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Determinants of HIV Preexposure Prophylaxis Adherence Among Female Sex Workers in a Demonstration Study in Cotonou, Benin: A Study of Behavioral and Demographic Factors

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Background: HIV preexposure prophylaxis (PrEP) efficacy is closely linked to adherence, and factors associated with PrEP adherence are not well understood and may differ across populations. As PrEP demonstration projects and implementation are ongoing, it is essential to understand factors associated with adherence to oral PrEP to design effective adherence interventions and maximize the public health impact of PrEP. We thus

aimed to assess demographic and behavioral factors associated with optimal PrEP adherence (100%) among female sex workers (FSWs) participating in a demonstration project in Cotonou, Benin.

Methods: Female sex workers were provided with daily Truvada and followed quarterly for 1 to 2 years. Sociodemographics, partners, and behaviors were collected through face-to-face questionnaires. Another questionnaire based on sexual the theory of planned behavior and the theory of interpersonal behavior was also administered. Generalized estimating equations were used to identify factors associated with optimal daily adherence.

Results: At baseline, 255 FSWs were followed up. One-year increase in age of FSWs was associated with a 3% increase in optimal adherence (prevalence ratio, 1.03; 95% confidence interval, 1.01–1.05; P for trend = 0.0003), and optimal adherence decreased by 31% for every 6 months of follow-up (prevalence ratio, 0.69; 95% confidence interval, 0.59–0.79; P for trend < 0.0001). For the participants who have completed the behavioral questionnaires, high intention to adhere to the treatment was also a predictor of optimal adherence.

Conclusions: Efforts should be geared toward FSWs intending to use PrEP to help them reach adequate adherence levels for effective HIV protection.

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Preexposure prophylaxis (PrEP; the use of antiretroviral drugs by HIV-seronegative individuals) has been demonstrated to effectively prevent HIV acquisition.¹ Researchers have noted, however, that PrEP efficacy is closely linked to adherence, the degree to which users follow their prescribed daily regimen.² In clinical trials, PrEP efficacy varied substantially among adherers and nonadherers.^{1,3} Two randomized trials among high-risk women in Africa did not show PrEP efficacy against HIV acquisition because of low adherence.^{4,5} Success of PrEP intervention is therefore based on the capability to maintain good adherence within the cohort under investigation.⁶

In the literature, some factors shown to be associated with suboptimal adherence to PrEP are younger age, heavy alcohol use, no sexual activity, not being married, and longer duration in the study.^{4,7,8} However, factors associated with PrEP adherence may differ across populations.⁹ As PrEP demonstration projects and implementation are ongoing,¹⁰ it is essential to understand factors associated with adherence to oral PrEP to design effective adherence interventions and maximize the public health impact of PrEP.¹¹ In Africa, limited data on PrEP demonstration projects among female sex workers (FSWs) are available. In South Africa, self-reported adherence to PrEP among FSWs varied over time between 70% and 85%.¹² In Senegal, adherence measured by MEMS (was initially 80% but dropped rapidly to 50% in the first 2 months).¹³ Moreover, both these studies did not evaluate factors associated with adherence.

Given the behavioral challenges associated with PrEP adherence, we hypothesized that the theory of planned behavior (TPB) coupled with the theory of interpersonal behavior (TIB) could help explain adherence to PrEP. The TPB has been used previously to address adherence issues related to antiretroviral treatment in HIV-positive individuals.¹⁴ The TBP was developed by Ajzen¹⁵ to predict human behavior. The TPB postulates that attitudes toward the behavior, subjective norm, and perceived behavioral control influence the intention of performing the behavior. The TIB was developed by Triandis¹⁶ and proposes several additions to the model proposed in the TPB. Indeed, according to the TIB, behavior in any situation is a function of the intention, the habitual responses, and the situational constraints and conditions. The intention is influenced by social and affective factors as well as by rational deliberations. Given the paucity of data on PrEP implementation in the West African region, especially on adherence determinants, we aimed to evaluate behavioral and demographic factors associated with PrEP adherence among FSWs participating in a demonstration project conducted in Cotonou, Benin, where the HIV epidemic is concentrated among key populations and HIV prevalence among FSWs was estimated at 15.7% in 2015.¹⁷

