexual partners for those initiating PrEP. There were no significant differences in baseline characteristics, including sexual behaviors, between groups.
Conclusions: We found no evidence of sexual risk compensation among HIV-negative MSM in South Africa. Instead we found PrEP initiation to be protective against additional risk. In this study that provided PrEP in the context of a comprehensive HIV prevention package with regular HIV/STI testing, counseling, and condom provision, PrEP initiation did not lead to increases in reported sexual risk behavior among MSM. Future studies should consider the impact of combination HIV prevention services on PrEP-related risk compensation.

Key Words: risk compensation, sexual risk behavior, pre-exposure prophylaxis, PrEP, HIV, men who have sex with men, MSM

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INTRODUCTION

Daily antiretroviral pre-exposure prophylaxis for HIV prevention (PrEP) is a highly efficacious and well tolerated biomedical intervention for preventing HIV transmission. HIV disproportionately affects men who have sex with men (MSM), who are at a greater risk of acquiring HIV due to the high biological risk of HIV transmission through unprotected receptive anal sex(1-3), making them a key population for HIV prevention. The 2010 iPrEx study, the first randomized, controlled PrEP efficacy trial among MSM and transgender women, found that daily tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) reduced the rate of HIV transmission by 44%(4). Further open-label extension projects and trials including iPrEx OLE, PROUD, and IPERGAY demonstrated evidence of PrEP effectiveness, and supported the feasibility of PrEP delivery in both high- and low-income settings within existing health systems(5-7).

The Centers for Disease Control and Prevention (CDC) released interim clinical recommendations for prescribing PrEP to individuals at high risk of HIV infection in 2012, formalized those recommendations in 2014, and provided an update in 2017(8). The guidelines indicated individuals at "substantial risk" of HIV infection for PrEP, including MSM not in a monogamous partnership with a known HIV-negative man and having any unprotected (condomless) anal intercourse in the past 6 months, or MSM experiencing any bacterial STI diagnosis in the past 6 months(8).

Despite the overwhelming evidence supporting PrEP for HIV prevention, real-world uptake outside of research settings has been slower than optimal(9). Among a number of established barriers to attaining PrEP prescriptions(10-12), clinician awareness of and willingness to prescribe PrEP has been consistently identified. Some clinicians report hesitations

to prescribe PrEP due to possible risk compensation among individuals on PrEP(13). The theory of risk compensation posits that decreases in an individual's perceived risk may result in increases in their risk behavior(14). Opponents of PrEP suggest that the benefits of PrEP for HIV prevention among treated individuals may be negated by increases in other risk behaviors, such as increased occurrence of condomless sex acts and a greater overall number of sexual partners, due to the decreased perceived risk of HIV transmission while on PrEP(14-16).

Increased incidence of sexually transmitted infections (STIs) among PrEP users may be evidence of risk compensation among PrEP users(17-21). STI incidence rates from PrEP studies are somewhat limited as markers for risk compensation because the increased testing for STIs (recommended quarterly) that accompanies PrEP prescriptions likely will result in increased rates of newly diagnosed STIs. Several recent mathematical modeling studies have found that increased scale-up of PrEP coverage may in fact result in a substantial overall decrease of STIs among MSM as a result of increased testing and treatment as part of the CDC PrEP guidelines(22, 23). There is a growing body of evidence from numerous RCTs and open-label studies indicating that uptake of PrEP does not lead to changes in self-reported sexual risk behavior among PrEP users(4, 24-26).

To assess the association between PrEP use and risk compensation, it is important to monitor behavioral markers such as reported condom use and number of sexual partners, however such studies assessing risk compensation are notoriously difficult to design due to the information bias that accompanies self-report behavioral measures and the statistical power needed to detect differences in risk behaviors among groups. There is a need for carefully designed studies that use longitudinal cohort data to track sexual risk behavior over time in order to obtain valid estimates of potential changes in sexual risk behavior (risk compensation) among

individuals using PrEP for HIV prevention. The Sibanye Health Project, a prospective one-year cohort study of MSM in Cape Town and Port Elizabeth, South Africa, is one such study that can offer valuable insight into risk compensation among MSM initiating PrEP in sub-Saharan Africa.

