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# Sexual Relationships Outside Primary Partnerships and Abstinence are Associated with Lower Adherence and Adherence Gaps: Data from the Partners PrEP Ancillary Adherence Study

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# Sexual relationships outside primary partnerships and abstinence are associated with lower adherence and adherence gaps: data from the Partners PrEP Ancillary Adherence Study

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## Abstract

**Objective—**To assess the role of sexual relationships on levels and patterns of adherence to medication for pre-exposure prophylaxis (PrEP) against HIV.

**Methods—**We enrolled 1,147 HIV-negative individuals in long-term serodiscordant relationships at three sites in Uganda from the Partners PrEP Study- a randomized placebo-controlled trial of daily oral tenofovir and emtricitabine/tenofovir. We used generalized estimation equations to assess the effects of sexual relationships on low adherence (<80%) and on gaps in adherence.

**Results—**Fifty-three percent were male, 51% were 18-34 years and 24% were polygamous. Participants who reported sex in the past month with someone other than their primary partner and with <100% condom use were more than twice as likely to have low adherence (aOR 2.48, 95% CI: 1.70-3.62) compared to those who had sex with only their primary partners and 100% condom

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use. Using the same reference group, those who abstained from sex in the previous month had 30% increased odds of low adherence (aOR 1.30, 95% CI: 1.05-1.62), and participants in non-polygamous marriages who reported sex with both their primary and other partners and <100% condom use were almost twice as likely to be low adherers (aOR 1.76, 95% CI: 1.01-3.08). At least one 72-hour gap in adherence was seen in 598 participants (54.7%); 23.2% had at least one one-week gap.

**Conclusions—**Risk of low overall adherence was higher in participants who reported sex outside primary partnerships and suboptimal condom use, as well as in those who abstained from sex. Adherence gaps were common, potentially creating risk for HIV acquisition.

### Keywords

HIV pre-exposure prophylaxis; sexual behavior; adherence

## Introduction

HIV antiretroviral medications have been shown to reduce the transmission of the virus when used for prophylaxis by HIV-negative individuals. [1-3] Based on these studies, the US Food and Drug Administration (FDA) approved the use of tenofovir/emtricitabine; an antiretroviral drug for pre-exposure prophylaxis (PrEP) by HIV-negative individuals with a high risk of acquiring sexually transmitted HIV. [4] PrEP is now one of the few available HIV prevention strategies in a field where vaccines and a cure have long been elusive.

Adherence to prescribed antiretroviral medication is known to be vital to successful viral suppression and better clinical outcomes in HIV treatment settings. [5] Additionally, adherence has been identified to be a key component of effective PrEP. [6] Poor adherence to assigned medication is likely the primary reason for the null findings in the FEM-PREP and VOICE studies, which assessed the efficacy of oral and topical tenofovir for HIV pre-exposure prophylaxis among heterosexual African women. [7]

Because PrEP is a new tool in HIV prevention, there are limited data on the associations of adherence to this medication. However we recently reported that several factors including age, heavy alcohol use, being in a polygamous marriage and sexual behavior might affect adherence to HIV PrEP. [8] For the purposes of this study polygamy status was defined at baseline and referred to one of two situations: 1) an HIV-negative man with more than one wife, one of whom was HIV-positive, or 2) an HIV-negative woman whose HIV-infected husband had more than one wife. Marriage was be defined by law, religious or local custom. We assessed quarterly sexual behavior via interviewer-administered questionnaires and quarterly adherence was assessed using the medication event monitoring system (MEMS: Aardex, Switzerland). We found that HIV-negative participants who reported sex with only people other than their primary sexual partners were twice as likely to have low rates of adherence as compared to those who only reported sex with their primary partners (aOR 2.3, 95% C.I: 1.3 to 3.8). In a second study using SMS surveys for assessing sexual behavior [9], participants who did not have sex on a particular day were almost twice as likely to miss a dose of PrEP medication on that same day (aOR 1.87, 95% C.I: 1.35 to 2.60).

