Alignment of PrEP use and sexual behavior over four months among men who have sex with men in the southern United States

Jeb Jones1 · Sanjana Pampati1 · Aaron J. Siegler1

Abstract
Unlike antiretrovirals for HIV treatment, pre-exposure prophylaxis (PrEP) does not require continual adherence to be fully effective; rather, PrEP adherence is important only in the context of episodes of sexual risk. Therefore, studies of PrEP adherence and persistence must incorporate contemporaneous measurement of sexual behavior. Short, frequent surveys of PrEP use and sexual behavior allow for the measurement of the alignment between PrEP use and sexual behavior. We assessed the feasibility of using biweekly PrEP use and sexual behavior questionnaires to measure adherence and persistence on PrEP over a period of four months. We also measured the alignment of PrEP use and condomless anal sex. PrEP-using MSM in the southern US were recruited using online advertisements. Participants completed a baseline survey followed by brief surveys every two weeks for 16 weeks to report their PrEP use and sexual behavior over the preceding two-week period. Study retention was high: 91% of participants completed the baseline and final survey and, overall, 86% of study surveys were completed. Self-reported PrEP adherence and persistence were high, but instances of PrEP non-adherence were observed to frequently overlap with episodes of condomless anal sex. The most prominent reasons cited for missing PrEP doses were being too busy, not having PrEP on hand, and not being sexually active. Completing short, biweekly surveys of PrEP use and sexual behavior is feasible and acceptable to MSM in the southern US. Future studies should investigate incorporating biomarker measurements to validate self-reported adherence.

Keywords Pre-exposure prophylaxis · HIV · Men who have sex with men · Adherence · Persistence

Introduction
Pre-exposure prophylaxis (PrEP) is a highly effective HIV prevention intervention, providing near complete protection against HIV acquisition via anal sex for men who have sex with men (MSM) who take at least four of seven daily doses per week[1]. PrEP use has increased steadily since Truvada (emtricitabine/tenofovir disoproxil fumarate) was first approved for use by the Food and Drug Administration as a HIV prevention medication in 2012[2]. Truvada is now available in a generic form, reducing the cost of prescriptions. A second formulation, Descovy (emtricitabine/tenofovir alafenamide), has also been approved for use as PrEP. However, uptake of PrEP still remains lower than levels modeling studies suggest are needed to achieve meaningful population-level reductions in HIV incidence[3].

The burden of new diagnoses of HIV is disproportionately high in the US South[4]. In 2019, the South had the highest rate of new HIV diagnoses and accounted for 52% of all new HIV diagnoses in the US. MSM account for the majority of new HIV diagnoses in the South: 68% of new diagnoses in the South in 2019 were among MSM. This disparity in risk is accompanied by a disparity in PrEP use. The South continues to be the region of the US with the lowest PrEP uptake. In 2017, the prevalence of PrEP use in the South was 29.8 per 100,000 population compared to 30.1, 36.0, and 62.3 per 100,000 population in the Midwest, West, and Northeast, respectively[2] The South is also home to many counties that have had the lowest increases in the ratio of PrEP use to MSM population from 2012–2018.[5] A number of studies have highlighted unique challenges to PrEP access and persistence in the US South, including HIV-related training gaps among providers and other staff, stigma, and time- and resource-related constraints.[6–8].
The Ending the HIV Epidemic (EHE) initiative identifies increasing PrEP coverage as a primary strategy for reaching the goal of achieving a 90% reduction in new HIV infections by 2030[9]. Understanding predictors of uptake, adherence following PrEP initiation, and prolonged persistence on PrEP is critical to meeting the promise of PrEP as a key HIV prevention tool. In addition to interventions such as PrEP, EHE identifies priority jurisdictions in need of expansion of HIV prevention services.[10] Almost half of the county-level priority jurisdictions in EHE are in the South. Of seven states that are identified as priority states, six are in the southern US.

To fully understand patterns of PrEP use, it is critical that assessments of PrEP adherence and persistence measure contemporaneous sexual behavior. Indeed, PrEP discontinuation is not necessarily indicative of increased HIV risk if an individual’s sexual risk profile has changed. Thus, to accurately characterize PrEP adherence and persistence in the context of PrEP indication, sexual behavior must be fully assessed concurrently with reporting of PrEP usage.[11, 12].

