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Acceptability of Injectable and On-Demand Pre-Exposure Prophylaxis Among an Online Sample of Young Men Who Have Sex with Men in California

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Abstract

Purpose: Pre-exposure prophylaxis (PrEP) is an effective strategy to prevent HIV. However, low uptake of daily oral PrEP since Food and Drug Administration approval and low medication adherence among users have stimulated the investigation of other modalities for delivery, such as injectable PrEP and on-demand PrEP. The objective of this study was to determine the demographic and behavioral predictors of willingness to try alternative PrEP delivery mechanisms among young men who have sex with men (YMSM) who stated that they were unwilling to try daily oral PrEP.
Methods: YMSM in California were recruited through geosocial networking applications; we analyzed a subsample who stated that they were either ambivalent about trying or unwilling to try daily oral PrEP ($n = 265$). We used chi-square and Fisher's exact tests to determine characteristics associated with willingness to try injectable PrEP, willingness to try on-demand PrEP, and willingness to try either alternative form.
Results: For individuals who stated that they would not be willing to try daily oral PrEP, ~85% were willing to try on-demand and/or injectable PrEP. Individuals who reported some college or more reported greater willingness to try injectable PrEP (adjusted odds ratio [aOR]: 2.92; 95% confidence interval [CI]: 1.32–6.46), on-demand PrEP (aOR: 2.28; 95% CI: 1.06–4.90), or either method (aOR: 5.54; 95% CI: 1.78–17.22).
Conclusion: Future research should determine how to enhance uptake of emerging forms of PrEP among the individuals most at risk for HIV.

Keywords: gay/bisexual men, HIV pre-exposure prophylaxis, HIV prevention, men who have sex with men

Introduction

Pre-exposure prophylaxis (PrEP) is a biomedical HIV prevention strategy that can greatly reduce the chances of acquiring HIV among HIV-negative individuals.[1] In 2012, the U.S. Food and Drug Administration approved emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) for daily oral PrEP.[2] Models indicate that daily oral PrEP can reduce an individual's likelihood of contracting HIV by between 96% and 99% for rectal exposures.[3] PrEP represents a promising strategy for reducing HIV burden among the most heavily affected communities, including gay, bisexual, and other men who have sex with men (MSM), but low uptake of daily oral PrEP and suboptimal adherence to daily oral PrEP indicate that other modalities may be warranted.

In the largest PrEP trials and demonstration projects to date, between 32% and 86% of participants had detectable tenofovir (TFV) or TFV-diphosphate levels in plasma or peripheral blood mononuclear cells, and much lower proportions had biomarker evidence of daily adherence.[1,4–7] In addition, uptake of daily oral PrEP has been low. In the One Thousand Strong Cohort study of MSM in the United States, Parsons et al. found that 4% of participants had been prescribed PrEP and proposed a motivational cascade for improving uptake and adherence.[8] A study by Hoots et al. found similar uptake among men participating in the

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National HIV Behavioral Surveillance (NHBS) survey with only 4% of men reporting PrEP use.[9] In contrast, 57% of NHBS participants have an indication for PrEP based on Centers for Disease Control and Prevention (CDC) Guidelines.[9] To increase uptake and acceptability, more episodic regimens, such as injectable and on-demand PrEP, have recently been investigated.[10,11]

Cabotegravir is an investigational integrase inhibitor that has been shown in animal models to provide robust protection against simian/human immunodeficiency virus (SHIV) challenge through rectal, vaginal, and intravenous routes.[12] The first Phase IIa study that investigated cabotegravir as long-acting injectable (LAI) PrEP in HIV-negative men found that two simultaneous gluteal injections of long-acting cabotegravir (2 mL each, 800 mg total) every 12 weeks was a suboptimal regimen.[13] In response to these findings, a second Phase IIa trial (HPTN 077 in Brazil, sub-Saharan Africa, and the United States) was modified to evaluate an alternative dose of 600 mg (given as a single 3 mL injection) every 8 weeks after an initial 4-week injection interval.[14] Results from the primary analysis showed that LAI cabotegravir was tolerated well by low-risk HIV-negative men and women and the findings supported development of LAI cabotegravir for HIV prevention in men and women using the 600 mg dose (given as a single 3 mL injection) administered every 8 weeks after an initial 4-week injection interval.[14]

