

UCLA

UCLA Previously Published Works

Title

Incidence and Correlates of Sexually Transmitted Infections Among Black Men Who Have Sex With Men Participating in the HIV Prevention Trials Network 073 Preexposure Prophylaxis Study

Permalink

<https://escholarship.org/uc/item/9066w82r>

Journal

Clinical Infectious Diseases, 69(9)

ISSN

1058-4838

Authors

Hightow-Weidman, Lisa B

Magnus, Manya

Beauchamp, Geetha

et al.

Publication Date

2019-10-15

DOI

10.1093/cid/ciy1141

Peer reviewed

Incidence and Correlates of Sexually Transmitted Infections Among Black Men Who Have Sex With Men Participating in the HIV Prevention Trials Network 073 Preexposure Prophylaxis Study

Lisa B. Hightow-Weidman,¹ Manya Magnus,² Geetha Beauchamp,³ Christopher B. Hurt,¹ Steve Shoptaw,⁴ Lynda Emel,³ Estelle Piwowar-Manning,⁵ Kenneth H. Mayer,⁶ LaRon E. Nelson,^{7,8} Leo Wilton,^{9,10} Phaedrea Watkins,¹¹ Darren Whitfield,¹² Sheldon D. Fields,¹³ and Darrell Wheeler¹⁴

¹Institute for Global Health & Infectious Diseases, University of North Carolina at Chapel Hill; ²Department of Epidemiology and Biostatistics, Milken Institute School of Public Health at the George Washington University, District of Columbia; ³Statistical Center for HIV/AIDS Research & Prevention, Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, Washington; ⁴Department of Family Medicine, David Geffen School of Medicine, University of California, Los Angeles; ⁵Department of Pathology, John Hopkins School of Medicine, Baltimore, Maryland; ⁶Fenway Institute, Fenway Health and the Division of Infectious Diseases, Department of Medicine, Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, Massachusetts; ⁷School of Nursing, University of Rochester, New York; ⁸Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Canada; ⁹Department of Human Development, State University of New York, Binghamton; ¹⁰Faculty of Humanities, University of Johannesburg, Auckland Park, South Africa; ¹¹Syneos Health, Clinical Development, Raleigh, North Carolina; ¹²School of Social Work, Department of Psychiatry, School of Medicine, University of Pittsburgh, Pennsylvania; and ¹³School of Health Professions, New York Institute of Technology, Old Westbury, and ¹⁴Iona College, New Rochelle, New York

Background. The HIV Prevention Trials Network (HPTN) Study 073 (HPTN 073) assessed the feasibility, acceptability, and safety of preexposure prophylaxis (PrEP) for black men who have sex with men (BMSM). The purpose of this analysis was to characterize the relationship between PrEP uptake and use and incident sexually transmitted infections (STIs) among participants enrolled in HPTN 073.

Methods. A total of 226 human immunodeficiency virus (HIV)–uninfected BMSM were enrolled in 3 US cities; all participants received client-centered care coordination (C4) and were offered daily oral PrEP. Participants were followed for 12 months with STI testing (rectal and urine nucleic acid amplification test for gonorrhea and chlamydia, rapid plasma reagin for syphilis) conducted at baseline, week 26, and week 52. Logistic regression was used to examine associations between STI incidence and PrEP uptake. Generalized estimating equations were used to evaluate associations between age, PrEP acceptance, sexual behaviors, and incident STIs.

Results. Baseline STI prevalence was 14.2%. Men aged <25 years were more likely to have a baseline STI (25.3% vs 6.7%; odds ratio [OR], 4.39; 95% confidence interval [CI], 1.91, 10.11). Sixty participants (26.5%) acquired ≥ 1 STI during follow-up; the incidence rate was 34.2 cases per 100 person-years (95% CI, 27.4, 42.9). In adjusted analyses, baseline STI diagnosis (OR, 4.23; 95% CI, 1.82, 9.87; $P < .001$) and additional C4 time (OR, 1.03; 95% CI, 1.00, 1.06; $P = .027$) were associated with having an incident STI. STI incidence was not associated with PrEP acceptance or adherence.

Conclusions. While we found higher rates of STIs in younger BMSM, overall rates of STI were lower than in prior PrEP trials, with no increase over time. BMSM with STIs at PrEP initiation may require additional interventions that target STI acquisition risk.

Clinical Trials Registration. NCT01808352.

Keywords. African-American; gay; PrEP; sexually transmitted infections.

Human immunodeficiency virus (HIV) incidence in the United States is slowly declining, but an estimated 40 000 new infections still occur each year [1]. Since persons living with HIV who achieve virologic suppression have effectively no risk of transmitting the virus to others [2, 3], linkage to care and initiation of antiretroviral therapy have likely contributed greatly

to trends in incidence. However, the benefits of “treatment as prevention” and other new biomedical prevention technologies [4] are not distributed equally across subpopulations affected by HIV. Black communities continue to experience the most severe burden of HIV among all racial/ethnic groups in the United States, with black men who have sex with men (BMSM) disproportionately impacted [5]. In 2016, BMSM accounted for 26% of the 39 782 new HIV diagnoses in the United States. While the overall rate among BMSM has not changed, there was a 30% increase in HIV infection rates among those aged 25–34 years between 2011 and 2015 [5]. Modeling studies have estimated that if the current trends continue, 1 in 2 BMSM will be diagnosed with HIV in his lifetime [6], and that if current incidence rates persist, 40% of BMSM will be HIV infected by age 30 [7].