Methods are needed to understand how best to accurately measure concurrent sexual behavior and PrEP use. Short message service (i.e., text message) surveys have been shown to be an acceptable method to assess PrEP use and sexual behavior among serodiscordant couples in Kenya and Uganda.[13, 14] Another study of young MSM in US cities found that self-report of adherence frequently overestimated adherence compared to biological measures.[15] However, adherence was measured infrequently and with relatively long lookback windows, which might make it more challenging for participants to accurately recall their PrEP use. Long lookback windows also make it more difficult to temporally align reported occurrences of condomless sex with periods of non-adherence.

Daily assessments of sexual behavior have been found to be acceptable over short periods of time (i.e., one month) [16]; however, longer follow-up periods are needed to observe the full trajectory of PrEP use and its alignment with sexual behavior. One study of a small, clinic-based sample of MSM using PrEP measured adherence using electronic pill bottles and assessed sexual behavior via a sex diary every two weeks, finding frequent periods of PrEP non-use that overlapped with periods of sexual risk.[17]

Additional data are needed to support these findings and to assess methods for measuring adherence in the absence of electronic pill bottles.

Although there are existing data on PrEP adherence and persistence, more data are needed on functional adherence (i.e., adherence during periods of sexual risk). To measure functional adherence, more frequent reporting is necessary to determine whether an episode of sexual risk was protected by PrEP. The goal of the current study was to assess the feasibility of measuring PrEP adherence and persistence and sexual behavior using frequent, brief, online surveys of PrEP-using MSM in the southern US. We assessed feasibility through survey completion rates and overall retention, analyzed how PrEP adherence and persistence aligned with periods of sexual risk, and assessed STI testing over the follow-up period.

**Materials and methods**

**Participants and follow-up schedule**

Participants were recruited via advertisements on Facebook and Grindr targeted towards men living in the southern US and via emails sent to previous research participants who indicated willingness to participate in future studies. After clicking on an advertisement, participants were redirected to an eligibility screener, securely hosted on a HIPAA-compliant survey platform. Participants were eligible to participate if they were cisgender male, 18–34 years old, lived in the US South as defined by the United States Census Bureau, had anal sex with a man in the previous 6 months, were HIV-negative, and reported current use of oral PrEP.

Eligible participants were contacted to verify their contact information. Following verification, participants were sent the baseline survey. Participants who passed the fraud prevention protocol (described below) following the baseline survey were enrolled in the prospective cohort. Participants were followed for 16 weeks and completed check-in surveys every two weeks to report sexual behavior and PrEP use in the previous 14 days. Participants were compensated $20 for each of the baseline and final surveys and $5 for each completed biweekly check-in survey. Compensation was in the form of an electronic gift card to the participant’s choice of Amazon, Target, or Walmart. This study was approved by the Emory University Institutional Review Board.

**Fraud Prevention**

Contact and demographic information was confirmed using spokeo.com, a personal data aggregator, to verify that the contact information provided was associated with a real person. We also compared the answers to select questions (e.g., ZIP code, age) in the screening and baseline surveys to confirm that participants provided consistent information at each time point. Any discrepancies were resolved by contacting the participant[18].
Measures

Demographics

The baseline survey included demographics (age, race/ethnicity, education, income), health insurance status, ZIP code of residence, sexual behavior in the previous 12 months, and HIV/STI testing history. Participant urbanicity was categorized based on county of residence using the National Center for Health Statistics urban-rural classification scheme[19]. Participants living in large or fringe metro areas were categorized as urban; participants in the other four categories (medium and small metro, micropolitan, and noncore) were categorized as non-urban.