To better understand the relationship between sexual behavior and adherence to PrEP, in this study, we assessed the associations of sexual behavior with monthly adherence rates, which may better assess short-term effects of sexual behavior, as well as with patterns of adherence to PrEP. Patterns may be more informative than summary measures of adherence (e.g., median values) because lengthy gaps may expose an individual to more risk for HIV acquisition compared to occasional missed doses. [10] We also explore the effect condom use on adherence within all strata of sexual behavior. We further evaluated the influence of polygamy within strata of sexual behavior to explore more closely the role of polygamy on adherence to PrEP.

## Methods

### Study setting and population

We analyzed data from the Partners Ancillary Adherence Study, a sub-study of the Partners PrEP Study. [1] The Partners PrEP Study was a multisite, phase III, randomized, double-blind, placebo-controlled clinical trial that assessed the efficacy and safety of tenofovir (TDF) and emtricitabine/tenofovir (FTC/TDF) for pre-exposure prophylaxis against HIV acquisition. This clinical trial enrolled 4758 heterosexual serodiscordant couples at four sites in Kenya and five sites in Uganda. Heterosexual couples were defined as “sexual partners of the opposite gender who were married, had been living together, or otherwise considered each other a primary partner”. The adherence study took place at three of the Ugandan sites including Kampala (an urban setting) and Kabwohe and Tororo (rural settings; Figure 1). We have previously described details of this study [8], but briefly, we enrolled 1147 HIV-negative individuals in long-term serodiscordant relationships. All PrEP study participants at these sites were eligible for participation as long as they consented for study procedures and had at least six or more months of follow-up in the parent clinical trial. Enrollment was offered on a rolling basis and all participants provided written informed consent. In addition to monthly follow up visits at the clinics, we conducted unannounced home visits for pill counts monthly for the first 6 months and then quarterly thereafter. We also used the medication event monitoring system [MEMS] to monitor the date and time of pill bottle openings. Lastly, participants with <80% monthly adherence to PrEP were started on multi-session adherence intervention. [11] Data for this analysis was censored at July 10, 2011, the date of unbinding of the placebo arm.

### Ethical statement

The study was approved by the institutional review boards of participating study sites and those of Massachusetts General Hospital/Partners Healthcare and of the University of Washington.

### Assessment of sexual behavior

Sexual behavior was assessed via interviewer-administered questionnaires completed at monthly clinic visits. Face-to-face interviews have not been validated in a PrEP setting but have been shown to consistently assess sexual behavior. [12] At each visit, study participants met with counselors and discussed several issues relating to HIV-discordancy including sexual behavior in the past month. The interviewers queried the number of sexual acts,

condom use, and sexual acts with anyone besides the primary partner. Whenever ‘sex’ or ‘sexual intercourse’ was stated in a question, it included vaginal and anal sex, but not oral sex. Interviews were conducted in either English or in a local language of a participant's preference and participants were given the option of being interviewed by a counselor of their choice.

We categorized monthly sexual behavior as follows: participants who abstained, those who had sex with only their primary partners, those who had sex with only other partners (but not with their primary partner) and those that had sex with both the primary and other partner(s). Each of the above categories was dichotomized into either 100% condom use or <100% condom use. The “other partner” category included participants who in the previous month did not have sex with their primary partner but reported sex with someone else. We were unable to stratify this category by polygamy status at baseline due to small numbers. The number of participants was sufficient however to make this stratification for the category reporting sex with both the primary and other partner(s).