Received 30 August 2018; editorial decision 17 December 2018; accepted 4 January 2019; published online January 7, 2019.

Correspondence: L. B. Hightow-Weidman, Institute for Global Health & Infectious Diseases, University of North Carolina at Chapel Hill, 130 Mason Farm Rd, Chapel Hill, NC 27599-7030, NC (lisa_hightow@med.unc.edu).

Clinical Infectious Diseases® 2019;69(9):1597–1604

© The Author(s) 2019. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com. DOI: 10.1093/cid/ciy1141

Low uptake of preexposure prophylaxis (PrEP) among BMSM may further amplify disparities in HIV incidence [8]. Since US Food and Drug Administration approval of oral emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) as PrEP in 2012, the number of PrEP users has steadily increased, but utilization is concentrated among white MSM (WMSM) [9]. While black persons in the United States have the highest rate of HIV infections, it is estimated that only about 10% of PrEP users are black [9]. An evaluation of the PrEP care continuum on an Atlanta cohort of MSM (n = 562) found that while BMSM were equally likely to report awareness of and willingness to use PrEP compared to WMSM, BMSM were less likely to be prescribed PrEP (24.2% vs 34.8%) and achieve protective drug levels (12.3% vs 17.8%) [10].

Further complicating prevention efforts among high-risk groups is the complex relationship between HIV and other sexually transmitted infections (STIs). Individuals with active STIs are more likely to acquire HIV, and vice versa [11]. Among MSM, STIs have dramatically increased in the last decade [12]. There is general concern that expanded use of PrEP may lead to increased incidence of bacterial STIs, but available data thus far have been mixed [13, 14]. Higher STI incidence among PrEP users could be a true effect of behavioral disinhibition [15] or an apparent effect from increased screening of persons engaged in preventive sexual healthcare [13]. Limited data exist regarding STI risk among BMSM PrEP users, despite epidemiological data that show greater burdens of both HIV and STIs [5, 6, 16].

We sought to examine STI incidence among PrEP users by studying a unique cohort of BMSM recruited for HIV Prevention Trials Network (HPTN) Study 073. This multisite, open-label demonstration study explored whether provision of a culturally tailored intervention (client-centered care coordination [C4]) could improve acceptance of and adherence to oral FTC/TDF among BMSM. The C4 model integrates an evidence-based, public health strategy with a self-determination theory-based approach to counseling and client engagement [17]. Objectives of the parent study included description of the initiation, acceptability, safety, and feasibility of PrEP for BMSM [18]. The purpose of this secondary analysis was to characterize the relationship between PrEP uptake and use and incident STIs among participants enrolled in HPTN 073.

METHODS

Parent Study

HPTN 073 enrolled 226 HIV-uninfected BMSM between August 2013 and September 2014 in 3 US cities: Los Angeles, California; Washington, D.C.; and Chapel Hill, North Carolina. To be eligible, participants had to provide informed consent, be aged ≥ 18 years, be assigned male at birth, be black (multiracial/multiethnic men were also eligible), and self-report at least 1 of the following HIV risk behaviors or characteristics: condomless

anal intercourse (CAI) with a male partner; anal intercourse with more than 3 male partners; exchanging any anal sex with a male partner for money, gifts, shelter, or drugs; anal intercourse with a male partner while using drugs or alcohol; or having a male sex partner and an STI diagnosis in the prior 6 months. All participants had to be clinically eligible to receive FTC/TDF based on laboratory testing [19]. The institutional review boards at the University of California at Los Angeles, University of North Carolina at Chapel Hill, and George Washington University approved the parent study protocol.

At baseline, all participants were offered HIV and STI testing along with C4 (which included as-needed referrals for health-care and prevention services and harm reduction counseling, including a focus on psychosocial and structural barriers potentially impacting PrEP acceptance and adherence). FTC/TDF and all related clinical testing was offered free of charge. Participants could choose to initiate oral PrEP at any study visit until week 48, per their request and upon confirmation of a nonreactive antigen/antibody combination HIV test and eligible clinical laboratory results. Participants could also choose to discontinue PrEP at any point during the study. Study visits occurred at weeks 4, 8, and 13 and quarterly thereafter, up to 12 months. At screening weeks 26 and 52, rapid plasma reagin testing for syphilis was performed using plasma specimens; reactive titers were confirmed using a treponemal-specific assay per local testing protocols. At those same visits, urine and rectal swab samples were obtained for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) testing by the HPTN Laboratory Center, using the Aptima Combo 2 Assay for CT/NG assay (Hologic, San Diego, CA). Pharyngeal swabs were not specifically obtained per protocol, but cases of pharyngeal gonorrhea were reported as adverse events (AEs) if detected through clinical care. STIs diagnosed outside of the study were also recorded as AEs. At every visit, participants completed an audio computer-assisted self-interview (ACASI).

Measures

Sexual Risk Behaviors

At baseline and each follow-up ACASI, participants were asked about engagement in insertive and receptive condomless anal intercourse (CAI) with primary (main) and casual male partners. Engagement in CAI (insertive and/or receptive) was dichotomized into reporting ≥ 1 instance in CAI in the past 3 months vs no instances.