Table I  Demographic characteristics of PrEP-using men who have sex with men in the southern United States enrolled in longitudinal study of PrEP use and sexual behavior

| Characteristic                  | Overall (N = 78) |
|--------------------------------|-----------------|
| Age                            |                 |
| 18–24                          | 35 (45)         |
| 25–34                          | 43 (55)         |
| Race/Ethnicity                 |                 |
| Hispanic                       | 12 (16)         |
| Non-Hispanic Black             | 20 (27)         |
| Non-Hispanic White             | 35 (47)         |
| Other/Multiple                 | 8 (11)          |
| Education                      |                 |
| High School or Less            | 9 (12)          |
| At least some college          | 67 (88)         |
| Income                         |                 |
| Less than $20/year             | 12 (16)         |
| $20k/year - $74,999/year       | 46 (63)         |
| $75k or more/year              | 15 (21)         |
| Insurance Status               |                 |
| Private                        | 64 (83)         |
| Public                         | 4 (5)           |
| None                           | 8 (10)          |
| Other                          | 1 (1)           |
| Urbanicity                     |                 |
| Urban                          | 53 (68)         |
| Non-urban                      | 25 (32)         |
| Sexual Identity                |                 |
| Gay                            | 71 (91)         |
| Bisexual                       | 7 (9)           |
| Unstable Housing               |                 |
| Yes                            | 5 (7)           |
| No                             | 71 (93)         |

PrEP use

PrEP questions on the baseline survey included reasons for using PrEP, source of PrEP (e.g., health department, telehealth provider), barriers to PrEP access, and adherence over the previous 30 days.

PrEP use was measured using a consistent set of questions across the follow-up surveys. First, participants were asked if they were still taking PrEP. A participant who reported that they were no longer taking PrEP was considered to no longer be persistent; however, participants could report being on PrEP again at a later time point. Persistence was defined as continuing to report using PrEP whether adherent or not. Participants who reported continuing PrEP were asked a series of questions about their PrEP use over the past 14 days. PrEP adherence was determined based on the reported dosing schedule (i.e., daily or event-based). Daily PrEP adherence was categorized as full (i.e., no missed doses), sufficient (i.e., ≥ 8 doses in past 14 days), or non-adherent (< 8 doses in past 14 days). Daily oral PrEP has been shown to be fully protective against sexual transmission of HIV among MSM when taken at least 4 out of 7 days in a week[1]. We approximated this by defining sufficient adherence as at least 8 doses in a 14-day period because our surveys were administered biweekly. Event-based PrEP adherence was categorized as full (i.e., no missed doses) or non-adherent (i.e., one or more missed doses). Participants were categorized as having a misalignment of PrEP and sexual risk if they were non-adherent or reported no longer being on PrEP in an interval in which condomless anal sex was reported. In the final survey, participants were also asked about long-term plans regarding PrEP use.

Sexual behavior and STI-related outcomes

At all time points, sexual behavior questions assessed number of partners in the preceding interval and serostatus of partners (HIV-positive, HIV-negative, unknown status). For each partner serostatus, participants were asked about condom use during receptive and insertive anal sex. For those reporting HIV-positive partners, participants were asked if the partner’s viral load was suppressed, unsuppressed, or unknown. The final survey also assessed STI testing and diagnoses throughout the study period.

Statistical analyses

Demographic characteristics of participants enrolled in the study were summarized (i.e., number and percent). Retention in the study (operationalized as completed all surveys) and differences in retention by demographic characteristics was examined. PrEP adherence, persistence, alignment with
sexual risk, and dosing at each follow-up wave were summarized using univariate statistics. All bivariate comparisons were conducted using Fisher exact tests, and results were considered statistically significant at a threshold of \( \alpha < 0.05 \). All analyses were completed using SAS v9.4.

**Results**

A total of 78 participants completed a baseline survey and were enrolled in the cohort (Table I). Approximately half (47%) of the study population was non-Hispanic white, most (88%) had at least some college education, and most (83%) were privately insured. Most participants lived in urban areas (68%).

Overall and timepoint-specific retention suggest that this method of assessing PrEP use and sexual behavior is feasible. Most (67/78, 86%) participants completed both the baseline and final survey. Retention was 85% or higher at all follow-up visits except week 2. Among the 74/78 participants who completed at least one follow-up survey, full retention, defined as completing all follow-up surveys, was achieved with 48 (65%) participants (Table II). No statistically significant differences were observed between those who were fully retained and those who missed at least one survey based on the demographic characteristics examined.

