Understanding the Association Between PrEP Stigma and PrEP Cascade Moderated by the Intensity of HIV Testing

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Research Article

Keywords: Men who have sex with men, Pre-exposure prophylaxis, PrEP stigma, United States, HIV testing

Posted Date: February 21st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1326890/v1

Abstract

Background

In the United States, men who have sex with men (MSM) account for the majority of new HIV infections. On the other hand, pre-exposure prophylaxis (PrEP) is an effective strategy to curb HIV transmission, but it is widely underutilized. It is unknown how stigma affects PrEP care in the context of other HIV prevention strategies (e.g., HIV testing).[17] In the current study, we explored how PrEP and HIV-related stigma affect the PrEP care cascade (i.e., awareness, willingness, and uptake) and how the intensity of HIV testing services moderates the association.

Methods

We recruited a group of MSM from two cities in the U.S. With informed consent being collected, we included a total of 318 MSM in the current analysis. We employed bivariate and multivariable analyses to assess the association between PrEP stigma and PrEP cascade while controlling for potential confounders on each specific pathway. We further used a series of moderation analyses based upon the intensity of HIV testing within different timeframes to assess the association between PrEP stigma and PrEP cascade. In addition, we conducted the trend-analyses to assess the pattern of PrEP cascade across different time points of HIV testing.

Results

Compared with MSM who used PrEP, those who never used PrEP reported higher internalized (0.59 vs. 2.99) and vicarious PrEP stigma (3.66 vs. 5.56). Internalized PrEP stigma has significantly reduced the likelihood of PrEP willingness and PrEP uptake among this group. With the increased frequency of HIV testing, stigma became stronger to negatively impact the likelihood of PrEP willingness and PrEP uptake in MSM. The *Jonckheere–Terpstra test with Monte Carlo permutations* showed significant trend patterns across different frequencies of HIV testing. The same patterns have been identified under other timeframes (i.e., in the past 12m, 6m, and 3m).

Conclusions

Findings indicated that HIV prevention services might discourage MSM from PrEP use under the influence of stigma. A structural-level reform is urgently needed to turn the HIV service encounters into opportunities to facilitate and optimize the PrEP cascade among this group who may benefit from PrEP use.

Background

Men who have sex with men (MSM) are the most disproportionally burdened sexual minority by HIV.[1,2] Although targeted efforts have stabilized new HIV diagnoses and increased awareness of HIV status, MSM continue to be the most affected, accounting for 69% of newly HIV-diagnosed infections in 2018 in the United States.[1,2] The burden is exceptionally high for young MSM who disproportionately experience HIV diagnosis, suboptimal linkage to care, and HIV prevention services.[3–5]

HIV Prevention Continuum Framework conceptualizes the specific steps (i.e., HIV testing, linkage to prevention services, retention in services, and adherence support) along the HIV prevention spectrum. As the critical components of the *Framework*, HIV testing and pre-exposure prophylaxis (PrEP) are interconnected and play critical roles in the prevention spectrum.[6] As a gateway of initiating the continuum, HIV testing determines the direction of the following path. It is recommended that MSM at elevated HIV risks undergo HIV testing every 3-6 months.[1] With a negative HIV testing result, an uninfected person with HIV risk will be linked with and retained in HIV prevention services, such as PrEP care. With the ongoing engagement in the prevention process, the person will be retained in the prevention continuum as long as the risk remains to maintain the desired protective effect.[6] Furthermore, PrEP is an efficacious HIV prevention strategy when taken as prescribed, especially among MSM.[7]

Despite HIV testing and PrEP use having being considered crucial tools for ending the epidemic, HIV testing rates among MSM remain suboptimal in the United States.[8] Besides, a significant discrepancy was observed from lifetime HIV testing (i.e., 88.2%) to frequent HIV testing (i.e., 42.2%).[9] Furthermore, little data are available to assess the PrEP linkage and uptake rates initiated from HIV testing programs.[10] Although an upward trend in PrEP use has been observed among MSM across years, inadequate PrEP knowledge, limited awareness, and low uptake have been observed continuously.[11]

Unique barriers to the HIV prevention continuum have been identified among MSM, such as poverty, mental health status, access to healthcare, and insurance coverage.[9,11] HIV or PrEP related stigma also plays a crucial role in preventing MSM from seeking HIV care.[2,7,12,13] Even for individuals who are actively seeking HIV prevention services (e.g., HIV testing, linkage to PrEP), the internalized (e.g., self-perceived stigmatization) and vicarious stigma (e.g., stigmatized attitudes from health providers or significant others) that embedded within their life contexts impeding them from HIV prevention care, such as PrEP.[14]