PrEP Adherence Examined in 2 Ways

PrEP adherence was measured by self-report (via ACASI) and by pharmacological testing of 2 types of participant specimens, plasma, and peripheral blood mononuclear cells (PBMCs) [20]. The visual analogue scale was used to measure self-reported adherence to PrEP in the prior 30 days [21]. PrEP adherence was defined as meeting the 90% sensitivity threshold for ≥ 4

doses of FTC/TDF per week from either of the 2 sample types (plasma or PBMC) related to tenofovir (TFV) or FTC measurements: ≥ 4.2 ng/mL for TFV and ≥ 4.6 ng/mL for FTC in plasma; 9.9 fmol/ 10^6 for TFV diphosphate (TFV-DP) and $.4$ fmol/ 10^6 for FTC triphosphate in PBMCs [22].

Statistical Analyses

Descriptive statistics were computed and stratified by PrEP acceptance. Associations between the binary outcome of new STI cases and factors of interest (age, PrEP acceptance, PrEP adherence, and sexual behaviors) were evaluated using logistic regression with site as a covariate. Generalized estimating equations were used to account for repeated outcomes in both unadjusted and adjusted analyses. Incidence rates and confidence intervals (CIs) were calculated based on a Poisson distribution. Person-years (PY) of follow-up time were calculated to the first STI diagnosis or last STI date from either the PrEP acceptance date (among PrEP acceptors) or from study enrollment date (among PrEP decliners). Among participants who acquired HIV during study follow-up, STI diagnoses after HIV seroconversion were excluded, since different psychosocial and physiologic states may obscure the relationship between PrEP and STIs. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Characteristics of Participants

Detailed characteristics of participants in HPTN 073 are described elsewhere [23]. Briefly, of 226 enrolled participants, 86% self-identified as black only, 25% had a high school diploma or less, 48% reported an annual income $< \$20,000$, and 73% and 20% identified as gay or bisexual, respectively. The median age was 26 years (interquartile range [IQR], 23 to 32), and 91 men (40.3%) were aged < 25 years.

Baseline and Incident STIs

STI prevalence was 14.2% at baseline. The most common STI at baseline was chlamydia (10.2%; 1.8% urethral and 9.1% rectal) followed by gonorrhea (5.3%; .9% urethral and 4.6% rectal) and syphilis (1.3%). These proportions did not change significantly at week 26 (16.2%) or week 52 (18.2%; $P = .85$; Figure 1). Rectal STIs accounted for the largest proportion of infections at all 3 time points (11.5%, 11.8%, and 9.6%). At baseline, men aged < 25 years had a higher STI prevalence than older men (25.3% vs 6.7%), equating to a 4.4-fold greater odds of an STI in younger men (odds ratio [OR], 4.39; 95% confidence interval [CI], 1.91, 10.11).

Sixty men (26.5%) acquired an STI during follow-up, and 9 men (4%) had an STI at both follow-up visits where measured. Incident STIs by visit and short-term PrEP adherence demonstrated by blood levels at each visit are described in Table 1. Regardless of PrEP acceptance, compared to men who were aged ≥ 25 years, men younger than 25 were more likely to have STIs at both week 26 (9.2% [11/120] vs 26.5% [22/83]) and week 52 (16.0% [19/119] vs 22.0% [18/82]). At week 26, those who accepted PrEP had similar rates of STIs whether or not they reported any CAI in the prior 3 months (19.3% any CAI; 15.5% no CAI). Among the 4 participants at week 26 who were diagnosed with an STI (3 of whom had rectal infections) and had not opted to take PrEP, none reported CAI in the past 3 months. At week 52, 18 participants who reported no CAI in the past 3 months were diagnosed with a new STI (9 of which were rectal infections), including 15 men who accepted PrEP and 3 who did not.

Over the entire study follow-up period, there was an STI incidence rate of 34.2 cases/100 person-years (95% CI, 27.4, 42.9; Table 2). No statistically significant differences in STI incidence were found by study visit week or by PrEP acceptance. Among those men with 1 or more incident STIs, adherence (both self-report and drug level) was low at both 26 weeks

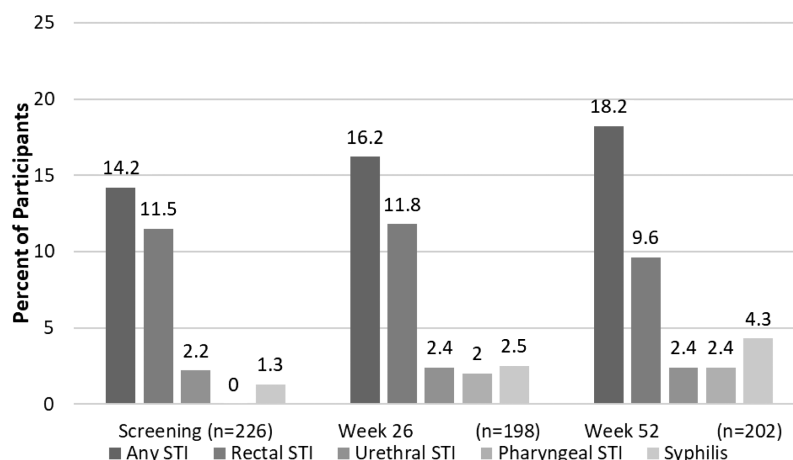


Figure 1. Sexually transmitted infections at screening and follow-up. Abbreviation: STI, sexually transmitted infection.

