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Does HIV Pre-Exposure Prophylaxis Modify the Effect of Partnership Characteristics on Condom Use? A Cross-Sectional Study of Sexual Partnerships Among Men Who Have Sex with Men in San Francisco, California

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Abstract

Increasing rates of sexually transmitted infections (STIs) in the United States among men who have sex with men (MSM) have raised concerns that pre-exposure prophylaxis (PrEP) has been associated with higher engagement in condomless anal intercourse (CAI). While partnership characteristics have previously been found to influence condom use, the extent to which PrEP use may modify their effect on CAI remains unknown. A secondary analysis of 535 sexual partnerships from a cross-sectional study in San Francisco was conducted to evaluate interactions between PrEP use and partnership characteristics on CAI. Bivariate and multivariate generalized estimating equation (GEE) logistic regression models were used to estimate relative measures of association, adjusted for confounding by seroconcordance and partnership type, as well as account for repeated partnerships per respondent. Partnerships where both partners used biomedical prevention had significantly greater odds of CAI [odds ratio (OR) = 5.19, 95% confidence interval (CI): 2.27–11.9] compared to those where only one partner used biomedical prevention, while those where neither partner used biomedical prevention had significantly lower odds of CAI (OR = 0.61, 95% CI: 0.40–0.93). There was no significant association between meeting place (online vs. offline) and sexual risk taking (OR = 1.03, $p = 0.894$). Having one partner disclose their HIV status (compared to neither partner having disclosed) was associated with significantly higher odds of CAI among partnerships of PrEP-using MSM [adjusted OR (aOR) = 5.28, 95% CI: 1.91–14.61], while the association was not significant among the partnerships of non-PrEP-using MSM (aOR = 1.29, 95% CI: 0.75–2.21). Differences in condom use among MSM using PrEP may not be well explained by differences in the effect of partnership characteristics. MSM using PrEP appear to commonly practice biomedical matching and high engagement in CAI with other biomedical prevention users, which could indicate relatively concentrated sexual networks and partly explain their disproportionate risk for STIs. Future studies should further investigate biomedical matching to develop interventions that further promote the sexual health of those using PrEP.

Keywords: pre-exposure prophylaxis, HIV/AIDS, MSM, prevention, condom use, sexual behavior

Introduction

HIV INFECTION REMAINS a concentrated epidemic, disproportionately affecting men who have sex with men (MSM) in the United States.¹ In San Francisco, 72% of the new HIV infections in 2015 occurred among MSM.² However, recent biomedical discoveries have led to promising new HIV prevention strategies, such as treatment as pre-

vention (TasP) and pre-exposure prophylaxis (PrEP), ushering in the biomedical HIV prevention era.³

This new era has coincided with increasing rates of sexually transmitted infections (primarily chlamydia, gonorrhea, and syphilis) and a decreasing trend in condom use among MSM.^{4,5} These trends have raised concerns that risk compensation may lead to increased sexual risk taking, such as condomless sex, among PrEP users and their partners, owing

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to the perceived reduction in risk afforded by PrEP.⁶ A recent systematic review and meta-analysis of 17 recent longitudinal studies of PrEP found that PrEP has been associated with both an increased risk for sexually transmitted infections (STIs) and condomless sex among MSM, further highlighting the need for an improved understanding of decreased condom use as a result of risk compensation.⁷

Condom use among MSM is a complex behavior affected by converging individual, social, and partnership characteristics.^{8,9} While the majority of research continues to focus on differences between individuals to explain sexual risk taking,¹⁰ a growing body of research suggests that a significant proportion of the variability in condom use during anal intercourse exists within individuals across different sexual partnerships.^{11–24} Within the sexual partnerships of MSM, the strongest associations between condom use and partnership characteristics have been observed based on partnership type and agreement of serostatus between partners (seroconcordance). Mathematical models based on data from five US cities during the 2003–2005 cycle of the National HIV Behavioral Surveillance (NHBS) System suggested that 68% of HIV transmissions among MSM occurred within main partnerships, as a result of the higher number of sex acts and lower condom use during anal sex with main partners compared to casual or exchange partners (i.e., those where money and/or other gifts were exchanged for sex).²⁵ Seroconcordant partnerships, in which sexual partners share the same HIV status, have been similarly found to be associated with a higher likelihood of condomless anal intercourse (CAI).^{13,16,17,24} Self-reported serodiscussion, or the mutual discussion of HIV status between sexual partners, has also been independently associated with greater engagement in CAI.^{18–20} In addition, the rising popularity of geosocial networking apps has raised concerns about increased sexual risk taking among MSM who meet partners online, yet the evidence remains inconclusive as to whether online-initiated partnerships have a higher likelihood of CAI compared to offline-initiated partnerships.^{21–23}

