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Evaluation of sexual risk behavior among study participants in the TDF2 PrEP study among heterosexual adults in Botswana

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Abstract

Objective—Among participants of a clinical trial to test the efficacy of tenofovir/emtricitabine in protecting heterosexual men and women living in Botswana from HIV infection, determine 1) if sexual risk behavior, specifically condomless sex acts and number of sex partners, changed over time, 2) factors associated with condomless sex acts and number of sex partners and 3) the effect of participant treatment arm perception on risk behavior to address the possibility of risk compensation.

Methods—A longitudinal modeling of rates of risk behaviors was used to determine if the rate of condomless sex acts (#acts/person) and rate of sex partners (#partners/person) changed over time and which factors were associated with behavior change.

Results—1200 participants were analyzed over 1 year. There was a 25% decrease in the rate of sex partners among participants sexually active in the last 30 days. The rate of reported condomless sex acts was greater for males (RR=1.34, CI=1.07–1.67) and participants whose sexual debut in years was ≤ 15 years of age (RR=1.65, CI=1.14–2.38) and 16–17 (RR=1.68, CI=1.22–2.31) compared to ≥20 years. Rate of reported sex partners was greater for males (RR=3.67, CI=2.86–4.71) and participants whose age at sexual debut in years was ≤15 (RR=2.92, CI=2.01–4.22) and 16–17 (RR=2.34, CI=1.69–3.24) compared to ≥20. There was no effect of participant treatment arm perception on risk behavior.

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Conclusions—Our study of PrEP to prevent HIV infection found no evidence of risk compensation which may have been due to participants' motivations to reduce their risk behaviors and risk-reduction counseling.

Keywords

clinical trial; tenofovir/emtricitabine; risk compensation; sexual risk behavior

Introduction

A clinical trial (TDF2 study) to test the efficacy of TDF/FTC as pre-exposure prophylaxis (PrEP) in protecting heterosexual men and women living in Botswana from HIV infection found a 63% reduced risk of infection [1]. Three other clinical trials also demonstrated the efficacy of tenofovir-based PrEP. The iPrEx trial found a 42% reduced risk of HIV infection among gay men and transgender women [2, 3]. The Partners PrEP trial, discontinued early after an interim data review, found that daily oral TDF/FTC (75%) and TDF (67%) reduced risk the of HIV acquisition for the HIV-negative partner in a discordant couple [4]. The Bangkok Tenofovir study found a 49% reduced risk of HIV among injection drug users [5]. In contrast, two trials, FEM-PrEP [6] and VOICE [7], both involving women, were stopped early because there was lack of evidence of effectiveness. Follow-up analysis of the VOICE and FEM-PREP [6] trials showed that the lack of effectiveness was due, at least in part to low adherence [8]. Because of the large role poor adherence plays in explaining variability of PrEP trial outcomes, an improved understanding of pharmacological variables [9] and psychological and social determinants of behavior [10, 11] will be needed. In 2012, TDF/FTC was approved for oral daily use as PrEP by the U.S. Food and Drug Administration (FDA).

Several factors will influence the effectiveness of PrEP in the real world including adherence and risk compensation [11]. Risk homeostasis theory postulates that persons attempt to produce an output or given level of risk to health that matches the target level of risk [12]. In the case of PrEP, if a person believes that it will prevent HIV, they would theoretically reduce restrictions on their risk behaviors [13]. Risk compensation behaviors and their frequency, likely to differ depending upon the prevention intervention and various social and individual level factors [13], have long been an area of concern when considering biomedical HIV prevention interventions [2, 14].

The purpose of the present analysis of the TDF-2 study data was to determine, among a general population of adult heterosexual men and women in Botswana participating in the study, 1) if sexual behavior, specifically condomless sex acts and number of sex partners, changed over time, 2) the factors associated with condomless sex acts and number of sex partners and 3) the effect of participant treatment arm perception on risk behavior to address the possibility of risk compensation. To supplement the self-report data, a secondary analysis was done to determine the frequency of pregnancy or sexually transmitted infection (STI) diagnosis during the study, and factors associated with each.

Methods

The TDF-2 study, a phase 3 randomized, double-blind, placebo-controlled clinical trial to determine if PrEP was effective in preventing HIV among heterosexual men and women, was carried out in the cities of Francistown and Gaborone, Botswana, between May 2007 and May 2010 (ClinicalTrials.gov Identifier: NCT00448669). The full description and results of the TDF2 study can be found in the primary report [1].