Overall self-reported adherence and persistence were high (Table III). At the final study visit, 59 of 66 (89%) participants reported continuing to take PrEP. The vast majority of participants reported complete adherence or adherence sufficient to provide protection against sexual transmission of HIV. More than 90% of participants reported using a daily dosing regimen at each follow-up survey, with the remainder reporting event-based dosing. Although non-adherence and discontinuation were not common, having an episode of condomless anal sex during a period of non-adherence or discontinuation was very common.

| Characteristic | All Study Activities Completed (n = 48) | Missed At Least One Survey (n = 26) |
|---------------|----------------------------------------|----------------------------------|
| Age           | N (%)                                 | n (%)                            |
| 18–24         | 20 (65)                                | 11 (35)                          |
| 25–34         | 27 (69)                                | 12 (31)                          |
| Race/Ethnicity|                                        |                                  |
| Hispanic      | 8 (73)                                 | 3 (27)                           |
| Non-Hispanic Black | 10 (63) | 6 (38) |
| Non-Hispanic White | 23 (70) | 10 (30) |
| Other/Multiple | 5 (71)                                 | 2 (29)                           |
| Education     |                                        |                                  |
| High School or Less | 7 (88) | 1 (13)  |
| At least some college | 39 (65) | 21 (35) |
| Income        |                                        |                                  |
| Less than $20/year | 6 (67) | 3 (33)   |
| $20k/year - $74,999/year | 26 (60) | 17 (40) |
| $75k or more/year | 12 (92) | 1 (8)    |
| Insurance Status|                                       |                                  |
| Private       | 35 (61)                                | 22 (39)                          |
| Public        | 4 (100)                                | 0 (0)                            |
| None          | 7 (88)                                 | 1 (13)                           |
| Other         | 1 (100)                                | 0 (0)                            |
| Urbanicity    |                                        |                                  |
| Urban         | 36 (72)                                | 14 (28)                          |
| Non-urban     | 11 (55)                                | 9 (45)                           |

**Table III** PrEP adherence, persistence, alignment with sexual risk, and dosing

| Characteristic | Week 2 N = 61 | Week 4 N = 67 | Week 6 N = 69 | Week 8 N = 71 | Week 10 N = 67 | Week 12 N = 66 | Week 14 N = 66 | Week 16 N = 66 |
|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
| PrEP Persistence<sup>a</sup> | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Full Adherence | 60 (98) | 65 (98) | 67 (97) | 68 (97) | 64 (96) | 64 (97) | 60 (91) | 59 (89) |
| Sufficient Adherence<sup>c</sup> | 32 (54) | 44 (69) | 42 (64) | 43 (65) | 48 (75) | 47 (75) | 43 (73) | 45 (78) |
| Non-adherent | 7 (12) | 3 (5) | 3 (5) | 4 (6) | 2 (3) | 1 (2) | 2 (3) | 1 (2) |
| PrEP Sexual Risk Misalignment<sup>d</sup> | 3 (38) | 1 (25) | 2 (40) | 4 (67) | 1 (20) | 2 (67) | 1 (13) | 4 (50) |
| Dosing Strategy<sup>e</sup> | Daily | 56 (93) | 64 (100) | 64 (97) | 64 (97) | 62 (97) | 62 (97) | 59 (98) | 57 (97) |
| Event-Based | 4 (7) | 0 (0) | 2 (3) | 2 (3) | 2 (3) | 2 (3) | 1 (2) | 1 (2) |

<sup>a</sup>Answering “No” to the question “Are you still taking PrEP?”

<sup>b</sup>Among those still on PrEP

<sup>c</sup>\( \geq 4/7 \) doses/week

<sup>d</sup>Episode of condomless anal sex during a period of PrEP non-adherence or discontinuation; proportion is calculated among participants who were non-adherent or had discontinued PrEP

<sup>e</sup>During week 16, one participant reported that they switched to every other day until “covid-19 clears/stay home orders removed”
Among participants who reported missed doses of PrEP (Table IV), the most frequently reported reasons for missing a dose were being too busy (34/53, 64%), not having their pills with them (25/53, 47%), and not being sexually active (16/53, 30%). Among the 10 participants who discontinued PrEP at some point during the study, reported reasons were not being sexually active (7/10, 70%), ending a relationship (2/10, 20%), beginning a monogamous relationship (2/10, 20%), cost (3/10, 30%), and inability to obtain a refill (3/10, 30%).