MATERIALS AND METHODS

Overview of the PrEP Demonstration Study

We analyzed data from the PrEP arm of a prospective demonstration study that aimed to assess the feasibility and usefulness of early antiretroviral treatment (E-ART; or “test-and-treat”) and PrEP among professional FSWs (e.g., women whose main revenue comes from sex work) in Benin (ClinicalTrials.gov NCT02237). Study procedures are detailed elsewhere.¹⁷ Briefly, from September 2014 to December 2015, 256 FSWs were recruited and followed up until December 2016. The follow-up period varied from 12 to 24 months depending on the moment of the recruitment. Eligible women were provided monthly with once-a-day Truvada tablet (tenofovir [TFV] disoproxil fumarate/emtricitabine [FTC]) during the follow-up period but could be supplied for up to 3 months if needed. At recruitment, participants provided free and informed consent to participate in the study;

however, they were not aware of drug measurements at specific study visits until the end of the study to avoid influencing drug-taking behavior. Counseling on adherence was provided in the field and at the clinic during study visits. The study protocol (including deferred information on drug measurements) was approved by the ethics committee of the CHU de Québec-Université Laval and the National ethics committee in Benin.

Analysis of Drug Concentrations

Adherence assessment was described elsewhere.¹⁸ Briefly, TFV measurements were taken 14 days after recruitment (D-14) and at months 6, 12, 18, and 24 (or early final visit) follow-up visits. The concentrations of TFV in plasma were analyzed in batch using a previously described liquid chromatographic–mass spectrometric assay. The lower limit of quantification for TFV of the assay was 0.31 ng/mL. The assay was validated following US Food and Drug Administration bioanalytical recommendations and can detect drug usage within the past week.¹⁹ Optimal adherence (all 7 pills taken in the last week) was defined as a TFV concentration ≥ 35.5 ng/mL (this cutoff was shown to reflect daily adherence with a sensitivity of 90% in controlled studies).¹⁹ For the plasma drug concentrations, we only used TFV measures because only 3.5% of all samples were discordant between TFV and FTC when using the lower limit of quantification cutoff, and the correlation coefficient between TFV and FTC concentrations was high (correlation coefficient = 0.9).

Data Collection

Sociodemographics at screening, sexual partners, and behaviors at enrollment and quarterly visits were collected through face-to-face administered questionnaires. In addition, to assess which constructs are more likely to influence adherence intention and behavior, another questionnaire based on the TPB and the TIB was administered at the first follow-up visit (day 14). Figure 1 illustrates the conceptual framework we used based on these 2 theories. The first construct of the TPB is behavioral intention and is the motivating factor that influences behavior. The stronger the intention to execute a certain behavior, the more likely one is to engage in that behavior. The second construct is attitude toward behavior and refers to the extent to which a person perceives

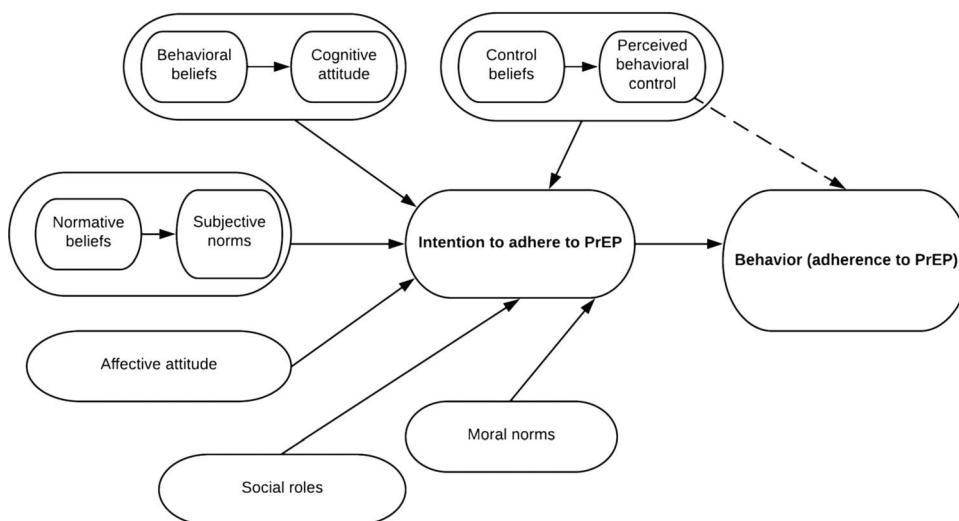


Figure 1. Theoretical framework used to explain adherence to PrEP among FSWs in the E-ART/PrEP demonstration project conducted in Benin (2014–2016). This framework is based on the TPB by Ajzen¹⁵ and the TIB by Triandis.¹⁶

favorable or unfavorable consequences of performing a behavior. Attitude involves behavioral convictions and outcome evaluations. The third construct, subjective norm, is a social pressure to perform a behavior or not. Subjective norm is composed of normative beliefs and motivation to comply. Perceived behavioral control also plays a major role in the TPB and indicates the individual's perception of the ease or difficulty of adopting the desired behavior.