Self-reported behavioral data were collected from participants at baseline and monthly thereafter using face to-face interviews augmented by audio computer-assisted self-interviews at baseline and semi-annually thereafter. HIV prevention services were provided to all participants and included individualized counseling on risk reduction, free male and female condoms, and screening for STIs. If indicated, partner notification and treatment for STIs were carried out.

Measures

Dependent Variables—Our primary analysis consisted of determining factors associated with two longitudinal measures of sexual risk behavior as well as two cumulative proxy measures of condomless sex. The two longitudinal dependent variables that measured sexual behavior were:

1. Number of condomless vaginal sexual acts (“number of condomless sex acts”) with both casual and main partners among those who reported having had at least one sexual partner in the previous 30 days and
2. Number of casual and main vaginal sex partners in the last 30 days (“number of sex partners”) among all study participants.

The two cumulative proxy measures of condomless sex were pregnancy (among women) or STI diagnosis during the course of the study. The STIs included were laboratory-confirmed gonorrhea, syphilis, chlamydia, trichomoniasis or herpes simplex virus 2. See main study paper for specifics on laboratory assessments. [1]

Independent variables—Independent variables included time, treatment group (TDF/FTC, placebo) to which the subject was assigned at randomization, treatment arm perception (or the treatment group that the respondent believed that he/she had been assigned to [TDF/FTC/placebo/unsure]) measured at baseline, 6 months, and 12 months, demographic factors (age, gender, educational attainment, screening site (Gaborone or Francistown), marital status, occupational status), and age at sexual debut. Laboratory results for STIs were also considered as independent variables in the analysis of self-reported sexual behavior.

Analysis

To measure the potential impact of selection bias at both enrollment and randomization, we assessed demographic characteristics and risk behaviors at screening by enrollment status (screened and enrolled versus screened and not enrolled) as well as among those enrolled by treatment group (TDF/FTC and placebo). For time-varying outcomes (i.e., number of condomless sex acts and number of sex partners), we used negative binomial hurdle (NBH)

random-effects models [15, 16] to estimate the occurrence and rate of condomless sexual acts (#acts/person) and sexual partners (#partners/person) over time and determine factors associated with sexual behavior. To assess factors associated with a pregnancy or STI diagnosis occurring at any time during the study, we estimated the risk ratios associated with each predictor using log binomial regression.

Our NBH models analyze the data for each outcome measure independently using two components: logistic regression to estimate the odds of reporting zero condomless sex acts (or zero sex partners) and negative binomial regression to estimate the rate ratio (RR) of condomless sex acts (or sex partners) over time and across subgroups. Thus, in the analysis of number of condomless sex acts, our model estimates the odds of reporting no condomless sex acts, and for respondents reporting at least one condomless sex act we estimate the rate ratio of condomless sex acts (i.e., number of condomless sex acts per person) at different time points or across different subgroups during the previous 30 days. This allowed us to determine if the number of participants who reported always using condoms changed over time or was significantly associated with selected predictors. Also, for those who had at least one condomless sex act in a time period, this modeling strategy allowed us to determine if the rate of reported condomless sex acts changed over time or was significantly associated with selected predictors. The analysis of number of sex partners was done similarly and allowed us to determine if having no sex partners changed over time (or differed with regard to selected predictors) and, for those who had at least one sex partner, if the rate of reported sex partners changed over time (or differed with regard to selected predictors).

We accounted for correlated responses (multiple observations within subject) by treating the participant as a random effect in both components of the NBH model (i.e., logistic regression and negative binomial components). Additionally, we identified predictors associated with the outcome. Factors that were significant at the $p \leq 0.20$ level in base models were considered for inclusion in the final multivariable model. However, time and treatment perception were used regardless of statistical significance. We performed a backwards elimination variable selection process to arrive at our final multivariable models. The final model for each outcome measure consisted of predictors that were significant in each model component independently at the 0.05 level.

Results

Of the 2533 volunteers who were screened for the study, 52.2% were eligible for enrollment. The enrolled and not-enrolled participants were significantly different on several variables. Compared to not-enrolled participants, a greater proportion of enrolled participants were 30–39 years of age, had post-secondary school education, were from Gaborone, and were employed. The enrolled versus not enrolled participants also differed on variables related to eligibility criteria (Supplemental Table 1). The final number of persons who were enrolled and randomized in the TDF2 study was 1219. Of the 1219, 19 participants were excluded from analysis (3 were HIV infected at enrollment and 16 never started study medication), leaving 1200 study participants.