Studies suggested that MSM receiving more intensive HIV testing services were more likely to engage in safer sex practices (e.g., condom use) than those who received less intensive services.[15,16] Moreover, the impact of HIV testing services on risk reduction behaviors (e.g., frequency of condom use, multi-partnership) is more substantial among HIV-positive MSM than among HIV-negative ones.[17] HIV testing services may represent an opportunity to enhance the HIV prevention care continuum. However, it is understudied how HIV testing services moderate the association between PrEP/HIV stigma and PrEP care linkage and uptake.[17] In the current study, we explored how PrEP and HIV-related stigma affect the PrEP care cascade (i.e., awareness, willingness, and uptake) and how the intensity of HIV testing services moderates the association. We hypothesized that the more intensive a man received HIV testing services, the more likely he engaged in PrEP care.

METHODS:

Methods

Study Design and Participants

The sampling and recruiting strategies have been documented in detail elsewhere.[18] Briefly, starting from 2019 May, we conducted a cross-sectional study in two cities (Nashville, Tennessee, and Buffalo, New York) in the

United States. We employed a multi-pronged recruiting strategy including peer referral, flyer distribution, social media posts, and venue-based and event-based recruitment. The study protocol was reviewed and approved by the Institutional Review Boards at the University of Rochester and Buffalo. With informed consent being collected, a total of 318 MSM were included in the current analysis.

Data collection and Measures

Participants were asked to complete a self-administered survey via the Research Electronic Data Capture (REDCap) to report data regarding demographics, sexual behaviors, history of substance use, HIV testing experience, mental health status, PrEP/HIV related stigma, and PrEP cascade (i.e., awareness, willingness, and uptake).

Demographics include their age (in years), race (Black vs. White), education level, housing status (stable vs. unstable), insurance coverage, marital status. Risk behaviors were measured by their sexual practice (e.g., condomless insertive or receptive sex, sex with HIV-positive partners, substance use during sex, and sex position). A series of indicators measured mental health status. Anxiety was assessed using the 7-item Generalized Anxiety Disorder Assessment (GAD-7) Scale (e.g., “Have you been feeling nervous, anxious, or on edge in the past four weeks?”; Cronbach’s α =0.93).[19] Depression was measured using the 9-item Patient Health Questionnaire (e.g., “In the past four weeks, how often did you feel little interest or pleasure in doing things?”; Cronbach’s α =0.94).[20,21] Loneliness was measured using the University of California at Los Angeles (UCLA) Loneliness Scale (e.g., “I feel left out”; Cronbach’s α =0.80).[22] Perceived stress was assessed using the 10-item Perceived Stress Scale (PSS) that measures stress in the past four weeks (e.g., “how often have you been upset because of something that happened unexpectedly?”; Cronbach’s α =0.89).[23] Suicide was measured using a four-question scale adapted from validated studies (e.g., “have you ever thought about or attempted to kill yourself?”; Cronbach’s α =0.83).[18,24] Internalized homophobia was measured by a four-item Internalized Homophobia Scale that measures the extent to which gay and bisexual individuals do not accept their sexual orientation or sexual identity (e.g., “Sometimes I dislike myself for being gay or bisexual”; Cronbach’s α =0.91).[25] Resilience was measured by the 10-item Conner-Davidson Resilience Scale (CD-RISC-10) (e.g., “I am able to adapt to change”, Cronbach’s α =0.88). The Condom use Self-Efficacy Scale measured confidence of condom use to assess one’s confidence with using a condom or asking sexual partners to use condoms (e.g., “I would feel comfortable discussing condom use with a potential partner before we engaged in sex.”; Cronbach’s α =0.88). A 12-item scale measured HIV testing self-efficacy (e.g., “Knowing where you can go for an HIV test”, “Getting tested for HIV at least every 3-6 months”; Cronbach’s α =0.91) to ask them how confident they were they about enacting behaviors concerning HIV testing.[30] HIV testing was measured by asking participants whether they had (yes vs. no) tested for HIV in the past 3, 6, or 12 months. PrEP and HIV related stigma was measured by internalized PrEP stigma (e.g., “I should avoid taking PrEP because it is only for slutty people”; Cronbach’s α =0.93), vicarious PrEP stigma (e.g., “I’ve seen/heard people not wanting to hang out with folks who are taking PrEP”; Cronbach’s α =0.93) and perceived HIV stigma toward MSM (e.g., “People I care about would stop being in touch with me after if I had HIV”; Cronbach’s α =0.94) that adopted from a recent study.[31] PrEP cascade was assessed using PrEP awareness, willingness to PrEP use in general and at specific scenarios (e.g., “If PrEP may cause mild side effects, such as nausea, headaches, and rashes in a small number of people, would still you take PrEP EVERY DAY so you can lower your HIV risk by 90%?”, “If you need to see a clinician every 3-6 months for a new prescription, would you still consider taking PrEP everyday to lower your HIV risk by 90%?”), and PrEP

uptake (i.e., ever used and currently using). This study used indicators along the PrEP cascade (i.e., PrEP awareness, willingness, and uptake) as dependent variables.

