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## MSM at highest risk for HIV acquisition express greatest interest and preference for injectable antiretroviral PrEP compared to daily, oral medication

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### Abstract

Men who have sex with men (MSM) account for nearly 70% of new HIV diagnoses, with young black MSM at the highest risk for infection in the United States. Pre-exposure prophylaxis (PrEP) can decrease HIV acquisition in at-risk individuals by over 90%. However, therapeutic efficacy requires a daily pill, posing adherence challenges. Experimental modalities, including injectable PrEP given once every two months, may improve adherence among those most in need. To assess interest in and preference for injectable PrEP, an online survey was mounted on two popular MSM sexual networking apps. Differences by age, race, and other characteristics were examined using multinomial logistic regressions. Of 4,638 respondents, 73% expressed interest in injectable PrEP and 47% indicated they would prefer an injection (compared to 17% who prefer a daily pill and

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#### **Conflicts of Interest:**

Dr. Kenneth H. Mayer has received unrestricted research grants from ViiV Healthcare, Inc. and Gilead Sciences. The remaining authors declare that they have no conflict of interest.

#### **COMPLIANCE WITH ETHICAL STANDARDS**

##### *Ethical Approval*

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

##### *Informed Consent*

Informed consent was obtained electronically from all individual participants included in the study. A waiver of documentation of consent was approved by the Fenway Health Institutional Review Board.

36% who were unsure). Within this sample, interest in and preference for injectable PrEP was highest among MSM at highest risk for HIV infection (i.e., younger age groups, racial/ethnic minorities, those with riskier sexual behavior). As a result, if proven effective in clinical trials, injectable PrEP has the potential to reduce social disparities in HIV transmission among MSM.

### Keywords

HIV transmission; men who have sex with men; youth; racial/ethnic minorities; pre-exposure prophylaxis

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## INTRODUCTION

In 2015, nearly 40,000 people were diagnosed with HIV in the United States (U.S.), with men who have sex with men (MSM) accounting for nearly 70% of these infections (1). Important HIV transmission disparities exist, particularly by race and age. Blacks represent 12% of the U.S. population but account for 40% of HIV cases among MSM. Moreover, while HIV diagnoses among white MSM have fallen by 18% over the last decade, they rose by over 20% among black and Hispanic MSM (2). Gaps in the age of diagnosis have also grown. Adolescents and young adults (ages 13 to 29) represent over 40% of all new cases of HIV; 80% of youth diagnoses occur in young men who have sex with men (YMSM) (2). Black YMSM are at the highest risk for HIV infection in the U.S. Despite this subpopulation being the focus of enhanced HIV prevention initiatives (3), disparities persist.

In addition to behavioral risk reduction, pharmacological pre-exposure prophylaxis (PrEP) has the potential to effectively curtail new transmissions by protecting uninfected individuals from HIV transmission (4, 5). Currently, the only U.S. FDA-approved and recommended formulation of PrEP is the once daily, oral antiretroviral combination pill consisting of tenofovir disoproxil fumarate and emtricitabine (TDF/FTC). When taken as prescribed, PrEP users can decrease their risk for HIV infection by over 90% compared to non-users (4). However, maximizing the efficacy of PrEP can only be achieved through consistent medication adherence. In the intention-to-treat analysis of the 2010 iPrEx study, PrEP lowered HIV transmission among MSM and transgender women by 44% (6). Further, the as-treated analysis for iPrEx demonstrated that participants with TDF/FTC blood levels indicative of four or more pills per week had 92% lower transmission (6). This was subsequently supported by findings from the 2015 open-label extension (iPrEx OLE), which found that no participants with TDF/FTC blood levels indicative of four or more pills per week contracted HIV, demonstrating the importance of good adherence (7).

The CDC estimates that almost half a million U.S. MSM are PrEP candidates, however PrEP has not been scaled up to achieve a population-wide impact (8). In spite of reinforced evidence of PrEP's ability to reduce the risk for HIV acquisition, PrEP uptake initially remained low due to limited awareness and access barriers (9). Between 2012 and 2015, Gilead Sciences, Inc. (Foster City, CA), the sole manufacturer of TDF/FTC in the U.S., reported nearly 50,000 new PrEP prescriptions, an increase of over 500%, but with prominent discrepancies: only 7.5% of new users were under the age of 25 and only 10% were black (10).