## Assessment of adherence

Monthly adherence to PrEP medication was assessed using the medication event monitoring system [MEMS]. This system uses an electronic microchip in the cap of a pill bottle to record dates and times the pill bottle was opened and closed. The underlying assumption is that every opening and closure of the pill bottle translates to a swallowed dose of the study drug. Recorded adherence data was then downloaded during monthly clinic visits. Although MEMS is a proxy measure and is subject to misclassification, it allows for assessment of adherence patterns by documenting daily pill taking behavior [13] and has been shown to have a high positive predictive value of treatment outcomes. [14]

We assessed execution of adherence as a dichotomous variable, with 80% or greater adherence defined as ‘high adherence’ and < 80% adherence defined as ‘low adherence’. The level of adherence required for effective PrEP is not known. However, we recently found 100% PrEP efficacy if participants' adherence rates are maintained at 80% and above. [8] We also assessed patterns of adherence (i.e., the number of periods of at least 48 hours, 72 hours and 1 week during with the pill bottle was unopened). We looked at a range of patterns because there is limited data on how much tenofovir must be present in blood and tissue to offer protection against HIV. Data are also limited on how gaps in adherence before and after achievement of stable states affect this protection. Using the heuristic that drugs remain in the body for about 4 half-lives [15], it is likely that tenofovir (half life $\sim$ 17 hours) is undetectable after a gap of 68 hours, or approximately three days.

## Assessments of other covariates

We collected baseline data on the study participant's age, gender, social economic status and level of education, all of which have been shown to be associated with adherence in HIV treatment settings. [16] We assessed partnership characteristics including how long the couple had been living together, the number of children they had, whether one of them was in a polygamous marriage and how long they had known that they were HIV discordant. Social economic status was assessed using the Filmer-Pritchett index, which uses household items

to estimate wealth. [17] For this study, the wealth index for a couple's home reflected the presence of a concrete floor, running water, electricity, a television and a house with two or more rooms of residence.

Time varying characteristics assessed included heavy alcohol use, depression, number of study drug side effects, the participant's perceived risk of HIV acquisition and CD4 cell counts of the HIV-infected partner. Depression was assessed using the Hopkins Symptom Checklist, a functional impairment assessment instrument that can be used to approximate a DSM-IV depression diagnosis, which has been validated in similar populations. [18] Heavy alcohol use was assessed using the Rapid Alcohol Problems Screen that has been shown to have good sensitivity and specificity in identifying detrimental drinking patterns and has cross-nation validity. [19]

### Statistical analysis

We performed bivariate analyses between each possible covariate and adherence using generalized estimating equations (GEE). Monthly adherence execution was modeled using a binomial distribution, whereas adherence patterns were modeled with a Poisson distribution. For model selection, the initial multivariate model included all variables with a p-value ≤0.20 from the bivariate analyses. Starting with variables with the highest p-values we assessed the scale of maximum likelihood, one at a time and dropped those with p-values >0.10 from the final multivariate model. We used a similar method to assess possible interaction effects between sexual behaviors with age, gender, study site and social economic status, all chosen a priori and used a p-value of <0.10 as a cutoff for statistical significance. Data were analyzed using SAS version 9.3 (SAS Institute Inc., Cary, NC).

## Results

### Study participants

A total of 1,751 HIV-negative participants enrolled in the parent clinical trial at the three sites. Of these, 1,182 were offered participation in the adherence study and 1,147 (97%) were enrolled. Reasons for not being offered participation included having less than 6 months remaining for follow-up while on study drug, logistical reasons that would make study procedures difficult to conduct and stopping of the parent clinical trial before participation could be offered. Thirty-five participants did not meet the criteria for enrollment resulting in a final analysis dataset of 1,093 participants (Table 1). Of these, 53.4% were male, 51.2% were aged between 18 and 34 years, the median number of years living with the HIV-positive partner was 8.5 years, and 24.2% were in polygamous marriages. The mean follow-up duration was 11 months.