Statistical Analysis: Descriptive statistics were displayed for both continuous and categorical variables. We used *Chi-square* and *Independent t-test* to examine if demographics, risk behaviors, and mental health status varied by different stages of the PrEP cascade. We employed bivariate and multivariable analyses to assess the association between PrEP stigma and PrEP cascade while controlling for potential confounders on each specific pathway. Furthermore, a series of moderation analyses were conducted using *Hayes' PROCESS macro*[32] with 2,000 times bootstrapping samples to assess the effect of frequency of HIV testing under different timeframes (e.g., in the past 3, 6, 12, and 24month) on the association between PrEP/HIV stigma and PrEP cascade. Adjusted odds ratios and corresponding 95% confidence intervals were reported. In addition, trend analyses using the *Jonckheere–Terpstra test with Monte Carlo permutations* were used to assess the trend of PrEP cascade across different time points of HIV testing. We conducted all statistical analyses using *Stata 16.0TM* (StataCorp LP, College Station, Texas, USA).

Results

Participants Characteristics

A total of 318 MSM who self-reported as Black (n=209) or White (n=109) were included in the current analysis. The mean age of included participants was 25.86 years old (standard deviation [SD]=4.94), and 74.21% of them lived in Nashville, TN, and 25.79% lived in Buffalo, NY. The majority of them had some college degree or above (80.51%), reported insurance coverage (81.76%), had stable housing (75.79%), and were never married (90.57%). Among these MSM, 60.32% reported having condomless insertive sex, and 56.27% reported having condomless receptive sex. About one-quarter of them reported having sex with HIV-positive partners, 58.49% reported alcohol use during sex, and 39.49% reported recreational drug use during sex. MSM who were older, White, and had stable housing reported a higher prevalence of PrEP awareness and PrEP uptake than their peers. In addition, MSM who reported risk behaviors were more likely to report PrEP awareness, willingness, and uptake than those who did not. Furthermore, MSM who reported worse depression and loneliness conditions, better resilience, confidence in condom use, and HIV testing self-efficacy were more likely to report PrEP awareness and willingness and uptake (Table 1-2).

Table 1
Demographics and risk behaviors by PrEP cascade status (n=318)

		PrEP awareness (n=255, 80.19%)		PrEP willingness (n=260, 81.76%)		PrEP uptake (n=106, 33.33%)	
Demographics	**Overall**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**
Age [mean (sd)]	25.86 (4.94)	22.21 (4.05)****	26.76 (4.72)	25.17 (4.94)	26.01 (4.94)	24.89 (5.00) ****	27.79 (4.21)
Site							
Nashville	236 (74.21%)	25.85%****	74.15%	19.92%	80.08%	74.15%****	25.85%
Buffalo	82 (25.79%)	2.44%	97.56%	13.41%	86.59%	45.12%	54.88%
Race							
White	109 (34.28%)	5.50%****	94.50%	10.09%***	89.91%	49.54%****	50.46%
Black	209 (65.72%)	27.27%	72.73%	22.49%	77.51%	75.60%	24.40%
Education							
High School or less	62 (19.50%)	38.71%****	61.29%	16.13%*	83.87%	88.71%****	11.29%
Some college	129 (40.57%)	27.13%	72.87%	24.81%	75.19%	74.42%	25.58%
College and above	127 (39.94%)	3.15%	96.85%	12.60%	87.40%	48.03%	51.97%
Having Insurance coverage							
No	58 (18.24%)	34.48%****	65.52%	20.69%	79.31%	70.69%	29.31%
Yes	260 (81.76%)	16.54%	83.46%	17.69%	82.31%	65.77%	34.23%
Housing							
Stable	241 (75.79%)	12.86%****	87.14%	16.18%	83.82%	61.83%***	38.17%
Unstable	77 (24.21%)	41.56%	58.44%	24.68%	75.32%	81.82%	18.18%
Marital status							
Never married	288 (90.57%)	19.79%	80.21%	17.01%	82.99%	68.75%*	31.25%