Specific to MSM using PrEP, recent preliminary qualitative evidence has suggested that partnership characteristics are also influential in their decision to engage in CAI, and that the role of these characteristics in modifying risk behaviors among PrEP users may be distinct from MSM not using PrEP.^{26,27} For example, recent observational evidence has suggested that a new partnership characteristic, coined “biomed matching,” has emerged in the biomedical HIV prevention era. Biomed matching refers to partnerships in which MSM are more likely to engage in CAI when both partners are currently utilizing biomedical prevention (either using PrEP or having an undetectable viral load).²⁸

Among randomized clinical trials, concerns about risk compensation and longitudinal reductions in condom use following PrEP initiation were not substantiated.^{29–31} However, the generalizability of these early clinical trials is rather limited and may not be reflective of the more general experience of PrEP use by MSM today. For example, biomed matching would not have been possible to detect within the context of the initial clinical trials of PrEP when its use by MSM was rare and participants were blinded to their treatment assignment. Such limitations highlight the need for additional observational research into how PrEP may be changing the sexual behaviors of MSM as its use becomes more widespread.

Since licensure by the Food and Drug Administration in 2012, San Francisco has widely promoted PrEP among MSM to support the city’s Getting to Zero initiative and to meet the UNAIDS target of zero new HIV infections by 2020.^{32,33} Thus, the increasing popularity of PrEP among MSM in San Francisco provides an early opportunity to assess how this novel prevention method may be affecting condom use in a more generalizable population of MSM outside of randomized clinical trial settings. Given the concerns of a decreasing trend in condom use and increasing rates of STIs among MSM in San Francisco, an improved understanding of how PrEP use interacts with partnership characteristics to influence condom use is vital to understanding the behavioral mechanisms behind risk compensation. Further understanding the potentially unique aspects of the sexual networks of PrEP users may help explain the dynamics driving ongoing STI transmission in the context of widespread biomedical prevention use and inform effective strategies for further promoting the sexual health of MSM.

Thus, the primary purpose of this analysis was to assess if PrEP use (by the respondent or at the individual level) modifies the effect of partnership characteristics on odds of CAI among the sexual partnerships of MSM. In addition, we sought to assess whether biomed matching was occurring within our sample and if it was associated with greater engagement in CAI. We hypothesized that PrEP use would reduce the magnitude of previously reported associations between partnership characteristics and CAI, except for biomedical matching, which would be amplified among PrEP users.

Methods

This secondary data-analysis used data from the SEEDS study conducted from March 2015 to July 2017 in San Francisco, CA. SEEDS was a cross-sectional study that utilized respondent-driven sampling to assess alcohol use patterns and correlates of hazardous use in a diverse sample of alcohol-using MSM.³⁴ Participation involved completing a 30-min survey through audio computer-assisted self-interview (ACASI). Ultimately, the study recruited 252 participants meeting the following inclusion criteria: (1) used alcohol at least once in the past year, (2) had sex with men, (3) were at least 18 years of age, (4) resided in the San Francisco Bay Area, and (5) had been assigned male sex at birth and/or identified as male. All study procedures were reviewed and approved by the UCSF Institutional Review Board (IRB approval number 14-14481).

