# Sexual Frequency and Planning Among At-Risk Men Who Have Sex With Men in the United States: Implications for Event-Based Intermittent Pre-Exposure Prophylaxis

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**Abstract:** Intermittent dosing of pre-exposure prophylaxis (iPrEP) has potential to decrease costs, improve adherence, and minimize toxicity. Practical event-based dosing of iPrEP requires men who have sex with men (MSM) to be sexually active on fewer than 3 days each week and plan for sexual activity. MSM who may be most suitable for event-based dosing were older, more educated, more frequently used sexual networking websites, and more often reported that their last sexual encounter was not with a committed partner. A substantial proportion of these MSM endorse high-risk sexual activity, and event-based iPrEP may best target this population.

**Key Words:** intermittent pre-exposure prophylaxis, pre-exposure prophylaxis, event-based dosing, men-who-have-sex-with-men, HIV, sexual frequency, sexual planning

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## INTRODUCTION

The Pre-exposure Prophylaxis Initiative (iPrEx) trial recently demonstrated a 42% efficacy of daily oral tenofovir/emtricitabine (TDF/FTC) pre-exposure prophylaxis (PrEP) for prevention of HIV acquisition among men who have sex with men (MSM) who were also provided a comprehensive package of prevention services.[1] Two more recent studies have confirmed the efficacy of PrEP both for high-risk heterosexual men and women in Botswana and for HIV-uninfected men and women in HIV-serodiscordant relationships in Kenya and Uganda.[2,3] However, 2 studies of PrEP in African women were terminated early or had one of the oral PrEP arms discontinued due to futility.[4,5]

In iPrEx, efficacy of PrEP increased with improved drug adherence. However, adherence to daily pill dosing was suboptimal for a substantial proportion of study participants, with drug being detected in fewer than half of the participants when randomly sampled.[6] Intermittent dosing has the potential to improve adherence if costs and side effects are lower and men only perceive themselves to be at risk at certain periods (eg, weekends, vacations), and thus are not willing to take a daily pill. Animal studies have provided promising evidence that different intermittent PrEP dosing strategies may be effective,[7,8] and clinical trials to evaluate the feasibility of iPrEP in MSM are currently underway.

Several alternative dosing strategies have been proposed. An intermittent event-based dosing strategy would involve both pre-exposure and postexposure doses taken with potential exposures.[9] This intervention will only be feasible in populations with infrequent risk activity because exposures on 3 or more days each week would necessitate near-daily dosing. Further, pre-exposure dosing requires that men both correctly identify potential exposures and plan for these exposures by having medication available in advance.

Patterns of risk behavior for HIV acquisition are critical to determine whether an event-based dosing strategy with a pre-exposure dosing boost is feasible and plausibly effective in different at-risk populations. To assess the potential appropriateness of event-based dosing of iPrEP among MSM in the United States, we evaluated anal sex frequency, planning, and patterns of sexual risk among MSM using online social networking websites. Because it is thought that event-based dosing of iPrEP will most benefit high-risk MSM who have sex on fewer than 3 days each week and who plan for

sexual activity, the current study was designed to further characterize these men.

## METHODS

MSM from the United States were recruited from 2 online social networking sites (Facebook and Black Gay Chat) to complete a secure anonymous online survey administered through SurveyGizmo. Banner ads were used for recruitment, and men were subsequently screened using an online self-administered survey that gathered information on age, sex, and sexual activity with male partners in the prior 12 months. Eligible participants included men age ≥18 who reported anal sex with male partners in the prior 12 months. The study was reviewed by the Emory University Institutional Review Board (Protocol 00047677) and was determined to be exempt from Institutional Review Board review because no identifying information was collected; therefore, documentation of informed consent was not required. No incentive for participation was given. We restricted the following analysis to men who reported being HIV uninfected.

Our primary outcomes were "less frequent sex" and "planned sex." Men who reported anal sex on 0, 1, or 2 days in the past week were defined as having "less frequent sex." "Planned sex" was defined as arranging to meet someone to have sex, going to a place to potentially meet a sex partner, or setting up a time to have sex with a partner. Men who reported sexual planning were then asked if this planning occurred more than 3 days, 1–3 days, several hours, or minutes before their last anal sex encounter. This outcome was treated as "planned sex" only when planning occurred at least several hours before the last reported anal sex encounter.

Demographic explanatory variables considered for analyses included age, race/ethnicity, educational attainment, home region of the United States (West, South, Midwest, Northeast), employment status, and health insurance status. The survey also included questions related to sexual practices, use of condoms during the last anal sex encounter, and HIV-testing history. In our survey, a committed partner was defined as someone that the participant felt committed to above all others and could be a boyfriend, significant other, life partner, or husband. Websites, such as adam4adam.com and manhunt.com, were considered sexual networking websites if primarily used for dating and sexual hook-ups.

Stata 11.0 was used for analyses. Comparisons were examined using $\chi^2$ and Kruskal–Wallis tests, and $P$ values less than 0.05 were considered statistically significant.