Notes: ****<0.0001, ***<0.001, **<0.01, *<0.05

		PrEP awareness (n=255, 80.19%)		PrEP willingness (n=260, 81.76%)		PrEP uptake (n=106, 33.33%)	
Ever married	30 (9.43%)	20.00%	80.00%	30.00%	70.00%	46.67%	53.33%
Risk behaviors							
Condomless insertive							
Never	123 (39.68%)	26.02%***	73.98%	23.58%	76.42%	75.61%**	24.39%
Ever	187 (60.32%)	13.37%	86.63%	14.97%	85.03%	59.36%	40.64%
Condomless receptive							
Never	136 (43.73%)	25.00%***	75.00%	24.26%*	75.74%	76.47%**	23.53%
Ever	175 (56.27%)	13.14%	86.86%	13.71%	86.29%	57.71%	42.29%
Sex with HIV+ partners							
Never	230 (74.43%)	19.13%	80.87%	20.00%	80.00%	70.87%**	29.13%
Ever	79 (25.57%)	16.46%	83.54%	13.92%	86.08%	50.63%	49.37%
Alcohol use during sex							
Never	132 (41.51%)	33.33%****	66.67%	22.73%	77.27%	81.06%****	18.94%
Ever	186 (58.49%)	10.22%	89.78%	15.05%	84.95%	56.45%	43.55%
Recreational drug use during sex							
Never	192 (60.38%)	25.52%***	74.48%	20.83%	79.17%	71.88%*	28.13%
Ever	126 (39.62%)	11.11%	88.89%	14.29%	85.71%	58.73%	41.27%
Sex position							
Insertive	103 (32.39%)	25.24%	74.76%	23.30%	76.70%	69.90%	30.10%

Notes: ****<0.0001, ***<0.001, **<0.01, *<0.05

		PrEP awareness (n=255, 80.19%)		PrEP willingness (n=260, 81.76%)		PrEP uptake (n=106, 33.33%)	
Receptive	87 (27.36%)	13.79%	86.21%	13.79%	86.21%	59.77%	40.23%
Versatile	128 (40.25%)	19.53%	80.47%	17.19%	82.81%	68.75%	31.25%

Notes: ****<0.0001, ***<0.001, **<0.01, *<0.05

Table 2
Mental health, HIV prevention strategy, and HIV related stigma by PrEP cascade status (n=318)

		PrEP awareness		PrEP willingness		PrEP uptake	
	Overall	No	Yes	No	Yes	No	Yes
Mental Health							
Anxiety (α = 0.93)	7.57 (5.74)	6.75 (7.17)	7.78 (5.32)	6.14 (7.06)*	7.89 (5.36)	7.42 (5.95)	7.87 (5.30)
Depression (α = 0.94)	9.79 (7.47)	7.40 (8.20)**	10.38 (7.17)	7.95 (8.05)*	10.20 (7.28)	9.17 (7.67)*	11.03 (6.92)
Loneliness (α = 0.80)	19.07 (5.08)	17.40 (5.42)**	19.48 (4.91)	16.29 (5.59)****	19.68(4.75)	18.75 (5.15)	19.71 (4.88)
Perceived Stress (α = 0.89)	18.37 (5.77)	19.53 (4.23)*	18.09 (6.07)	18.72 (5.43)	18.30 (5.85)	18.58 (5.60)	17.95 (6.11)
Suicide (α = 0.83)	5.56 (3.17)	5.86(4.10)	5.49 (2.89)	4.71(2.65)*	5.75(3.24)	5.50 (3.29)	5.68 (2.91)
Internalized homophobia (α = 0.91)	1.78 (1.06)	1.87 (1.16)	1.76(1.04)	1.71 (1.04)	1.80 (1.07)	1.86 (1.12)*	1.63 (0.93)
Resilience (α = 0.96)	2.81 (0.92)	2.50 (1.36)**	2.89(0.76)	2.70 (1.15)	2.83 (0.86)	2.80 (1.03)	2.83 (0.65)
Confidence of condom use (α = 0.88)	4.13 (0.86)	3.88 (1.19)**	4.19 (0.74)	4.01 (1.20)	4.15 (0.76)	4.15 (0.88)	4.08 (0.81)
HIV testing self-efficacy (α = 0.91)	3.90 (0.90)	3.64(1.12)**	3.96 (0.83)	3.86 (1.15)	3.91 (0.84)	3.77 (0.94)	4.14 (0.75)***
HIV Prevention strategies							
HIV testing in the past 3m	203 (63.84%)	46.03%**	68.24%	31.03%****	71.15%	51.42%****	88.68%
HIV testing in the past 6m	236 (74.21%)	65.08%	76.47%	53.45%****	78.85%	66.51%****	89.62%
HIV testing in the past 12m	258 (81.13%)	76.19%	82.35%	63.79%****	85.00%	75.47%****	92.45%