Exposure measures

The SEEDS study’s survey instrument assessed sexual risk behaviors and partnership-level characteristics by asking questions pertaining to respondents’ three most recent male sexual partners in the past 6 months. For each sexual partner, respondents were asked the number of anal intercourse events in the past 6 months, of those, how many were condomless, the HIV status of their sexual partner, where they met the sexual partner, if they and their partner had each disclosed their HIV status, the type of relationship, and if their partner had disclosed PrEP use or an undetectable viral load.

Partnership type was classified as either being a main or casual partnership. Main partnerships were those where

participants identified their sexual partner as a “boyfriend, primary partner, or spouse” or “an ex-boyfriend or former partner.” Casual partnerships included any partner described as “a fuck buddy,” “one night stand,” “anonymous encounter,” “a person I pay or who pays me for sex or sex play” or “Other.”

Participants were asked where they had first met each sexual partner, which originally included 12 specific categories of meeting places. These were collapsed into online (“Internet, phone app, social networking site”) and offline (bars, nightclubs, sex clubs, gyms, introduced by friends, restaurants, work/school, etc.) meeting venues to avoid over parameterization and ensure adequate sample sizes.

Concordance variables were created for HIV status, biomed matching, and serodiscussion to be indicative of whether both, neither, or only one of the partners had the characteristic of interest within the sexual partnership. HIV statuses of each study participant (“respondent”) and their reported partners were used to categorize sexual partnerships as seroconcordant (positive), seroconcordant (negative), or serodiscordant (in either direction). The partnerships of respondents who reported their sexual partner’s HIV status as “Unknown” were presumed to be serodiscordant as done in previous studies.^{13,24} Similarly, a biomed matching concordance variable was built, which categorized sexual partnerships as concordant (neither used biomedical prevention), concordant (both partners used biomedical prevention), or discordant (only one partner biomedical prevention). Both having an undetectable viral load for HIV-positive persons and using PrEP for HIV-negative persons were considered biomedical prevention methods. HIV-positive participants self-reported the results of their last plasma HIV RNA level (or viral load) during the survey, which was then transformed into a categorical variable to be indicative of viral suppression as defined as 50 or fewer copies per milliliter. Participants were asked if their sexual partners were virally suppressed or had an undetectable viral load to the best of their knowledge. Finally, a serodiscussion concordance variable was created with three categories to indicate whether both sexual partners had disclosed their HIV status (serodiscussion concordant), only one partner had disclosed (serodiscussion discordant), or neither partner had disclosed (non-serodiscussion concordant).

Current use of PrEP by respondents was assessed using the question, “Are you currently taking pre-exposure prophylaxis, also known as PrEP or Truvada?”

Outcome measures

The outcome of interest for this analysis was CAI, measured by asking participants how many condomless insertive and receptive anal sex events they had with each respective sexual partner. A binary variable for CAI was created for each reported partnership, indicating at least one act of either receptive or insertive CAI within the partnership. CAI was dichotomized to characterize partnerships with potential for the transmission of STIs.

Statistical analyses

Bivariate associations between each partnership-level characteristic (seroconcordance, partnership type, meeting place, serodiscussion, and biomed matching) and CAI were

estimated using generalized estimating equation logistic regressions, accounting for repeated partnerships reported by an MSM respondent using an exchangeable working covariance matrix. Analogous methods were used to estimate partially adjusted associations between each partnership characteristic and CAI, including an interaction term for PrEP use by the respondent. Finally, a multivariable model for each relationship characteristic was constructed, which additionally adjusted for seroconcordance and partnership type, motivated by the strong associations of these partnership characteristics with condom use among MSM previously reported in the literature.^{13,15–17,25} Interaction terms were considered statistically significant using an alpha level of 0.05.

Results

Descriptive characteristics of sexual partnerships

Our original dataset contained 602 partnerships nested within 241 respondent MSM; however, after removal of all partnerships missing any of the variables used in this secondary analysis ($n=67$), we were left with 535 partnerships nested within 227 respondent MSM. Among the 67 excluded partnerships, the missing variable(s) were as follows: 18 (26.9%) for seroconcordance, 22 (32.8%) for partnership type, 24 (35.8%) for meeting place, 27 (40.3%) for serodiscussion, and 28 (41.8%) for biomed matching. Of the 227 respondent MSM included in this analysis, 141 (62.1%) contributed 3 sexual partnerships, 38 (16.7%) contributed 2 partnerships, and 48 (21.2%) contributed only 1 partnership toward our analysis.