Data from the ECLAIR study found that participant satisfaction with cabotegravir was high, with most individuals indicating a desire to continue receiving PrEP through injections instead of taking an oral version of cabotegravir.[15] In the P18 cohort study among young MSM in New York, 81% of respondents stated that they were willing to use injectable PrEP and 79% of respondents stated that they would prefer injectable PrEP at 3-month intervals when compared with a daily oral pill.[16] In another study among 1071 MSM in the United States, Parsons et al. found that LAI PrEP administered every 3 months was acceptable among 54% of respondents and preferred when compared with daily oral formulations.[17] In contrast, 35% preferred daily oral pills, 34% preferred nonvisible implants, 25% preferred injections, and 4% preferred visible implants among another sample of MSM in the United States.[10]

On-demand PrEP involves an individual taking two doses of FTC/TDF between 2 and 24 hours before sexual activity and then subsequently taking one dose each at 24 and 48 hours after the initial two doses.[18] In the IPERGAY study, Molina et al. showed that MSM who took active FTC/TDF on-demand had a significantly lower incidence of HIV compared with individuals who took placebo in an on-demand schedule.[18] The authors reported that the active FTC/TDF group had a relative reduction in HIV incidence of 86%. However, the median number of doses used each month was 15. Given the high median number of doses each month, it is still unclear if truly episodic PrEP is sufficient to prevent HIV infection given exposure.[19,20] In addition, Parsons et al. have shown that individuals may be particularly inaccurate in predicting their future sexual behavior.[21]

Although previous studies have compared the likelihood of using different modalities of PrEP administration,[22] no studies to date have looked exclusively at respondents who stated that they were unwilling to try daily oral PrEP. The objective of this analysis was to determine the demographic and behavioral predictors of willingness to try alternative PrEP delivery mechanisms among the subset of respondents in a large online sample of young MSM (YMSM) in California who stated that they were unwilling to try daily oral PrEP.

Methods

Participants and procedures

From July 9, 2015 to August 20, 2015, participants were recruited in California through geosocial networking applications (apps) to complete a survey about PrEP. Geosocial networking apps displayed push notifications and prospective participants were directed to a screener to assess eligibility. To meet screening criteria, prospective participants needed to be (1) 18 to 29 years of age, (2) assigned a male sex at birth and identify their gender as male, (3) sexually active with other men in the past 5 years, (4) HIV negative, and (5) a resident of California. Although participation was based on sexual behavior with men as opposed to sexual orientation identity, we also asked, ''Do you consider yourself to be…'' with options of (1) Heterosexual or straight, (2) Gay, (3) Lesbian, (4) Bisexual, (5) Decline to Answer, or (6) Something else, with an option to specify.

Individuals who met the screening criteria were directed to the survey, which took ~20 minutes to complete. The last question collected the email address of the participant so that they could receive a $25 gift card for participation. The original sample was comprised of HIV-negative YMSM in California, 18–29 years of age. The present analysis was conducted with a subset of individuals from the original study with complete responses who identified as male, had never used PrEP, and indicated that they were either ambivalent about trying or unwilling to try daily oral PrEP.

Consent and institutional review board approval

Participants were recruited through push notifications on a geosocial networking app. When they clicked on the notification, they were redirected to a study website, which screened for eligibility. An informed consent document was displayed if participants passed the eligibility screener. After reading the informed consent, participants could agree to participate by clicking forward or decline study participation by exiting the website. The study was approved by the North General Institutional Review Board of the University of California, Los Angeles.

Measures

Demographic measures included race/ethnicity (White, Black/African American, Hispanic/Latino, or other/mixed), age (dichotomized as 18–25 and 26–29), sexual orientation identity (gay, bisexual, something else), sexual behavior (with men only or men and women), employment (full time, part time, full-time student, or other), education (dichotomized as less than college or some college and above), income ($0–$9,999, $10,000–$29,000, or $30,000 or more), current insurance (yes or no), and citizenship status (yes or no). Decline to answer options were provided for all demographic questions. Race/ethnicity was a multiselect question, whereas sexual orientation identity, sexual behavior,

employment, education, income, current insurance, and citizenship status were single-select questions.