METHODS

Study Design and Procedures

Data were collected between February 2015 and September 2016 for the Sibanye Health Project, one of a number of NIH-funded Methods for Prevention Packages Program (MP3) grants(27). Sibanye was a prospective longitudinal cohort study of men who have sex with men (MSM) and transgender women in South Africa and was a single-arm intervention pilot study with no control group. This study was designed to demonstrate feasibility, acceptability, and uptake of a combination package of HIV prevention services to include biomedical, behavioral, and community-level interventions and services for this population.

The Sibanye intervention included provision of an assortment of condom and lubricant choices, risk reduction counseling, couples voluntary counseling and testing (CVCT), individual HIV testing and counseling, STI screening and treatment, linkage to care services for persons living with HIV (PLHIV), PrEP with TDF/FTC for eligible participants, and post-exposure prophylaxis (PEP) for HIV-negative participants with a high-risk exposure to HIV. Apart from mandatory HIV/STI screening, all participants could choose which of these services they utilized. Community-level interventions provided as part of the intervention included health care provider training on the delivery of lesbian, gay, bisexual, and transgender (LGBT)-specific services, LGBT sensitization training, and MSM and transgender community efforts to improve health literacy and uptake of services.

The study protocol and procedures have been previously published(27). In brief, participants were recruited from community events, venues known to be frequented by MSM and transgender women, online social networks, and referrals from existing participants. Study visits included a baseline visit and 3-, 6-, and 12-month follow-up visits after enrollment. A computer-assisted self-interview (CASI) survey was completed by participants at baseline and each subsequent study visit to assess demographics and behavioral characteristics. A clinical exam and biological testing for HIV was conducted for all participants at baseline and all follow-up visits; screening for sexually transmitted infections (STIs) was conducted at baseline, 6-, and 12-month visits. PrEP eligibility screenings were conducted at both the baseline and the 3-month study visit. An additional monitoring visit with laboratory tests for kidney function occurred 1 month after PrEP initiation, and standard PrEP monitoring occurred every 3 months thereafter(8). All study procedures were approved by Emory and South African Institutional Review Boards and informed consent was obtained from all study participants.

Study Population

The study enrolled 292 participants at four study sites in South Africa: the Desmond Tutu HIV Foundation in Cape Town (N=115), and three public health clinics in Port Elizabeth (N=177). All participants were assigned male at birth, were 18 years of age or older (mean age of 26 years), had self-reported anal intercourse with a man in the past year, and were a current resident of Port Elizabeth or Cape Town. Of the 292 enrolled participants, 167 (57%) were HIV-negative at baseline and all were followed prospectively. Of the 125 participants who were HIV-positive at baseline, 34 were followed prospectively to allow for a maximum of 20% HIV-positive participants per site in the prospective cohort. The remaining 91 participants were

referred to care but not followed prospectively and stopped after their baseline visits. Further demographic description of the study population has been published elsewhere(27). For the purposes of analyses for this manuscript, the study population was restricted to only those participants who were HIV-negative at baseline (N=167). None of the HIV-negative participants were on PrEP at baseline. All 167 participants completed the baseline visit, 156 (93%) completed the 3-month follow-up, 150 (90%) completed the 6-month follow-up, and 145 (87%) completed the 12-month follow-up. There was no significant difference in levels of retention by study site.

Measures

Sexual Risk Behavior

Behavioral surveys conducted at each study visit collected information on demographics, history of HIV and STI testing, alcohol and substance use, history of sexual activity and recent sexual activity, and condom and lubricant use. At baseline, participants were asked about the number of male, female, and transgender sexual partners both over the past 12 months and past 3 months, as well as frequency of condom use with their male, female, and transgender partners and if they had any condomless anal or vaginal sex with any partners. At each follow-up visit, participants were asked about recent sexual activity with male, female, and transgender partners, to include number of partners, consistency of condom use, and condomless sex acts with any partners since the previous study visit. Participants were able to report detailed partner-level data for up to 4 sexual partnerships at each visit, including partner's HIV status if known, sexual activity, and condom use within each partnership.