Of the 535 sexual partnerships included in this analysis, 116 (21.7%) were reported by PrEP-using MSM respondents. The majority of sexual partnerships reported by PrEP-using MSM were concordantly HIV negative (67.2%), casual (85.3%), had met offline (56.9%), had both engaged in serodiscussion (65.5%), and had engaged in at least one episode of CAI in the past 6 months (74.1%). The majority of sexual partnerships reported by non-PrEP-using MSM were similarly HIV-negative concordant (41.5%), casual (80.2%), had met offline (76.1%), had both engaged in serodiscussion (51.3%), and had engaged in at least one episode of CAI in the past 6 months (55.4%). Conversely, the slight majority of sexual partnerships of PrEP-using respondents were discordant in their biomedical prevention use (50.9%), while those reported by non-PrEP-using respondents were primarily concordant in their nonuse of biomedical prevention (73.8%). Descriptive statistics of the sexual partnerships stratified by PrEP-use (by respondent MSM) are presented in Table 1.

In unadjusted analyses, CAI was significantly associated with seroconcordance, partnership type, serodiscussion concordance, and biomed matching. Partnerships where both partners were HIV positive had significantly greater odds of CAI [odds ratio (OR)=2.34, 95% confidence interval (CI): 1.36–4.05] compared to serodiscordant partnerships. Casual partnerships had significantly lower odds of CAI compared to main partnerships (OR=0.53, 95% CI: 0.34–0.81). Partnerships where neither partner had disclosed their HIV status had significantly lower odds of CAI compared to partnerships where only one partner had disclosed (OR=0.60, 95% CI: 0.37–0.97). Partnerships where both partners were using biomedical prevention had significantly greater odds of CAI

TABLE 1. DESCRIPTIVES OF SEXUAL PARTNERSHIPS OF MEN WHO HAVE SEX WITH MEN STRATIFIED BY RESPONDENT PRE-EXPOSURE PROPHYLAXIS USE IN SAN FRANCISCO, CA (N=535)

Partnership characteristics	Partnerships of egocentric PrEP users (n=116)		Partnerships of egocentric non-PrEP users (n=419)	
	n	%	n	%
Seroconcordance				
Concordant (Both HIV-)	78	67.2	174	41.5
Concordant (Both HIV+)	—	—	131	31.3
Discordant (HIV+ and HIV-)	38	32.8	114	27.2
Partnership type				
Main partner	17	14.7	83	19.8
Casual partner	99	85.3	336	80.2
Meeting place				
Offline	66	56.9	319	76.1
Online	50	43.1	100	23.9
Serodiscussion				
Concordant (both disclosed)	76	65.5	215	51.3
Concordant (neither disclosed)	22	19.0	105	25.1
Discordant (only 1 partner disclosed)	18	15.5	99	23.6
Biomed matching				
Concordant (neither use biomedical prevention)	—	—	309	73.8
Concordant (both use biomedical prevention)	57	49.1	19	4.5
Discordant (only 1 partner uses biomedical prevention)	59	50.9	91	21.7
CAI in the past 6 months				
Yes	86	74.1	232	55.4
No	30	25.9	187	44.6

CAI, condomless anal intercourse; PrEP, pre-exposure prophylaxis.

(OR=5.19, 95% CI: 2.27–11.9) compared to those where only one partner was using biomedical prevention, while those where neither partner was using biomedical prevention had significantly lower odds of CAI (OR=0.61, 95% CI: 0.40–0.93). In addition, PrEP use by the respondent MSM was associated with significantly higher odds of CAI within a sexual partnership (OR=2.10, 95% CI: 1.16–3.80). There was no significant difference in the odds of CAI between partnerships that had formed online compared to those that had formed offline (OR = 1.03, $p = 0.89$). The full result of all unadjusted associations between partnership characteristics and CAI is presented in Table 2.