We asked about perceptions of the risk of getting HIV (low, moderate, or high) and concern about becoming infected with HIV (not concerned, somewhat concerned, or very concerned). We also asked about timing of last HIV test (less than 6 months ago, between 6 months and 1 year ago, and more than 1 year ago/never), last sexually transmitted infection (STI) test (same categories), and if they had been diagnosed with an STI in the past year (yes or no). Lastly, we asked about substance use in the last 6 months, number of male sex partners in the last 6 months, whether the participant used a condom all the time for anal sex, had receptive anal sex with a man without a condom, insertive anal sex without a condom with an HIV-positive man, or had any HIV-positive male partners (all in the last 6 months). CDC risk score was calculated using age group (18–28 vs. 29), number of male sex partners in the last 6 months, number of times the individual had receptive anal sex with a man without a condom in the last 6 months, number of HIV-positive male partners in the last 6 months, number of times the individual had insertive anal sex with an HIV-positive man without a condom in the last 6 months, and use of methamphetamine in the last 6 months.

Willingness to use daily oral PrEP was measured on a 6-item scale ranging from extremely likely to extremely unlikely. Those who answered anything other than extremely or very likely were considered either ''ambivalent or unwilling'' to try daily oral PrEP. Therefore, individuals who stated that they were somewhat likely, somewhat unlikely, very unlikely, or extremely unlikely were classified in this ambivalent or unwilling category. In addition, we used a sensitivity analysis for participants who said that they were somewhat unlikely, very unlikely, or extremely unlikely to try daily oral PrEP to determine the validity of results.

Outcome measures

Participants were asked two additional yes/no questions about different forms of PrEP, injectable and on-demand. To assess willingness to try injectable PrEP, participants were asked ''Would you be more likely to take PrEP if it was only a shot every 3 months instead of a daily pill? (Assuming that both are equally effective).'' To assess attitudes about on-demand PrEP, participants were asked ''Would you be more likely to take PrEP if you only had to take the pill when you had sex instead of every day? (Assuming that both are equally effective).'' Participants who answered yes to these questions were considered willing to try the respective method(s). A third variable was created to indicate those who were willing to try either alternative method versus those who were not willing to try any form of PrEP.

Data analysis

Chi-square or Fisher's exact tests were used to determine the demographic and behavioral predictors of willingness to try alternative PrEP delivery mechanisms (willing to try injectable PrEP, willing to try on-demand PrEP, and willing to try either alternative forms), adjusting for multiple comparisons with the Benjamini–Hochberg correction. Variables that were significant at the bivariate level (alpha <0.05) were included in separate multivariate logistic regression models for each outcome.

Results

A total of 3842 individuals took the screener to assess survey eligibility. Of those who were screened, 1777 (46%) met the inclusion criteria to complete the survey. The removal of incomplete and duplicate surveys left a total of 761 unique participants. Of the original sample of 761 participants, 687 (90.3%) had never taken PrEP, and 265 (38.6%) of those who had complete responses were either ambivalent about trying or unwilling to try daily oral PrEP (subsequently referred to as ''unwilling''). In the sensitivity analysis, 105 participants were somewhat unlikely, very unlikely, or extremely unlikely to try daily oral PrEP.

When compared with those who were willing to try daily oral PrEP, respondents who were unwilling to try daily oral PrEP were more likely to be 18–25 years of age ($p = 0.002$), have an income of $30,000 or more ($p = 0.01$), report receiving an HIV test within the last year ($p = 0.008$), and report not being at all concerned about becoming infected with HIV ($p = 0.001$).

The subset sample was racially/ethnically diverse: Black (28.7%), Hispanic (27.5%), White (23.0%), and other/mixed race (20.8%) (Table 1). Two-thirds of the sample was 18–25 (66.8%) years of age and over three quarters identified as gay (76.6%). Most of the sample indicated they had sex with men only in the past 5 years (77.4%). Forty-four percent of the sample was employed full time and 75.5% completed some college or more. Many of the participants (62.6%) indicated that they were at least somewhat concerned about becoming infected with HIV. Only 6.8% of the sample indicated that they felt their risk of getting HIV was high, but 58% of individuals had a CDC risk score that indicated that they were at high risk for HIV infection (Supplementary Table S1; Supplementary Data available online at www.liebertpub.com/lgbt). The CDC risk score was constructed based on an article by Smith et al. using data on age group (18–28 vs. 29), number of male sex partners in the last 6 months, number of times the individual had receptive anal sex with a man without a condom in the last 6 months, number of HIV-positive male partners in the last 6 months, number of times the individual had insertive anal sex with an HIV-positive man without a condom in the last 6 months, and use of methamphetamine in the last 6 months.[23] This is also the risk algorithm that the CDC has used in its clinical practice guidelines for PrEP.[24] Individuals with scores greater than or equal to 10 were classified as high risk based on our risk score.