Individuals who initiate daily oral PrEP may continue to face challenges related to adherence, particularly younger people (11). In order to offset adherence barriers, new PrEP modalities will need to alleviate challenges specific to daily oral therapy, including remembering to take a pill consistently. The safety and acceptability of injectable PrEP, or cabotegravir, has been established (12,13), and large-scale randomized controlled trials comparing injectable PrEP to a daily oral pill is underway to establish its efficacy among MSM (i.e., HPTN 083) and heterosexual women (i.e., HPTN 084) (14). Injectable PrEP has the potential to prevent unintended dosing interruptions because an injection would only be required once every two months according to the current regimen under study (14). Few studies have analyzed the perceived acceptability of injectable PrEP, particularly among those subpopulations most at risk for HIV (15–17), and to the best of our knowledge, no studies have examined acceptability of and preferences for injectable PrEP since trials have been undertaken and publicized. Understanding how to facilitate the incorporation of alternative medication regimens into individuals' schedules and lifestyles is essential to reducing HIV transmission.

The aim of this study was to assess differences in interest in and preference for oral vs injectable PrEP, and for reasons for not being interested in injectable PrEP, among a national sample of MSM in the U.S. Moreover, we examined variances in interest and preference by sociodemographics—particularly age and race/ethnicity—and behavioral factors, given the disproportionate burden of new infections in racial and ethnic minorities and in the young.

## METHODS

### Participants and Procedures

Data were collected from an anonymous online survey of adult (18 years of age or older) members of two MSM social/sexual networking apps. The study protocol and survey, conducted over 10 days in March 2016, was developed in collaboration with researchers at academic institutions, a community health center specializing in the care of MSM, and key personnel working with social/sexual networking platforms. A link to the survey was sent to desktop, mobile web and mobile app users who had been active in the past 90 days. In total, 16,466 members clicked the provided link to the survey, 4,638 of whom consented and were eligible. Eligibility included: being 18 years of age or older, being assigned male sex at birth and/or identifying as male (i.e., cis-man, transgender man or transgender woman), ever having sex with another man, and being HIV-uninfected or not knowing one's HIV status. This study was approved by the Institutional Review Board of The Fenway Institute of Fenway Health in Boston, MA.

### Study Instrument

In addition to sociodemographics, the measures for this study included history of PrEP use, interest in diverse PrEP modalities, and sexual risk behaviors. Participants took an average of 10 minutes to complete the survey. At the end of the survey, those who wished to be entered into a raffle for a chance to win one of three iPads were taken to a page separate from their survey responses to provide an email address.

## Sociodemographics

Sociodemographics included age, race/ethnicity, health insurance status, education, and employment status.

## Sexual and Condom Use Behaviors

Sexual and condom-use behaviors were measured using items adapted from previous MSM research studies (18) and included an inquiry of the number of male sexual partners in the past three months. Individuals who reported any intercourse with males in the past three months (i.e., “sexually active”) were asked the number of times they had condomless anal sex (CAS) with these partners. Respondents were then classified as: no CAS, one time, or two or more times.

## PrEP Use and Modality Preferences

Prior PrEP use was assessed by asking: *“Have you ever heard about PrEP (i.e., pre-exposure prophylaxis, medication taken by mouth BEFORE sex as protection against HIV infection)?”* Those who responded affirmatively were then asked if they had ever taken PrEP. Participants were also provided with a short description of injectable PrEP: *“Another form of PrEP that is currently being tested is an injection, or a shot, given by a doctor or nurse every two months. Instead of taking a pill by mouth every day, studies are underway to determine if having a shot every two months will offer protection against HIV.”* Individuals were then asked how interested they would be in injectable PrEP (categorized into: very/somewhat interested vs neutral or somewhat/very uninterested), reasons they might not be interested in this modality (informed by our prior formative study (19)), level of difficulty of taking injectable PrEP compared to a daily pill as prescribed, and their preference for injectable PrEP compared to a daily, oral pill (categorized into: prefer injectable vs unsure vs. prefer daily pill).