Subjects were randomized to TDF or placebo groups and were followed for 1563 person-years (median, 1.1 years; maximum, 3.7 years). There were no significant differences in demographic characteristics, presence of STIs in the last year, or sexual behaviors in the last 30 days between the treatment and placebo groups at enrollment (Table 1). Participant perception of their study arm assignment was recorded at baseline (TDF2 n=228 (19.4%), placebo n=72 (6.1%), not sure n=878 (74.5%)), 6 months (TDF2 n=164 (20.8%), placebo n=79 (10.0%), not sure n=546 (69.2%)), and 12 months (TDF2 n=81 (18.2%), placebo n=50 (11.3%), not sure n=313 (70.5%)).

Condomless Sex Acts

Twenty-four participants (2.0%) reported no sex acts during the study period and were, therefore, not included in this analysis. Of the remaining 1176 subjects, 15 (1.3%) always reported no condomless sex acts (i.e., consistent condom use). Six hundred thirty-three (53.8%) reported both condomless sex acts as well as sex with a condom (i.e., inconsistent condom users) and 528 (44.9%) never reported using a condom (i.e., non-condom users). The number of reported condomless sex acts in a given 30-day period ranged from 0–168 acts.

The percent or rate of reported sex acts with 100% condom use in the last 30 days showed no apparent change over time (Fig. 1a), however the odds of reporting no condomless sex acts in the past 30 days increased approximately 16% per year (p=0.0042) (Supplemental Table 2). The percent or rate of reported condomless sex acts among those with 1 or more reported condomless sex acts in the past 30 days showed no significant change over time (p=0.3683)(Supplemental Table 2) (Fig. 1b).

Number of sex partners

Of the 1200 subjects, 20 (1.7%) reported no sex partners throughout the entire study. Seven hundred and two participants (58.5%) reported having 1 or more sex partners during each 30-day window of observation. In addition, 478 participants (39.8%) reported having 1 or more sex partners during at least one but not all 30-day periods. The number of reported sex partners in a given 30-day period ranged from 0–17 partners (mean=1.0; SD=0.76 median=1.0; IQR=1.0–1.0).

The percent of participants who reported no sex partners in the last 30 days increased (Fig. 1c). In addition, the odds of reporting no sex partners in the past 30 days increased approximately 40% per year (p≤0.0001) (Supplemental Table 3). For those who reported at least 1 sex partner during a time period, the rate of reported sex partners decreased approximately 25% per year (p≤0.0001) (Supplemental Table 3) (Fig. 1d).

Multivariable Analysis: Factors associated with reporting no condomless sex acts, and for no sex partners in past 30 days—The adjusted odds of reporting no condomless sex acts significantly increased by approximately 23% per year (adjusted odds ratio (aOR)=1.23, 1.10–1.37). Odds of no condomless sex were significantly lower for participants whose sexual debut in years was ≤15 years of age (aOR=0.37, CI=0.23–0.61) and 16–17 (aOR=0.49, CI=0.32–0.72) compared to ≥20 and for participants who were

diagnosed with an STI during the study (aOR=0.43, CI=0.27–0.69). There was no significant effect of participant perception that they were receiving TDF-2 compared to participant perception that they were receiving a placebo (aOR=1.05, CI=0.77, 1.44) (Table 2).

The adjusted odds of reporting no sex partners significantly increased approximately 2% per year (aOR=1.02, CI=1.01–1.03). Odds of reporting no sex partners were significantly lower for participants who were married (aOR=0.33, CI=0.17–0.62), employed (OR=0.76, CI=0.58–1.00), and participants who tested HSV-2 positive during the study (aOR=0.58, CI=0.44–0.76). There was no significant effect of participant perception that they were receiving TDF-2 compared to participant perception that they were receiving a placebo (aOR=0.92, CI=0.68, 1.22) (Table 3).

