

Medication Adherence Among Men Who Have Sex with Men at Risk for HIV Infection in the United States: Implications for Pre-Exposure Prophylaxis Implementation

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Abstract

Pre-exposure prophylaxis (PrEP) is a promising HIV prevention approach for men who have sex with men (MSM), however non-adherence could limit its effectiveness. Understanding the experiences of HIV-uninfected MSM taking routine medications can provide valuable insights into open label PrEP adherence in real world settings and guide development of PrEP adherence interventions. In this study, we examined self-reported medication-taking experiences and facilitators and barriers of medication adherence among a geographically-diverse online sample of HIV-uninfected US MSM. Among 1480 participants, 806 (54%) reported taking medications regularly, of whom 80% reported taking medications for treatment and 55% for prevention purposes. Facilitators of medication adherence included establishing a routine, keeping medication visible, and using a pill-box; barriers included forgetting, changes in routine, and being busy or away from home. Only 45% rated their medication-taking ability as excellent, and 36% reported not missing any doses in the past 30 days. In multivariable analyses, older men and those not reporting any adherence barriers were more likely to report excellent adherence, and men willing to use PrEP were more likely to report perfect 30-day adherence. Counseling strategies to build pill-taking routines and support younger MSM are suggested to maximize the public health impact of PrEP.

Introduction

PRE-EXPOSURE PROPHYLAXIS (PrEP) is a rapidly emerging HIV prevention strategy, with four large clinical trials demonstrating the safety and efficacy of daily oral chemoprophylaxis in HIV-uninfected populations.¹⁻⁴ In 2012, the United States (US) Food and Drug Administration (FDA) approved emtricitabine/tenofovir (FTC/TDF) as a once-daily pill to prevent HIV acquisition in at-risk adults,⁵ and several demonstration projects are underway to evaluate its application in real-world settings.⁶

One group that has great potential to benefit from PrEP is HIV-uninfected, sexually-active men who have sex with men (MSM). In 2011, the CDC issued interim guidance for PrEP

use in MSM at high-risk for HIV acquisition⁷ and in May 2014 comprehensive PrEP guidelines were released.⁸ MSM account for the greatest proportion of new HIV infections in the US,⁹ with a 34% increased incidence among 13- to 29-year-old MSM and a 48% increased incidence among young African-American MSM between 2006 and 2009.¹⁰

Researchers and the US FDA have noted that PrEP efficacy is closely tied to adherence.^{1,3,11-13} In the iPrEx study conducted in MSM and transgender women across four continents, preventive efficacy of FTC/TDF was 42% in the overall cohort, and rose to an estimated >90% among participants with detectable drug levels in blood.¹ More recently, two large PrEP trials failed to demonstrate efficacy in women, likely due in part to low adherence.^{11,14}

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Presently, rates of open-label PrEP use as an HIV-prevention strategy are largely unknown, and there are limitations in generalizing from adherence observed in placebo-controlled clinical trials to real-world PrEP use.^{15–17} The experiences of HIV-uninfected MSM taking routine medication regimens, including prescription and over-the-counter medications,¹⁸ could provide valuable insights into potential adherence rates and facilitators and barriers to daily PrEP regimens, and inform the development of intervention approaches to support PrEP adherence among MSM.

The objectives of this study were to examine medication-taking experiences to identify facilitators and barriers of regular medication use and characterize overall self-reported adherence rates and correlates of medication adherence among a geographically-diverse sample of HIV-uninfected, sexually active US MSM.

Methods

US MSM were recruited from two online social networking sites (Facebook and Black Gay Chat) and asked to complete a secure, anonymous online survey. Data were collected from November 30 to December 19, 2010, shortly after the release of iPrEx results.⁵ Details on recruitment methods have been published previously.¹⁹ In brief, the online self-administered survey gathered information on demographics, HIV testing and infection, sexual activity, and experience with taking medications (prescribed, over-the-counter, vitamins, and supplements). Eligible participants included men age 18 or older. The study was reviewed by the Emory University Institutional Review Board and was determined to be exempt.

The study sample was restricted to men who reported being HIV-uninfected and completed survey questions on sexual practices and medication use. Barriers to regular medication use were assessed by answers to “what is the main thing that makes taking your medication every day difficult or just not possible to do on some days?” and facilitators were assessed by answers to “what helps the most in remembering to take your medication daily?”