### Overall adherence and sexual behavior

A total of 402 (36.7%) participants had at least one month with <80% adherence; this translated into 13.3% of the observed months of low adherence. Levels of adherence are presented by category of sexual activity and condom use in Table 2. Participants who reported sex with other partners only (i.e., no sex with their primary sexual partner) and also reported < 100% condom use (N=92) were more than twice as likely to be low adherers as

compared to those who had sex only with their primary partners with 100% condom use (aOR 2.48, 95% CI: 1.70 to 3.62). The number of other sexual partners had no effect on odds for low adherence (OR: 0.98, 95% CI: 0.68-1.40). Using the same reference group, those who abstained from sex in the previous month (N=465) had 30% increased odds of low adherence (aOR 1.30, 95% CI: 1.05 to 1.62). Participants who reported sex with both their primary and other partners (not including polygamous marriages) with < 100% condom use (N=60) were almost twice as likely to be low adherers (aOR 1.76, 95% CI: 1.01 to 3.08). However, those with similar sexual behavior in the past month but in polygamous marriages did not have significantly higher odds of low adherence (aOR: 1.10 95% CI: 0.49 to 2.53).

Participants who reported sex with only their primary partners were more likely to have 100% condom use as compared to those who had sex with both their primary partners and other partner(s), and with those who had sex with only other partners (79%, 33% and 36% respectively). Those with low or moderate concern of contracting HIV had 41% lower odds of low adherence as compared to those who had no concern of HIV acquisition. Men were 34% more likely to be low adherers than women. We did not find any significant interaction effects of sexual behavior with age (P=0.91), social economic status (P=0.23) or study site (P=0.17) on the likelihood of having <80% monthly adherence to PrEP.

### Patterns of adherence

Prevalence of gaps in adherence by sexual behavior is presented in Table 3. A total of 598 (54.7%) of the participants had at least one gap of 72 consecutive hours of non-adherence and 254 (23.2%) of these also had at least one one-week gap of non-adherence. Of the participants who reported <100% use of condoms in a previous month (N=546), 38.8% had at least one 72-hour gap in adherence in that month and 17% had a one-week gap in adherence in that month.

Participants who reported sex with other partners only and <100% condom use had 50% higher odds of having at least one 72-hour gap in adherence as compared to those who had sex with only their primary partners with 100% condom use (aOR 1.50, 95% CI: 1.19 to 1.91), while those who abstained from sex in the previous month had 17% elevated odds (aOR=1.17, 95% CI: 1.01 to 1.35; Table 4). Adherence gaps of 72 hours were not associated with reporting sex with both primary and other partners in the previous month, regardless of polygamy status. We found similar results when assessing odds of having 48-hour gaps in adherence (data not shown). Men were more likely to have had a one-week gap as compared to women (aOR: 1.54, 95% CI: 1.04 to 2.27).

## Discussion

In this prospective observational study within a randomized clinical trial, HIV-negative participants who reported sex with people other than their primary partner and those who abstained from sexual activity in the previous month were more likely to be low adherers. We found similar, although somewhat weaker associations between sexual activity and gaps in adherence. Our findings also indicate that <100% condom use was more common in participants who reported sex with only other partners and that participants in polygamous marriages did not have increased odds of being low adherers.

These findings extend results from our previous study. [8] The current study however, observed somewhat weaker associations among participants that had abstained in the past month, which suggests that the association of abstinence with adherence may be stronger if this sexual behavior is sustained over a longer period (in this case, quarterly versus monthly). We also found that participants who had sex with only other partners had the highest odds of low adherence and having gaps of non-adherence. We are however unable to distinguish whether this other partner was a new sexual partner or a partner in a polygamous marriage. Nonetheless, these findings indicate that participants who had sex with only other partners are more likely to be low adherers. A similar pattern has been observed in some HIV treatment settings, where patients with risky sexual behaviors are also more likely to be poor adherers to therapy. [20, 21] Also, the highest odds of low adherence were observed in participants who had sex with only other partners and in the same month also had less than 100% condom use. Further research is needed on the dynamics influencing condom use with primary partners (HIV-infected) and with other partners. However, one possible explanation for both lower adherence and <100% condom use is low perceived risk of acquiring HIV from the other partner.