Notes: ****<0.0001, ***<0.001, **<0.01, *<0.05

		PrEP awareness		PrEP willingness		PrEP uptake	
HIV testing in the past 24m	274 (86.16%)	76.19%*	88.63%	70.69%****	89.62%	82.08%**	94.34%
Risk-based HIV test	87 (27.36%)	14.29%***	30.59%	31.03%	26.54%	24.53%	33.02%
Sero-adaption	241 (75.79%)	38.10%****	85.10%	68.97%	77.31%	70.75%**	85.85%
Sero-sorting	205 (64.47%)	39.68% ****	70.59%	48.28%**	68.08%	64.15%	65.09%
Stigma							
Internalized PrEP stigma (α = 0.93)	1.99 (4.02)	–	–	2.03 (4.06)	1.99 (4.02)	2.99 (4.85)****	0.59 (1.57)
Vicarious PrEP stigma (α = 0.93)	4.77 (7.69)	–	–	5.88 (7.82)	4.61 (7.68)	5.56 (8.16)*	3.66 (6.86)
Perceived HIV stigma toward MSM (α = 0.94)	28.99 (9.42)	26.33 (10.39)**	29.65 (9.07)	25.28 (10.23)***	29.99 (9.42)	29.17 (9.85)	28.64 (8.54)
Notes: ****<0.0001, ***<0.001, **<0.01, *<0.05							

Associations Between Prep Stigma And Prep Cascade

Compared with MSM who used PrEP, those who never used PrEP reported higher internalized (0.59 vs. 2.99) and vicarious PrEP stigma (3.66 vs. 5.56). MSM who reported higher perceived HIV stigma towards MSM usually had a higher prevalence of PrEP awareness (29.65 vs. 26.33). While controlling for confounders on these pathways, internalized stigma significantly reduced the odds of being willing to use PrEP under various hypothetical scenarios, such as if PrEP may cause mild side effects (adjusted odds ratios [*aOR]=0.90, 95% confidence interval [CI]= 0.83, 0.97*), if need to see a clinician every 3-6 months for a new prescription (*aOR=0.90, 95%CI= 0.83, 0.97*), if need to get a blood test every 3-6 months to check if the pill has affected your kidney function (*aOR=0.89, 95%CI= 0.82, 0.97*), if need to get a regular HIV test every 3-6 months to determine your eligibility for PrEP (*aOR=0.88, 95%CI= 0.81, 0.96*), if it will not work well if don't use it daily (*aOR=0.92, 95%CI= 0.85, 0.99*), and if a friend or your partner(s) finds out you are taking PrEP and might suggest you are at risk for HIV (*aOR=0.84, 95%CI= 0.76, 0.92*). The internalized stigma also reduced the odds of ever using PrEP by 24% (*aOR=0.76, 95%CI= 0.65, 0.89*). Besides, mixed findings were identified for vicarious stigma and PrEP HIV stigma towards MSM on the PrEP cascade (Table 3).

Table 3
Association between PrEP stigma and PrEP cascade (PrEP willingness, and PrEP uptake) among men who have sex with men (n=318)

		Internalized stigma	Vicarious stigma	Perceived HIV stigma toward MSM
Willingness to use PrEP	Willingness (Overall)	0.96 (0.91, 1.01)	1.00 (0.89, 1.12)	**1.05 (1.00,1.11)**
	Willingness1	0.96 (0.88, 1.04)	1.01 (0.97, 1.06)	0.98 (0.94, 1.01)
	Willingness2	**0.90 (0.83, 0.97)**	1.00 (0.96, 1.04)	0.99 (0.96, 1.03)
	Willingness3	**0.90 (0.83, 0.97)**	1.00 (0.97, 1.05)	0.99 (0.96, 1.03)
	Willingness4	**0.89 (0.82, 0.97)**	1.00 (0.96, 1.04)	1.00 (0.96, 1.03)
	Willingness5	**0.88 (0.81, 0.96)**	1.00 (0.96, 1.05)	0.99 (0.95, 1.03)
	Willingness6	0.95 (0.88, 1.02)	**1.05 (1.01, 1.09)**	0.99 (0.96, 1.03)
	Willingness7	**0.92 (0.85, 0.99)**	1.01 (0.97, 1.05)	0.98 (0.94, 1.01)
	Willingness8	**0.84 (0.76, 0.92)**	0.98 (0.94, 1.02)	1.01 (0.98, 1.06)
PrEP uptake	Ever take PrEP	**0.76 (0.65, 0.89)**	0.97 (0.93, 1.01)	**0.96 (0.91, 0.99)**
	Currently taking PrEP	1.08 (0.75, 1.55)	1.03 (0.94, 1.12)	1.04 (0.96, 1.13)