## Statistical Analysis

Response percentages were calculated overall, as well as by interest in and preference for injectable PrEP, for sociodemographic characteristics and sexual behaviors. Chi-squared tests were performed to examine differences in these measures by interest in and preference for injectable PrEP. To examine independent correlates of interest in and preference for injectable PrEP, multivariable binomial and multinomial logistic regression models were fit, respectively. All analyses were done in SAS v9.3.

As is common in online surveys, attrition occurred throughout the questionnaire. As a result, many sociodemographic characteristics, which were asked at the end of the survey, had substantial missing data. However, given the exploratory and descriptive nature of this study, we did not impute missing data, and missing observations were excluded.

## RESULTS

Of the 4,638 who completed the survey, participants came from all 50 states, Washington DC, and four U.S. territories. Sample characteristics are described in Table I. Briefly, 10.6% were 18 to 21 years old, 14.9% were 22 to 25 years old, and 13.7% were 26 to 29 years old.

Nearly half of the respondents (47.7%) identified as white, 25.1% as black and 11.4% as Hispanic. One in eight (11.9%) did not have any health insurance and 16.1% had public health insurance (e.g., Medicaid/Medicare). More than half (52.8%) reported CAS two or more times in the past three months. Approximately 15% reported ever having used oral PrEP.

### Interest in Injectable PrEP

Over two-thirds of respondents (73.2%) expressed interest in injectable PrEP; 44.7% were very interested and 28.5% were somewhat interested. Among those not interested in injectable PrEP, common reasons included: concern about long-acting side effects (50.8%), dislike of needles (30.0%), and dislike of having a foreign substance injected into their body (18.4%). Less common reasons were: not feeling that they need it (14.4%) and not thinking it would work (7.8%). In bivariate analyses (Table II), individuals who were interested in injectable PrEP were significantly more likely to: be 26–29 years old or 30–39 years old compared to 18–21 years old; be black or Hispanic compared to white; have completed high school or less compared to graduating college; report more CAS; and be oral PrEP experienced. In the multivariable model (Table II), participants who reported being interested in injectable PrEP had higher odds of: being younger (e.g., aOR 18–21 vs. 50+ = 1.55, 95% CI 1.03 to 2.32); being black (aOR = 1.44, 95% CI 1.14 to 2.09) or Hispanic (aOR = 1.53, 95% CI 1.11 to 2.09) compared to white; engaging in more CAS (aOR for 2+ vs 0 = 1.74, 95% CI 1.46 to 2.08); and previously using oral PrEP (aOR = 2.64, 95% CI 2.00 to 3.49). Those who reported being interested in injectable PrEP had lower odds of: being a college graduate (aOR = 0.79, 95% CI 0.64 to 0.97) compared to having less education than college.

### Preference for Injectable PrEP Vs Daily Pill

Nearly half (47.2%) of respondents indicated that they would prefer injectable PrEP compared to 16.8% who preferred a daily pill and 36.0% who were unsure; moreover, 47.0% also indicated that injectable PrEP would be less difficult than a daily pill to take as prescribed. In bivariate analyses (Table III), participants that preferred injectable PrEP were significantly more likely to: be younger; be black or Hispanic compared to white; have completed high school or less compared to graduating college; be born outside of the U.S.; and engage in more CAS. In the multivariable, multinomial model (Table III), respondents who reported preferring injectable PrEP to oral PrEP had higher odds of: being younger (e.g., aOR 18–21 vs. 50+ = 1.71, 95% CI 1.05 to 2.79); being black (aOR = 1.58, 95% CI 1.17 to 2.12) or Hispanic (aOR = 1.45, 95% CI 1.00 to 2.12) compared to white; engaging in more CAS (aOR for 2+ vs 0 = 1.52, 95% CI 1.21 to 1.91); and being oral PrEP experienced (aOR = 1.39, 95% CI 1.02 to 1.89). Compared to those who preferred a daily oral pill, those who reported being unsure about their preference had higher odds of being oral PrEP experienced (aOR = 1.63, 95% CI 1.18 to 2.23).

