Journal

Journal of acquired immune deficiency syndromes (1999), 80(1)

ISSN

1525-4135

Authors

Milam, Joel
Jain, Sonia
Dubé, Michael P
et al.

Publication Date

2019

DOI

10.1097/qai.0000000000001885

Peer reviewed

Sexual Risk Compensation in a Pre-exposure Prophylaxis Demonstration Study Among Individuals at Risk of HIV

Joel Milam, PhD, Sonia Jain, PhD,† Michael P. Dubé, MD,* Eric S. Daar, MD,‡§‖ Xiaoying Sun, MS,† Katya Corado, MD,‡ Eric Ellorin, MA,† Jill Blumenthal, MD,† Richard Haubrich, MD,¶ David J. Moore, PhD,† and Sheldon R. Morris, MD,† the CCTG Team*

Background: A public health concern regarding HIV pre-exposure prophylaxis (PrEP) is sexual risk compensation (ie, increased unsafe sex among PrEP users that may undermine prevention efforts).

Methods: This demonstration study (NCT#01761643; initiated in 2013) included 398 men who have sex with men who initiated PrEP and were followed over 48 weeks at 4 sites in Southern California. Wilcoxon signed-rank tests compared previous 30-day number of sex partners and condomless insertive anal sex and receptive anal sex (CIAS and CRAS, respectively) acts at weeks 4, 12, 24, 36, and 48 to baseline. At 2 sites, PrEP users were also compared with a lagged, comparison group of 99 men who have sex with men who did not receive PrEP over 24 weeks using linear regression models, adjusting for age, race/ethnicity, education, and respective baseline scores. Logistic regression compared week 24 sexually transmitted infection (STI) rates.

Results: Over 48 weeks in the PrEP group, there were significant decreases in the number of unknown HIV status sex partners and increases in CRAS at all study visits; there was no consistent change in number of HIV+ sex partners or CIAS. Among participants at 2 sites, there were no significant differences between PrEP and non-PrEP users in change in number of partners, CIAS, CRAS, or STI rates at week 24.

Conclusions: Among early adopters of PrEP, there is some evidence for sexual risk compensation. Results support current guidelines of regular STI screening and behavioral risk reduction and adherence counseling with the provision of PrEP.

Received for publication May 30, 2018; accepted September 27, 2018.

From the *Keck School of Medicine, University of Southern California, Los Angeles, CA; †University of California, San Diego, San Diego, CA; ‡Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA; §Long Beach Department of Health and Human Services, Long Beach, CA; ‖University of Colorado Denver, Denver, CO; and ¶Gilead Sciences Inc, Foster City, CA.

Supported by National Institute of Mental Health (R21MH100979) and the California HIV Research Program (CHRP: MC08-SD-700 and EI-11-SD-005). Additional funding includes NIAID grants: AI 064086 (K24 to R. H.); AI 36214 (CFAR Clinical Investigation Core and Biostatistics and Modeling Core). Study drug was provided by Gilead Sciences.

R.H. is Professor Emeritus at UCSD and a current employee of Gilead Sciences. E.S.D. receives research support from Gilead, Merck, and ViiV and has been a consultant for Gilead, Merck, and Theratechnologies. The remaining authors have no funding or conflicts of interest to disclose.

Correspondence to: Joel Milam, PhD, Department of Preventive Medicine, University of Southern California, 2001 Soto Building, MC9239, Los Angeles, CA 90032 (e-mail: milam@usc.edu).

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

(*J Acquir Immune Defic Syndr* 2019;80:e9–e13)

INTRODUCTION

Tenofovir disoproxil fumarate (TDF) combined with emtricitabine (FTC) is the first Food And Drug Administration (FDA)-approved drug to reduce the risk of HIV infection in persons at risk of HIV acquisition.[1] The efficacy of TDF/FTC for pre-exposure prophylaxis (PrEP) to HIV is well-documented in several randomized controlled trials among populations at risk for HIV, including men who have sex with men (MSM)[2,3] and HIV serodiscordant heterosexual couples.[3,4] One concern about PrEP as an HIV prevention strategy is risk compensation, where those who take PrEP subsequently increase sexual behaviors that place them at risk for HIV and other sexually transmitted infections (STIs).