One outcome variable used in the present analysis was dichotomized condomless sex at each time point. If a participant reported any condomless sex on either the participant-level or

partner-level questionnaire, they were coded as having had condomless sex during that time period. This included reporting no condom use or inconsistent condom use. Dichotomizing the complex variable of condom usage over a given period into any condomless sex is a common way to determine sexual risk in studies of sexual risk behavior(25, 26), and aligns with CDC guidelines for determining PrEP eligibility(8).

The second outcome variable of total number of sex partners was dichotomized as 0-2 partners or more than 2 partners at each time point. At baseline and each follow-up visit, participants were asked separate questions about how many male partners, female partners, and transgender partners they had in the last three months (baseline) or since the previous study visit (months 3, 6, and 12). The outcome of total number of sex partners at each study visit was assessed using the participant-level data because partner-level data was limited to a maximum of 4 partnerships. The outcome variable of total number of partners was derived as the sum of the participants' self-reported number of male, female, and transgender partners, then dichotomized as discussed above. At baseline, we used the variables corresponding to the number of partners over the three months prior to enrollment to provide the most consistent reporting period from baseline through 12-month follow-up.

For analyses, both outcome variables were dichotomized due to significant missing data for more nuanced sexual behavior data at follow-up assessment periods. Utilizing dichotomized outcome variables provided the most stable estimates of association.

PrEP Use

Optional PrEP with TDF/FTC was made available as part of the comprehensive HIV prevention package to all participants who met clinical and behavioral PrEP eligibility criteria at

their screening visit. Participants who were PrEP eligible and interested were allowed to initiate treatment 1 month after study enrollment; participants who were uninterested or ineligible based on behavioral criteria at baseline but whose interest or risk profile changed throughout the first three months were allowed to initiate PrEP at the subsequent study visit, month 4. Participants who initiated PrEP were able to discontinue and re-start PrEP treatment throughout the study period, either by personal choice or as instructed by the study physician. Continued PrEP eligibility was assessed throughout the 12-month follow-up period.

For this analysis, PrEP coverage was dichotomous and measured at baseline and months 3, 6, and 12. Current literature suggests that PrEP taken 4 days per week for men is as effective in preventing HIV infection as daily PrEP(28), thus participants were considered to be PrEP-covered over any given follow-up period if they were on PrEP for at least 4/7 of the total number of days between corresponding study visits. 10 of the 82 participants who initiated PrEP discontinued use before reaching this threshold for being effectively PrEP-covered during any follow-up period and were considered not PrEP-covered in analysis.

Statistical Analysis

We used the following primary outcome measures to assess changes in sexual risk behavior over the study period: any condomless anal or vaginal sex, and number of sexual partners (dichotomous, 0-2 sexual partners and >2 sexual partners). Exposure (PrEP coverage during each follow-up period) was coded as a dichotomous variable (PrEP covered and not PrEP covered) and was assessed at each follow-up visit based on the recorded start and stop dates of PrEP, without regard to self-reported adherence or measured TDF/FTC blood levels.

We fit logistic regression models for outcomes of any condomless sex and number of sex partners. All models were fit using generalized estimating equations (GEE) for repeated measures with an exchangeable working correlation structure and robust standard errors to account for correlation within subjects. Data was analyzed in long format, and GEE models used the variable for PrEP coverage at each time point to estimate the associations between the primary outcomes of interest and PrEP coverage. Participants were excluded from final analysis if they did not have at least one follow-up visit at which exposure status and sexual risk behavior outcome data were collected. Participants with incident HIV infection were excluded from analysis after the visit at which they were diagnosed with HIV.