Perceived behavioral control may also be an immediate determinant of behavior if the behavior is not completely volitional (i.e., not free of practical constraints).^{15,20} The TIB builds on the TPB, and the main constructs added by this theory are affective attitude, social roles, and moral norm. Affective attitude is the emotional response to a particular situation that is based on instinctive and unconscious process in the mind. Social roles refer to the pressures

TABLE 1. Factors Associated With Optimal Daily Adherence Measured by Tenofovir Plasma Concentration

Factors	PR _{adherence} Nonadjusted (95% CI)	P	PR _{adherence} Adjusted (95% CI)	P
Age, y		0.0056*		0.0005 [†]
<25	Ref		Ref	
25–34	1.67 (0.95–2.95)		1.84 (1.04–3.23)	
35–44	2.41 (1.34–4.31)		2.77 (1.56–4.91)	
≥45	2.18 (1.77–4.05)		2.52 (1.36–4.64)	
Nationality		0.4893		
Beninese	Ref			
Togolese	1.11 (0.81–1.52)			
Nigerian	1.36 (0.92–2.00)			
Others	0.87 (0.43–1.77)			
Marital status		0.9701		
Married	Ref			
Divorced, separated	1.09 (0.38–3.14)			
Widow	1.19 (0.40–3.53)			
Single	1.09 (0.38–3.15)			
Education		0.9999		
Not educated	Ref			
Primary school	1.00 (0.72–1.40)			
Secondary school or higher	1.00 (0.71–1.41)			
No. clients in the last 14 d		0.1969*		
0	Ref			
1–14	1.33 (0.90–1.98)			
>14	1.40 (0.94–2.09)			
Condom breakage during sexual relationship with clients in the last 14 d		0.1513*		
No	Ref			
Yes	1.30 (0.94–1.79)			
Condom usage frequency with different types of partners		0.1415*		
Never	Ref			
Sometimes	1.78 (0.86–3.69)			
Always	1.72 (0.84–3.52)			
Consistent condom use without breakage with clients and not having regular partners or other paying partners		0.1421*		
No	Ref			
Yes	1.24 (0.95–1.63)			
Recent sex work cessation		0.1453*		
Yes	Ref			
No	1.29 (0.93–1.79)			
Heavy alcohol drinking		0.2196		
Yes	Ref			
No	1.19 (0.91–1.57)			
Follow-up visit		<0.0001*		<0.0001 [‡]
Day 14	Ref		Ref	
Month 6	0.60 (0.48–0.76)		0.57 (0.46–0.72)	
Month 12	0.48 (0.35–0.65)		0.44 (0.32–0.60)	
Month 18	0.42 (0.27–0.66)		0.40 (0.26–0.63)	
Month 24	0.30 (0.16–0.58)		0.27 (0.14–0.52)	

Optimal daily adherence means all pills were taken in the last week. The numbers of individuals contributing data at day 14, month 6, month 12, month 18, and month 24 are, respectively, 225, 189, 151, 76, and 30, for a total of 671 observations. Heavy alcohol drinking is defined for women as consuming 8 or more drinks per week.²¹

*Significant variables with $P < 0.20$ in univariate models were included in a multivariate model. Less significant variables were eliminated using backward selection to only keep variables significant with $P < 0.05$ in the final model.

[†] P for trend = 0.0003 when including age as a continuous variable in the model.

[‡] P for trend < 0.0001 when including duration of follow-up as a continuous variable in the model.

Ref indicates reference category.

and expectations of others that can cause an individual to behave in a given manner. Moral norm is the feeling of obligation felt by the person to adopt or not adopt the behavior.¹⁶

Intention to adhere to PrEP was measured on a scale of 1 (not likely at all) to 7 (very likely) using these following 3 questions: (1) "In the coming weeks, do you intend to take your tablets daily as prescribed by the doctor?" (2) "In the coming weeks, will you be willing to take your pills daily as prescribed by your doctor?" and (3) "In the coming weeks, are you sure you will always take your pills daily as prescribed by the doctor?" Other constructs measured with the questionnaires were affective attitude, cognitive attitude, subjective norms, perceived behavioral control, behavioral beliefs, social roles, normative beliefs, and moral norm. All these constructs were also measured on a scale of 1 (not likely at all or very low) to 7 (very likely or very high).