Mathematical modeling suggests that if risk compensation occurs, PrEP can paradoxically increase the transmission of (TDF/FTC) resistant HIV strains.[5] In addition, PrEP does not prevent other STIs, which could also increase with sexual risk compensation behaviors. On the other hand, some mathematical models indicate that despite potential risk compensation behaviors among those on PrEP, there is a net benefit at the population level through greater health care engagement (eg, increased STI screening and treatment).[6,7] Thus, because TDF/FTC will not always prevent HIV infection and does not prevent other STIs, safer sex/risk reduction counseling and regular HIV testing are components of the TDF/FTC product label and Risk Evaluation and Mitigation Strategy program.[8]

The results from the placebo-controlled PrEP efficacy trials supporting FDA approval indicated no risk compensation.[2,3] However, sexual practices were self-reported; participants in these studies were counseled that PrEP was unproven, and there was no guarantee of reducing the risk of acquiring HIV. Now that PrEP is accessible as a prevention strategy and declared as safe and efficacious by the FDA, the "real-world" experiences and large-scale implementation of PrEP will likely differ from trial results.[9] For example, data from MSM at risk of HIV who were given hypothetical scenarios regarding availability of PrEP (before FDA approval) found that more than 35% planned to decrease

condom use in response.[10] Data since FDA approval (July 2012) suggest variability in sexual behavior in response to PrEP.[11] A recent demonstration study (n = 112) found a significant reduction in condom use and increase in STIs in the 12 months after PrEP initiation.[12] Thus, sexual risk compensation remains a concern for PrEP as an HIV prevention strategy. This study examined the potential for sexual risk compensation in a demonstration study of PrEP that enrolled participants during 2013–2015.

METHODS

Study Setting

The California Collaborative Treatment Group (CCTG) is a multi-institutional, HIV clinical research network including 4 Southern California medical centers/care sites [University of California, San Diego (UCSD); University of Southern California (USC); Harbor-University of California Los Angeles; and Long Beach Health Department]. The CCTG 595 PrEP demonstration study (TAPIR) was a randomized controlled trial initiated in 2013 to test the effectiveness of a text messaging system vs. standard of care to support PrEP adherence over 48 weeks (NCT#01761643).[13] In the primary outcome study, overall PrEP adherence was high in both study arms, and all participants received PrEP regardless of study arm. The CCTG 595 study enrolled a convenience sample through recruitment with outreach in the community, internet, social network referral, and word of mouth of 398 MSM and transgender women from 435 screens at the 4 sites. Screen fails included 8 new HIV diagnoses, 19 that decided not to participate before baseline. Immediately after recruitment for this trial, at 2 of the sites (UCSD and USC), a lagged comparison group was recruited using the same recruitment methodology and eligibility criteria, except that PrEP use was an exclusion criteria for this group. Those who declined PrEP at the screening for the PrEP demonstration trial were the initial enrollees into this group. Those in the non-PrEP group were followed for 24 weeks.

Eligibility Criteria

Eligible participants for both the TAPIR study and the non-PrEP–using group were English- or Spanish-speaking HIV-uninfected MSM and transgender women (age $>$ 18 years). HIV was confirmed by a negative fourth generation antigen–antibody assay or an antibody assay in addition to HIV nucleic acid amplification test (NAAT).[13] Participants needed to have persistent elevated risk of HIV infection as determined by one or more of the following criteria: (1) at least 1 HIV-infected sexual partner for $\geq$4 weeks; (2) no condom use during anal intercourse with $\geq$3 male sex partners who are HIV-positive or of unknown HIV status during the last 3 months; or (3) no condom use during anal sex with $\geq$1 male partner plus an STI diagnosis during the last 3 months.

Study Procedures and Measures

For PrEP initiators (TAPIR participants), study visits occurred at baseline, weeks 4, 12, 24, 36, and 48. These participants were provided study drug (TDF/FTC) and received brief HIV prevention and adherence counseling with provision of study drug by trained study staff consistent with Centers for Disease Control and Prevention guidelines.[14] Participants were allowed to continue past week 48 on study drug through week 96 or until the last enrolled subject completed their week 48 visit. For non-PrEP users, 2 study visits occurred at baseline and week 24. After baseline assessment, these participants also received the same brief HIV prevention counseling that was provided to the TAPIR participants.