In our partially adjusted models to assess cross-level interaction between PrEP and the associations of partnership characteristics and CAI, a statistically significant interaction was found only between serodiscussion and PrEP use (by the respondent MSM). Among PrEP-using MSM, partnerships in which one partner or both partners had disclosed their HIV status were significantly more likely to engage in CAI compared to partnerships in which neither partner had disclosed their status [adjusted OR (aOR)=5.89, 95% CI: 1.59–21.83 and aOR=5.28, 95% CI: 1.91–14.61, respectively], while among non-PrEP-using respondent MSM, serodiscussion was not significantly associated with CAI (aOR=1.29, 95% CI: 0.75–2.21 and aOR=1.05, 95% CI: 0.65–1.67, respectively). All partially adjusted associations between partnership characteristics and CAI, including cross-level interactions with PrEP use by the respondent, are presented in Table 2. The interaction term between serodiscussion and PrEP use by the respondent MSM remained statistically

significant in our fully adjusted model that additionally controlled for seroconcordance and partnership type (aOR=5.86, 95% CI: 1.50–22.83 and aOR=5.59, 95% CI: 1.85–16.89, respectively). Partially adjusted and fully adjusted interaction plots between PrEP use and the effect of serodiscussion on CAI are presented in Fig. 1. All fully adjusted associations between partnership characteristics and CAI, including cross-level interactions with PrEP use, are presented in Table 2.

Discussion

In this secondary analysis of a cross-sectional study of the sexual partnerships reported by PrEP using and nonusing MSM in San Francisco, we found limited evidence of significant modifications of the associations between partnership characteristics and sexual risk taking by PrEP use. However, we did find that PrEP use moderated the association between serodiscussion and CAI among MSM. In addition, our finding of a strong association between biomedical matching and CAI confirms biomed matching as both a common and highly influential partnership characteristic affecting condom use among MSM. These findings taken together suggest that MSM using PrEP may not be using condoms differently in the majority of their sexual partnerships, and instead, differences in the types of partnerships that constitute their sexual networks may better explain risk compensation and higher engagement in sexual risk taking.

Sexual partnerships of PrEP-using MSM had significantly higher odds of engaging in CAI when one partner or both

TABLE 2. UNADJUSTED, PARTIALLY ADJUSTED, AND FULLY ADJUSTED GEE LOGISTIC REGRESSIONS FOR CROSS-LEVEL INTERACTIONS BETWEEN PRE-EXPOSURE PROPHYLAXIS AND PARTNERSHIP-LEVEL CORRELATES OF CONDOMLESS ANAL INTERCOURSE AMONG SEXUAL PARTNERSHIPS OF MEN WHO HAVE SEX WITH MEN IN SAN FRANCISCO, CA (N=535)