Nearly three-quarters (73.6%) of the sample indicated that they would be more willing to try injectable PrEP than daily oral PrEP. Race/ethnicity, employment status, education level, insurance status, concern with getting HIV, time since last HIV test, time since last STI test, any alcohol use in the last 6 months, and having had an HIV-positive male partner in the last 6 months were significantly associated with willingness to try injectable PrEP in bivariate analysis. After adjustment in a multivariate model, only education level remained significant. Those who had some college or more had higher odds of willingness to try injectable PrEP (adjusted odds ratio [aOR]: 2.92; 95% confidence interval [CI]: 1.32–6.46) (Table 2).

Among the sample, 74.3% indicated that they would be more willing to try on-demand dosing than daily oral PrEP. With the exception of having had an HIV-positive male

Table 1. Demographic and Behavioral Predictors of Willingness to Try Alternative Pre-Exposure Prophylaxis Delivery Mechanisms Among Young Men Who Have Sex with Men in California ($N = 265$)

		Injectable			*On demand*			*Either*		
	Overall n *(%)*	*Yes* n *(%)*	*No* n *(%)*	p	*Yes* n *(%)*	*No* n *(%)*	p	*Yes* n *(%)*	*No* n *(%)*	p
Total	265	195 (73.6)	70 (26.4)		197 (74.3)	68 (25.7)		226 (85.3)	39 (14.7)	
Race/Ethnicity										
White	61 (23.0)	43 (22.1)	18 (25.7)	*	50 (25.4)	11 (16.2)	**	55 (24.3)	6 (15.4)	**
Black/African American	76 (28.7)	47 (24.1)	29 (41.4)		40 (20.3)	36 (52.9)		51 (22.6)	25 (64.1)	
Hispanic/Latino	73 (27.5)	62 (31.8)	11 (15.7)		59 (29.9)	14 (20.6)		68 (30.1)	5 (12.8)	
Other/mixed	55 (20.8)	43 (22.1)	12 (17.1)		48 (24.4)	7 (10.3)		52 (23.0)	3 (7.7)	
Age										
18–25	177 (66.8)	130 (66.7)	47 (67.1)		132 (67.0)	45 (66.2)		149 (65.9)	28 (71.8)	
26–29	88 (33.2)	65 (33.3)	23 (32.9)		65 (33.0)	23 (33.8)		77 (34.1)	11 (28.2)	
Sexual orientation identity										
Gay	203 (76.6)	148 (75.9)	55 (78.6)		153 (77.7)	50 (73.5)		171 (75.7)	32 (82.1)	