Participant age, race, marital status, alcohol and substance use, education level, income, and partner's HIV status were identified as possible covariates of interest based on literature review and a directed-acyclic graph (DAG, Figure 1). Bivariate analyses did not show any significant associations ($p < 0.05$) between these covariates and PrEP coverage or either outcome of interest, however this is not surprising given the small size of the study population. To assess whether the association between PrEP use and unprotected sex or number of sexual partners was modified by time or partner's HIV status, we tested for interactions between these variables and PrEP coverage. No evidence of effect modification was found for either interaction term. Age (continuous), partner's HIV status (dichotomous, 1=any *HIV*-positive partner or any partner of unknown status, 0=all partners known to be HIV-negative), marital status (dichotomous) and income (trichotomous, coded as in Table 1) were kept in the final models as they comprise the minimally-sufficient set to control for confounding based on the DAG in Figure 1. Race was not included in the final models due to adequate control for confounding by other covariates and a lack of variation in race in the analytic sample. A *P* value of <0.05 was considered statistically

significant, and no adjustments were made for multiple comparisons. All analyses were performed in SAS 9.4.

RESULTS

Participant Characteristics

Among 156 participants with at least one follow-up assessment after baseline, all were born male and 14 (8.4%) identified as female or transgender women. The mean age of participants was 25 years (range 18-46) at baseline. More than three-quarters of participants identified as Black African, 15.8% identified as Coloured, and the remaining identified as White. The majority of all participants (95.1%) were not married. There were no significant differences in baseline characteristics between individuals ever experiencing a PrEP coverage period and those without any PrEP coverage periods. Table 1 shows the demographic characteristics of all participants included in the analytic sample. Table 2 shows sexual health and risk behavior of the analytic sample at baseline by PrEP group; no statistically significant associations were observed between PrEP users and nonusers. Overall study retention was high, with 14% lost to follow-up (LTFU) by month 12.

Incident HIV Infection

Among the 167 PrEP-eligible participants, 9 (5%) had incident HIV infection during follow-up: one at month 3, two at month 6, and six at month 12. Four of the nine incident HIV infections were among participants who were not PrEP covered at any time point (incidence rate = 5.9 infections per 100 person-years), while five HIV infections occurred among participants who were PrEP-covered at any point during the study period (incidence rate = 6.7 infections per 100 person-years). Of the five PrEP-covered participants with incident HIV infection, four had

no free tenofovir in their blood at seroconversion. This group also had either a self-reported physician initiated PrEP stop or had not picked up PrEP medication prior to incident HIV diagnosis. One PrEP-covered participant with incident HIV infection had detectable tenofovir levels consistent with recent PrEP use at seroconversion, but had a poor history of self-reported adherence. There was no evidence of drug resistance to TDF/FTC among the PrEP-covered participants with incident HIV infection.

PrEP Use & Sexual Risk Behavior

Of the 167 PrEP-eligible participants, 82 chose to initiate PrEP treatment at baseline or 3-month follow-up periods; of the 82 participants who initiated PrEP, 72 were considered to be "PrEP-covered" during at least one follow-up period. Overall, instances of condomless sex declined over the study period; 104 (62.3%) participants reported any condomless anal or vaginal sex in the past 12 months at baseline, 47 (28.1%) reported any condomless sex at the month 3 assessment, 41 (24.6%) reported any condomless sex at month 6, and 35 (21.0%) reported any condomless sex at month 12. The 167 participants reported a total of 895 male, female, and transgender sexual partnerships from baseline to 12-month follow-up. At baseline, participants reported a mean of 2.4 sexual partners in the past 3 months (SD=2.8), with the mean number of partners in the overall analytic sample decreasing at each subsequent time point.

Before controlling for confounding, repeated measures models identified that participants who were PrEP-covered had a 56% lower risk of reporting any condomless sex compared to those who were not PrEP-covered (Table 3, RR=0.44, 95% CI: 0.30 to 0.64). Adjusting for partner's HIV status, yearly income, marital status, and age did not substantially change this estimate (aRR=0.39, 95% CI: 0.25 to 0.62). The unadjusted model found that PrEP use was not

statistically significantly associated with a change in risk for having more than two sexual partners compared to participants who were not PrEP-covered (Table 3, RR=0.68, 95% CI: 0.38 to 1.20). Multivariable models adjusting for partner's HIV status, yearly income, marital status, and age also showed no significant association in the risk of having more than two sexual partners between PrEP-covered and non-PrEP-covered participants (aRR=0.66, 95% CI: 0.33 to 1.34).