To our knowledge no study has explicitly assessed the role of polygamy on adherence. Several studies have however found that polygamy offers a protective effect against HIV-acquisition. [22, 23] Our previous findings showed that participants in polygamous marriage had a 60% reduced odds for low adherence as compared to those from monogamous marriages. [8] We did not find a protective effect in this study but did find no increased risk among polygamous partners. We hypothesize that HIV-negative partners in discordant and polygamous marriages receive extra social support to adhere to PrEP so as to prevent transmission of HIV within the polygamous marriage. This concept is consistent with our recent findings that spousal support plays a key role in PrEP adherence. [24] The lack of a protective effect in our study could be multifactorial. First, we had small numbers of people in these stratifications. Secondly, the one-month exposure period might not be long enough to assess the protective effect that was observed in quarterly assessment of sexual behavior on adherence.

This is the first study to assess the effect of sexual behavior on patterns of adherence. Though previous studies have shown that participants in Partners PrEP Study had high rates of adherence [8], we found that many participants had gaps of not taking their medication. Such intermittent dosing is likely to increase the risk of acquiring HIV since every subsequent day of non-adherence results in a lower concentration of active drug. This increased risk is consistent with findings from the FEM-PrEP study that showed high rates of inconsistent use of the study drug that could have contributed to the lack of a protective effect in the active study arms. [25] Some of the observed gaps, however, could have been due to pocket doses (i.e., removal of multiple tablets with one opening for later use) —a well-established limitation of electronic adherence measurement, and may not reveal true gaps in adherence. The correlation of adherence gaps with other potentially risky sexual behaviors, like sex with other partners, suggests that many are real. Additionally, we do not know if these gaps in adherence were covered by other forms of HIV prevention (e.g., condoms). This highlights the need for a better understanding of the use of combination prevention strategies. Additionally, among participants who reported abstinence in the previous month,

some extended gaps could have could been intentional because of no perceived risk of HIV transmission in that period. Such practices may be logical; however, the correlation of specific dosing patterns with achievement and maintenance of drug levels sufficient for providing effective protection against HIV infection are unknown. Such an understanding will be crucial in advising individuals on how to start and stop PrEP (i.e., periodic dosing) with the confidence that it will be effective. These findings can be used in designing HIV prevention programs with a PrEP component. For example, PrEP might not be the recommended HIV prevention method for people who know that they will not be having sex for certain periods. Also, individuals with outside partners may benefit from additional counseling on risk perception and strategies for including PrEP when they are with these other partners.

Our study's strengths include the use of a prospective study design to assess the effects of short-term sexual behaviors on low adherence. Our large sample size enabled us to assess the effects of many aspects of sexual behavior. One study limitation was that few participants reported sexual activity with both their primary and other partners. We therefore had limited statistical power to assess associations between sexual behavior and adherence within some strata of sexual behavior. Also, we did not have data on relationship discord, a risk factor that has been suggested to be critical to adherence to PrEP medication [26] and were therefore unable to evaluate possible confounding by this factor. Also, data on sexual behavior were collected using self-report which is subject to social desirability bias, which may result in to less reporting of some risky sexual behaviors. Lastly, we could not distinguish if other partners were actually within polygamous marriages.

In conclusion, our findings identify groups of people in HIV serodiscordant relationships who may require extra adherence support during PrEP implementation programs-- namely, those with multiple partners but are not in polygamous marriages. In addition, PrEP eligible persons who are likely to abstain from sex may need prevention methods that are more suitable to intermittent need. Also, we found that though overall adherence rates were high, many participants missed taking their study pills for relatively long periods of time, potentially creating risk for HIV acquisition. Further research is needed on the use and efficacy of intermittent and periodic PrEP from trials and demonstration projects. We also found that polygamy might be a factor influencing better adherence due to the desire to prevent HIV transmission within a polygamous marriage. However, more work is needed to ascertain this effect using a study with more people that report this behavior and one that distinguishes whether or not the “other partner” is part of the polygamous marriage.