Multivariable Analysis: Factors associated with reporting ≥1 condomless sex acts, and for ≥1 sex partners in past 30 days—For those who reported ≥1 condomless sex act during a time period, the rate of reported condomless sex acts was significantly greater for participants who tested positive for HSV-2 (aRR=1.32, CI=1.06–1.66), males (aRR=1.34, CI=1.07–1.67), and for participants whose age at sexual debut in years was ≤15 (aRR=1.65, CI=1.14–2.38) and 16–17 (aRR=1.68, CI=1.22–2.31) compared to ≥20 of age. There was no significant effect of participant perception that they were receiving TDF2 compared to participant perception that they were receiving a placebo (aRR=0.95, CI=0.73, 1.24) (Table 2).

For those reporting ≥1 sex partners during a time period, the rate of reported sex partners significantly decreased by approximately 3% per year (aRR=0.97, CI=0.97–0.98). There was a significantly increased rate of reported sex partners for those whose age at sexual debut in years was ≤15 (aRR=2.92, CI=2.01–4.22) or 16–17 (aRR=2.34, CI=1.69–3.24) compared to ≥20 and among males (aRR=3.67, CI=2.86–4.71). The rate of reported sex partners was also significantly greater for participants 21–29 years of age (aRR=3.12, CI=1.18–8.24) compared to 18–20 years of age and for participants diagnosed with an STI during the course of the study (aRR=1.79 CI=1.34–2.41). There was no significant effect of participant perception that they were receiving TDF-2 compared to participant perception that they were receiving a placebo (aRR=1.04, CI=0.84, 1.29) (Table 3).

STI diagnosis and Pregnancy

Factors associated with being diagnosed with an STI or becoming pregnant during the course of the study—During the course of the study, of participants enrolled 155 of 1200, 12.9%, were diagnosed with an STI, while 96 of the 544 women, 17.6%, became pregnant. Although nearly all participants reported condomless sex at some point during the study, of the 155 persons diagnosed with an STI, 109 (70.3%) reported no condomless sex acts during the month immediately preceding the STI diagnosis. Also, of the 96 women who became pregnant during the study, only 1 (1.0%) reported consistent condom use. As noted previously, only 15 participants (8 females and 7 males) reported consistently using condoms throughout the entire study. One of these 15 participants was diagnosed with an STI and 1 of the female participants became pregnant during the study.

No variables, including perception of treatment arm assignment, were significantly associated with pregnancy or STI diagnosis during the study.

Discussion

Using our measures, risk compensation was not observed in our study of PrEP to prevent HIV infection among heterosexual participants living in Botswana. While some studies have provided data suggesting that risk compensation is possible [17, 18], our findings concur with the findings of other HIV prevention interventions such as male circumcision [19], vaccines [20], and microbicides [21] as well as other PrEP trials [2, 3, 14, 22–24], including the open label extension of iPrEX [25]. Not only was there no evidence of risk compensation in our study, there was, in fact, a trend toward less reported sexual risk over time. For those reporting no condomless sex in the last 30 days, the absence of condomless sex continued over the trial and the odds increased 16% per year. Although the odds increased 16% it equates to approximately a 3% increase in the 100% condom use. In addition, for those reporting no sex partners in the past 30 days, the odds of continued reporting of no sex partners increased 40% per year. There are several potential reasons for the reduction in risk behavior. First, participants in controlled trials may join the trial to obtain help in reducing their risk behaviors because they have already made a decision to change their behavior to avoid HIV infection. For instance, in the VAX004 HIV vaccine trial, 56% of participants reported joining the trial to reduce their risk behavior [26]. Second, it may be that the risk-reduction counselling and testing, as well as provision of condoms, a key part of our study, was effective in motivating participants to reduce their high-risk sexual behavior. Third, it may be that the participants did not know to which treatment arm they were assigned nor even if the drug would protect them. In fact, the message given to the participants from study staff was that assignment to treatment arm and efficacy of the drug were unknown. There is also the possibility of social desirability bias [27]. Finally, there may be regression to the mean where extreme behaviors even out due to natural fluctuations [28]. In the context of this randomized controlled clinical trial, it is not possible to exclude any or assess the relative contributions of these factors.