DISCUSSION

The Sibanye Health Project was one of the earliest longitudinal cohort studies that focused on MSM and transgender women in South Africa. This study of a comprehensive HIV prevention package found no evidence of risk compensation among at-risk MSM on pre-exposure prophylaxis over a 12-month follow-up period. Of particular interest, PrEP use was found to have a strong protective effect on any condomless sex in our analyses, demonstrating that PrEP-covered participants had lower levels of condomless sex. The association between PrEP use and participants' number of sexual partners was not statistically significant, however a similar trend in the protective effect of PrEP was found. Furthermore, there was no increase in either risk behavior after PrEP initiation.

Though the existing literature surrounding risk compensation on PrEP is mixed, there is a growing body of evidence with no indication of risk compensation among MSM on PrEP. The findings of this analysis are consistent with studies showing that PrEP may in fact have a protective effect on sexual risk behaviors over time(4, 5, 24-26). These findings differ from those in other longitudinal RCT settings, likely due to different measures and cultural context. As part of the study design, all MSM and transgender women in this study received the HIV prevention package of risk-reduction counseling, condoms, lubricants, PrEP provision, and regular HIV and

STI testing and treatment. Participants who initiated PrEP treatment during this study had more frequent interactions with culturally competent health practitioners, risk-reduction counseling, and more consistent access to a variety of condoms and lubricants from the study sites. These factors may partially explain the observed decrease in sexual risk behaviors over the study period, and may help mitigate any risk compensation among individuals who initiate PrEP.

This study has several strengths. Overall, retention was high and we identified no significant differences in retention by participants who were on PrEP during the study period and those who were not. Our non-experimental, longitudinal study design and analysis allowed us to estimate the real-world effect of PrEP on sexual risk behavior over time, which may be more generalizable than results from carefully controlled clinical trials. There were no baseline differences in sexual risk behavior or demographics between groups, thus minimizing the potential effects of confounding on our results. Our findings were unlikely to be due to chance given the large effect size we identified (aRR=0.39 and aRR=0.66).

We note a number of limitations for this study. First, we were unable to look at more detailed measures of risk behavior due to the small sample size and missing data. The study had insufficient power to examine differences in biomarkers of sexual risk, such as STI incidence. Because our sexual risk behavior measures were self-reported and participants on PrEP had increased interaction with health providers, our results may be subject to social desirability bias. It is possible that participants on PrEP could have reported a change in sexual behaviors without an actual change, though this bias was likely mitigated through the use of computer self-administered surveys. There were some inconsistencies between participant- and partner-level data in the total number of sexual partners, which may have led to misclassification of the outcome, though this misclassification was likely non-differential and would have biased our

result towards the null. Finally, because this pilot study was conducted in only two cities in South Africa (Cape Town and Port Elizabeth) and the majority of participants were Black South Africans, results may not be generalizable outside this population.

We found no evidence of risk compensation among MSM benefiting from PrEP coverage for HIV prevention. Rather than an increase in sexual risk behavior, we found that taking PrEP in the context of comprehensive care may be protective against increased sexual risk. More frequent clinic visits, increased access to free condoms and lubricants, and HIV/STI testing and counseling with clinicians trained in LGBTQ service provision may motivate at-risk individuals to practice safer sexual behaviors, even after initiating PrEP. It is important for programs to continue offering comprehensive prevention approaches for HIV prevention, and future research should explore the impact of comprehensive services on outcomes relating to PrEP care.

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TABLES

Table 1. Baseline demographics of all HIV-negative participants by PrEP treatment group*