At baseline and week 24, participants in all groups completed a screening for STIs and confidential, computer assisted self-interview (CASI). STI screening included syphilis (serum rapid plasma reagin and if positive, confirmatory treponemal test), as well as NAAT of urine and swabs of pharynx and rectum for chlamydia and gonorrhea (Hologic Aptima). Referrals were made to providers or local sexually transmitted disease clinic for newly diagnosed STIs. STI treatment was confirmed by completion of a medication record review. Self-reported sexual risk behavior assessments at baseline and week 24 were identical in the PrEP and non-PrEP groups, and asked about sexual activity over the previous 30 days, including the number of HIV-positive partners, HIV status unknown partners, condomless insertive anal sex (CIAS) acts, and condomless receptive anal sex (CRAS) acts. Results of these assessments were not available to study staff and were transmitted electronically to a central location and not stored locally. Among PrEP users, at 3 months after their last visit that included study-provided PrEP, a subset of these participants reported on whether they continued their PrEP use (through a nonstudy source) and their sexual risk behaviors.

Statistical Analysis

Primary analyses were performed among PrEP initiators. Wilcoxon signed-rank test was used to compare the number of sex partners and sex acts at weeks 4, 12, 24, 36, and 48 to baseline.

Only data from the 2 sites that recruited the lagged non-PrEP comparison group were used to compare PrEP initiators with non-PrEP users. Baseline characteristics were summarized and compared between PrEP initiators and non-PrEP users using Fisher's exact test for categorical variables and Wilcoxon rank-sum test for continuous variables. Multivariable regression models were then performed to assess the change in sexual risk behaviors from baseline to week 24 adjusting for the following baseline variables: age, race/ethnicity, education, and respective baseline score for each outcome variable. Incidence of HIV infection and STIs during the study was calculated and compared between study groups using Fisher's exact test. A P value of <0.05 was considered statistically significant. No adjustments were made for multiple comparisons. Statistical analyses were performed in R (http://cran.r-project.org), version 3.3.2.

RESULTS

Study Flow

From 435 completing a screening visit, a total of 398 individuals (395 MSM and 3 transgender women) met the study eligibility criteria and enrolled into the TAPIR PrEP demonstration study. From 100 completing a screening visit, a total of 99 MSM met the study eligibility criteria and enrolled into the lagged, non-PrEP comparison arm. Retention in the PrEP initiation (TAPIR) group was n = 346 (87%) at week 24 and n = 324 (81%) at week 48. There were 2 seroconversions in this group over this period. Retention in the no PrEP group was n = 70 (71%) at week 24. Of the 29 early discontinuations, 2 were due to the initiation of PrEP and 2 were due to HIV seroconversion (remainder lost to follow-up).

Risk Behaviors Among PrEP Initiators Over 48 Weeks

The mean age of PrEP participants was 35.2 years (range 19–64; Table 1). Fifty percent were non-Hispanic white, 28% were nonblack Hispanic, and 15% identified as black alone or as part of multiple racial identity.

Compared with baseline, the number of previous 30-day HIV unknown status partners decreased at all visits (mean difference of 0.21–0.46 partners; Table 2). There was no consistent change in number of HIV+ partners, which significantly increased at week 36 only. The number of CRAS acts increased across all study visits (mean increase = 0.49–0.87 acts, all P's < 0.05). The number of CIAS acts did not significantly change (all P values >0.05).

Risk Behaviors 3 Months After Discontinuation of Study-Provided PrEP

Three months after the conclusion of the TAPIR study, 199 participants were successfully recontacted and assessed. Of these, 34.2% (n = 68) were no longer taking PrEP. The most commonly endorsed reasons for stopping PrEP included being in a monogamous relationship (25%, n = 17), lack of insurance (23.5%, n = 16), and self-perception of no longer being at risk for HIV (14.7%, n = 10). Compared with those who continued PrEP, those who were no longer on PrEP reported fewer sex partners and unprotected sex acts in the previous 3 months (data not shown; all P's < 0.05).

Comparisons Between PrEP Initiators and Non-PrEP Users Over 24 Weeks

At baseline, the PrEP initiators reported higher education and income, and were less likely to have had an HIV-infected sexual partner during the past 4 weeks or longer compared with non-PrEP users (Table 1). There were no significant differences between these groups when examining change in risk behaviors over 24 weeks (Table 3). For example, although PrEP users had an increase in the number of HIV-positive partners at week 24, compared with a decrease reported among those not on PrEP, this difference was not statistically significant [unadjusted mean increase = 0.21 (SD = 2.86) vs. −0.24 (SD = 1.22), respectively, P = 0.081; Table 3]. Multivariable models (adjusting for age, race/ethnicity, education, and baseline number of positive