Overall, 45/63 (71%) participants were tested for STIs over the 4-month follow-up period. Of these, almost all received blood (98%) and urine (93%) tests. Approximately two-thirds received tests for rectal (64%) and pharyngeal (69%) STIs. Among those who reported any receptive anal sex over the follow-up period (n=17, 38%), 13 (76%) reported receiving a rectal STI test. Of those who reported a STI test, 5 (11%) participants were diagnosed with chlamydia, 4 (9%) were diagnosed with gonorrhea, and 2 (4%) were diagnosed with syphilis.

**Discussion**

We enrolled a cohort of PrEP-using MSM in the US South to assess the feasibility of measuring PrEP adherence and sexual behavior with frequent online surveys and to measure the alignment between PrEP use and periods of sexual risk. We observed high retention and biweekly survey completion over 16 weeks of follow-up, indicating that frequent, short assessments of PrEP use and sexual behavior are feasible to characterize PrEP use and its concordance with sexual risk longitudinally. Notably, we enrolled participants from throughout the southern US, including in rural areas, suggesting that mobile-based surveys like the ones we used are acceptable to PrEP-using MSM throughout the South. These results are in line with other studies of PrEP-using[20] and non-PrEP-using MSM[21] that have demonstrated willingness to complete daily assessments over shorter time periods (e.g., 1–2 months).

Although not statistically significant, the point estimate for retention over the study period was substantially lower among non-urban (55%) compared to urban participants (72%). Additional research is needed to determine if this relationship is significant in a larger sample and, if so, to explore reasons for the disparity and interventions to reduce it.

Overall, PrEP adherence and persistence were high during the 4-month follow-up. The high persistence and adherence might reflect a bias due to our reliance on self-report of PrEP use or due to enrolling existing PrEP users instead of newly-initiating PrEP users. At least one study has observed high levels of adherence across self-report and biomarker measures[22]. However, other studies have found lower levels of adherence when using biological measurements of adherence[23–26]. In a study of Black MSM and transgender women in Harlem, adherence following three months of follow-up was only 53%[25]. Notably, in that study there was substantial divergence of self-report from biological markers of adherence.

Among the minority who were non-adherent or discontinued PrEP, condomless anal sex was frequent, indicating a misalignment between PrEP use and opportunities for HIV transmission. This is similar to results from a trajectory-based analysis that found that one fourth of infrequent condom users had low PrEP adherence[26]. Sexual risk fluctuates over time[27]; PrEP discontinuation or nonadherence does not affect HIV transmission risk unless there is condomless sex during a period of medication nonadherence. It is critical that studies of PrEP adherence and persistence incorporate contemporaneous assessments of sexual behavior over sufficiently short recall periods to be able to accurately align periods of PrEP coverage with sexual behavior. We observed fluctuations in adherence across the study interval using a two-week recall interval. Lower resolution estimates (e.g., monthly, quarterly) of adherence and sexual behavior would be unable to identify whether missed doses overlapped with episodes of sexual risk or whether nonadherence only occurred during periods of no sexual

**Table IV** Reasons for PrEP non-adherence and discontinuation among PrEP-using men who have sex with men in the southern US over four months of follow-up

| Reason for PrEP non-adherence | n   | %   |
|-------------------------------|-----|-----|
| Missed >1 PrEP Dose           | 53  | 72  |
| Reasons for Missing           |     |     |
| Too Busy                      | 34  | 64  |
| Did not have pills with them  | 25  | 47  |
| Did not want to be seen taking PrEP | 3  | 6   |
| Side Effects                  | 0   | 0   |
| Not sexually active           | 16  | 30  |
| Only took when planning to have sex | 3  | 6   |
| Drunk or high                 | 3   | 6   |
| No refill                     | 6   | 11  |
| Cost                          | 3   | 6   |
| Discontinued PrEP             | 10  | 14  |
| Reasons for Discontinuing     |     |     |
| Not sexually active           | 7   | 70  |
| Diagnosed with HIV            | 0   | 0   |
| Ended relationship            | 2   | 20  |
| Began monogamous relationship | 2   | 20  |
| Side Effects                  | 0   | 0   |
| Cost                          | 3   | 30  |
| Disapproval from family or friends | 1  | 10  |
| Unable to obtain refill       | 3   | 30  |
activity or sexual episodes that included other forms of protection (e.g., condoms).