For our primary analysis, we adapted the single-item adherence rating scale, which has been demonstrated to have significantly less over-reporting²⁰ and has been used as a self-reported adherence measure across several PrEP trials. This item asks respondents to “Please rate your ability to take your medication every day over the last 30 days,” with five response categories (poor, fair, good, very good, excellent). We also asked “In the past 30 days, have you missed taking at least one dose of your medication.” Adherence was defined in two ways. First, high adherence was defined as having a self-rating of excellent versus the combined category of poor, fair, and good. Second, we evaluated individuals who reported not missing a single medication dose in the past 30 days compared to those who reported missing one or more doses. We used these two rigorous thresholds for defining high adherence because daily-dosing is currently the only recommended dosing schedule for PrEP, and participants may inflate self-reported adherence due to social desirability. Participants were also asked how interested they would be in taking PrEP for HIV prevention.

Participant characteristics were described using medians and inter-quartile ranges for continuous variables and fre-

quencies for categorical variables. Participants included in this analysis were compared to those excluded using chi-square tests for categorical variables and *t*- or nonparametric tests for continuous variables. Logistic regression was used to identify factors associated with high adherence, including demographic and behavioral characteristics, type of current medications (self-reported medications that were dichotomized by the authors as for prevention or treatment), and reporting one or more facilitators or barriers to adherence (open-ended questions categorized by the authors). All predictors with a *p*-value of <0.10 in an unadjusted model were included in a multivariable model. We assessed the robustness of the multivariable results in a more parsimonious model using backwards deletion to retain only variables for which *p* < 0.05, and used Pearson’s correlation coefficient to check for collinearity. Since individuals who reported barriers to taking their medication might have been more likely to report lower adherence, we performed a sensitivity analysis by removing the barrier variable from the multivariable models. Data were analyzed using STATA version 12.1.²¹

Results

Out of 2560 HIV-uninfected MSM who initiated the online survey and provided demographic information, 1480 (58%) provided complete data for the sexual practices and adherence variables analyzed in this study. Men without complete data were more likely to be younger, black, reside in the Southern US, and to report a lower educational level (*p* < 0.05).

Among these 1480 participants, 806 (54%) reported taking medications regularly, with 92% reporting daily recommended dosing. Table 1 compares the socio-demographic, sexual risk, and medication-taking profiles of the 806 participants who reported regular medication use with the 674 who reported not taking medications regularly. Medication use differed by age, race, education level, and type of health insurance (all *p*-values < 0.001). Those not taking medications regularly were more likely to have had anal sex with a man in the past 12 months (*p* = 0.003) and be less likely to have had an HIV test in the past 12 months (*p* = 0.001).

Among the 806 regular medication users, 55% reported taking medication for prevention (vitamins or supplements) and 80% for treatment. For treatment purposes, 33% reported taking medications for hypertension, hyperlipidemia, or diabetes; 34% for depression or mood disorders; 20% allergy medication; 17% pain medication; and 9% asthma medication. Thirty-six percent reported one or more facilitators to taking their medication regularly, 42% reported one or more adherence barriers, and 47% responded they would be very or extremely likely to use PrEP as a prevention strategy.

The most common facilitators of medication-taking included having a routine (25%), keeping medications visible (19%), using a pill-box (6%), experiencing physical effects or symptoms of not taking their medication (5%), being motivated to stay healthy (4%), and using cell-phone or digital alarms (4%). Common adherence barriers included forgetting to take the medication (45%), experiencing a change in daily routine (24%), being busy (23%), away from home (19%), or too tired (10%), medication cost (8%), trouble refilling medications (7%), not wanting to take the medication (6%), and being depressed, overwhelmed, or angry (6%).