Bisexual	57 (21.5)	43 (22.1)	14 (20.0)		41 (20.8)	16 (23.5)		51 (22.6)	6 (15.4)	
Something else	5 (1.9)	4 (2.1)	1 (1.4)		3 (1.5)	2 (2.9)		4 (1.8)	1 (2.6)	
Sexual behavior										
Men only	205 (77.4)	149 (76.4)	56 (80.0)		153 (77.7)	52 (76.5)		171 (75.7)	34 (87.2)	
Men and women	60 (22.6)	46 (23.6)	14 (20.0)		44 (22.3)	16 (23.5)		55 (24.3)	5 (12.8)	
Employment										
Employed full time	117 (44.2)	97 (49.7)	20 (28.6)	**	95 (48.2)	22 (32.4)	**	108 (47.8)	9 (23.1)	**
Employed part time	66 (24.9)	40 (20.5)	26 (37.1)		38 (19.3)	28 (41.2)		44 (19.5)	22 (56.4)	
Full-time student	48 (18.1)	38 (19.5)	10 (14.3)		39 (19.8)	9 (13.2)		45 (19.9)	3 (7.7)	
Other	34 (12.8)	20 (10.3)	14 (20.0)		25 (12.7)	9 (13.2)		29 (12.8)	5 (12.8)	
Education										
Less than college	65 (24.5)	36 (18.5)	29 (41.4)	**	37 (18.8)	28 (41.2)	**	43 (19.0)	22 (56.4)	**
Some college and above	200 (75.5)	159 (81.5)	41 (58.6)		160 (81.2)	40 (58.8)		183 (81.0)	17 (43.6)	
Income										
$0–$9,999	59 (22.3)	50 (25.6)	9 (12.9)		48 (24.4)	11 (16.2)		55 (24.3)	4 (10.3)	
$10,000–$29,000	109 (41.1)	77 (39.5)	32 (45.7)		75 (38.1)	34 (50.0)		87 (38.5)	22 (56.4)	
$30,000 or more	97 (36.6)	68 (34.9)	29 (41.4)		74 (37.6)	23 (33.8)		84 (37.2)	13 (33.3)	
Current insurance	192 (72.5)	153 (78.5)	39 (55.7)	**	154 (78.2)	38 (55.9)	**	177 (78.3)	15 (38.5)	**
U.S. citizen	244 (92.1)	179 (91.8)	65 (92.9)		178 (90.4)	66 (97.1)		206 (91.2)	38 (97.4)	
How would you rate your risk of getting HIV										
Low	130 (49.1)	100 (51.3)	30 (42.9)		101 (51.3)	29 (42.6)		117 (51.8)	13 (33.3)	*
Moderate	117 (44.2)	80 (41.0)	37 (52.9)		80 (40.6)	37 (54.4)		92 (40.7)	25 (64.1)	
High	18 (6.8)	15 (7.7)	3 (4.3)		16 (8.1)	2 (2.9)		17 (7.5)	1 (2.6)	
How concerned are you about becoming infected with HIV										
Not concerned	99 (37.4)	58 (29.7)	41 (58.6)	**	63 (32.0)	36 (52.9)	*	70 (31.0)	29 (74.4)	**
Somewhat concerned	70 (26.4)	55 (28.2)	15 (21.4)		58 (29.4)	12 (17.6)		67 (29.6)	3 (7.7)	
Very concerned	96 (36.2)	82 (42.1)	14 (20.0)		76 (38.6)	20 (29.4)		89 (39.4)	7 (17.9)	