	All participants (n=167)	**Ever PrEP Covered[a] (n=72)**	**Never PrEP Covered (n=95)**	
	n (%)	n (%)	n (%)	*P*
Age group, years				0.90
18-24	103 (61.7)	44 (61.1)	59 (62.1)	
≥ 25	64 (38.3)	28 (38.9)	36 (37.9)	
Gender identity				0.09
Male	153 (91.6)	69 (95.8)	84 (88.4)	
Other[b]	14 (8.4)	3 (4.2)	11 (11.6)	
Sexual identity				0.89
Gay	87 (52.1)	39 (54.2)	48 (50.5)	
Bisexual	61 (36.5)	25 (34.7)	36 (37.9)	
Other[c]	19 (11.4)	8 (11.1)	11 (11.6)	
Relationship status				0.26
Not married	154 (95.1)	65 (92.9)	89 (96.7)	
Married to a man or woman	8 (4.9)	5 (7.1)	3 (3.3)	
Race				0.36
Black African	135 (81.8)	55 (78.6)	80 (84.2)	
Coloured	26 (15.8)	12 (17.1)	14 (14.7)	
White	4 (2.4)	3 (4.3)	1 (1.1)	
Education level				0.11
Did not finish secondary	85 (50.9)	30 (41.7)	55 (57.9)	
Completed secondary	58 (34.7)	29 (40.3)	29 (20.5)	
Tertiary	24 (14.4)	13 (18.1)	11 (11.6)	
Annual income				0.40
None	91 (54.5)	35 (48.6)	56 (59.0)	
R1-R4,800	38 (22.8)	19 (26.4)	19 (20.0)	
>R4,800	38 (22.8)	18 (25.0)	20 (21.1)	

*Ns may not add up to column totals because of missing data on participant characteristics

[a]Includes participants who were on PrEP for at least 4/7th of any given follow-up period

[b]Includes participants who self-identify as female or transgender

[c]Includes participants who answered heterosexual or other

Table 2. Baseline sexual health related behavior characteristics among HIV-negative participants by PrEP treatment group*

	All participants (n=167)	Ever PrEP Covered[a] (n=72)	Never PrEP Covered (n=95)	
	n (%)	n (%)	n (%)	*P*
Sexual Risk Behaviors				
Any UAI[b] with a male partner, past 12 months				0.98
Yes	67 (48.2)	29 (48.3)	38 (48.1)	
No	72 (51.8)	31 (51.7)	41 (51.9)	
Number of male sex partners, past 12 months				0.09
0-2	111 (67.3)	42 (60.0)	69 (72.6)	
> 2	54 (32.7)	28 (40.0)	26 (27.4)	
Partner HIV status[c]				0.09
HIV+	5 (3.1)	0 (0.0)	5 (5.3)	
HIV-	40 (24.5)	20 (29.0)	20 (21.3)	
Unknown	118 (72.4)	49 (71.0)	69 (73.4)	
Transactional sex past 12 months				0.83
Yes	29 (19.2)	13 (20.0)	16 (18.6)	
No	122 (80.8)	52 (80.0)	70 (81.4)	
Sexual Health				
HIV test within past year				0.07
Yes	103 (61.7)	50 (69.4)	53 (55.8)	
No	64 (38.3)	22 (30.6)	42 (44.2)	
Any STI diagnoses[d], past 12 months				0.55
Yes	63 (37.7)	29 (40.3)	34 (35.8)	
No	104 (62.3)	43 (59.7)	61 (64.2)	
Substance Use				
Binge drinking 5+ days, past 30 days				0.31
Yes	27 (17.7)	14 (21.2)	13 (85.1)	
No	126 (82.4)	52 (78.8)	74 (14.9)	
Any drug use, past 6 months				0.59
Yes	57 (34.3)	26 (36.6)	31 (32.6)	
No	109 (65.7)	45 (63.4)	64 (67.4)	
Any cocaine or crack cocaine use, past 6 months				0.78
Yes	3 (2.0)	1 (1.6)	2 (2.3)	

No	148 (98.0)	61 (98.4)	87 (97.7)	
Any methamphetamine use, past 6 months				0.52
Yes	18 (11.5)	9 (13.4)	9 (10.1)	
No	138 (88.5)	58 (86.6)	80 (89.9)	
Injection drug use, past 6 months				0.65
Yes	5 (3.0)	3 (4.2)	2 (2.1)	
No	161 (97.0)	68 (95.8)	93 (97.9)	

*Ns may not add up to column totals because of missing data on participant characteristics.