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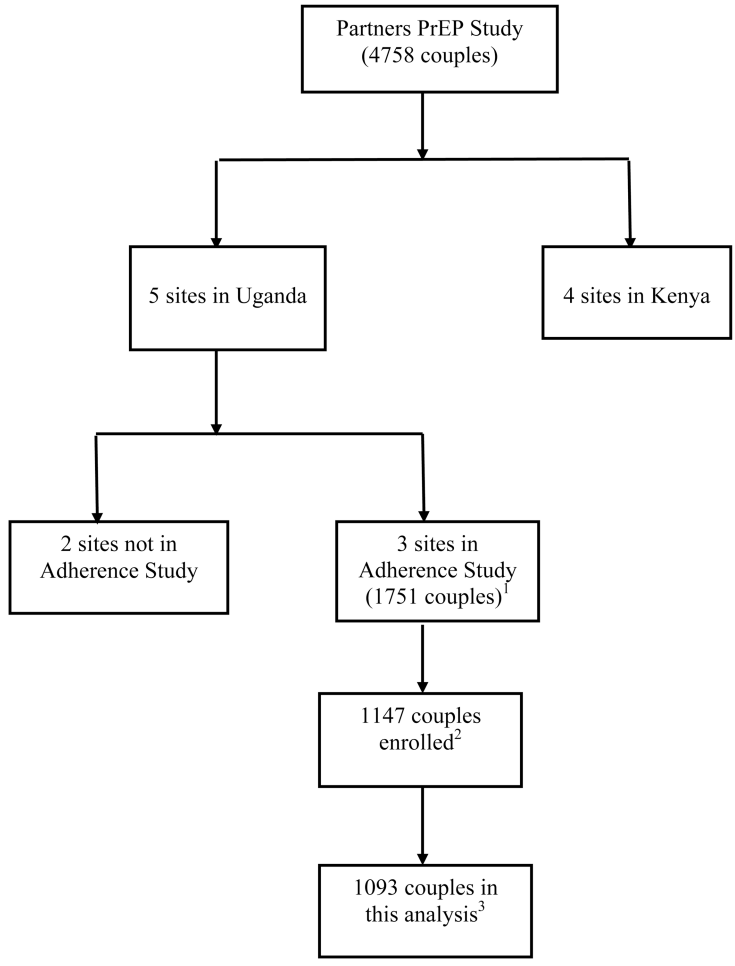


**Figure 1. Study populations for the Partners PrEP Study and the Ancillary Adherence Study**

[1]Two sites were in a rural settings and the third was in an urban setting.

[2]Reasons for not being enrolled included participant decline, not meeting inclusion criteria and not being offered participation into the study (after stopping of the parent clinical trial by the DSMB)

[3]Fiftyfour participants excluded due of censoring the analysis dataset to before July 10 2011

## Table 1
## Baseline characteristics of study participants (N=1093)

| Characteristic | N | % |
|---|---|---|
| Male (N, %) | 584 | 53.4 |
| Age (N, %) | | |
| 18-24 | 86 | 7.9 |
| 25-34 | 475 | 43.5 |
| 35-44 | 392 | 35.9 |
| 44+ | 140 | 12.8 |
| Education level (N, %) | | |
| Primary or less (≤ 7 years) | 821 | 75.1 |
| Secondary (8-13 years) | 244 | 22.3 |
| Post secondary (> 13 years) | 28 | 2.6 |
| Primary source of income (N, %) | | |
| Professional | 66 | 6.0 |
| Laborer | 220 | 20.1 |
| Trade/sales | 148 | 13.5 |
| Farming | 635 | 58.1 |
| Other | 24 | 2.2 |
| On placebo (N, %) | 387 | 35.4 |
| Duration of knowledge of discordance, years (median, range) | 1 | 0-14 |
| Number of years living together (median, range) | 8.5 | 0-39 |
| Polygamous marriage (N, %)[1] | 264 | 24.2 |
| Number of children in partnership (median, range) | 2 | 0-13 |
| CD4 cell count in HIV-infected partner, cells/$mm^3$ (N, %)[2] | | |
| < 200 | 30 | 2.8 |
| 200-350 | 246 | 22.5 |
| > 350 | 817 | 74.7 |