(*continued*)

TABLE 1. (CONTINUED)

		Injectable			*On demand*			*Either*		
	Overall n *(%)*	*Yes* n *(%)*	*No* n *(%)*	p	*Yes* n *(%)*	*No* n *(%)*	p	*Yes* n *(%)*	*No* n *(%)*	p
Condom use all the time for anal sex in the last 6 months	96 (36.2)	78 (40.0)	18 (25.7)		78 (39.6)	18 (26.5)		87 (38.5)	9 (23.1)	
Last HIV test										
Less than 6 months ago	138 (52.1)	109 (55.9)	29 (41.4)	**	105 (53.3)	33 (48.5)	**	126 (55.8)	12 (30.8)	**
Between 6 months and 1 year ago	65 (24.5)	34 (17.4)	31 (44.3)		38 (19.3)	27 (39.7)		41 (18.1)	24 (61.5)	
More than 1 year ago/never	62 (23.4)	52 (26.7)	10 (14.3)		54 (27.4)	8 (11.8)		59 (26.1)	3 (7.7)	
STI diagnosis in the past year										
Any STI	55 (20.8)	44 (22.6)	11 (15.7)		45 (22.8)	10 (14.7)		50 (22.1)	5 (12.8)	
Last STI test										
Less than 6 months ago	129 (48.7)	104 (53.3)	25 (35.7)	**	102 (51.8)	27 (39.7)	**	118 (52.2)	11 (28.2)	**
Between 6 months and 1 year ago	68 (25.7)	34 (17.4)	34 (48.6)		40 (20.3)	28 (41.2)		43 (19.0)	25 (64.1)	
More than 1 year ago/never	68 (25.7)	57 (29.2)	11 (15.7)		55 (27.9)	13 (19.1)		65 (28.8)	3 (7.7)	
Substances used in the last 6 months										
Alcohol	204 (77.0)	159 (81.5)	45 (64.3)	**	164 (83.2)	40 (58.8)	**	186 (82.3)	18 (46.2)	**
Marijuana/pot	116 (43.8)	89 (45.6)	27 (38.6)		90 (45.7)	26 (38.2)		103 (45.6)	13 (33.3)	
Poppers	60 (22.6)	48 (24.6)	12 (17.1)		50 (25.4)	10 (14.7)		57 (25.2)	3 (7.7)	*
Other illicit drugs	36 (13.6)	25 (12.8)	11 (15.7)		24 (12.2)	12 (17.6)		28 (12.4)	8 (20.5)	
Methamphetamine/crystal	9 (3.4)	8 (4.1)	1 (1.4)		8 (4.1)	1 (1.5)		9 (4.0)	0 (0)	
Number of male sex partners in the last 6 months										
0–5	181 (68.3)	127 (65.1)	54 (77.1)		128 (65.0)	53 (77.9)		151 (66.8)	30 (76.9)	
6–10	55 (20.8)	44 (22.6)	11 (15.7)		45 (22.8)	10 (14.7)		48 (21.2)	7 (17.9)	
11 or more	29 (10.9)	24 (12.3)	5 (7.1)		24 (12.2)	5 (7.4)		27 (11.9)	2 (5.1)	
Had receptive anal sex with a man without a condom in the last 6 months	113 (42.6)	88 (45.1)	25 (35.7)		91 (46.2)	22 (32.4)		105 (46.5)	8 (20.5)	**
Had an HIV-positive male partner in the last 6 months	24 (9.1)	12 (6.2)	12 (17.1)	**	16 (8.1)	8 (11.8)		17 (7.5)	7 (17.9)	
Had insertive anal sex without a condom with an HIV-positive man in the last 6 months	59 (22.3)	45 (23.1)	14 (20.0)		47 (23.9)	12 (17.6)		54 (23.9)	5 (12.8)	
Risk score[a]										
Low <10	112 (42.3)	77 (39.5)	35 (50.0)		77 (39.1)	35 (51.5)		88 (38.9)	24 (61.5)	**
High ≥10	153 (57.7)	118 (60.5)	35 (50.0)		120 (60.9)	33 (48.5)		138 (61.1)	15 (38.5)	

*$p < 0.05$; **$p < 0.01$.

[a]CDC risk score was calculated using age group (18–28 vs. 29), number of male sex partners in the last 6 months, number of times the individual had receptive anal sex with a man without a condom in the last 6 months, number of HIV-positive male partners in the last 6 months, number of times the individual had insertive anal sex with an HIV-positive man without a condom in the last 6 months, and use of methamphetamine in the last 6 months.

CDC, Centers for Disease Control and Prevention; STI, sexually transmitted infection.

Table 2. Multivariate Logistic Regressions of Acceptability of Alternative Methods of Pre-Exposure Prophylaxis by Demographic and Behavioral Characteristics Among Young Men Who Have Sex with Men in California ($N = 265$)