TABLE 1. Characteristics of PrEP Initiators and Non-PrEP Users

	PrEP Initiators (n = 398)	PrEP Initiator Comparison Group (n = 302)	Non-PrEP Users (n = 99)	P*
Gender				
Male, N (%)	395 (99.3)	301 (99.7)	99 (100)	
Transgender women. N (%)	3 (0.7)	1 (0.3)	0 (0)	
Age, mean (SD)	35.2 (9.3)	34.7 (9.3)	42.4 (12.8)	<0.001
Race, N (%)				0.002
Hispanic	112 (28.1)	85 (28.6)	40 (40.8)	
Non-Hispanic white	198 (49.7)	153 (51.5)	35 (35.7)	
Black	52 (13.1)	38 (12.8)	21 (21.4)	
Other	36 (9.1)	21 (7.1)	2 (2.0)	
Education, N (%)				<0.001
High school or less	35 (8.8)	29 (9.6)	30 (30.3)	
Some college	149 (37.4)	115 (38.1)	40 (40.4)	
College or advanced degree	214 (53.8)	158 (52.3)	29 (29.3)	
Household income, N (%)				<0.001
<$2000/month	85 (21.4)	66 (21.9)	58 (58.6)	
>$2000/month	249 (62.6)	202 (66.9)	32 (32.3)	
Refuse	64 (16.1)	34 (11.2)	9 (9.1)	
Any STI at baseline, N (%)	104 (26.1)	78 (25.8)	17 (17.2)	0.10
Risk behavior (previous 30 days), mean (SD)				
No. of HIV+ partners	0.96 (1.87)	0.99 (1.76)	0.75 (1.70)	0.078
No. of HIV unknown partners	1.32 (2.81)	1.37 (2.93)	1.25 (2.56)	0.874
# CIAS events	2.8 (7.6)	2.58 (7.15)	2.25 (3.73)	0.190
# CRAS events	2.16 (6.89)	1.98 (6.24)	1.50 (3.28)	0.719
Inclusion criteria				
≥1 HIV+ partner for ≥4 weeks, N (%)	197 (49.5)	140 (46.4)	33 (33.3)	0.026
Condomless sex with ≥3 HIV +/unknown partners past 3 months, N (%)	276 (69.3)	212 (70.2)	78 (78.8)	0.120
Condomless sex with ≥1 male partner and STI diagnosis	66 (16.6)	53 (17.6)	7 (7.1)	0.009

*Fisher's exact test or Wilcoxon rank-sum test for bivariate comparisons between non-PrEP and PrEP comparison group.

TABLE 2. Change in Sexual Partnerships and Anal Sex Acts Among PrEP Users

Study Week	Mean Change (SD) From Baseline in Reported No. of Partners/Acts in Past 30 Days			
	HIV+ Partners	HIV Unk. Partners	CIAS	CRAS
Week 4	−0.08 (2.27)	−0.35 (2.82)*	0.24 (9.27)	0.87 (9.72)*
Week 12	−0.06 (1.97)	−0.21 (3.19)	−0.03 (7.91)	0.67 (8.31)*
Week 24	0.16 (2.81)	−0.35 (2.92)*	−0.03 (7.50)	0.67 (8.31)*
Week 36	0.66 (7.25)*	−0.46 (3.15)*	−0.04 (8.21)	0.71 (8.25)*
Week 48	0.07 (2.17)	−0.46 (3.25)*	−0.25 (8.08)	0.49 (7.68)*

*Wilcoxon signed-rank test $P < 0.05$.
HIV Unk.: HIV status unknown.

partners) also indicated no differences between PrEP users and nonusers in changes in any of the risk behaviors (previous month) from baseline to week 24 (all P's > 0.09; *data not shown*). For example, in the adjusted models, PrEP users on average had a 0.58 increase in the number of positive partners at week 24 compared with non-PrEP users (adjusted mean diff = 0.58, SE = 0.35, $P = 0.096$).

The STI incidence rate at week 24 was not different between those not on PrEP compared with PrEP users (n = 9, 12.5% vs. n = 47, 17.22%, respectively; $P = 0.375$). In a multivariable logistic regression model of STI incidence at week 24, this remained nonsignificant. There were n = 2 and n = 1 HIV seroconversions among those not on PrEP and PrEP users, respectively, up to week 24.