The high frequency of condomless anal sex during periods of PrEP non-adherence or discontinuation is a potentially important finding with respect to increased risk among those who have discontinued PrEP or are non-adherent: these data indicate that, at least for some participants, these periods of reduced or discontinued PrEP use were not indicated. When identified, occurrences of non-adherence or discontinuation might also be appropriate triggers for intervention to ensure that PrEP use is no longer indicated or to identify strategies to resume PrEP. A very small minority of participants reported using event-based dosing; however, event-based dosing is one strategy that might increase PrEP use among those who cite daily dosing as a barrier to PrEP use.[27] Increasing awareness of event-based dosing might be another strategy for increasing functional adherence of PrEP.

The most common reasons participants reported for missing doses of PrEP were being too busy and not having access to their medication when they intended to take it. This indicates that behavioral interventions to support improved adherence strategies might be effective in increasing PrEP adherence. For example, social cognitive theory[28] includes factors of self-efficacy and goal setting that could form the foundation of interventions to mitigate PrEP adherence issues due to these reasons. Not being sexually active was also a common reason, indicating that participants were actively monitoring their ongoing sexual risk and altering their PrEP use accordingly. Smaller proportions indicated missing doses due to cost or lack of a refill. Similarly, the majority of participants who discontinued PrEP reported doing so due to not being sexually active, ending a relationship, or beginning a monogamous relationship. However, although numbers were small, a third of discontinuations were attributed to cost or inability to obtain a refill. This indicates that financial and healthcare access barriers remain important determinants of PrEP adherence and persistence.

Most participants reported STI testing during the four months of follow-up, with the majority of those reporting testing for urethral STIs and syphilis. Rectal STI testing was less frequent. STI testing is recommended at least every six months for PrEP users, so we might have missed some regular STI testing given that our follow-up period was only four months in duration. However, our results do indicate that there might be a need to increase rectal and pharyngeal screening for chlamydia and gonorrhea as these infections are site-specific and rectal infections tend to be asymptomatic.[29]

This is a non-random sample of PrEP-using MSM in the southern US, so we are limited in our ability to draw general conclusions about PrEP adherence and persistence among all PrEP users in the southern US. Larger studies with probabilistic sampling methods will be necessary to obtain reliable estimates of PrEP adherence and persistence and alignment of PrEP use with sexual risk. Using a 14-day lookback window required us to approximate a measure of sufficient adherence from 4 pills in a 7-day period to 8 pills in a 14-day period; however, our goal was to test a survey frequency that we thought might be sustainable for prolonged periods. Additionally, we enrolled existing PrEP users, thus our preliminary estimates of adherence and persistence might be biased upward given that these were experienced PrEP users. Monitoring men from the time of PrEP initiation will be necessary to obtain estimates among new users of PrEP, where the likelihood of discontinuation and suboptimal adherence might be greater. We also relied exclusively on self-report to assess PrEP use due to budget constraints. Although we attempted to minimize the potential for recall bias by limiting the recall period to the previous two weeks during follow-up, the accuracy to which participants are able to report their level of adherence to PrEP use is unknown. Future studies may consider biological measures or real-time assessments (e.g., ecological momentary assessments) to provide more accurate determination of PrEP adherence. Participants recruited online are not representative of all PrEP-using MSM, and our estimates of retention might not be replicated in other populations.

Finally, the study period overlapped with the beginning of the SARS-CoV-2 pandemic in the United States. Beginning in April 2020, previous participants were asked to complete a one-time survey on physical distancing protocols in place where they lived and whether they had altered their sexual behavior or PrEP use patterns in direct response to the pandemic or restrictions related to the pandemic. We found substantial decreases in sexual activity at the beginning of the pandemic accompanied by smaller changes in PrEP use; these results have been reported elsewhere[12]. For the present analysis, the number of participants whose study period overlapped with the pandemic precluded a meaningful assessment of its impact on adherence and persistence. However, we do not expect that the pandemic affected the overall measurement of the association between PrEP use and sexual risk.