## DISCUSSION

Social inequities in HIV infection are well-documented (1–3). PrEP has the potential to decrease the number of new infections. However, currently PrEP is only available as a daily

pill, and uptake data suggests that those most at risk for HIV, including youth and racial/ethnic minorities, are less likely to initiate PrEP (10). Among those who initiate PrEP, studies also indicate that adherence is lower for younger and racial/ethnic minority individuals (20). As such, in order to reduce demographic imbalances in HIV transmission, it is essential to develop diverse, effective prevention modalities that are acceptable to disproportionately affected groups.

Regardless of its efficacy, if injectable PrEP is not acceptable to those most in need, its reach and impact will be limited and may in fact widen sociodemographic gaps. In our study, nearly half expressed a preference for injectable PrEP; a smaller proportion than a study conducted among men in New York City (15) but similar levels to a national study conducted in 2014 (17). Nearly one-third of respondents reported being unsure about their preference for injectable or oral PrEP, suggesting a need for further PrEP education and outreach, particularly delineating potential advantages and disadvantages of the distinct modalities for individuals and their personal contexts.

Moreover, results of our survey of a large sample of MSM in the U.S. suggest that some subgroups of individuals who are at the highest risk for HIV infection and have the lowest uptake of and adherence to oral PrEP—including black and Hispanic MSM, younger MSM, and individuals with higher behavioral risk—are most likely to be interested in and prefer injectable PrEP to oral PrEP. If the clinical trials demonstrate efficacy of injectable PrEP, and if injectable PrEP access and uptake among younger, black and Hispanic MSM reflects the level of interest that was seen in this study, this new modality could profoundly curtail the HIV epidemic in the U.S.

Given these findings, it is important that promotional efforts for injectable PrEP, if proven efficacious and approved by the FDA, consider how to best engage YMSM and racial/ethnic minorities. Actions may include developing diverse and inclusive advertisements, considering culturally-relevant motivations for using PrEP, addressing culturally-specific stigma related to PrEP use, and performing focused outreach in communities most affected by HIV (21, 22).

### Limitations

Results should be interpreted in light of the limitations. We collected survey data online and based on self-report, which may have introduced non-response bias and social desirability bias. We are not able to assess the potential of differential non-response, and if participation and non-response were not random, our results may not be fully representative of the target population. Social desirability bias may have resulted in misclassification of important measures; however, because this survey was self-administered and anonymous, social desirability is likely limited. There were missing data for some measures; however, levels of missing data were comparable to those observed in other self-administered surveys of MSM online (23,24). Moreover, assessment of interest and preferences for injectable PrEP remain hypothetical and may not translate to real-life uptake. Relatedly, when assessing their preference for a daily oral pill vs. injectable PrEP, participants were operating under the assumption that oral PrEP is an available medication and injectable PrEP is still experimental. Therefore, those who preferred oral PrEP may have done so because of

assumptions about superior safety and efficacy, potentially underestimating interest in and preference for injectable PrEP. Finally, participants were asked to choose between two prevention modalities—daily oral pill and injectable PrEP given every two months. Given the state of the research, it is likely that additional options will be available (e.g., on-demand PrEP, rectal gel), likely impacting preferences for and interest in injectable PrEP. This would be an important area for future research.

## CONCLUSIONS

Among this sample of at-risk MSM recruited online, interest in and preference for injectable PrEP was highest among MSM at highest risk for HIV infection (i.e., younger age groups, racial/ethnic minorities, those with higher sexual risk behavior). As a result, if shown to be effective in ongoing clinical trials and if future uptake follows this current trend, injectable PrEP may be able to lessen social inequities in HIV transmission.

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**Table I**

## Sample Characteristics

Measure		N	%
Age (n = 4638)	18–21	490	10.6
	22–25	690	14.9
	26–29	636	13.7
	30–39	1056	22.8
	40–49	772	16.6
	50+	944	21.4
Race/ethnicity (n = 3397)	White	1619	47.7
	Black	854	25.1
	Hispanic	386	11.4
	Asian/Pacific Islander	244	7.2
	Multiracial	244	7.2
	Other	50	1.5
Insurance status (n = 3326)	No insurance	397	11.9
	Private	1983	59.6
	Public	535	16.1
	Other	411	12.4
Educational attainment (n = 3384)	High school/GED or less	1377	40.7
	College graduate	1193	35.2
	Graduate/professional degree	814	24.1
Employment status (n = 3355)	Full-time employment	1243	37.0
	Not full-time employment	2112	63.0
Country of birth (n = 3364)	United States	2976	88.5
	Outside United States	388	11.5
Number of condomless anal sex acts, past 3 months (n = 3502)	0	1281	36.6
	1	371	10.6
	2+	1850	52.8
Oral PrEP experienced (n = 4630)	No	3941	85.1
	Yes	689	14.9