## RESULTS

The data were collected from November 30 to December 19, 2010, shortly after the release of iPrEx results. Men who were HIV uninfected and reported anal sex in the past year were included in our analyses (n = 1013). The median age was 28 (range: 18–77). Most (56%) respondents reported that their last anal sex was unprotected. Table 1 summarizes demographic, psychosocial, and other sexual risk characteristics.

When asked about how many days participants had anal sex during the preceding week, 49.1% reported no sexual

**TABLE 1.** Demographic and Clinical Characteristics of 1013 Participants Meeting Eligibility Criteria

| Characteristic | Proportion of Total Sample (%) |
|---|---|
| Age | |
| <20 | 12.8 |
| 20–29 | 42.5 |
| 30–39 | 18.5 |
| 40–49 | 15.2 |
| ≥50 | 11.0 |
| Race | |
| White | 70.2 |
| Hispanic | 12.8 |
| Black | 8.4 |
| Multi-racial/Other | 8.6 |
| Education | |
| Completed college | 36.1 |
| Region | |
| West | 27.8 |
| South | 27.3 |
| Midwest | 24.6 |
| Northeast | 20.2 |
| Employed | 71.2 |
| Insured | 74.1 |
| Last sexual episode | |
| Planned several hours in advance | 41.5 |
| Last anal sex unprotected* | 56.0 |
| Last anal sex unprotected receptive | 21.5 |
| Last anal sex unprotected insertive | 17.4 |
| Last anal sex unprotected receptive and insertive | 13.0 |
| Last partner HIV+ or unknown serostatus | 29.8 |
| Last anal sex unprotected and HIV+ or unknown serostatus partner | 14.0 |
| Drug use | 7.2 |
| Alcohol use | 16.1 |
| Last sexual partner boyfriend, significant other, life partner or husband | 53.7 |
| Exchanged money or drugs for sex | 2.7 |
| Where sex occurred | |
| Home | 84.6 |
| Hotel room | 3.6 |
| Sex club/resort | 1.3 |
| Public venue | 3.2 |
| Other | 7.3 |
| Sexual practices in past week | |
| Anal sex on fewer than 3 days in the past week | 84.9 |
| Anal sex on fewer than 3 days in the past week and planned sex at last encounter | 30.5 |
| Other sexual practices | |
| Use of sexual networking websites at least once/week | 47.3 |
| All anal sex partners disclosed HIV status in past year | 49.9 |
| HIV test in the past 12 months | 48.7 |

*Unable to characterize type of last unprotected anal sex for 32 men given missing data.

activity, 27.3% reported anal sex on 1 day, and 8.5% on 2 days. The remaining participants (15.1%) reported anal sex on 3 or more days. Frequency of anal sex on different days of the week ranged from 14.1% on Wednesday to 18.0% on Saturday; 34.1% of our study sample reported anal sex during the preceding weekend and 35.7% reported anal sex on at least 1 weekday in the preceding week. Clustering of sexual activity was uncommon, with only 14 men (1.4%) and 7 men (0.7%) reporting anal sex on exactly 3 and 4 consecutive days, respectively.

Of all study participants, 50.4% reported no advanced planning before their last sexual encounter, whereas 8.2% reported planning only minutes in advance. The remaining men reported planning hours (22.4%), 1–3 days (10.7%), or more than 3 days in advance (8.4%).

Thirty-one percent of survey participants reported both planning and less frequent sex. In bivariate analysis, men who reported both planning and less frequent sexual activity were older, more highly educated, and more frequently reported that their last sexual episode was not with a committed partner, that they had received an HIV test in the past year, and that they used sexual networking websites (Table 2). Although not statistically different from men who reported more frequent or unplanned sex, 53.7% of these men reported that their last sexual encounter was unprotected, and 14.9% reported that their last anal sex encounter was without a condom with an HIV-infected or unknown serostatus partner.

## DISCUSSION

In this study of sexually active, self-reported HIV-uninfected MSM in the United States, we found that the men who may be most suitable for event-based iPrEP more frequently reported sexual activity outside of a committed relationship and use of online sexual networking websites. Notably, nearly half of these men who reported both less frequent sex and planning before sexual activity had not received an HIV test in the past year. A substantial proportion of these men also engaged in high-risk behavior for HIV acquisition such as unprotected anal sex, sometimes with HIV-infected or unknown serostatus partners. If event-based dosing proves effective, future iPrEP interventions may need to target the men who report sexual event planning and less frequent sex and who also report these high-risk sexual behaviors.

**TABLE 2.** Bivariate Analyses of Sexual Frequency and Sexual Planning

| Variable | Less Frequent and Planned Sex (%) | More Frequent or Unplanned Sex (%) | *P* |
|---|---|---|---|
| Age (median) | 30 yrs | 27 yrs | <0.001* |
| Completed college | 46.1 | 31.9 | <0.001 |
| Last sexual partner not a committed partner | 59.8 | 37.6 | <0.001 |
| HIV test in the past 12 months | 53.7 | 46.5 | 0.033 |
| Use of sexual networking website at least once weekly | 55.3 | 43.6 | 0.001 |

*Kruskal–Wallis equality-of-populations rank test.