Conclusions

We demonstrated that biweekly surveys are a feasible method to obtain high-resolution data on the concordance between PrEP use and sexual behavior. This type of data will be necessary to fully characterize PrEP use patterns over time because, from a HIV prevention perspective, PrEP
adherence is only important in as much as it corresponds to episodes of sexual risk. Future studies should explore data collection periods of longer duration and acceptability of accompanying biomarker-based adherence testing.

Although we observed high levels of PrEP adherence and persistence, condomless anal sex was common during periods of PrEP nonadherence or discontinuation. This indicates that potential HIV exposure might be common among MSM who have discontinued PrEP or who are nonadherent to the dosing regimen. These findings indicate that increased efforts will be necessary to ensure that once MSM initiate PrEP, they continue to use it as prescribed as long as it is indicated based on behavioral risk.

Acknowledgements This work was supported by the Center for AIDS Research at Emory University (P30AI050409).

Compliance with Ethical Standards The authors have no conflicts to disclose. This research was approved by the Emory University Institutional Review Board (approval number IRB00107373 and informed consent was obtained from all participants.

References

1. Grant RM, Anderson PL, McMahan V, Liu A, Amico KR, Mehrotra M, et al. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. Lancet Infect Dis. 2014;14:820–9.
2. Sullivan PS, Gilmer RM, Mouhanna F, Pemberton ES, Guest JL, Jones J, et al. Trends in the use of oral emtricitabine/tenofovir disoproxil fumarate for pre-exposure prophylaxis against HIV infection, United States, 2012–2017. Ann Epidemiol [Internet]. Elsevier; 2018 [cited 2018 Jul 24];2018/07/25. Available from: https://www.ncbi.nlm.nih.gov/pubmed/30037634.
3. Jenness SM, Goodreau SM, Rosenberg E, Beylerian EN, Hoover KW, Smith DK, et al. Impact of the Centers for Disease Control’s HIV Preexposure Prophylaxis Guidelines for Men Who Have Sex With Men in the United States. J Infect Dis. 2016;214:1800–7.
4. Centers for Disease Control and Prevention. Surveillance Report HIV, 2019; vol. 32 [Internet]. 2021 [cited 2021 Aug]. Available from: http://www.cdc.gov/hiv/library/reports/hiv-surveillance. html.
5. Mouhanna F, Castel AD, Sullivan PS, Kuo I, Hoffman HJ, Siegler AJ, et al. Small-area spatial-temporal changes in pre-exposure prophylaxis (PrEP) use in the general population and among men who have sex with men in the United States between 2012 and 2018. Ann Epidemiol. 2020;49:1–7.
6. Rolle C-P, Onwubiko U, Jo J, Sheth AN, Kelley CF, Holland DP. PrEP Implementation and Persistence in a County Health Department Setting in Atlanta, GA. AIDS Behav. 2019;23:296–303.
7. Rice WS, Stringer KL, Sohail M, Crockett KB, Atkins GC, Kudroff K, et al. Accessing Pre-exposure Prophylaxis (PrEP): Perceptions of Current and Potential PrEP Users in Birmingham, Alabama. AIDS Behav. 2019;23:2966–79.
8. Henny KD, Duke CC, Geter A, Gaul Z, Frazier C, Peterson J, et al. HIV-Related Training and Correlates of Knowledge, HIV Screening and Prescribing of nPEP and PrEP Among Primary Care Providers in Southeast United States, 2017. AIDS Behav. 2019;23:2926–35.