Table 1. Characteristics of Incident Sexually Transmitted Infections by Preexposure Prophylaxis Acceptance and Visit

Variable	Week 26 PrEP Accept, % (n/N)	Week 52 PrEP Accept, % (n/N)	Week 26 PrEP Not Accept, % (n/N)	Week 52 PrEP Not Accept, % (n/N)
Any STI	17 (29/167)	19 (31/166)	11 (4/36)	17 (6/35)
Age, years				
≥25	10.6 (10/94)	15.6 (15/96)	3.8 (1/26)	17.4 (4/23)
<25	26.0 (19/73)	22.9 (16/70)	30.0 (3/10)	16.7 (2/12)
Baseline any STI diagnosis				
No	12.9 (18/139)	15.7 (22/140)	12.1 (4/33)	18.8 (6/32)
Yes	39.3 (11/28)	34.6 (9/26)	.0 (0/3)	.0 (0/3)
Any CAI (past 3 months)				
No	15.5 (11/71)	18.1 (15/83)	17.4 (4/23)	12.0 (3/25)
Yes	19.3 (16/83)	17.8 (13/73)	.0 (0/11)	37.5 (3/8)
Any receptive CAI (past 3 months)				
No	17.2 (15/87)	15.7 (16/102)	14.8 (4/27)	11.5 (3/26)
Yes	17.9 (12/67)	22.2 (12/54)	.0 (0/7)	42.9 (3/7)
Any insertive CAI (past 3 months)				
No	20.2 (18/89)	15.6 (15/96)	15.4 (4/26)	11.1 (3/27)
Yes	13.8 (9/65)	21.7 (13/60)	.0 (0/8)	50.0 (3/6)
Any alcohol/drug use 2 hours before or during sex (past 3 months)				
No	16.3 (16/98)	15.8 (16/101)	8.3 (2/24)	18.5 (5/27)
Yes	19.6 (11/56)	21.8 (12/55)	20.0 (2/10)	16.7 (1/6)
Self-report adherence ≥60%				
No	22.6 (7/31)	26.3 (5/19)	n/a	n/a
Yes	16.8 (18/107)	15.7 (13/83)	n/a	n/a
PK short-term adherence ≥4 days/week				
No	19.0 (11/58)	17.1 (13/76)	n/a	n/a
Yes	16.7 (17/102)	20.9 (18/86)	n/a	n/a
Average client-centered care coordination minutes				
Mean (standard deviation)	30 (7.8)	29 (6.3)	30 (7.8)	36 (15.2)
Min, Max	20, 50	16, 41	23, 41	18, 60

Abbreviations: CAI, condomless anal intercourse; n/a, not applicable; PK, pharmacokinetic; PrEP, preexposure prophylaxis; STI, sexually transmitted infection.

and 52 weeks (26.7% self-reported adherence ≥60%; 28.4% had drug levels indicating dosing ≥4 days/week).

Correlates of Incident STIs

Several characteristics were associated with having an incident STI prior to adjustment for confounders (Table 3), including age <25 years, having a prevalent STI at baseline, and having C4 counselors spending more than the mean number of minutes performing care coordination activities. In adjusted analyses, only a baseline STI diagnosis (OR, 4.23; 95% CI, 1.82, 9.87; $P < .001$) and additional minutes of C4 (OR, 1.03; 95% CI, 1.00, 1.06; $P = .027$) remained associated with having an incident STI. We saw no statistically significant association with STI incidence and PrEP uptake, self-reported PrEP adherence, or PrEP adherence measured by drug levels (Table 3).

Changes in Condomless Anal Intercourse

While decreased rates of CAI (both receptive and insertive) were observed from baseline through week 52 among both men accepting and declining PrEP, this result was significant only among those accepting PrEP (Table 4). Overall, the proportion

of participants reporting CAI was lower for those declining PrEP compared to those accepting PrEP at all time points.

Relationship Between Incident HIV Infections and STIs

Eight incident HIV infections were diagnosed during the study. Two participants were also diagnosed with incident STIs at the time HIV seroconversion was detected (1 man who accepted PrEP was diagnosed with syphilis and 1 man who declined PrEP was diagnosed with urethral gonorrhea). Two participants who seroconverted were diagnosed with chlamydia at baseline (1 rectal and 1 urethral infection).

DISCUSSION

To our knowledge, this is the first study to evaluate longitudinal acquisition of STIs in a sample of US BMSM being offered PrEP. Overall, 26.5% of participants in HPTN 073 were diagnosed with an STI during study follow-up, a rate lower than what was seen in other recent PrEP studies [24, 25]. While direct comparisons cannot be made, particularly given how few BMSM were enrolled in other studies [24–26], these results provide valuable insight into the interplay between PrEP use, STIs, and ongoing

Table 2. Sexually Transmitted Infection Incidence Rate by Preexposure Prophylaxis Acceptance

Variable	Sexually Transmitted Infection (n)	Person-years	Incidence Rate (95% Confidence Interval) per 100 Person-years	P Value
Overall (all participants)	70	204.6	34.2 (27.4, 42.9)	...
All weeks4658
Not on PrEP	11	39.2	28.1 (15.5, 50.7)	...
On PrEP	59	165.4	35.7 (27.6, 46.0)	...
Week 26				
Not on PrEP	5	20.2	24.8 (10.3, 59.6)	.4363
On PrEP	28	77.3	36.2 (25.0, 52.4)	...
Week 52				
Not on PrEP	6	19.0	31.5 (14.2, 70.2)	.8048
On PrEP	31	88.1	35.2 (24.8, 50.0)	...