Statistical Analysis

The prespecified factors that we hypothesized might be associated with optimal daily adherence were included in the analysis. Baseline variables included age, nationality, education, and marital status. Time-dependent variables included number of clients in the last 14 days, condom failure during sexual relations with clients in the last 14 days, condom usage with all types of partners, consistent condom use without breakage with clients and not having regular partners or other nonpaying partners, short-term sex work interruption, heavy alcohol drinking (≥ 8 drinks per week²¹), and duration of follow-up. Factors associated with optimal daily adherence were identified using binomial regression with generalized estimating equations assuming an unstructured working correlation to account for repeated measures across visits. Bivariate analyses using a statistical significance of P value < 0.20 were first conducted followed by a multivariate analysis using a statistical significance of P value < 0.05 comprising all factors significantly associated with adherence in the bivariate analyses. For the participants who completed the behavioral questionnaires, descriptive statistics were performed and Cronbach α coefficient was computed to measure the reliability of the questionnaire. Logistic regression was used to identify the constructs associated with intention to adhere to treatment at the first study visit. Generalized estimating equations were then used to identify factors (including the variables from the TPB and TIB) associated with optimal daily adherence as measured at all visits. When a subject was not present at a given study visit, the data from all other scheduled visits that she attended were still used in the analysis.

RESULTS

In the PrEP arm of the E-ART/PrEP study, 256 FSWs were recruited. In this present study, 1 FSW was excluded from the analyses because of missing data on variables used to measure adherence predictors. Thus, at baseline, 255 FSWs were followed up and the numbers of included participants were 225 (88.2%) at D-14, 189 (74.1%) at month 6, and 151 (59.2%) at month 12. Because not all women could be followed up for more than 1 year, the actual participation rates were 55.5% (76/137) at M18 and 50.8% (30/59) at M24. Retention till the end of the study was 47.3%, and mean duration of follow-up was 11.8 ± 7.9 months. Participants' characteristics and reasons for withdrawal are detailed elsewhere.¹⁷ Briefly, the mean (SD) age was 32.5 (9.2) years, 49.0% of the FSWs were Beninese, 97.7% were not married, and 65.9% did not complete secondary school. Heavy alcohol use (≥ 8 drinks per week)²¹ at baseline was reported by 34.4% of the participants. A majority (55.5%, or 75/135) of the withdrawals from the study were due to participants moving away from the study site or returning to their country of origin. Two HIV seroconversions occurred during the 250.1 person-years of

follow-up (HIV incidence, 0.8/100 person-years; 95% confidence interval [CI], 0.3–1.9/100 person-years).

Factors Associated With Optimal Daily Adherence

Optimal adherence (all pills taken in the last 7 days) combining all study visits was 34.1% (210/615). Table 1 shows the factors associated with optimal adherence in univariate and multivariate analyses. Only age and duration in the study were significantly associated with optimal adherence in the multivariate models. When considering age and duration of follow-up as continuous variables, 1-year increase in age of FSWs was associated with a 3% increase in optimal adherence (prevalence ratio [PR], 1.03; 95% CI, 1.01–1.05; P for trend = 0.0003), whereas optimal adherence decreased by 31% for every 6 months of follow-up (PR, 0.69; 95% CI, 0.59–0.79; P for trend < 0.0001). Marital status, education, condom use with all types of partners, condom failure, number of clients in the last 14 days, recent trips outside of Cotonou, nationality, short-term sex work interruption, and heavy alcohol drinking were not associated with adherence.

Descriptive Statistics of the Constructs From the TPB and the TIB

Intention to adhere to PrEP at the D-14 visit was high among participants (mean [SD], 6.56 [1.05]). Other constructs with high means were affective attitude, cognitive attitude, and social roles. A high value for Cronbach α (> 0.70), indicating good internal consistency of the items in the scale, was observed for almost all constructs (Table 2).

Constructs From the TPB and the TIB Associated With Adherence Intention at the Beginning of the Study

In multivariate logistic regression, adherence intention was significantly associated with 2 of the theoretical constructs: perceived behavioral control (odds ratio [OR], 1.94; 95% CI, 1.10–3.40; $P = 0.0230$) and affective attitude (OR, 2.90; 95% CI, 1.82–4.6; $P = < 0.0001$; Table 3). All other theoretical constructs were not significantly associated with adherence intention.