	Unadjusted models			Partially adjusted models ^a			Fully adjusted models ^b		
	aOR	SE	p	aOR	SE	p	aOR	SE	p
Partnership characteristics (level 1)									
Seroconcordance									
Concordant (both HIV+)	2.34	0.66	0.002	2.56	0.75	0.001	2.53	0.75	0.002
Concordant (both HIV-)	1.16	0.24	0.474	0.90	0.22	0.663	0.77	0.19	0.284
Discordant (HIV+ and HIV-)	1.00 (ref.)	—	—	1.00 (ref.)	—	—	1.00 (ref.)	—	—
Partnership type									
Casual	0.53	0.12	0.003	0.63	0.15	0.052	0.58	0.15	0.035
Main	1.00 (ref.)	—	—	1.00 (ref.)	—	—	1.00 (ref.)	—	—
Meeting place									
Online	1.03	0.20	0.894	1.16	0.27	0.519	1.25	0.30	0.349
Offline	1.00 (ref.)	—	—	1.00 (ref.)	—	—	1.00 (ref.)	—	—
Serodiscussion									
Concordant (both disclosed)	1.46	0.31	0.077	1.05	0.25	0.850	1.18	0.33	0.561
Discordant (only 1 partner disclosed)	1.67	0.41	0.037	1.29	0.35	0.354	1.38	0.41	0.284
Concordant (neither disclosed)	1.00 (ref.)	—	—	1.00 (ref.)	—	—	1.00 (ref.)	—	—
Biomed matching									
Concordant (neither use)	0.61	0.13	0.022	0.54	0.14	0.017	0.67	0.19	0.156
Concordant (both use biomedical prevention)	5.19	2.20	<0.001	3.97	3.15	0.083	3.50	3.00	0.144
Discordant (only 1 partner uses)	1.00 (ref.)	—	—	1.00 (ref.)	—	—	1.00 (ref.)	—	—
Respondent characteristics (level 2)									
Current PrEP use									
Yes	2.10	0.64	0.02	—	—	—	—	—	—
No	1.00 (ref.)	—	—	—	—	—	—	—	—
Cross-level interactions terms between partnership characteristics and PrEP use									
Seroconcordance									
Concordant (both HIV+) × PrEP use	—	—	—	N/A ^c	N/A ^c	N/A ^c	N/A ^c	N/A ^c	N/A ^c
Concordant (both HIV-) × PrEP use	—	—	—	2.07	1.03	0.14	2.48	1.24	0.07
Partnership type									
Casual × PrEP use	—	—	—	N/A ^d	N/A ^d	N/A ^d	N/A ^d	N/A ^d	N/A ^d
Meeting place									
Online × PrEP use	—	—	—	0.52	0.25	0.168	0.60	0.29	0.289
Serodiscussion									
Concordant (both disclosed) × PrEP use	—	—	—	5.04	2.88	0.01	4.76	2.81	0.008
Concordant (neither disclosed) × PrEP use	—	—	—	4.57	3.30	0.04	4.25	3.15	0.051
Biomed matching									
Concordant (neither use) × PrEP use	—	—	—	N/A ^c	N/A ^c	N/A ^c	N/A ^c	N/A ^c	N/A ^c
Concordant (both use) × PrEP use	—	—	—	1.53	1.42	0.651	1.66	1.64	0.510

^aPartially adjusted models include the respective partnership characteristic, PrEP use, and a corresponding cross-level interaction term between the partnership characteristic and PrEP.

^bFully adjusted models additionally controlled for seroconcordance and partnership type.

^cEstimates were unattainable due to implausibility. For example, partnerships that are concordantly HIV+ are ineligible for either sexual partner to currently be using PrEP (must be HIV-).

^dThere were no observed main partnerships without CAI among PrEP using egocentrics.

aOR, adjusted odds ratio; CAI, condomless anal intercourse; GEE, generalized estimating equation; PrEP, pre-exposure prophylaxis.

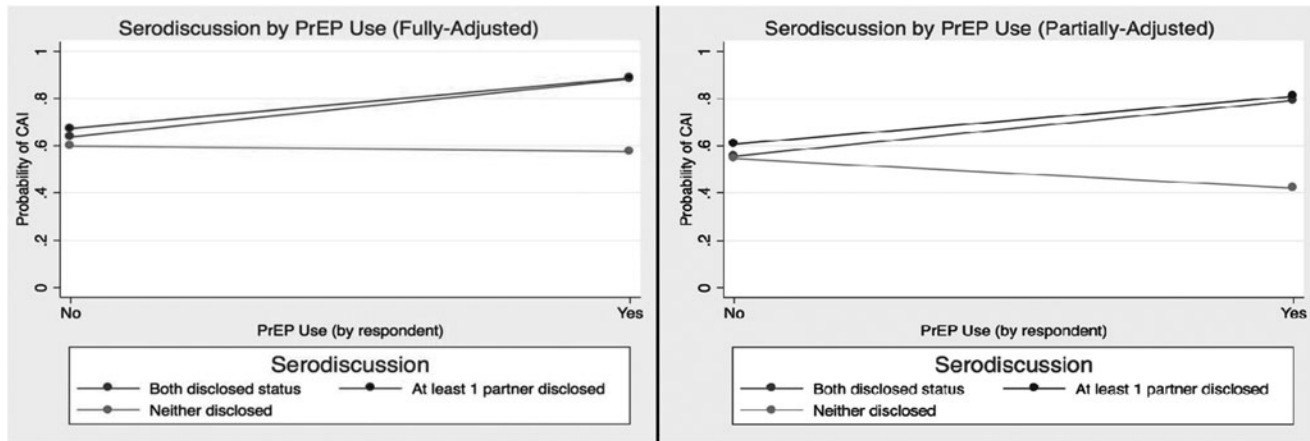


FIG. 1. Interaction plots: partially adjusted and fully adjusted interaction plots between PrEP use and the effect of serodiscussion on CAI. CAI, condomless anal intercourse; PrEP, pre-exposure prophylaxis.