TABLE 1. DEMOGRAPHIC AND BEHAVIORAL CHARACTERISTICS OF 1480 RESPONDENTS, STRATIFIED BY REGULAR USE OF MEDICATIONS

<i>Characteristic</i>	<i>Took medication regularly N = 806 N (%)</i>	<i>Did not take medication regularly N = 674 N (%)</i>	<i>p Value</i>
Age in years, median (interquartile range)	37 (25–47)	28 (20–33)	<0.0001
<i>Age group</i>			
18–25 years old	209 (26%)	402 (60%)	
26–35 years old	185 (23%)	140 (21%)	<0.0001
36–45 years old	187 (23%)	79 (12%)	
>45 years old	225 (28%)	53 (8%)	
<i>Race</i>			
White	621 (77%)	412 (61%)	
Hispanic	88 (11%)	99 (15%)	
Black	40 (5%)	85 (13%)	<0.0001
Multi-racial	27 (3%)	31 (5%)	
Other	26 (3%)	46 (7%)	
<i>Education</i>			
Completed college	329 (41%)	181 (27%)	
Some college, Associates degree, and/or technical school	351 (44%)	298 (44%)	<0.0001
High school or less	117 (15%)	193 (29%)	
<i>Region</i>			
West	209 (26%)	197 (30%)	
South	231 (29%)	175 (26%)	
Midwest	188 (23%)	163 (25%)	0.398
Northeast	173 (22%)	125 (19%)	
Islands	2 (<1%)	2 (<1%)	
<i>Employed</i>	535 (67%)	470 (70%)	0.208
<i>Insurance status</i>			
Private insurance/HMO	430 (53%)	271 (41%)	
Medicaid/Medicare	61 (8%)	37 (6%)	
Other government	19 (2%)	14 (2%)	<0.0001
Other type/multiple types	104 (13%)	63 (9%)	
No health insurance	165 (21%)	222 (33%)	
Don't know	25 (3%)	61 (9%)	
<i>Sexual practices</i>			
Had anal sex with a man in the past week	258 (32%)	248 (37%)	0.055
Had anal sex with a man in the past 12 months	543 (79%)	463 (86%)	0.003
UAI at last sex	291 (51%)	210 (51%)	0.906
Last partner HIV+ or unknown status	187 (33%)	135 (33%)	0.899
Drug use during last sexual encounter	39 (7%)	23 (6%)	0.474
Alcohol use during last sexual encounter	83 (15%)	64 (16%)	0.629
<i>Take medications on a regular basis</i>			
Take medication for prevention	444 (55%)	NA	
Take medication for treatment	642 (80%)	NA	
Not taking medication regularly	NA	674 (100%)	
<i>HIV testing</i>			
Had HIV test in last 12 months	387 (48%)	252 (37%)	<0.0001
<i>Willingness to use PrEP</i>			
Extremely/very likely to use PrEP	364 (48%)	287 (45%)	0.341
Not likely/slightly likely/moderately likely to use PrEP	396 (52%)	346 (55%)	
<i>Promoters/barriers to medication-taking</i>			
Reported ≥1 promoter for medication taking	527 (65%)	NA	
Reported ≥1 barrier for medication taking	620 (77%)	NA	

NA, not applicable; UAI, unprotected anal intercourse.

Among medication users, 45% rated their medication-taking ability as excellent, 28% very good, 13% good, 10% fair, and 4% poor. Furthermore, only 36% reported taking all their medication as recommended in the past 30 days. In bivariate analyses, self-reported excellent adherence was

associated with being over 25 years old, having had an HIV test in the last 12 months, and taking medications for treatment versus other reasons. Being uninsured, reporting one or more adherence barriers, and use of alcohol during last sexual encounter was associated with lower odds of reporting

TABLE 2. BIVARIATE AND MULTIVARIATE LOGISTIC REGRESSION FOR SELF-REPORTED EXCELLENT ADHERENCE TO MEDICATION TAKING AMONG SELF-REPORTED MEDICATION TAKERS

Variable	Bivariate odds ratio (95% CI)	Multivariate odds ratio (95% CI) N = 790
Age groups		
18–25 years old	1.0 [referent]	1.0 [referent]
26–35 years old	2.15 (1.4–3.3) p<0.001	2.54 (1.56–4.12) p<0.001
36–45 years old	2.22 (1.45–3.4) p<0.001	2.11 (1.29–3.44) p=0.003
>45 years old	5.66 (3.72–8.6) p<0.001	5.64 (3.50–9.11) p<0.001
Race		
White	1.0 [referent]	1.0 [referent]
Hispanic	0.83 (0.53–1.3) p=0.42	1.16 (0.68–1.97) p=0.59
Black	0.64 (0.33–1.26) p=0.19	1.01 (0.47–2.19) p=0.98
All other	0.61 (0.33–1.1) p=0.10	0.82 (0.41–1.63) p=0.57
Completed college	Not significant	
Employed	Not significant	
Uninsured	0.66 (0.46–0.94) p=0.02	0.88 (0.59–1.33) p=0.55
Region	Not significant	
HIV test in the past 12 months (yes or no)	1.34 (1.01–1.77) p=0.04	1.15 (0.83–1.6) p=0.40
Anal sex with a man in the past week (yes or no)	Not significant	
Had anal sex with a man in the past 12 months (yes or no)	Not significant	
UAI at last sex	Not significant	
Take medication for prevention (yes or no)	Not significant	
Take medication for treatment (yes or no)	1.69 (1.18–2.43) p=0.004	1.41 (0.91–2.17) p=0.12
Reported ≥1 promoter for medication taking	0.76 (0.57–1.02) p=0.07	1.15 (0.79–1.66) p=0.47
Reported ≥1 barrier for medication taking	0.1 (0.07–0.16) p<0.001	0.1 (0.06–0.16) p<0.001
Alcohol use during last sex		
No	1.0 [referent]	1.0 [referent]
Yes	0.56 (0.34–0.92) p=0.02	0.70 (0.39–1.23) p=0.21
missing	1.03 (0.75–1.4) p=0.86	1.03 (0.69–1.53) p=0.90
Drug use during last sex	Not significant	
Willingness to use PrEP		
not at all/moderately likely	1.0 [referent]	1.0 [referent]
extremely/very likely	1.3 (0.97–1.73) p=0.08	1.21 (0.86–1.70) p=0.27
missing	1.27 (0.68–2.38) p=0.4	1.32 (0.60–2.91) p=0.49