**Table II**

Factors Associated with Interest in Injectable PrEP, Bivariate and Multivariable<sup>a</sup>

Measure	Bivariate		Multivariable		
	N (%)	p	aOR (95% CI)	p	
Age	18–21	306 (63.7)	0.004	1.55 (1.03, 2.32)	0.037
	22–25	468 (68.9)		1.54 (1.11, 2.12)	0.009
	26–29	447 (71.4)		1.37 (1.00, 1.88)	0.049
	30–39	749 (72.2)		1.30 (1.01, 1.68)	0.040
	40–49	509 (66.8)		0.99 (0.77, 1.27)	0.940
50+	650 (66.5)		1.0		
Race/ethnicity	White	1148 (71.7)	<0.001	1.0	
	Black	670 (79.9)		1.44 (1.14, 1.82)	0.002
	Hispanic	304 (80.4)		1.53 (1.11, 2.09)	0.009
	Asian/Pacific Islander	178 (73.6)		1.16 (0.79, 1.71)	0.443
	Multiracial	181 (74.2)		1.02 (0.72, 1.44)	0.901
	Other	37 (75.5)		0.90 (0.45, 1.80)	0.773
Insurance status	No insurance	300 (76.1)	0.222	1.0	
	Private	1453 (73.9)		0.95 (0.71, 1.26)	0.712
	Public	407 (78.1)		1.24 (0.89, 1.73)	0.201
	Other	309 (76.1)		0.97 (0.69, 1.36)	0.850
Educational attainment	High school/GED or less	1050 (77.5)		1.0	
	College graduate	854 (72.5)	0.014	0.79 (0.64, 0.97)	0.022
	Graduate/professional degree	602 (74.6)		0.97 (0.77, 1.23)	0.804
Employment status	Full-time	916 (74.8)		1.0	
	Not full-time	1569 (75.2)	0.777	1.17 (0.97, 1.43)	0.108
Country of birth	United States	2204 (75.1)		1.0	
	Outside United States	287 (74.9)	0.955	0.90 (0.67, 1.20)	0.467
Condomless anal sex acts, past 3 months	0	842 (67.3)	<0.001	1.0	

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Measure	Bivariate		Multivariable	
	N (%)	P	aOR (95% CI)	P
Oral PrEP experienced	288 (79.3)		1.70 (1.27, 2.28)	<0.0001
	1461 (79.5)	1	1.74 (1.46, 2.08)	<0.0001
Oral PrEP experienced	563 (82.2)	Yes	2.64 (2.00, 3.49)	<0.0001
	2566 (66.3)	No	1.0	

Dependent variable=Being very or somewhat interested in injectable PrEP, compared to being neutral, somewhat or very uninterested