[1] Referred to one of two situations: 1) an HIV-negative man with more than one wife, one of whom was HIV-positive, or 2) an HIV-negative woman whose HIV-infected husband had more than one wife

[2] Assessed at beginning of adherence study

**Table 2**

**Univariable and multivariable analysis for < 80% adherence to PrEP**

Less than 80% adherence was seen in 402 study participants during 13.3% of all follow-up months.

| | | Unadjusted | | | Multivariable [2] | | |
|---|---|---|---|---|---|---|---|
| **Risk Category [1]** | **N, %** | **OR** | **95% C.I** | **p-value** | **aOR** | **95% C.I** | **p-value** |
| Primary partner only | | | | | | | |
| 100 % condom use | 929(85) | | Reference | | | Reference | |
| < 100% condom use | 418(39) | 1.06 | 0.90-1.25 | 0.52 | 0.95 | 0.70-1.30 | 0.76 |
| Abstinence | 465(43) | 1.32 | 1.13-1.54 | <0.01 | 1.30 | 1.05-1.62 | 0.02 |
| Other partner only | | | | | | | |
| 100 % condom use | 76(7) | 1.50 | 0.99-2.27 | 0.06 | 1.71 | 1.06-2.76 | 0.03 |
| < 100% condom use | 92(8) | 2.09 | 1.52-2.86 | <0.01 | 2.48 | 1.70-3.62 | 0.01 |
| Other partner + primary partner & polygamous[4] | | | | | | | |
| 100 % condom use | 56(5) | 0.96 | 0.67-1.37 | 0.82 | 1.10 | 0.49-2.53 | 0.82 |
| < 100% condom use | 81(7) | 0.92 | 0.61-1.39 | 0.68 | 1.45 | 0.86-2.43 | 0.16 |
| Other partner + primary partner & non-polygamous | | | | | | | |
| 100 % condom use | 60(5) | 1.10 | 0.65-1.88 | 0.72 | 1.76 | 1.01-3.08 | 0.04 |
| < 100% condom use | 91(8) | 1.40 | 0.99-1.98 | 0.06 | 1.41 | 0.88-2.27 | 0.16 |

[1] Some participants contributed to multiple categories due to change of monthly sexual behaviors

[2] Multivariable model controlled for:

Age[3], OR 0.96 (95%C.I: 0.93-0.98)

Social economic status index[3], OR 1.21 (95%C.I: 1.02-1.43)

Female, OR 0.66 (95%C.I: 0.47-0.93)

Adherence study duration[3], OR 1.03 (95%C.I: 1.01-1.06)

Duration of knowledge of discordance[3], OR 1.09 (95%C.I: 1.01-1.18)

Low or moderate concern for HIV acquisition vs. No concern, OR 0.59 (95%C.I: 0.42-0.83)

[3] Continuous variables

[4] Referred to one of two situations: 1) an HIV-negative man with more than one wife, one of whom was HIV-positive, or 2) an HIV-negative woman whose HIV-infected husband had more than one wife