Abbreviation: PrEP, preexposure prophylaxis.

risk behaviors among the population most impacted by HIV infection in the United States.

In registrational trials of FTC/TDF for PrEP, a high incidence of STIs was observed, but there was no conclusive evidence for risk compensation among PrEP users. Indeed, some studies reported a decline in key metrics of STI risk (eg, number

of sex partners or frequency of CAI) [20, 25, 27, 28]. Though there was a high incidence of STIs among participants in the US PrEP Demonstration Project, the rate did not increase over time while people were on PrEP [24]. However, other studies, including those among younger MSM, suggest higher rates of STIs among MSM who use PrEP compared to non-PrEP users

Table 3. Correlates of Incident Sexually Transmitted Infections

Variable	At Least 1 Incident Sexually Transmitted Infection, % (n/N)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age, years			
≥25	21.4 (27/126)	Ref	...
<25	38.6 (34/88)	2.39 (1.36, 4.20)	1.41 (.60, 3.31)
PrEP acceptance			
Not on PrEP	25.0 (10/40)	1.47 (.73, 2.96)	...
On PrEP	29.3 (51/174)	Ref	...
Baseline any sexually transmitted infection diagnosis			
No	24.0 (44/183)	Ref	...
Yes	54.8 (17/31)	3.20 (1.67, 6.11)	4.23 (1.82, 9.87)
Any CAI (past 3 months)			
No	26.5 (27/102)	Ref	...
Yes	30.5 (29/95)	1.20 (.69, 2.07)	...
Any receptive CAI (past 3 months)			
No	27.4 (32/117)	Ref	...
Yes	30.0 (24/80)	1.39 (.79, 2.45)	...
Any insertive CAI (past 3 months)			
No	28.1 (34/121)	Ref	...
Yes	28.9 (22/76)	1.14 (.67, 1.94)	...
Any alcohol/drug use 2 hours before or during sex (past 3 months)			
No	27.3 (35/128)	Ref	...
Yes	30.4 (21/69)	1.34 (.75, 2.40)	...
Self-report adherence ≥60%			
No	35.5 (11/31)	Ref	...
Yes	26.7 (28/105)	.60 (.27, 1.31)	...
PK short-term adherence ≥4 days/week			
No	33.3 (21/63)	Ref	...
Yes	28.4 (29/102)	1.16 (.65, 2.08)	...
Average client-centered care coordination minutes			
Mean (standard deviation)	30 (9.5)	1.02 (1.00, 1.05)	1.03 (1.00, 1.06)

Abbreviations: CAI, condomless anal intercourse; CI, confidence interval; OR, odds ratio; PK, pharmacokinetic; PrEP, preexposure prophylaxis; Ref, reference.

Table 4. Proportion of Participants Reporting Condomless Anal Intercourse by Preexposure Prophylaxis Acceptance and Week on Study

Preexposure Prophylaxis Acceptance		Baseline Visit	Week 26	Week 52	P Value
Yes	Overall CAI	105/177 (59.3%)	84/156 (53.9%)	73/161 (45.3%)	.0019
	Insertive CAI	90/177 (50.9%)	65/156 (41.7%)	60/161 (37.3%)	.0016
	Receptive CAI	83/177 (46.9%)	68/156 (43.6%)	54/161 (33.5%)	.0039
No	Overall CAI	19/48 (39.6%)	11/34 (32.4%)	10/38 (26.3%)	.2178
	Insertive CAI	13/48 (27.1%)	8/34 (23.5%)	8/38 (21.0%)	.5158
	Receptive CAI	18/48 (37.5%)	7/34 (20.6%)	8/38 (21.0%)	.0984

Abbreviation: CAI, condomless anal intercourse.

[26, 29–31]. This may simply be a function of the risk profile of early adopters of PrEP—a population of MSM who might already engage more often in CAI and/or have multiple sex partners [20]. An apparent increase in STI incidence among PrEP users could also be an artifact of more frequent and consistent screening in this population [15].

The low overall rate of STI acquisition we observed is encouraging as efforts to increase uptake of PrEP among BMSM expands. Irrespective of PrEP, rates of STIs in the United States are 4.6, 6.6, and 8.9 times higher among black men compared to white men for syphilis, chlamydia, and gonorrhea, respectively [16]. A recent cohort study found that among MSM accessing medical care at a Boston community health center between 2005 and 2015, STI diagnoses increased more than 8 fold. Though BMSM made up only 6% of the participants, multivariable analyses demonstrated that being an MSM of color was independently associated with acquiring an incident STI [32]. Thus, when situated within the context of disparate rates of STIs reported among BMSM compared with MSM of other races [33], the low overall rates of STIs are encouraging as efforts to increase uptake of PrEP in this population expand. While causality cannot be proven, it should be noted that the men in this study were offered a culturally tailored behavioral intervention, C4, which may have impacted their sexual risk behavior compared to a population not receiving this intervention, although our study design did not permit such a comparison.