Multivariable analyses showed that younger age at sexual debut, male gender, and other sexually transmitted infections were associated with more HIV risk. Young age at sexual debut is an important risk factor for HIV [29, 30]. One way to mitigate early sexual debut may be to reduce school drop-out [31–33]. Education is postulated to have an effect in reducing HIV infection not only through exposure to HIV prevention and health information, but more importantly, through the knowledge and skills obtained through a basic education [34, 35]. These skills help individuals to find and use information, translate knowledge into behavior change, and plan for the future. In addition, it keeps boys and girls in school, exposed to same age mates, and occupied with studying [36]. Male gender was associated with greater HIV risk in our study. This finding seems contradictory given that HIV prevalence in Botswana is 3 times as high among young females as among young males (15.3 percent of young women and 5.1 percent of young men living with HIV in 2007). However, the qualitative portion of a PrEP study carried out in Ghana revealed multiple reasons why women reduced their high-risk sexual behaviors in that study and may have relevance to our study results. Two of the reasons were: 1) because the study gave them

access to condoms and 2) knowing that they were negative reduced their number of sex partners [37]. STIs, including HSV-2, have long been associated with persons engaging in high-risk sexual behaviors and with increased risk for HIV infection [38].

Our study results must be interpreted in the context of several potential limitations. First, there may have been attrition bias as a result of higher than expected participant withdrawal from the study due to relocation or other obligations [1], though because we do not believe that this attrition occurred differentially among participants who were at different levels of treatment perception and degrees of change in risk behavior over time, this did not likely impact our findings. Second, our results indicating no risk compensation may not be predictive of a person's risk perception and their risk behaviors in the real world outside the study environment. It has been suggested that future studies of risk compensation should not only assess perception of treatment condition (which we did assess) but also perception of efficacy of whatever pill the participant was taking (regardless of whether the participant thought it was the placebo or active drug), which we did not assess [39]. Third, while there was a qualitative component to our study, a question as to specific reasons participants modified their sexual behavior was not asked. Finally, increasing safer sexual behaviors over the course of the study could be due to dropout of higher-risk individuals [1] or social desirability bias in reporting [27]. It is of note that the large difference in the 40% unadjusted and the 2% adjusted increase in odds of no sex partners in last 30 days over time indicates the strong influence of other factors such as being married, where the spouse could be living in a separate location, and being HSV-2 positive, where the infected person may withdraw from having sex partners.