DISCUSSION

This study among early adopters of PrEP indicates a significant increase in CRAS after PrEP initiation (to all study visits up to 48 weeks). For TAPIR participants, PrEP was provided free of charge. Three months after the conclusion of the demonstration study, participants who remained on PrEP (either out-of-pocket or through their own insurance) had higher risk behaviors compared with those who stopped taking PrEP. Thus, some degree of sexual risk compensation occurred in the context of PrEP usage, most notably for increases in previous 30-day CRAS acts at all study visits after PrEP initiation (mean increases ranging from 0.49–0.89 over 48 weeks). Although the HIV infection risk estimate for each CRAS act is 1.4% (with substantial variation based on the characteristics of the partner, such as viral load),[15] PrEP would conceptually reduce this risk by 90%. Thus, considering variability in infectiousness across partnerships/time and that other risk behaviors (CIAS, number of HIV+ partners) did not show sustained increases, it is unclear whether this level of risk compensation would meaningfully undermine the protective effects of PrEP.

TABLE 3. Unadjusted Mean (SD) Change in the Previous 30-Day Number of Sexual Partnerships and Anal Sex Acts Among PrEP and Non-PrEP Users Over 24 Weeks

	PrEP (n = 274)	Non-PrEP (n = 72)
No. of HIV+ sex partners	0.21 (2.86)	−0.24 (1.22)
No. of HIV unk. status sex partners	−0.41 (2.84)	−0.46 (2.77)
Total no. of partners (positive/unknown)	−0.20 (3.91)	−0.69 (2.93)
CIAS	−0.66 (7.91)	−0.58 (3.16)
CRAS	0.54 (8.30)	0.01 (4.27)
Total no. of unprotected sex acts	0.21 (12.99)	−0.72 (5.49)

All P values >0.05. for differences between groups.
HIV unk., HIV status unknown.

One unexpected finding among those on PrEP over the 48-week study was a significant decrease in the number of sex partners of unknown HIV status. Future research should examine the possibility that PrEP usage may empower individuals to have more conversations about safer sex and/or discussing HIV status with their partners before sexual encounters.

When comparing a subset of the PrEP group with a lagged comparison group of non-PrEP users (up to the first 24 weeks only), and controlling for potential measured covariates, no differences between groups were observed for CRAS, CIAS, or incidence of any STI (at week 24 only). There was a marginal relative increase in number of HIV-infected partners among PrEP (vs. non-PrEP) users. Thus, there was limited evidence that PrEP (vs. non-PrEP) users display high levels of risk compensation.

Caution is needed when interpreting the results from these group comparisons. Despite using a similar recruitment strategy, protocol, and inclusion/exclusion criteria, there were notable differences between the PrEP initiators and the lagged, non-PrEP user comparison group beyond desire to initiate PrEP therapy. PrEP initiators were more likely to be white and of higher socioeconomic status (SES), whereas PrEP nonusers were more likely to be Hispanic or African American, and lower SES. We characterize the PrEP participants as higher-risk "early adopters," who were enthusiastic about accessing PrEP. For example, because insurance coverage for PrEP was still emerging during this study period, PrEP participants may have enrolled in the study solely for easy/affordable access to this prevention strategy. Thus, although we statistically controlled for potential measured covariates in the multivariable models, there are likely additional, unmeasured differences (eg, attitudes/beliefs) that could potentially prohibit important comparisons between these groups. In addition, PrEP users in this study had additional structured follow-up visits (weeks 4 and 12) that provided routine safer sex counseling and STI screening (and treatment) that co-occurred with PrEP administration, which may have mitigated potential increases in CRAS, CIAS, HIV infection, and STI incidence attributed to risk compensation.[16]

This study had several strengths and limitations. We successfully enrolled and retained individuals at risk of HIV (HIV prevalence at screening was 1.8% and 1% for PrEP initiators and nonusers, respectively) with a high STI prevalence at entry who were predominantly MSM. Although we used a CASI format for data collection because our primary outcomes were based on self-report, it is possible that social desirability bias may have influenced our results (eg,

those who started/stopped PrEP may have felt compelled to report that their risk levels increased/decreased). Generalizability to community-based PrEP use may be limited because adherence/care-received and self-reported risk behaviors in a research study (performed at HIV outpatient clinics) are likely unique from what might be found in the general population. Additional research regarding PrEP usage in general practice is needed to further explore potential risk compensation as PrEP utilization becomes more commonplace.