Being younger than 25 quadrupled the odds of having an STI at screening, and those with STIs at baseline were more likely to have an incident STI at any follow-up visit. Thus, younger BMSM as well as those with STIs at PrEP initiation may require additional counseling or consideration for additional behavioral or biomedical sexual risk reduction interventions during follow-up. While a recent study showed that on-demand post-exposure prophylaxis with doxycycline reduced the incidence of chlamydia infection and syphilis in high-risk MSM enrolled in a PrEP study [34], the utility of this strategy for BMSM, particularly its durability and impact on antibiotic resistance, requires further investigation.

The overall low adherence to PrEP among those BMSM in this study with incident STIs is concerning. Given that MSM with a history of syphilis or anorectal STIs have a greater risk

of subsequent HIV acquisition [35, 36], additional efforts to develop effective adherence interventions for BMSM on PrEP is critical. This finding is echoed by a recent 24-week demonstration project of PrEP among young MSM (aged 18–22 years) that found that at all time points, median TFV-DP concentrations for BMSM participants were below levels considered protective against HIV infection [37].

Rates of STIs were similar among those who chose to start PrEP in this study compared to those who declined PrEP, with no increase in incidence over time. While this aligns with the lack of increase in participant self-reported CAI over time, self-report of sexual risk behaviors may not always be an accurate reflection of risk. Indeed, we found that nearly 50% of participants at both week 26 and week 52 who reported no CAI in the past 3 months were diagnosed with a new STI. While some discrepancy could be related to mismatch in the time interval (eg, past 3 months for sexual risk vs STI screening every 6 months), this is similar to findings from a cohort of 485 young BMSM recruited in Mississippi, among whom 19.4% of rectal STI infections would have been missed if screening had not occurred among those denying any receptive anal sex [38].

Men whose health or social needs required C4 counselors to provide more time performing care coordination activities were more likely to have an incident STI during study follow-up. This may indicate these participants had more complex social situations and higher needs, including ongoing risk behaviors for STI acquisition, that required more counseling time and referrals. Among BMSM, factors such as social isolation and experiences of racism and homophobia have been shown to drive sexual risk-taking [39]. Further, structural factors, including financial hardship, incarceration, and unstable housing, have been associated with increased STIs among BMSM [40, 41]. Additional planned analyses unpacking C4 care coordination activities addressing participants' sexual health needs will inform future interventions.

This study has several key limitations. Screening for STIs only occurred at baseline and week 26 and week 52 study visits, thus potentially underestimating the incidence of STIs among participants. Men were queried at each study visit regarding any interim testing they had undergone, resulting in our awareness of 5 additional diagnoses and 3 cases of presumptive treatment at other clinical sites. Given that these diagnoses could not be

verified, these cases were not included in our analyses. Recent data and Centers for Disease Control and Prevention guidelines suggest more frequent STI testing is warranted for those on PrEP (every 3 months) compared to what our participants received [19]. In addition, STI screening in this study did not include sampling for pharyngeal gonorrhea. Because asymptomatic infections of the throat have been implicated in the expansion of antibacterial resistance among gonococci, comprehensive screening is important for long-term prevention and control efforts among MSM [42, 43]. Though our study sample is the largest to date of BMSM in a US PrEP demonstration study, the numbers of participants do not allow for statistically meaningful comparisons to be made between groups accepting and declining PrEP. Among the 9 participants with STIs at both follow-up visits, we were not able to determine whether these infections represented recurrent vs inadequately treated infections. Finally, sexual risk behaviors were self-reported. While ACASI has been shown to minimize social desirability bias when reporting sexual risk behaviors [44], the fact that many men who reported no CAI were diagnosed with new STIs is concerning. Frequent routine screening of MSM even in the absence of reported risk behavior or STI symptoms remains an important strategy for mitigating STIs among those at risk.

CONCLUSIONS

The expansion of PrEP for HIV prevention provides a unique and timely opportunity to address the lack of progress to date in reducing HIV and STI incidence among BMSM [45]. Clearly, PrEP for BMSM must not be delivered “in isolation” but rather as part of a combination prevention package that incorporates frequent STI screening and treatment and addresses BMSM’s pervasive ongoing exposure to adverse social and structural conditions, as well as a confluence of individual factors that continue to impact their overall health.

Notes

Acknowledgments. The authors thank the study team and participants at the following research sites: the University of North Carolina at Chapel Hill (CTU: AI069423-08/CTSA: 1UL1TR001111); the George Washington University, Milken Institute School of Public Health, Clinical Research Site (5UM1AI069053), and the District of Columbia Center for AIDS Research, a National Institutes of Health (NIH)–funded program (AI117970); and the University of California Los Angeles. The authors also acknowledge support from the HIV Prevention Trials Network (HPTN) Leadership and Operations Center, Family Health International 360; HPTN Laboratory Center Quality Assurance, Johns Hopkins University; HPTN Laboratory Center Pharmacology, Johns Hopkins University; HPTN Statistical and Data Management Center, Statistical Center for HIV/AIDS Research and Prevention; and Division of AIDS at the NIH; and Gilead Sciences, Inc.: Staci Bush, Lindsey Smith, James Rooney, and Brenda Ng. Other HPTN 073 contributors include Black Gay Research Group, HPTN Black Caucus, and District of Columbia Center for AIDS Research, an NIH-funded program (AI117970).

Disclaimer. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Allergy and Infectious Diseases (NIAID) or the NIH.