Notes:

1. Willingness1: If a friend or your partner(s) finds out you are taking PrEP and might suggest you are at risk for HIV

2. Willingness2: if cause mild side effects

3. Willingness3: if see a clinician every 3-6 months

4. Willingness4: if get a blood test every 3-6 months

5. Willingness5: if get a regular HIV test every 3-6 months

6. Willingness6: if charged a co-pay (fee)

7. Willingness7: if it will not work well if you don't use it daily

8. Willingness8: if a friend or your partner(s) finds out you are taking PrEP and might suggest you are at risk for HIV

	Internalized stigma	Vicarious stigma	Perceived HIV stigma toward MSM
Willingness adjusted covariates include: race, site, education, age, alcohol and drug use during sex, condomless sex, sex position, HIV testing, condom use confidence, HIV testing self-efficacy, mental health comorbidity, resilience, homophobia			
Uptake adjusted covariates include: race, education, age, substance use during sex, insurance, HIV testing, condomless sex, HIV testing, condom use confidence, HIV testing self-efficacy, mental health comorbidity, resilience.			

Moderation effects by frequency of HIV testing under different timeframes

We conducted a series of moderation analyses based upon HIV testing at different timeframes (i.e., in the past 3-month, 6-month, 12-month, and 24-month). With the increased frequency of HIV testing, the effect of PrEP stigma became stronger to impact the likelihood of PrEP willingness and PrEP uptake negatively. Specifically, in the past 24-month HIV testing history, for every one-unit increase in PrEP stigma, the odds of reporting willingness to PrEP use gradually decreased from *0.97 (95%CI=0.93, 0.99)* when testing four times, *0.94 (95%CI=0.89, 0.99)* when testing six times, to *0.91 (95%CI=0.84, 0.98)* when testing eight times. Similarly, the odds gradually decreased from *0.77 (95%CI=0.65, 0.91)* when testing 2 times, *0.70 (95%CI=0.56, 0.87)* when testing 4 times, *0.63 (95%CI=0.44, 0.90)* when testing 6 times, to *0.57 (95%CI=0.34, 0.95)* when testing 8 times. The *Jonckheere–Terpstra test with Monte Carlo permutations* showed significant trend patterns across different frequencies of HIV testing. The same patterns have been identified under other timeframes (i.e., in the past 12-month, 6-month, and 3-month) (Table 4).

Table 4
Moderation effect of HIV testing at different time points between the association between PrEP stigma and the PrEP cascade (n=318) *

Moderation effect	Internalized stigma (aOR, 95% CI)		Vicarious stigma(aOR, 95% CI)		Perceived HIV stigma toward MSM(aOR, 95% CI)	
	PrEP willingness	PrEP uptake	PrEP willingness	PrEP uptake	PrEP willingness	PrEP uptake
24m testing (n=299)						
0 times	1.03 (0.99, 1.06)	0.99 (0.66, 2.44)	–	–	–	0.95 (0.89, 1.01)
2 times	0.99 (0.97, 1.02)	**0.77 (0.65, 0.91)**	–	–	–	**0.95 (0.91, 0.99)**
4 times	**0.97 (0.93, 0.99)**	**0.70 (0.56, 0.87)**	–	–	–	**0.95 (0.91, 0.99)**
6 times	**0.94 (0.89, 0.99)**	**0.63 (0.44, 0.90)**	–	–	–	0.95 (0.90, 1.01)
8 times	**0.91 (0.84, 0.98)**	**0.57 (0.34, 0.95)**	–	–	–	0.96 (0.89, 1.03)
Trend test[$]	**P<0.0001**	**P<0.0001**	**P<0.0001**	**P<0.0001**	**P<0.0001**	**P<0.0001**
12m testing (n=281)						
0 times	**1.03 (1.00, 1.06)**	0.84 (0.66, 1.07)	–	1.02 (0.94, 1.10)	–	0.98 (0.91, 1.04)
1 times	1.00 (0.98, 1.02)	**0.79 (0.66, 0.94)**	–	1.00 (0.94, 1.06)	–	0.97 (0.92, 1.02)
3 times	**0.94 (0.91,0.99)**	**0.69 (0.53, 0.89)**	–	0.96 (0.92, 1.00)	–	0.96 (0.92, 1.00)
5 times	**0.89 (0.83, 0.96)**	**0.60 (0.37, 0.97)**	–	**0.92 (0.85, 0.99)**	–	0.94 (0.88, 1.01)
Trend test[$]	**P<0.001**	**P<0.0001**	**P<0.001**	**P<0.0001**	**P<0.001**	**P<0.0001**
6m testing (n=255)						
0 times	1.02 (0.99, 1.05)	**0.86 (0.70, 0.95)**	–	–	–	0.98 (0.93, 1.04)