In conclusion, our study of PrEP to prevent HIV infection showed no significant increase in sexual risk behavior among heterosexual participants in Botswana. In fact, the proportion of participants who always reported using a condom and having no sex partners increased over time. Risk-reduction counselling, regular HIV testing and provision of condoms are the standard of care in HIV prevention and HIV prevention research, and likely contributed to the increase in reported safe sexual practices in the study. This increase is consistent with results from other studies of PrEP [2, 4, 6, 14, 22, 23]. In this regard, it is important to note that certain groups may respond differently to counseling [37]. Although there was no risk compensation in any of the PrEP trials to date or the iPrEx open label extension, it does not mean that perception of HIV risk could not change when there is a more widespread use of PrEP [40], similar to the perception by MSM outside a study environment that greater risks could be taken in the age of HAART [41]. PrEP will work best when it is part of a toolkit that includes behavioral interventions supported by structural interventions [42] that address poverty [43, 44], including food insecurity [45, 46] and general education [47–51], as well as the integration of health services (e.g. drug use, mental health, and primary care) [52].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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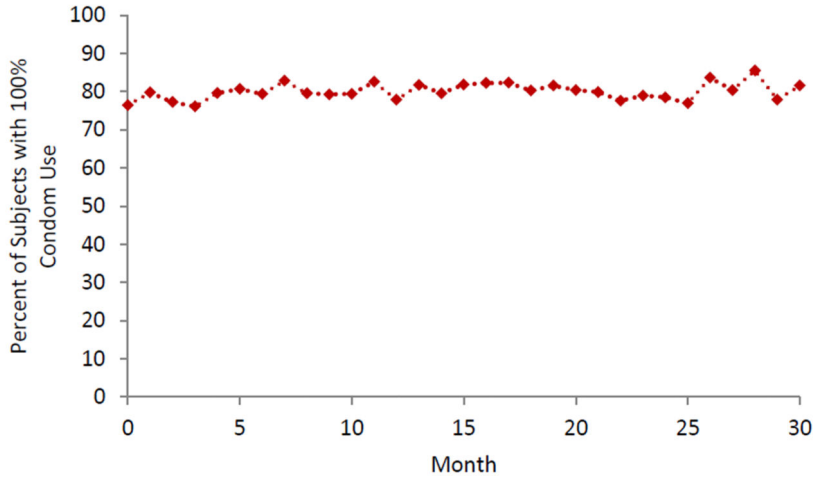
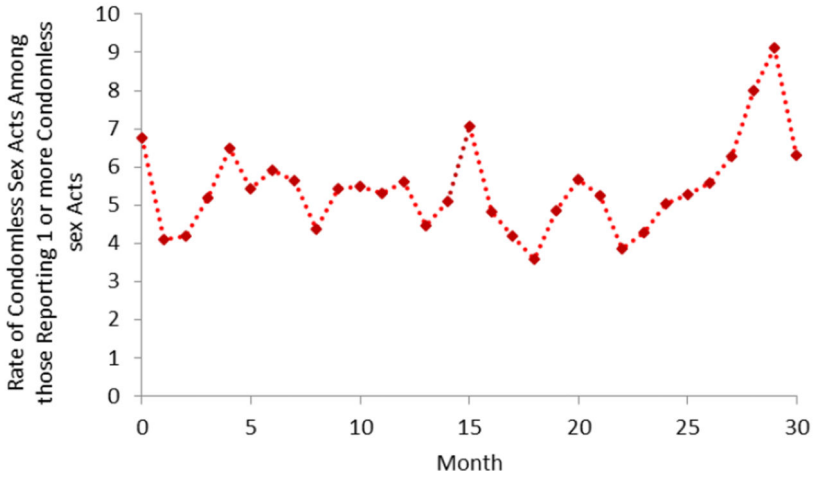
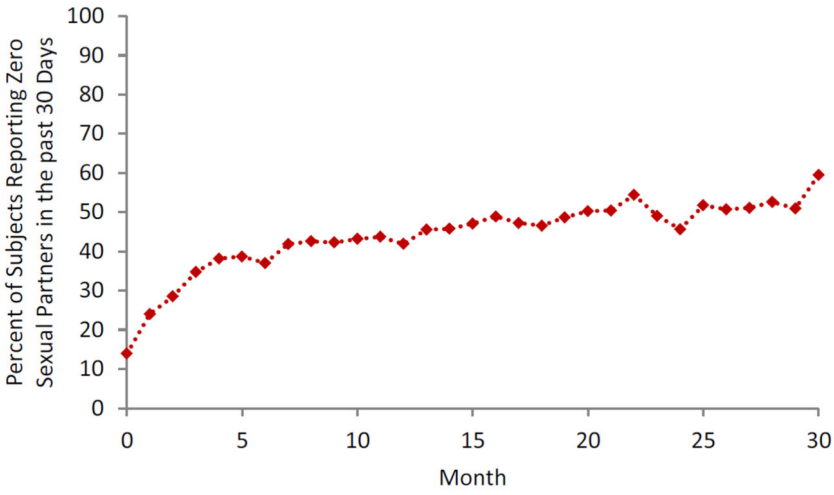
a. Percent of 1176 participants who reported 100% condom use (no condomless) sex acts in the past 30 days.



b. Rate of condomless sex acts (#acts/person) in the past 30 days among 1176 participants who reported 1 or more condomless sex acts.



c. Percent of 1200 participants who reported no sexual partners in the past 30 days.



d. Rate of sexual partners (#partners/person) in the past 30 days among 1176 participants who reported 1 or more partners.

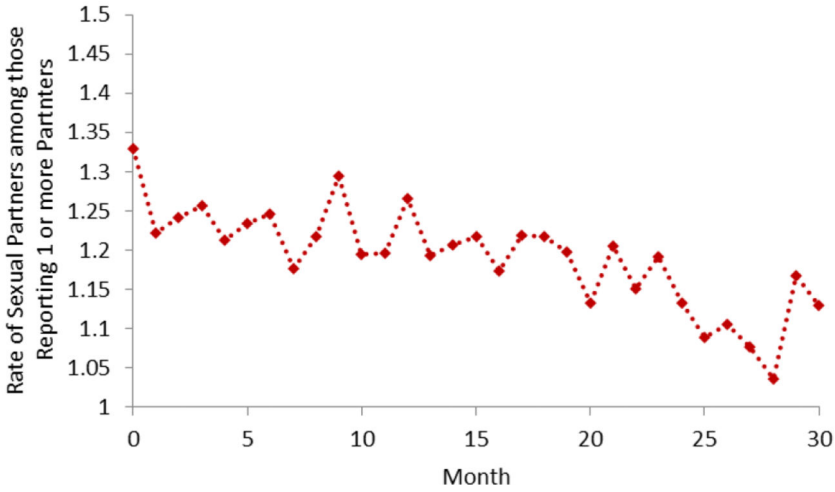


Figure 1.