Financial support. Overall support for the HPTN is provided by the NIAID of the NIH under award UM1AI068619 (HPTN Leadership and Operations Center), UM1AI068617 (HPTN Statistical and Data Management Center), and UM1AI068613 (HPTN Laboratory Center). Additional support was provided by the National Institute on Drug Abuse and the National Institute of Mental Health, of the NIH, US Department of Health and Human Services. The study product, tenofovir disoproxil fumarate/emtricitabine, was donated by Gilead Sciences, Inc.

Potential conflicts of interest. L. N. has a patent on client-centered care coordination pending. C. B. H. has received grant support from Gilead Sciences. M. M. reports textbook royalties from Jones and Bartlett Learning Inc unrelated to the present work. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

- Centers for Disease Control and Prevention. Estimated HIV incidence and prevalence in the United States, 2010–2015. HIV surveillance supplemental report. Vol. 23. CDC: Atlanta, GA; 2018.
- Cohen MS, Chen YQ, McCauley M, et al; HPTN 052 Study Team. Antiretroviral therapy for the prevention of HIV-1 transmission. *N Engl J Med* 2016; 375:830–9.
- Rodger AJ, Cambiano V, Bruun T, et al; PARTNER Study Group. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA* 2016; 316:171–81.
- Riddell J 4th, Amico KR, Mayer KH. HIV preexposure prophylaxis: a review. *JAMA* 2018; 319:1261–8.
- Centers for Disease Control and Prevention. HIV surveillance report, 2016. Volume 28. 2017. <http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Accessed 22 May 2018.
- Hess KL, Hu X, Lansky A, Mermin J, Hall HI. Lifetime risk of a diagnosis of HIV infection in the United States. *Ann Epidemiol* 2017; 27:238–43.
- Matthews DD, Herrick AL, Coulter RW, et al; POWER Study Team. Running backwards: consequences of current HIV incidence rates for the next generation of black MSM in the United States. *AIDS Behav* 2016; 20:7–16.
- Rolle CP, Rosenberg ES, Luisi N, et al. Willingness to use pre-exposure prophylaxis among Black and White men who have sex with men in Atlanta, Georgia. *Int J STD AIDS* 2017; 28:849–57.
- Mera R, Magnuson D, Hawkins T, Bush S, Rawlings K, McCallister S. Changes in Truvada® for HIV Pre-exposure Prophylaxis Utilization in the USA: 2012–2016. 9th IAS Conference on HIV Science (IAS 2017). Paris, France, 2017.
- Kelley CE, Kahle E, Siegler A, et al. Applying a PrEP continuum of care for men who have sex with men in Atlanta, Georgia. *Clin Infect Dis* 2015; 61:1590–7.
- Galvin SR, Cohen MS. The role of sexually transmitted diseases in HIV transmission. *Nat Rev Microbiol* 2004; 2:33–42.
- Stenger MR, Baral S, Stahlman S, Wohlfeiler D, Barton JE, Peterman T. As through a glass, darkly: the future of sexually transmissible infections among gay, bisexual and other men who have sex with men. *Sex Health* 2017; 14:18–27.
- Scott HM, Klausner JD. Sexually transmitted infections and pre-exposure prophylaxis: challenges and opportunities among men who have sex with men in the US. *AIDS Res Ther* 2016; 13:5.
- Freeborn K, Portillo CJ. Does pre-exposure prophylaxis for HIV prevention in men who have sex with men change risk behaviour? A systematic review. *J Clin Nurs* 2018; 27:3254–65.
- Calabrese SK, Underhill K, Mayer KH. HIV preexposure prophylaxis and condomless sex: disentangling personal values from public health priorities. *Am J Public Health* 2017; 107:1572–6.
- Centers for Disease Control and Prevention. STDs in racial and ethnic minorities—2016 STD surveillance. Available at: <https://www.cdc.gov/std/stats/16/minorities.htm>. Accessed 12 June 2018.
- Ng JY, Ntoumanis N, Thøgersen-Ntoumani C, et al. Self-determination theory applied to health contexts: a meta-analysis. *Perspect Psychol Sci* 2012; 7:325–40.
- Wheeler D, Fields S, Beauchamp G, et al. Pre-exposure prophylaxis initiation and adherence among black men who have sex with men (MSM) in three U.S. cities: results from the HPTN 073 study. *J Inter AIDS Soc* 2018; In press.
- Centers for Disease Control and Prevention. Updated PrEP clinical practice guideline and PrEP clinical providers’ supplement—2017. https://www.cdc.gov/hiv/pdf/guidelines/PrEPGL2017_CommentNotice.pdf. Accessed 12 June 2018.
- Grant RM, Anderson PL, McMahan V, et al; iPrEx Study Team. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *Lancet Infect Dis* 2014; 14:820–9.