9. U.S. Department of Health and Human Services., Ending the HIV Epidemic: About Ending the HIV Epidemic: Plan for America: Overview [Internet]. 2020 [cited 2021 Jan 14]. Available from: https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview.
10. U.S. Department of Health and Human Services., Priority Jurisdictions: Phase I [Internet]. 2020 [cited 2020 Jun 26]. Available from: https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/jurisdictions/phase-one.
11. Haberer JE. Current concepts for PrEP adherence in the PrEP revolution: from clinical trials to routine practice. Curr Opin HIV AIDS. 2016;11:10–7.
12. Haberer JE, Kidoguchi L, Heffron R, Mugo N, Bukusi E, Katahira E, et al. Alignment of adherence and risk for HIV acquisition in a demonstration project of pre-exposure prophylaxis among HIV serodiscordant couples in Kenya and Uganda: a prospective analysis of prevention-effective adherence. J Int AIDS Soc. 2017;20:21842.
13. Muwonge TR, Ngure K, Katahira E, Mugo N, Kimemia G, Burns BFO, et al. Short Message Service (SMS) Surveys Assessing Pre-exposure Prophylaxis (PrEP) Adherence and Sexual Behavior are Highly Acceptable Among HIV-Uninfected Members of Serodiscordant Couples in East Africa: A Mixed Methods Study. AIDS Behav. 2019;23:1267–76.
14. Curran K, Mugo NR, Kurth A, Ngure K, Heffron R, Donnell D, et al. Daily short message service surveys to measure sexual behavior and pre-exposure prophylaxis use among Kenyan men and women. AIDS Behav. 2015;17:2977–85.
15. Baker Z, Javanbakht M, Mierzwia S, Pavel C, Lally M, Zimet G, et al. Predictors of Over-Reporting HIV Pre-exposure Prophylaxis (PrEP) Adherence Among Young Men Who Have Sex With Men (YMSM) in Self-Reported Versus Biomarker Data. AIDS Behav. 2018;22:1174–83.
16. Wray TB, Kahler CW, Monti PM. Using Ecological Momentary Assessment (EMA) to Study Sex Events Among Very High-Risk Men Who Have Sex with Men (MSM). AIDS Behav. 2016;20:2231–42.
17. Wray TB, Chan PA, Kahler CW, Simpanen EM, Liu T, Mayer KH. Vulnerable Periods: Characterizing Patterns of Sexual Risk and Substance Use During Lapses in Adherence to HIV Pre-exposure Prophylaxis Among Men Who Have Sex With Men. J Acquir Immune Defic Syndr. 2019;80:276–83.
18. Bauermeister J, Pingel E, Zimmerman M, Couper M, Carballo-Dieguez A, Strecher VJ. Data Quality in web-based HIV/AIDS research: Handling Invalid and Suspicious Data. Field methods. 2012;24:272–91.
19. Ingram DD, Franco SJ. 2013 NCHS Urban-Rural Classification Scheme for Counties. Vital Health Stat 2. 2014;2:1–73.
20. Liu AY, Laborde ND, Coleman K, Vittinghoff E, Gonzalez R, Wilde G, et al. DOT Diary: Developing a Novel Mobile App Using Artificial Intelligence and an Electronic Sexual Diary to Measure and Support PrEP Adherence Among Young Men Who Have Sex With Men. AIDS Behav. 2016;20:21842.
21. Wray TB, Monti PM. Characteristics of Sex Events, Partners, and Motivations and Their Associations with HIV-Risk Behavior in a Daily Diary Study of High-Risk Men Who Have Sex with Men (MSM). AIDS Behav. 2020;24:1851–64.
22. Liu AY, Cohen SE, Vittinghoff E, Anderson PL, Doblec-K-Lewis S, Bacon O, et al. Preexposure Prophylaxis for HIV Infection Integrated With Municipal- and Community-Based Sexual Health Services. JAMA Intern Med. 2016;176:75–84.
23. Wheeler DP, Fields SD, Beauchamp G, Chen YQ, Emel LM, Hightow-Weidman L, et al. Pre-exposure prophylaxis initiation and adherence among Black men who have sex with men (MSM)
24. Hoenigl M, Morgan E, Franklin D, Anderson PL, Pasipanodya E, Dawson M, et al. Self-initiated continuation of and adherence to HIV pre-exposure prophylaxis (PrEP) after PrEP demonstration project roll-off in men who have sex with men: associations with risky decision making, impulsivity/disinhibition, and sensation seeking. J Neurovirol [Internet]. 2019;2019/01/09. Available from: https://link.springer.com/article/10.1007%2Fs13365-018-0716-3.
25. Colson PW, Franks J, Wu Y, Winterhalter FS, Knox J, Ortega H, et al. Adherence to Pre-exposure Prophylaxis in Black Men Who Have Sex with Men and Transgender Women in a Community Setting in Harlem, NY. AIDS Behav [Internet]. 2020;2020/05/10. Available from: https://link.springer.com/article/https://doi.org/10.1007/s10461-020-02901-6.

Publisher’s note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.