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## Table 3

### Participants with gaps of non-adherence

| | 48-hour gap | | 72-hour gap | | 1-week gap | |
|---|---|---|---|---|---|---|
| **Description** | **Prevalence** | **Months with at least one gap (N,%)** | **Prevalence** | **Months with at least one gap (N,%)** | **Prevalence** | **Months with at least one gap (N,%)** |
| Overall [1] | 85.2 | 5001 (42.8) | 54.7 | 1966 (16.8) | 23.2 | 641 (5.5) |
| **Sexual behavior** [2] | | | | | | |
| Abstinence | 82.7 | 3466 (29.6) | 46.4 | 1268 (10.8) | 19.3 | 404 (3.5) |
| Partner only | 63.4 | 722 (6.2) | 36.6 | 329 (2.8) | 14.0 | 110 (0.9) |
| Other only | 67.4 | 248 (2.1) | 44.9 | 140 (1.2) | 22.5 | 66 (0.6) |
| Primary partner + other partner | 73.1 | 551 (4.7) | 46.3 | 220 (1.9) | 14.5 | 61 (0.5) |
| **Condom use** | | | | | | |
| 100% | 70.5 | 2968 (25.4) | 39.2 | 1133 (9.7) | 15.4 | 185 (1.6) |
| <100% | 36.0 | 1310 (11.2) | 19.4 | 503 (4.3) | 8.2 | 346 (3.0) |
| **Polygamy status** | | | | | | |
| Polygamous[3] | 83.3 | 1088 (9.3) | 53.8 | 386 (3.3) | 16.3 | 84 (0.7) |
| Non Polygamous | 85.5 | 3891 (33.3) | 54.8 | 1565 (13.4) | 25.3 | 551 (4.7) |

[1] Overall prevalence = # of participants with at least one gap/1093.

[2] Sexual behavior prevalence = # participants that had at least one gap of non-adherence/# of participants that ever reported that sexual behavior

[3] Referred to one of two situations: 1) an HIV-negative man with more than one wife, one of whom was HIV-positive, or 2) an HIV-negative woman whose HIV-infected husband had more than one wife

## Table 4

**Univariable and multivariable analysis for having gaps of 72 hours or more without taking the study drug. Treatment gaps were observed in 598 participants during 16.8% of all follow-up months**

| | | Unadjusted | | | Multivariable [2] | | |
|---|---|---|---|---|---|---|---|
| **Risk Category [1]** | **N, %** | **OR** | **95% C.I** | **p-value** | **aOR** | **95% C.I** | **p-value** |
| Primary partner only | | | | | | | |
| 100 % condom use | 929(85) | | Reference | | | Reference | |
| < 100% condom use | 418(39) | 0.94 | 0.81-1.09 | 0.43 | 0.91 | 0.78-1.06 | 0.21 |
| Abstinence | 465(43) | 1.20 | 1.03-1.40 | 0.02 | 1.17 | 1.01-1.35 | 0.04 |
| Other partner only | | | | | | | |
| 100 % condom use | 76(7) | 1.51 | 0.93-2.44 | 0.09 | 1.32 | 0.93-1.87 | 0.12 |
| < 100% condom use | 92(8) | 1.69 | 1.26-2.26 | <0.01 | 1.50 | 1.19-1.91 | 0.01 |
| Other partner + primary partner & polygamous[4] | | | | | | | |
| 100 % condom use | 56(5) | 1.00 | 0.72-1.40 | 0.98 | 1.01 | 0.65-1.55 | 0.98 |
| < 100% condom use | 81(7) | 1.09 | 0.79-1.51 | 0.61 | 1.16 | 0.84-1.62 | 0.36 |
| Other partner + primary partner & non-polygamous | | | | | | | |
| 100 % condom use | 60(5) | 1.18 | 0.62-2.23 | 0.62 | 1.17 | 0.73-1.88 | 0.51 |
| < 100% condom use | 91(8) | 1.21 | 0.91-1.62 | 0.19 | 1.07 | 0.83-1.37 | 0.61 |

[1] Some participants contributed to multiple categories due to change of monthly sexual behaviors

[2] Multivariable model controlled for:

Age[3], aOR 0.98 (95% C.I: 0.96 to 0.99)

Social economic status index[3], aOR 1.12 (95% C.I: 1.01 to 1.25)

Female, aOR 0.60 (95% C.I: 0.48 to 0.76)

Adherence study duration[3], aOR 1.03 (95% C.I: 1.01 to 1.04)

[3] Continuous variables

[4] Referred to one of two situations: 1) either an HIV-negative man with more than one wife, one of whom was HIV-positive, or 2) an HIV-negative woman whose HIV-infected husband had more than one wife