**Table III**  
Factors Associated with Preference for Injectable PrEP, Bivariate and Multivariable

Measure	Bivariate			Multivariable <sup>a</sup>				
	Prefer Injectable PrEP	Unsure	Prefer Oral Pill	p	Prefer Injectable PrEP aOR (95% CI)	p	Unsure aOR (95% CI)	p
N (%)								
Age	170 (53.3)	96 (30.1)	53 (16.6)	<0.001	1.71 (1.05, 2.79)	0.031	0.98 (0.58, 1.65)	0.943
18-21	258 (49.3)	185 (35.4)	80 (15.3)		1.71 (1.14, 2.55)	0.010	1.32 (0.87, 1.99)	0.188
22-25	278 (52.2)	175 (32.8)	80 (15.0)		1.97 (1.33, 2.93)	0.001	1.18 (0.78, 1.77)	0.444
26-29	474 (52.7)	311 (34.6)	115 (12.8)		1.94 (1.41, 2.68)	<0.001	1.19 (0.85, 1.66)	0.303
30-39	280 (43.1)	238 (36.6)	132 (20.3)		1.11 (0.81, 1.51)	0.528	0.87 (0.64, 1.20)	0.403
40-49	327 (38.0)	358 (41.6)	176 (20.4)		1.0		1.0	
50+								
Race/ethnicity	635 (42.0)	594 (39.3)	282 (18.7)	<0.001	1.0		1.0	
White	423 (52.7)	275 (34.3)	104 (13.0)		1.58 (1.17, 2.12)	0.003	1.30 (0.95, 1.77)	0.097
Black	213 (58.4)	100 (27.4)	52 (14.2)		1.45 (1.00, 2.12)	0.053	0.90 (0.60, 1.36)	0.626
Hispanic	102 (44.2)	94 (40.7)	35 (15.2)		1.18 (0.71, 1.96)	0.513	1.36 (0.81, 2.28)	0.244
Asian/Pacific Islander	113 (49.3)	75 (32.8)	41 (17.9)		1.03 (0.67, 1.57)	0.906	0.84 (0.54, 1.31)	0.438
Multiracial	23 (47.9)	18 (37.5)	7 (14.6)		1.12 (0.46, 2.73)	0.801	1.15 (0.46, 2.85)	0.768
Other								
Insurance status	182 (49.1)	137 (36.9)	52 (14.0)	0.511	1.0		1.0	
No insurance	895 (48.0)	660 (35.4)	310 (16.6)		1.07 (0.74, 1.55)	0.704	0.75 (0.51, 1.10)	0.137
Private	243 (48.2)	182 (36.1)	79 (15.7)		1.11 (0.73, 1.68)	0.639	0.89 (0.58, 1.36)	0.581
Public	163 (43.1)	145 (38.4)	70 (18.5)		0.67 (0.44, 1.04)	0.072	0.73 (0.47, 1.14)	0.168
Other								
Educational attainment	649 (51.2)	415 (32.7)	204 (16.1)	0.008	1.0		1.0	
High school/GED or less	497 (44.2)	440 (39.1)	187 (16.6)		0.91 (0.71, 1.18)	0.481	1.20 (0.92, 1.56)	0.178
College graduate	357 (46.1)	291 (37.5)	127 (16.4)		0.98 (0.73, 1.32)	0.899	1.12 (0.83, 1.52)	0.465
Graduate/professional degree	549 (47.4)	412 (35.6)	197 (17.0)	0.815	1.0		1.0	
Full-time	946 (47.5)	722 (36.3)	322 (16.2)		0.92 (0.72, 1.18)	0.511	0.92 (0.71, 1.18)	0.509
Not full-time	1299 (46.6)	1021 (36.7)	465 (16.7)	0.051	1.0		1.0	
United States								
Country of birth								

Measure	Bivariate				Multivariable <sup>†</sup>			
	Prefer Injectable PrEP	Unsure	Prefer Oral Pill	p	Prefer Injectable PrEP aOR (95% CI)	p	Unsure aOR (95% CI)	p
	N (%)							
	195 (53.4)	117 (32.1)	53 (14.5)		1.27 (0.88, 1.85)	0.207	1.02 (0.69, 1.52)	0.909
Outside United States								
Condomless anal sex acts, past 3 months								
0	513 (43.8)	433 (36.9)	226 (19.3)	0.001	1.0		1.0	
1	165 (48.1)	114 (33.2)	64 (18.7)		1.11 (0.78, 1.57)	0.559	0.84 (0.59, 1.21)	0.358
2+	873 (49.6)	638 (36.3)	249 (14.1)		1.52 (1.21, 1.91)	<0.001	1.18 (0.93, 1.49)	0.165
Oral PrEP experienced								
Yes	293 (47.0)	258 (41.4)	72 (11.6)	<0.001	1.39 (1.02, 1.89)	0.038	1.63 (1.18, 2.23)	0.003
No	1494 (47.2)	1105 (34.9)	564 (17.8)		1.0		1.0	

<sup>†</sup> Multinomial regression, dependent variable=Preferring injectable PrEP or being unsure, compared to preferring a daily oral pill