partners had disclosed their serostatus compared to when neither partner had. However, there was no significant association between serostatus disclosure and CAI among the sexual partnerships of non-PrEP-using MSM. MSM have previously reported using PrEP as part of a larger prevention strategy, in which PrEP is used to complement rather than replace existing risk reduction strategies such as condom use and seropositioning.²⁶ Data from NHBS in 2014 similarly revealed that the majority of MSM using PrEP in San Francisco (80%) reported utilizing additional preventative or seroadaptive strategies in conjunction with PrEP.³⁵ Serodiscussion, or the mutual disclosure of HIV status, is a prerequisite for many of the common risk reduction strategies that inform condom use. In NHBS, exclusive serosorting (46.7%) and seropositioning (16.7%) were the most commonly used among PrEP users and both require knowledge of a partner's serostatus.³⁵ In partnerships where condom use is already intended, serodiscussion is likely to become less relevant. This may help explain the higher relative ORs between serodiscussion and CAI among the sexual partnerships of PrEP users compared to nonusers, as those using PrEP may be more likely to be implementing secondary seroadaptive risk reduction strategies. Thus, the MSM using PrEP who participated in CAI after serodiscussion cannot be assumed to be taking fewer precautions with their sexual partners, as they may instead be combining several behavioral approaches to sexual risk reduction.

Among our sample of sexual partnerships, the majority of associations between partnership characteristics and CAI were not significantly moderated by an individual's PrEP use; however, power to detect such interactions was limited. Approximately half of the sexual partnerships of MSM using PrEP were concordant in their use of biomedical prevention, which was found to be highly associated with greater engagement in CAI. Recent evidence has similarly suggested that MSM using PrEP engage in PrEP sorting, or a behavior in which they seek out and exclusively engage in CAI with partners who are similarly using PrEP or other means of biomedical prevention.^{27,28} Similarly, PrEP-related stigma (i.e., the "Truvada whore" stereotype) coupled with reducing HIV-related stigma may also alter the sexual networks of PrEP-using MSM to be more assortative in regard to biomedical prevention use. Previous qualitative studies have found that MSM using PrEP paradoxically report both a re-

duction in their own held HIV-related stigma (and being more likely to have HIV-positive partners after initiating PrEP), while also experiencing PrEP-related stigma and discrimination from other MSM (i.e., the "Truvada whore" stereotype and being assumed to be promiscuous).^{36,37} Thus, it is difficult to determine whether PrEP users are actively shaping their sexual networks by seeking sexual partners using biomedical prevention (i.e., biomedical matching and PrEP sorting) or if stigma (both PrEP and HIV-related) is driving the observed changes in their sexual networks. Regardless, the implications of this assortativity may be that the sexual networks of MSM using PrEP are becoming relatively concentrated, which could explain, in part, the disproportionate risk for STIs among MSM using PrEP. A recent case-crossover study in Los Angeles, CA, found an increased risk of rectal chlamydia and syphilis among MSM using PrEP in the year following PrEP initiation compared to the year before; however, only a small segment (28%) of PrEP users experienced an increase in STIs between periods.³⁸ Possible differences in sexual networks may help explain the disproportionate risk of STIs experienced by some segments of MSM using PrEP, primarily those practicing a high degree of biomedical matching. However, the relatively small sample size (especially among PrEP users) and nonindependent nature of our hierarchical data limited our statistical power to detect relatively small associations and may explain our null findings. A recent retrospective cohort study of MSM in Montreal similarly found an increased risk for STIs in the year after PrEP initiation compared to the year before among PrEP users and a higher relative risk of acquiring an STI among PrEP users compared to PEP users.³⁹ Biomedical matching within the sexual networks of PrEP users may also help to explain both these findings of an increased risk of STIs after PrEP initiation and relatively higher risk of STIs compared to PEP users. However, as previously pointed out, these findings may also be largely explained by temporal trends in STI rates among MSM and current prescribing patterns of PrEP.⁴⁰