An event-based dosing strategy likely will require both pre-exposure and postexposure doses around the time of potential HIV exposures. There are several additional iPrEP-dosing strategies that have also been proposed. A second strategy is to use a fixed number of doses each week independent of HIV risk exposure, and the feasibility of this approach will be primarily dependent on drug pharmacokinetics. A third approach is more infrequent periodic dosing during periods of increased risk behavior such as vacations or between relationships.[9]

Our study adds to the limited data in the literature that describe frequency of sexual activity and sexual planning behavior in HIV-uninfected MSM. Ultimately, these data may be critical for informing which iPrEP dosing strategy is most likely to be acceptable to the MSM who would be eligible to use it. One previous study of HIV-uninfected MSM in Bangkok, Thailand, observed that although iPrEP may be feasible, many of the men at highest risk for HIV acquisition may not be eligible because of lack of planning and more frequent sexual activity.[10] However, these results may not be generalizable to other populations of MSM.

Although the effectiveness and optimal dosing of iPrEP are still uncertain, early data suggest that sexual frequency and planning will be critical determinants of success if event-based dosing is used. Drug pharmacokinetics have not been well characterized in HIV-uninfected individuals, yet both TDF and FTC are appealing for iPrEP given their long intracellular half-lives, coformulation, penetration into tissues and cells susceptible to infection, and relatively mild side-effects.[11,12] In macaque studies, pre-exposure and postexposure dosing of TDF/FTC provided protection against multiple rectal exposures to simian-human immunodeficiency virus infection.[7]

Clinical trials of iPrEP are underway. The HPTN 067 Alternative Dosing to Augment PrEP Pill-Taking Study is a randomized, open-label, feasibility study of iPrEP enrolling high-risk HIV-uninfected MSM and women who have sex with men in Thailand and South Africa, respectively. In addition to a daily-dosing arm, some participants will be randomized to event-based dosing with TDF/FTC both before and after all potential HIV exposures or twice weekly dosing with a postexposure boost.[13] A second randomized iPrEP trial began enrolling MSM in France in January 2012, with the treatment arm taking 2 doses of TDF/FTC before sexual activity and 1 dose afterwards.[14] Notably, data from another study of iPrEP in MSM and female sex workers in Kenya and HIV discordant couples in Uganda suggest that adherence to postcoital dosing is especially challenging.[15]

Several methodological limitations should be acknowledged in interpreting these results. First, our cross-sectional sample of MSM only included men who use social networking websites and who chose to participate in an online survey, and these participants may not reflect demographic and risk characteristics among the larger community of MSM. Second, the majority of black MSM in this study was recruited from Black Gay Chat rather than Facebook, and it is likely that these men may not be comparable given this difference in

recruitment. Unfortunately, the methods employed during data collection to protect participant anonymity preclude data analyses stratified by recruitment strategy. We recruited men from Black Gay Chat to be more inclusive of black MSM. Third, because we chose not to collect identifying data, including IP address, we could not rigorously deduplicate responses; however, our experience with similar unincentivized surveys accessible only through banner referrals is that duplicate IP addresses comprise fewer than 3% of responses. In addition, our data captured frequency of sexual encounters rather than the number of different sexual partners, and consequently, we are unable to distinguish men having frequent sex with the same partner from men with multiple different sexual partners. Although an increased number of sexual partners confers significant risk for HIV acquisition,[16] unprotected sexual activity with even 1 partner remains an important risk factor, especially in communities with high HIV prevalence. Notably, men in seroconcordant monogamous relationships may have been included in our analyses despite being at lower risk for HIV acquisition.

Finally, our cross-sectional data fail to capture changes in behavior over time. The use of condoms at the last anal sex encounter may not be representative of long-term behavior and likely underestimates the proportion of men who sometimes engage in unprotected anal sex. We chose this measure to maximize specificity and to minimize recall bias,[17] similar to other online surveys of sexual risk in MSM.[18] Further, as we only obtained data regarding sexual frequency in the preceding week, we may have missed men who may engage in intermittent periods of increased sexual frequency. These men with infrequent high-risk sexual activity may be ideal candidates for periodic dosing of iPrEP during times of increased risk behavior. Additionally, if iPrEP proves to be effective, it is likely that some MSM may alter their behavior and start to plan their sexual encounters to make event-based dosing of iPrEP feasible. Developing strategies to help men plan for sexual encounters may be critical for the success of future iPrEP interventions, and further research will be needed to evaluate this potential for behavior change.

Despite these limitations, our study serves to better characterize MSM who may most benefit from event-based dosing of iPrEP. Upcoming trials of iPrEP will determine clinical efficacy and hopefully clarify the optimal dosing strategies. Additional knowledge regarding sexual frequency and planning will be critical in identifying MSM who may most benefit from this intervention. With use of TDF/FTC as PrEP, daily dosing will likely still remain necessary for the majority of high-risk MSM who report more frequent sexual activity or less planning.

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