21. Giordano TP, Guzman D, Clark R, Charlebois ED, Bangsberg DR. Measuring adherence to antiretroviral therapy in a diverse population using a visual analogue scale. *HIV Clin Trials*. **2004**;5:74–9.
22. Hendrix CW, Andrade A, Bumpus NN, et al. Dose frequency ranging pharmacokinetic study of tenofovir-emtricitabine after directly observed dosing in healthy volunteers to establish adherence benchmarks (HPTN 066). *AIDS Res Hum Retroviruses* **2016**; 32:32–43.
23. Wheeler D, Fields S, Beauchamp G, et al. HPTN 073: PrEP uptake and use by black men who have sex with men in 3 US cities. Conference on Retroviruses and Opportunistic Infections (CROI). Boston, MA, **2016**.
24. Liu AY, Cohen SE, Vittinghoff E, et al. Preexposure prophylaxis for HIV infection integrated with municipal- and community-based sexual health services. *JAMA Intern Med* **2016**; 176:75–84.
25. McCormack S, Dunn DT, Desai M, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet* **2016**; 387:53–60.
26. Traeger MW, Schroeder SE, Wright EJ, et al. Effects of pre-exposure prophylaxis for the prevention of human immunodeficiency virus infection on sexual risk behavior in men who have sex with men: a systematic review and meta-analysis. *Clin Infect Dis* **2018**; 67:676–86.
27. Liu AY, Vittinghoff E, Chillag K, et al. Sexual risk behavior among HIV-uninfected men who have sex with men participating in a tenofovir preexposure prophylaxis randomized trial in the United States. *J Acquir Immune Defic Syndr* **2013**; 64:87–94.
28. Marcus JL, Glidden DV, Mayer KH, et al. No evidence of sexual risk compensation in the iPrEx trial of daily oral HIV preexposure prophylaxis. *PLoS One* **2013**; 8:e81997.
29. Newcomb ME, Moran K, Feinstein BA, Forscher E, Mustanski B. Pre-exposure prophylaxis (PrEP) use and condomless anal sex: evidence of risk compensation in a cohort of young men who have sex with men. *J Acquir Immune Defic Syndr* **2018**; 77:358–64.
30. Milam J, Jain S, Dubé MP, et al; CCTG Team. Sexual risk compensation in a pre-exposure prophylaxis demonstration study among individuals at risk of HIV. *J Acquir Immune Defic Syndr* **2019**; 80:e9–e13.
31. Hoornenborg E, Coyer L, van Laarhoven A, et al; Amsterdam PrEP Project Team in the HIV Transmission Elimination Amsterdam Initiative. Change in sexual risk behaviour after 6 months of pre-exposure prophylaxis use: results from the Amsterdam Pre-exposure Prophylaxis Demonstration Project. *AIDS* **2018**; 32:1527–32.
32. Mayer KH, Maloney KM, Levine K, et al. Sociodemographic and clinical factors associated with increasing bacterial sexually transmitted infection diagnoses in men who have sex with men accessing care at a Boston community health center (2005–2015). *Open Forum Infect Dis*. **2017**; 4:ofx214.
33. Grey JA, Bernstein KT, Sullivan PS, et al. Rates of primary and secondary syphilis among white and black non-Hispanic men who have sex with men, United States, 2014. *J Acquir Immune Defic Syndr* **2017**; 76:e65–73.
34. Molina JM, Charreau I, Chidiac C, et al; ANRS IPERGAY Study Group. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial. *Lancet Infect Dis* **2018**; 18:308–17.
35. Bernstein KT, Marcus JL, Nieri G, Philip SS, Klausner JD. Rectal gonorrhoea and chlamydia reinfection is associated with increased risk of HIV seroconversion. *J Acquir Immune Defic Syndr* **2010**; 53:537–43.
36. Aziz S, Sweat D. Subsequent HIV diagnosis risk after syphilis in a southern black population. *Sex Transm Dis* **2018**; 45:643–7.
37. Hosek SG, Rudy B, Landovitz R, et al; Adolescent Trials Network for HIV/AIDS Interventions. An HIV preexposure prophylaxis demonstration project and safety study for young MSM. *J Acquir Immune Defic Syndr* **2017**; 74:21–9.
38. Chamberlain N, Crosby RA, Mena L, Chan PA, Mayer KH. Is patient-reported exposure a reliable indicator for anogenital gonorrhoea and chlamydia screening in young black men who have sex with men? *Sex Transm Dis* **2017**; 44:390–2.
39. Saleh LD, van den Berg JJ, Chambers CS, Operario D. Social support, psychological vulnerability, and HIV risk among African American men who have sex with men. *Psychol Health* **2016**; 31:549–64.
40. Nelson LE, Wilton L, Moineddin R, et al; HPTN 061 Study Team. Economic, legal, and social hardships associated with HIV risk among black men who have sex with men in six US cities. *J Urban Health* **2016**; 93:170–88.
41. Jeffries WL, Marks G, Lauby J, Murrill CS, Millett GA. Homophobia is associated with sexual behavior that increases risk of acquiring and transmitting HIV infection among black men who have sex with men. *AIDS Behav* **2013**; 17:1442–53.
42. Weinstock H, Workowski KA. Pharyngeal gonorrhoea: an important reservoir of infection? *Clin Infect Dis* **2009**; 49:1798–800.
43. Lewis DA. Will targeting oropharyngeal gonorrhoea delay the further emergence of drug-resistant *Neisseria gonorrhoeae* strains? *Sex Transm Infect* **2015**; 91:234–7.
44. Newman JC, Des Jarlais DC, Turner CE, Gribble J, Cooley P, Paone D. The differential effects of face-to-face and computer interview modes. *Am J Public Health* **2002**; 92:294–7.
45. Singh S, Song R, Johnson AS, McCray E, Hall HI. HIV incidence, prevalence, and undiagnosed infections in U.S. men who have sex with men. *Ann Intern Med* **2018**; 168:685–94.