Our analysis is subject to several other limitations that must be considered when interpreting our findings. First, we were unable to determine if PrEP was being used by the respondent during their reported sexual partnerships. Our survey instrument asked if respondents were currently using PrEP at the time of the survey, but then asked participants

questions about their last three sexual partners (which could have been anytime in the past 6 months). This may have led to misclassification of PrEP use for a partnership in either direction; however, we have no evidence to believe that the degree of misclassification would be differential. Due to the cross-sectional nature of our data, we are relatedly also unable to establish temporality between our observed differences in the effects of partnership characteristics by PrEP use, further highlighting the need for future longitudinal studies. Second, we are limited to self-reported data reported by the respondents to our survey instrument. Our analysis was limited to information reported about sexual partnerships by only the respondent MSM, and there is the possibility that we misclassified partnerships for multiple partnership characteristics (i.e., whether a respondent MSM was able to accurately report the undetectability or viral load of an anonymous or casual partner). However, we believe that the perception of a partners' undetectability (opposed to accurate knowledge of) may still be quite an influential decision in whether to engage in CAI. Future studies should consider assessing the confidence of a respondent's assessment of their partners' undetectability (and other partnership characteristics) to evaluate the extent that perception affects engagement in sexual risk taking. In addition, self-reporting of our outcome (i.e., sexual behaviors) remains the only feasible means of data collection and our use of ACASI has been shown to reduce social desirability bias.⁴¹ Based on the primary analysis of the SEEDS study and prior respondent driven sampling (RDS) studies that have shown the robustness of unweighted estimates,³⁴ we did not pursue the use of RDS-weighted measures in this exploratory secondary analysis. This limits our ability to generalize our findings, which should not be interpreted as population-based estimates. Similarly, our sample was drawn from alcohol-using MSM (such that the inclusion criteria required the use of alcohol at least once in the past 12 months), which limits the generalizability of our findings to MSM who abstain from alcohol use.

Despite these limitations, our analysis also had several strengths. First, our partnership-level approach to studying sexual risk taking allowed for us to quantify the relative importance of partnership characteristics among PrEP users and nonusers. Traditional analyses that use individuals as the unit of analysis are unable to adequately account for partnership characteristics and situational condom use. The second strength of our analysis is its use of respondent-driven sampling in an observational study setting, which allowed for recruitment of a relatively diverse and generalizable sample of the sexual partnerships compared to traditional sampling strategies and clinical trials with strict eligibility criteria. Although we did not apply individual RDS weights to this analysis, the results of our study are likely subject to less selection bias than the predominant sampling strategy (convenience sampling) for this population.

Our findings suggest that differences in condom use and risk compensation among MSM using PrEP may not be well explained by differences in situational condom use across sexual partnerships alone. The observed higher engagement in CAI may be better explained by a difference in the types of partnerships that constitute the sexual networks of MSM using PrEP, who appeared to commonly practice high engagement in CAI with other biomedical prevention users. This may result in potentially concentrated and interconnected sexual networks, which could help explain the disproportionate risk for sexually transmitted infections within this population. Future PrEP

implementation efforts should further investigate the role of sexual networks to develop relevant adjunct interventions that further promote the sexual health of those experiencing risk compensation and disproportionate risk for other STIs.

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Authors' Contributions

M.R.P., G.M.S., J.H., and M.P. collaborated in the writing of the article. G.M.S. and J.H. were involved in the design and conducting of the study. M.R.P., G.M.S., and M.P. collaborated on the main directions for data analysis and interpretation of results. M.R.P. performed all statistical analyses. M.R.P., G.M.S., J.H., and M.P. revised the article before submission.

Author Disclosure Statement

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