Notes: *Willingness adjusted covariates include: race, site, education, age, alcohol and drug use during sex, condomless sex, sex position, condom use confidence, HIV testing self-efficacy, mental health comorbidity, resilience, homophobia; Uptake adjusted covariates include: race, site, education, age, substance use during sex, insurance, HIV testing, condomless sex, HIV testing, condom use confidence, HIV testing self-efficacy, mental health comorbidity, resilience. [$]Exact p-value is calculated by 10,000 Monte Carlo permutations using the *Jonckheere–Terpstra test.*

Moderation effect	Internalized stigma (aOR, 95% CI)		Vicarious stigma(aOR, 95% CI)		Perceived HIV stigma toward MSM(aOR, 95% CI)	
	PrEP willingness	PrEP uptake	PrEP willingness	PrEP uptake	PrEP willingness	PrEP uptake
2 times	**0.96 (0.93, 0.99)**	**0.65 (0.51, 0.84)**	–	–	–	0.96 (0.92, 1.00)
4 times	**0.90 (0.85, 0.96)**	**0.50 (0.79, 0.85)**	–	–	–	0.93 (0.87, 1.00)
5 times	**0.87 (0.81, 0.94)**	**0.43 (0.22, 0.87)**	–	–	–	0.92 (0.83, 1.02)
Trend test[$]	**P<0.0001**	**P<0.0001**	**P<0.0001**	**P<0.0001**	**P<0.0001**	**P<0.0001**
3m testing (n=219)						
0 times	**1.03 (1.00, 1.07)**	0.80 (0.62,1.04)	–	1.04 (0.97, 1.11)	–	0.99 (0.94, 1.05)
1 times	**0.97 (0.95, 0.99)**	**0.71 (0.60, 0.85)**	–	**0.96 (0.91, 1.00)**	–	**0.96 (0.92, 1.00)**
2 times	**0.91 (0.88, 0.95)**	**0.64 (0.48, 0.85)**	–	**0.89 (0.82, 0.96)**	–	**0.93 (0.87, 0.99)**
3 times	**0.87 (0.81, 0.92)**	**0.58 (0.37, 0.90)**	–	**0.83 (0.73, 0.95)**	–	**0.99 (0.82, 0.99)**
Trend test[$]	**P<0.0001**	**P<0.0001**	**P<0.0001**	**P<0.0001**	**P<0.0001**	**P<0.0001**

Notes: *Willingness adjusted covariates include: race, site, education, age, alcohol and drug use during sex, condomless sex, sex position, condom use confidence, HIV testing self-efficacy, mental health comorbidity, resilience, homophobia; Uptake adjusted covariates include: race, site, education, age, substance use during sex, insurance, HIV testing, condomless sex, HIV testing, condom use confidence, HIV testing self-efficacy, mental health comorbidity, resilience. [$]Exact p-value is calculated by 10,000 Monte Carlo permutations using the *Jonckheere–Terpstra test.*

Discussions

To our knowledge, the current study is the first one to assess the moderation effect of intensity of HIV testing on the association between PrEP stigma and PrEP cascade among MSM in the United States. Consistent with literature, PrEP stigma remains a formidable barrier to engaging in PrEP cascade by discouraging them from seeking information, care and support, preventing them from getting tested, and linking and retaining in care.[33] For instance, in a Demo project in San Francisco, MSM reported a feeling of being stigmatized by their significant others (e.g., sex partners, friends, and health providers) due to their decision to start using PrEP.[34] These stigmatized feelings and experiences hindered MSM from accessing and engaging in care with a reduced quality of care and deteriorated intervention effectiveness.[35,36]