[a]Includes participants who were on PrEP for at least 4/7th of any given follow-up period

[b]UAI=unprotected anal intercourse

[c]Partner HIV status was participant reported, if known, and is a combined status covering all reported partners at baseline

[d]STI diagnoses includes rectal and urinary gonorrhea, chlamydia, herpes, and syphilis

Table 3. Logistic regressions of unprotected sex and number of sex partners on PrEP use among HIV-negative, PrEP-eligible participants

Outcome	**RR (95% CI)**	***P***
Adjusted models[a]		
Any unprotected sex	0.39 (0.25 to 0.62)	<0.0001
Number of partners[b]	0.66 (0.33 to 1.34)	0.249
Unadjusted models		
Any unprotected sex	0.44 (0.30 to 0.64)	<0.0001
Number of partners	0.68 (0.38 to 1.20)	0.182

[a]Models are adjusted for partner's HIV status (any positive partner or status-unknown partner), income, marital status, and age

[b]Number of partners was dichotomized at 0-2 and greater than 2 partners based on univariate distribution of the data

FIGURES

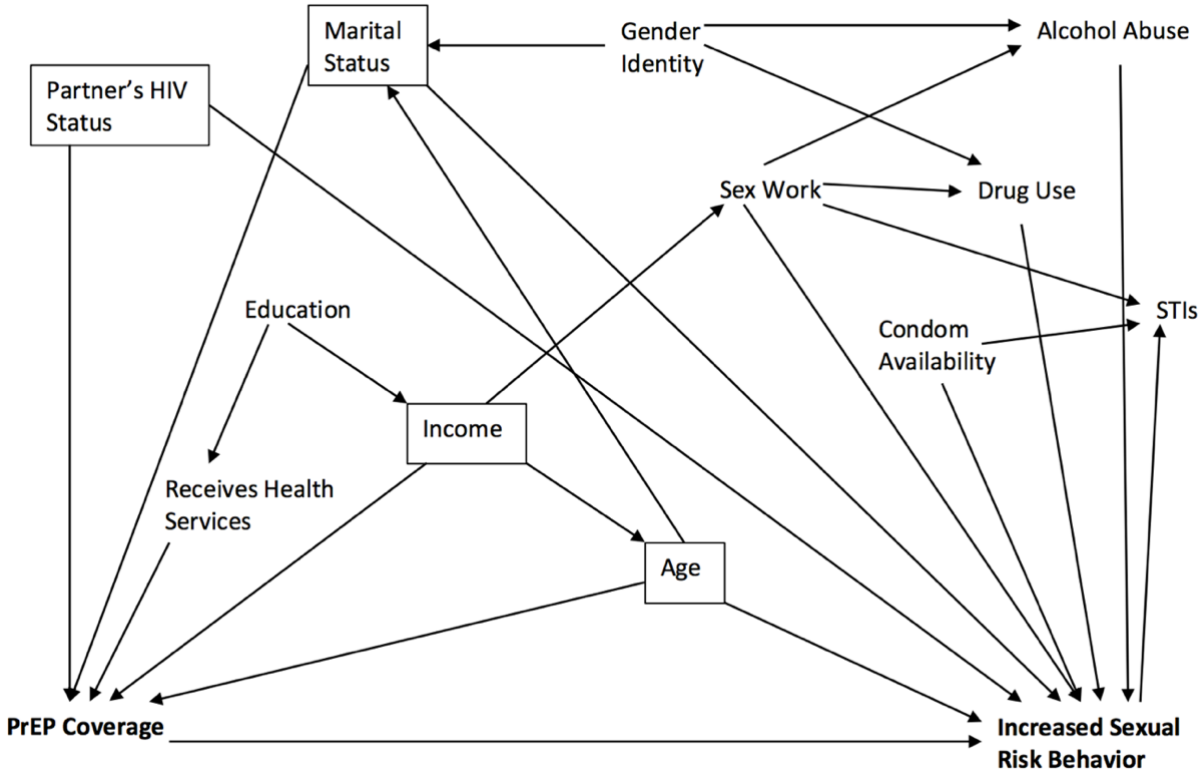

Figure 1. Directed acyclic graph to examine the relationship of potential covariates between exposure (PrEP coverage) and outcome (increased sexual risk behavior).