Change in the occurrence and frequency of sexual risk behavior over time. TDF2 clinical trial, Botswana 2007–2010.

Table 1

Demographic and clinical characteristics and risk behaviors at enrollment by treatment group in the TDF2 clinical trial. Botswana 2007–2010.

Demographic Characteristic or Risk Behavior	Combined (N=1219)	TDF/FTC (N=611)	Placebo (N=608)	p-value
Gender				
Male	662 (54.3)	331 (54.2)	331 (54.4)	0.9254
Female	557 (45.7)	280 (45.8)	277 (45.6)	
Education				
Primary or less	40 (3.3)	20 (3.3)	20 (3.3)	0.9962
Secondary (Jr/Sr)	891 (73.1)	446 (73.0)	445 (73.2)	
Postsecondary	288 (23.6)	145 (23.7)	143 (23.5)	
Marital Status				
Married or Cohabitating	70 (5.7)	32 (5.2)	38 (6.3)	0.4465
Single	1145 (93.9)	578 (94.6)	567 (93.3)	
Separated or Divorced	4 (0.3)	1 (0.2)	3 (0.5)	
Screening Site				
Gaborone	651 (53.4)	326 (53.4)	325 (53.5)	0.9724
Francistown	568 (46.6)	285 (46.6)	283 (46.6)	
Occupational Status Employed Unemployed	480 (39.4) 739 (60.6)	245 (40.1) 366 (59.9)	235 (38.7) 373 (61.4)	0.6052
HIV				
Positive	3 (0.3)	1 (0.2)	2 (0.3)	0.5603
Negative	1216 (99.8)	610 (99.8)	606 (99.7)	
Syphilis				
Positive	14 (1.2)	5 (0.8)	9 (1.5)	0.5462
Negative	1182 (97.0)	594 (97.2)	588 (96.7)	
Missing	23 (1.9)	12 (2.0)	11 (1.8)	
Gonorrhea				
Positive	24 (2.0)	12 (2.0)	12 (2.0)	0.4820
Negative	1119 (91.8)	566 (92.6)	553 (91.0)	
Missing	76 (6.2)	33 (5.4)	43 (7.1)	
Trichomonas*				
Positive	33 (5.9)	19 (6.8)	14 (5.1)	0.5400
Negative	471 (84.6)	237 (84.6)	234 (84.5)	
Missing	53 (9.5)	24 (8.6)	29 (10.5)	
Chlamydia				
Positive	97 (8.0)	43 (7.0)	54 (8.9)	0.2435
Negative	1047 (85.9)	535 (87.6)	512 (84.2)	
Missing	75 (6.2)	33 (5.4)	42 (6.9)	

Demographic Characteristic or Risk Behavior	Combined (N=1219)	TDF/FTC (N=611)	Placebo (N=608)	p-value
HSV-2				
Positive	428 (35.1)	208 (34.0)	220 (36.2)	0.2082
Negative	766 (62.8)	392 (64.2)	374 (61.5)	
Indeterminate	7 (0.6)	1 (0.2)	6 (1.0)	
Missing	18 (1.5)	10 (1.6)	8 (1.3)	
Number of Sex Partners Last Month				
0	151 (12.4)	73 (12.0)	78 (12.8)	
1	815 (66.9)	410 (67.1)	405 (66.6)	
2	172 (14.1	86 (14.1)	86 (14.1)	
3+	60 (4.9)	32 (5.2)	28 (4.6)	
Missing	21 (1.7)	10 (1.6)	11 (1.8)	0.9732
Total Number of All Sex Acts with Any Partner Last Month				
0	175 (14.4)	87 (14.2)	8 (14.5)	0.9815
1	94 (7.7)	45 (7.4)	849 (8.1)	
2	143 (11.7)	74 (12.1)	69 (11.4)	
3+	786 (64.5)	395 (64.7)	391 (64.3)	
Missing	21 (1.7)	10 (1.6)	11 (1.8)	
Number of Condomless Sex Acts (Any) Last Month				
0	805 (66.0)	402 (65.8)	403 (66.3)	0.1976
1	67 (5.5)	31 (5.1)	36 (5.9)	
2	38 (3.1)	27 (4.4)	11 (1.8)	
3+	137 (11.2)	68 (11.1)	69 (11.4)	
Did Not Have Sex	151 (12.4)	73 (12.0)	78 (12.8)	
Missing	21 (1.7)	10 (1.6)	11 (1.8)	