Covariate	*Injectable OR (95% CI)*	*On demand OR (95% CI)*	*Either injectable or on demand OR (95% CI)*
Race/Ethnicity (ref = White)			
Black/African American	1.12 (0.45–2.79)	0.40 (0.16–1.01)	0.39 (0.09–1.58)
Hispanic/Latino	1.80 (0.64–5.03)	1.22 (0.43–3.47)	1.29 (0.26–6.47)
Other/mixed	1.09 (0.41–2.92)	1.59 (0.52–4.89)	1.53 (0.27–8.59)
Employed (ref = employed full time)			
Employed part time	0.56 (0.24–1.32)	0.56 (0.25–1.26)	0.40 (0.12–1.29)
Full-time student	0.89 (0.33–2.40)	1.38 (0.50–3.76)	2.19 (0.40–11.84)
Other	0.46 (0.18–1.21)	1.09 (0.40–3.00)	1.47 (0.33–6.52)
Education (ref = less than college)			
Some college and above	2.92 (1.32–6.46)*	2.28 (1.06–4.90)*	5.54 (1.78–17.22)*
Current insurance (ref = yes)			
No	0.65 (0.31–1.37)	0.81 (0.39–1.67)	0.63 (0.21–1.88)
How concerned are you about becoming infected with HIV (ref = not concerned)			
Somewhat concerned	1.60 (0.70–3.68)	1.53 (0.65–3.61)	5.05 (1.14–22.47)
Very concerned	2.44 (1.08–5.51)	1.26 (0.58–2.76)	2.14 (0.65–7.09)
Last HIV test (ref = less than 6 months ago)			
Between 6 months and 1 year ago	0.80 (0.21–3.05)	0.94 (0.25–3.58)	0.21 (0.03–1.47)
More than 1 year ago/never	1.21 (0.28–5.21)	3.91 (0.92–16.56)	0.23 (0.02–2.76)
Last STI test (ref = less than 6 months ago)			
Between 6 months and 1 year ago	0.43 (0.12–1.58)	0.64 (0.17–2.43)	1.14 (0.17–7.54)
More than 1 year ago/never	1.18 (0.28–4.95)	0.44 (0.12–1.70)	12.41 (0.87–176.42)
Alcohol use in the last 6 months (ref = yes)			
No	0.77 (0.33–1.81)	0.59 (0.27–1.28)	0.74 (0.22–2.50)
Had an HIV-positive male partner in the last 6 months (ref = no)			
Yes	0.25 (0.09–0.69)	—	—
How would you rate your risk of getting HIV (ref = low)			
Moderate	—	—	0.69 (0.24–2.00)
High	—	—	0.90 (0.09–9.05)
Popper use in the last 6 months (ref = no)			
Yes	—	—	0.53 (0.13–2.20)
Had receptive anal sex with a man without a condom in the last 6 months (ref = no)			
Yes	—	—	2.30 (0.74–7.13)

*$p < 0.05$.
CI, confidence interval; OR, odds ratio.

partner in the last 6 months, all variables significant in the bivariate injectable PrEP analysis were significant in the bivariate on-demand analysis. After adjusting for other variables, those with some college or more had 2.28 times higher odds (95% CI: 1.06–4.90) of being willing to try on-demand PrEP, but no other variables were significant in the model.

A large portion (85.3%) of the sample was willing to try injectable and/or on-demand PrEP. In addition to the variables that were significant in the bivariate on-demand analysis, there were a few additional significant bivariate associations: An individual's own HIV risk rating, use of nitrates/poppers, and having had receptive anal sex without a condom in the last 6 months were also associated with willingness to try either injectable or on-demand PrEP. Similarly, only education level remained significant in a multivariate model. Those who had at least some college had a higher odds (aOR: 5.54; 95% CI: 1.78–17.22) of willingness to try either injectable or on-demand PrEP. Results were similar in the sensitivity analyses (Supplementary Table S2).

Discussion

Among an internet sample of YMSM recruited in California, we found that 39% ($n = 265$) of PrEP-naive respondents were either ambivalent about trying or unwilling to try daily oral PrEP. Of the 265 individuals in this subset, 12% were only unwilling to try injectable PrEP, 11% were only unwilling to try on-demand PrEP, 15% were unwilling to try either form of alternative PrEP, leaving 62% who were willing to try both forms. YMSM who are unwilling to try any form of PrEP are good candidates for nonbiomedical HIV prevention strategies. Correct and consistent condom use may remain their best option for disease prevention. That said, more can be done to educate these YMSM on the benefits of PrEP, especially as it becomes more widely available in alternative formulations.

We did not detect associations between willingness to try alternate forms of PrEP and concern for acquiring HIV or having an HIV-positive partner in the last 6 months. Educational status was the only significant predictor of willingness

to try alternate forms of PrEP in all three multivariate models. This finding could be explained by the hypothesis that educated individuals have better access to, or better discernment of, health resources and information.