Contrary to our hypothesis, findings indicated that the increased intensity of HIV testing services might discourage MSM from PrEP uptake or willingness to use. With the higher intensity of HIV testing, MSM who

encounter stigma were less likely to use or be willing to use PrEP. The same patterns have been observed under different periods (i.e., in the past 24, 12, 9, 6, and 3-month timeframe). Several reasons may explain the observed but unexpected phenomenon. *First*, studies revealed that MSM might have HIV testing experience in an unfriendly testing environment created by health professionals.[33,37] The hostile feeling was strong in young and racial/ethnic minority MSM.[37–39] The hostile environment discouraged MSM from engaging in other HIV prevention services, including PrEP care.[33,37] *Second*, some MSM may use frequent HIV testing as a strategy for HIV prevention. Instead of using PrEP, MSM use HIV testing to assess their risks. Furthermore, the cost of HIV testing is usually much lower than the cost of taking PrEP. *Third*, scarcity of comprehensive support for MSM was identified as a barrier for MSM engaging with PrEP care. Some MSM reported a lack of PrEP education and PrEP care navigation in HIV testing centers. MSM may not be aware of PrEP availability or clear about the PrEP care procedure.[37] *Lastly*, there may be a lack of provider knowledge preventing MSM from getting recommendations for PrEP care in HIV testing sessions.[40] In contrast, providers may play a key role in comparing the pros and cons of PrEP uptake decisions.[41] On the other hand, interventions have successfully linked MSM with PrEP care in educational and supportive settings. For instance, a study conducted in an HIV clinic successfully navigated 21% of HIV testing patients to PrEP care, and 16.3% initiated PrEP by simply providing HIV prevention information.[10]

Findings in this study are subject limitations. *First of all*, as the nature of the cross-sectional study design, we cannot make causal inferences between the association between PrEP stigma and PrEP cascade. Future longitudinal studies are needed to explore this temporal association. *Second*, participants' self-reported risk behaviors may be underreported due to social desirability bias. Their self-reported behaviors may also be subject to recall biases. *Third*, due to the limited sample size, we cannot stratify the moderation analyses by other effect modifiers (i.e., race, site locations). However, we have controlled them as confounders when assessing the associations. *Fourth*, as the original purpose was not designed to explore PrEP stigma and PrEP cascade, some unidentified confounders may affect the accuracy of the reported effect sizes. Future studies are needed to be specifically designed to explore the studied associations. Fifth, due to the sample scheme, we only included Black and White MSM in the current analysis. As MSM with other racial/ethnic identities may experience various risk factors and respond differently to the HIV prevention services, findings from the current study may suffer limited generalizability to broader MSM populations in the United States.

Conclusions

Increasing PrEP use is part of the national HIV/AIDS strategy,[42] and it is considered as one of the four pillars in the *Ending the HIV Epidemic* initiative in the United States.[8] Despite the Center for Disease Control and Prevention (CDC) and United States Prevention Service Task Force offering comprehensive guidelines for prescribing and managing PrEP,[43,44] and an upward trend has been observed across years since its approval,[7] the current PrEP uptake among MSM is still suboptimal to substantially reduce HIV incidence.[11,45] On the other hand, most MSM had participated in HIV testing at different time points.[9,46] Health providers may miss opportunities to provide PrEP to MSM patients who would benefit from using it on HIV prevention services. For instance, health professionals who conduct routine and regular HIV testing can assess patients' risk behaviors and prescribe PrEP as needed. They can play a critical role in this effort.[40,45] Therefore, a structural-level reform (e.g., educational programs at testing settings, consultation services for MSM at testing settings, education

among health professionals) is urgently needed to turn the HIV service encounters into opportunities to facilitate and optimize the PrEP cascade among this group who may benefit the most from PrEP use.

List Of Abbreviations

MSM
Men Who Have Sex With Men
PrEP
Pre-exposure Prophylaxis
REDCap
Research Electronic Data Capture
GAD-7
Generalized Anxiety Disorder Assessment
UCLA
University of California at Los Angeles
PSS
Perceived Stress Scale
CD-RISC-10
10-item Conner-Davidson Resilience Scale
SD
Standard Deviation
aOR
Adjusted ODDs Ratios
CI
Confidence Interval
CDC
Center for Disease Control and Prevention

Declarations

Ethics approval and consent to participate: The study protocol was reviewed and approved by the Institutional Review Boards at the University of Rochester and the University at Buffalo. All participants provide written consent to participate in the current research

Consent for publication: All authors read and approved the final manuscript

Availability of data and material: Limited de-identified raw data available from the corresponding author upon reasonable request

Competing interests: not applicable

Funding: The study was supported by the University of Rochester School of Medicine and Dentistry and School of Nursing Joint Award for Excellence in HIV Research). The content is solely the responsibility of the authors and does not necessarily represent the official views of University of Rochester.

Authors' contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Chen Zhang and Yu Liu. The first draft of the manuscript was written by Chen Zhang and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Acknowledgements: We would like to thank all study participants for their time, as well as staff from the Nashville Council on AIDS, Resources, Education and Support, MyHouse at Nashville (My Voice Community Engagement and Research Council), and Evergreen Health at Buffalo for their facilitation of participant recruitment and data collection process.

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