Note: There were 1219 subjects enrolled in the study. However, 18 of these subjects were carried over from the TDF1 study and were never screened for the TDF2 analysis. So, the “Screened and Enrolled” population for the TDF2 study consists of the original 1219 minus the 18 carryover subjects (n=1201). The analytic dataset for this study was constructed using a different set of inclusion criteria. We included the carryover participants. Our analysis, however, excludes 3 subjects because they were diagnosed HIV+ by blood test at enrollment. Also, 16 subjects were excluded because they never received their medication. So there were 1200 subjects included in the actual analysis (the original 1219 minus the 19 who were deemed ineligible).

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Table 2

Multivariable risk factors for condomless sex acts in the past 30 days. TDF2 clinical trial, Botswana 2007–2010.

Demographic Characteristic or Risk Behavior	No condomless sex acts			≥1 condomless sex acts		
	Odds Ratio	95% CI	p-value	RateRatio	95% CI	p-value
Time (per year)	1.23	1.10, 1.37	.0002	0.98	0.89, 1.11	.6910
Treatment Arm Perception						
TDF	1.05	0.77, 1.44	.7422	0.95	0.73, 1.24	.7135
Not Sure	1.06	0.80, 1.38	.6967	0.89	0.70, 1.11	.2954
Placebo	REF			REF		
Sexual Debut						
15 or less	0.37	0.23, 0.61	<.0001	1.65	1.14, 2.38	.0081
16–17	0.49	0.32, 0.72	.0005	1.68	1.22, 2.31	.0016
18–19	0.72	0.50, 1.04	.0857	1.34	1.00, 1.81	.0551
20+	REF			REF		
Gender						
Female	--	--	--	REF		
Male	--	--	--	1.34	1.07, 1.67	.0100
STI						
Yes	0.43	0.27, 0.69	.0003	--	--	--
No	REF			--	--	--
HSV-2						
Yes	--	--	--	1.32	1.06, 1.66	.0147
No	--	--	--	REF		

Note: "—" indicates the variable was not included in that component of the final multivariable model.

Table 3

Multivariable risk factors for number of sex partners in the past 30 days. TDF2 clinical trial, Botswana 2007–2010.

Characteristic	No sex partners			1 or more sex partners		
	Odds Ratio	95% CI	p-value	Rate Ratio	95% CI	p-value
Time (per year)	1.02	1.01, 1.03	<.0001	.97	.97, .98	<.0001
Treatment Arm Perception						
TDF	0.92	0.68, 1.22	.5476	1.04	0.84, 1.29	.7328
Not Sure	0.94	0.73, 1.20	.6008	1.02	0.85, 1.23	.8357
Placebo	REF			REF		
Marital Status						
Single	REF			--	--	--
Married	0.33	0.17, 0.62	.0006	--	--	--
Age						
18–20	--	--	--	REF		
21–29	--	--	--	3.12	1.18, 8.24	.0224
30+	--	--	--	2.14	0.75, 6.12	.1568
Occupational Status						
Employed	0.76	0.58, 1.00	.0467	--	--	--
Unemployed	REF			--	--	--
Sexual Debut						
15 or less	--	--	--	2.92	2.01, 4.22	<.0001
16–17	--	--	--	2.34	1.69, 3.24	<.0001
18–19	--	--	--	1.23	0.91, 1.67	.1834
20+	--	--	--	REF		
Gender						
Female	--	--	--	REF		
Male	--	--	--	3.67	2.86, 4.71	<.0001
STI						
Yes	--	--	--	1.79	1.34, 2.41	.0001

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Characteristic	No sex partners			1 or more sex partners		
	Odds Ratio	95% CI	p-value	Rate Ratio	95% CI	p-value
No	--	--	--	REF		
HSV-2						
Yes	0.58	0.44, 0.76	.0001	--	--	--
No	REF			--	--	--

Note: "--" indicates the variable was not included in that component of the final multivariable model.