UAI, unprotected anal intercourse.

excellent adherence (Table 2). In multivariable analyses, older men and those not reporting any adherence barriers were more likely to report excellent adherence. Results were similar in multivariable analyses of not missing any doses in the last 30 days, with the addition that men who were willing to use PrEP were more likely to report perfect 30-day adherence for their current medications (data not shown). Backward stepwise elimination did not change the inferences, and there was no evidence of collinearity among the variables in the multivariable model. In sensitivity analyses omitting the barrier variable from multivariable models, older age was still associated with reporting excellent adherence.

Discussion

In this national online survey of sexually-active, HIV-uninfected US MSM, approximately half of the respondents reported currently taking a routine regimen of prescribed or over the counter medications, supplements, or vitamins. Most took medications for treatment purposes and over half for prevention. Among regular medication users, less than half rated their medication taking ability as excellent and only one-third reported not missing any doses in the past month. Potential PrEP users were more likely to report perfect

30-day adherence, suggesting MSM who are willing to take PrEP may be more likely to have good adherence patterns. We also found that older men and those who did not report any adherence barriers were more likely to report high adherence. Establishing a routine and keeping medication visible were the most common facilitators of adherence, and forgetting, being busy, or away from home, and experiencing a change in routine were the most common adherence barriers; these findings are similar to those reported in the literature in HIV-infected^{22,23} and uninfected^{17,24,25} populations.

Several studies among HIV-infected populations have demonstrated that younger individuals may have more difficulties with adherence to antiretroviral therapy.^{26–30} Lower adherence to study product among younger individuals has been seen in several PrEP trials, including iPrEx in sexually active MSM^{31,32} and the VOICE trial in at-risk women in Africa.³³ Younger populations also had higher HIV incidence in these trials^{1,33,34} and highlight the critical need to evaluate potential adherence interventions in these populations.

Men who have sex with men who are already taking medication for treatment may have an easier time adhering to PrEP compared to MSM not currently taking medication for treatment. Of note, a significant proportion of the US adult population uses one or more medications on a regular basis to

manage chronic conditions,¹⁸ and in this surveyed population of MSM, approximately 43% reported taking a regular medication for treatment. For those who choose to take PrEP for prevention, leveraging experiences with medication taking and established routines should be prioritized in developing adherence plans. Of note, we did not find an association between reporting anal intercourse without a condom and adherence, suggesting that individuals who have risky sex may not necessarily have lower adherence to PrEP. The following strategies may be beneficial in supporting open-label PrEP use: counseling approaches that explore facilitators and barriers to adherence; anticipate changes in routine, travel, and/or substance use; and use problem-solving to identify relevant adherence tactics.^{16,17,35,36}

The CDC recommends HIV-testing at least annually for sexually active MSM to identify new infections and prevent ongoing transmission.³⁷ Among the 1006 MSM in this study who reported anal sex with a man in the past 12 months, only 52% reported having an HIV test during this period. As the guidance for PrEP requires frequent HIV testing,⁸ PrEP use could facilitate increased HIV-testing rates among high-risk MSM.

This study has both strengths and limitations. This investigation provided a snap-shot of medication-taking behaviors across a large, geographically diverse sample of US MSM. However, several methodological weaknesses should be acknowledged. First, our cross-sectional sample only included men who used social-networking websites and elected to participate in an online survey and may not be representative of all at-risk US MSM. Second, all data, including information on medications, were self-reported and are subject to recall and social desirability biases. Of note, self-reported adherence rates in PrEP trials have generally overestimated PrEP use when compared to objective measures such as pharmacokinetic drug levels.³⁸ Third, this study was anonymous and therefore we could not insure that each survey was from a unique respondent.

By evaluating adherence to routine medication-taking regimens in HIV-uninfected US MSM, we provide valuable insights into potential facilitators and barriers that may generalize to open-label PrEP adherence. Important next steps are to develop interventions to support PrEP adherence, particularly for young PrEP users, to maximize the public health benefit of this promising new HIV prevention strategy.

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