These findings have implications for how to manage sexual risk reduction counseling when prescribing PrEP. Our data would suggest on average that there was less than 1 additional CRAS act per month over the baseline of 2 CRAS per month; so, if the HIV risk was 1% per CRAS with a HIV-infected untreated partner, then risk would be 2% at baseline that would go up to 3% with increased CRAS. However, with a 90% reduction with PrEP, it would be reduced to 0.3%, which is much lower than the 2% before PrEP. Although risk compensation behaviors occur, these data indicate that they are likely not large enough to warrant a public health concern regarding undermining the protective effect of PrEP against new HIV infections. Still, risk reduction counseling and STI screening, which are guideline recommendations for PrEP administration, remain critically important. Although all participants in this study received risk reduction counseling and regular STI testing, their real-world implementation in mitigating risk compensation among PrEP users is unknown. Additional approaches could include materials for PrEP prescribers that emphasize the importance of risk reduction counseling (eg, practicing safer sex) and regular HIV testing.[8] Prescribing PrEP should not be conditional on acceptance of any behavioral risk reduction. However, counseling for risk reduction behaviors should be provided to anyone who is being started on PrEP to minimize risk of HIV and in particular for the reduction of STI risk. The results from this study support policies for physicians to provide appropriate nonjudgmental safer sex and behavioral counseling, and regular STI screening,[16] when administering PrEP to their patients.

ACKNOWLEDGMENTS

The authors thank our participants for volunteering for this study. They acknowledge the efforts of our study nurses Edward Seefried, Connie A. Funk, Sadia Shaik, Ruben Lopez, Sandra Diaz, and Robert Jimenez, as well as other study staff including Kelly Walsh, Marvin Hanashiro, Daisy Villafuerte, Janisse Mercado, Ramiro Correa, Michael Crump, Fang Wang, and Luis Mendez.

REFERENCES

1. FDA. Truvada approved to reduce the risk of sexually transmitted HIV in people who are not infected with the virus Avaiable at: http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm312264.htm. Accessed July 30, 2012.
2. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med.* 2010;363:2587–2599.
3. Smith DK, Thigpen MC, Nesheim SR, et al. Interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults. *MMWR Morb Mortal Wkly Rep.* 2012;61:586–589.
4. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med.* 2012;367:399–410.
5. Supervie V, García-Lerma JG, Heneine W, et al. HIV, transmitted drug resistance, and the paradox of preexposure prophylaxis. *Proc Natl Acad Sci U S A.* 2010;107:12381–12386.
6. Jenness SM, Sharma A, Goodreau SM, et al. Individual HIV risk versus population impact of risk compensation after HIV preexposure prophylaxis initiation among men who have sex with men. *PLoS One.* 2017;12:e0169484.
7. Punyacharoensin N, Edmunds WJ, De Angelis D, et al. Effect of preexposure prophylaxis and combination HIV prevention for men who have sex with men in the UK: a mathematical modelling study. *Lancet HIV.* 2016;3:e94–e104.
8. Kadan-Lottick NS, Robison LL, Gurney JG, et al. Childhood cancer survivors' knowledge about their past diagnosis and treatment: Childhood Cancer Survivor Study. *JAMA.* 2002;287:1832–1839.
9. Leibowitz AA, Parker KB, Rotheram-Borus MJ. A US policy perspective on oral preexposure prophylaxis for HIV. *Am J Public Health.* 2011;101:982–985.
10. Golub SA, Kowalczyk W, Weinberger CL, et al. Preexposure prophylaxis and predicted condom use among high-risk men who have sex with men. *J Acquir Immune Defic Syndr.* 2010;54:548–555.
11. Fonner VA, Dalglish SL, Kennedy CE, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. *AIDS.* 2016;30:1973–1983.
12. Lal L, Audsley J, Murphy DA, et al. Medication adherence, condom use and sexually transmitted infections in Australian preexposure prophylaxis users. *AIDS.* 2017;31:1709–1714.
13. Moore DJ, Jain S, Dube MP, et al. Randomized controlled trial of daily text messages to support adherence to PrEP in at-risk for HIV individuals: the TAPIR study. *Clin Infect Dis.* 2018;66:1566–1572.
14. CDC. Interim guidance: preexposure prophylaxis for the prevention of HIV infection in men who have sex with men. *MMWR Morb Mortal Wkly Rep.* 2011;60:65–68.
15. Baggaley RF, White RG, Boily MC. HIV transmission risk through anal intercourse: systematic review, meta-analysis and implications for HIV prevention. *Int J Epidemiol.* 2010;39:1048–1063.
16. Jenness SM, Weiss KM, Goodreau SM, et al. Incidence of gonorrhea and chlamydia following human immunodeficiency virus preexposure prophylaxis among men who have sex with men: a modeling study. *Clin Infect Dis.* 2017;65:712–718.