Given low PrEP uptake[9] as well as adherence barriers to the once-daily oral PrEP formulation,[25] individual, community, and structural interventions are needed to increase awareness of daily, injectable, and on-demand PrEP. For example, the Los Angeles County Department of Public Health deployed a social marketing campaign called GetPrEPLA.com, which depicts PrEP users as superheroes in a comic book format.[26] In New York City, the health department launched the ''We Stay Sure'' campaign depicting same-sex couples as well as racial/ethnic minority models.[27] These innovative, sex-positive social marketing campaigns should be adopted by health departments in other jurisdictions. In addition, the State of California now requires information about PrEP to be delivered with HIV post-test counseling through the recently passed AB 2640.[28]

In addition to these efforts underway, high school sexual education curricula should consider including PrEP as an HIV prevention option as many already do with condoms. Although conversations on LGBT health issues are not often included in such curricula,[29] PrEP can be discussed as an option that is available for everyone regardless of gender or sexual orientation. Individual-level education may confer the additional benefit of reducing social stigma and fear of side effects that may be associated with PrEP and result in greater willingness to try one or more formulations of PrEP as they become available. These multilevel efforts can provide more widespread understanding of PrEP and allow more individuals to decide whether PrEP is right for them.

Approximately 10% ($n = 15$) of individuals who had a high-risk score according to the CDC PrEP screener stated that they were unwilling to try either injectable or on-demand PrEP. While this group is small, it is important to understand why these individuals are not amenable to any form of PrEP since these high-risk individuals could benefit the most from PrEP use. By understanding the factors that drive individuals from PrEP contemplation to PrEParation along the motivational PrEP cascade, we can more fully ensure that at-risk individuals are educated about all HIV prevention strategies.[8]

Limitations

This study has important limitations as well as notable strengths. First, the survey was asked among a convenience sample of YMSM living in California who were recruited through geosocial networking apps. Therefore, it may not be generalizable to older MSM, younger MSM who do not use geosocial networking apps in California, and/or YMSM outside of California. Second, due to the small sample size of the subset analyzed, we may not have been able to detect associations in multivariable models due to power issues (i.e., Type II errors). Third, intentions to use PrEP may not reflect actual usage trends. In a study comparing willingness and intentions to use PrEP, Rendina et al. found that 43% of respondents were unwilling, 41% were willing but not intending, and 16% were willing and intending to take PrEP.[30] These differences highlight the need to further incorporate intentions into future surveys of potential PrEP users. Fourth, these proportions must be interpreted cautiously as recent data indicate that injectable PrEP needs to be administered at 2-month intervals as opposed to the quarterly timeframe asked about in the present and previous studies.[16,17] Greater frequency of injectable PrEP formulations may lower acceptability of this formulation for certain groups. Furthermore, the acceptability of on-demand PrEP was ascertained by asking the following question, ''Would you be more likely to take PrEP if you only had to take the pill when you had sex instead of every day? (Assuming that both are equally effective)?'' On-demand PrEP requires taking two doses of FTC/TDF between 2 and 24 hours before sexual activity and then subsequently taking one dose each at 24 and 48 hours after the initial two doses,[18] and the way the question was asked does not account for this nuance, which may bias estimates. Fifth, our survey did not ask about reasons for not wanting to initiate PrEP, but this information is key for future interventions that aim to increase uptake among the most at-risk populations. Sixth, the willingness to use daily oral PrEP question was asked on a 6-item scale, whereas the willingness to use either on-demand or injectable PrEP was asked as binary yes/no questions; this different methodology prevented a more nuanced analysis of individuals who may have been more ambivalent about these alternative forms of PrEP. Lastly, attitudes about both once-daily oral PrEP and alternative forms of PrEP have likely evolved since these data were collected.

Numerous education campaigns at both the state and local levels have led to greater uptake of PrEP. However, data from the current study are informative given that injectable PrEP is still undergoing clinical trials, and the findings can be used to tailor further education efforts. Study strengths include recruitment of participants through MSM-specific online outlets, and the possibility for reduced social desirability bias due to online assessment (compared with face-to-face assessment).

Conclusion

PrEP will only be as successful as the rate of uptake by populations who are the most at risk for HIV infection. A perceived inability to adhere to a daily medication may be a significant reason for unwillingness to try daily oral PrEP, but the reasons for rejection of either injectable or on-demand PrEP are still unclear. It is quite possible that as more scientific evidence supporting these alternative dosing schedules becomes available, willingness to try on-demand and injectable PrEP may increase. Future studies should focus on the small subset of individuals who are at risk for HIV, but who are unwilling to try any form of PrEP. Understanding their perceptions about PrEP and perceived barriers to uptake will allow HIV prevention efforts to maximize the utility of PrEP against HIV.

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Disclaimer

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Author Disclosure Statement

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