Factors Associated With Optimal Adherence Using the TPB and the TIB

For the 169 participants who completed the questionnaire based on the TPB and the TIB administered at D-14 and had at

TABLE 2. Descriptive Statistics of the Constructs Used to Evaluate Optimal Daily Adherence to PrEP in a Demonstration Project Conducted Among Female Sex Workers in Benin (2014–2016)

Constructs	Mean	SD	Cronbach α Coefficient
Intention	6.56	1.05	0.93
Perceived behavioral control	5.48	0.97	0.44
Affective attitude	6.07	1.21	0.85
Cognitive attitude	6.45	0.90	0.82
Behavioral beliefs	5.00	1.53	0.80
Social roles	6.18	1.24	0.76
Subjective norms	3.95	2.82	—*
Normative beliefs	3.51	1.88	0.83
Moral norms	5.68	1.55	0.64

All constructs were measured on a scale of 1 (not likely at all) to 7 (very likely). The number of participants who have completed the behavioral questionnaire is 169.

*Construct composed of only one question.

TABLE 3. Constructs From the Theory of Planned Behavior (TPB) Associated With Optimal Adherence Intention at the Beginning of the Study

Constructs	OR _{intention} Not Adjusted (95% CI)	P	OR _{intention} Adjusted (95% CI), Full Model	P	OR _{intention} Adjusted (95% CI), Final Model	P
Perceived behavioral control	3.14 (1.88–5.25)	<0.0001	1.96 (1.06–3.48)	0.0327*	1.94 (1.10–3.4)	0.0230
Affective attitude	3.48 (2.23–5.44)	<0.0001	3.00 (1.65–5.47)	0.0003*	2.90 (1.82–4.6)	<0.0001
Cognitive attitude	2.51 (1.60–3.91)	<0.0001	1.13 (0.62–2.09)	0.6793		
Behavioral beliefs	1.54 (1.22–1.94)	0.0003	0.88 (0.56–1.38)	0.5870		
Social roles	1.39 (1.07–1.80)	0.0132	1.26 (0.85–1.87)	0.2494		
Subjective norms	1.09 (0.96–1.23)	0.1864	1.17 (0.93–1.48)	0.1735		
Normative beliefs	1.10 (0.91–1.32)	0.3361	0.74 (0.51–1.08)	0.1193		
Moral norms	1.38 (1.11–1.71)	0.0035	1.11 (0.79–1.55)	0.5647		
Age [†]	1.02 (0.98–1.06)	0.3521	0.98 (0.93–1.03)	0.4987		
Nationality		0.2795		0.7190		
Beninese	Ref		Ref			
Others	0.69 (0.35–1.36)		0.84 (0.32–2.19)			
Stayed until the end of the study		0.0538		0.3720		
Yes	Ref		Ref			
No	0.51 (0.26–1.01)		0.65 (0.25–1.69)			

Optimal daily adherence means all pills were taken in the last week. The outcome variable intention to adhere to PrEP was measured on a scale of 1 (not likely at all) to 7 (very likely) using 3 questions from the TPB. The variable was then dichotomized into high intention (7) or less high intention (<7). For the other constructs, mean scores were computed from the questions composing the constructs and the continuous variables were evaluated in the models. All the constructs were measured on a scale of 1 (not likely at all or very low depending on the construct) to 7 (very likely or very high depending on the construct). The number of participants who have completed the behavioral questionnaire is 169.

*Significant variables with $P < 0.05$ in univariate models were included in a multivariate model.

[†]Age (in years) was treated as a continuous variable in this analysis.

Ref indicates reference category.

least 1 measure of TFV plasma concentration during follow up, intention to adhere to PrEP was significantly associated with adherence (OR, 2.65; 95% CI, 1.46–4.81; $P = 0.0013$). Age (OR, 1.04; 95% CI, 1.01–1.07; $P = 0.00037$) and duration in the study (OR, 0.56; 95% CI, 0.45–0.69; $P = 0.00037$) were also significant predictors of adherence, as is in the previous model using data from all participants (Table 4).

DISCUSSION

In this analysis, we assessed demographic and behavioral factors associated with PrEP adherence among FSWs participating in a demonstration project in Benin. To our knowledge, this is the first study evaluating factors associated with PrEP adherence in the West African region, where the HIV epidemic is largely concentrated among FSWs and men who have sex with men.²² We found that older age, shorter duration in the study, and high intention to adhere to the treatment at the beginning were predictors of optimal adherence in this cohort. Our results are in accordance with the growing literature on PrEP experiences in diverse populations. Older age has been found to be associated with higher adherence in previous studies on PrEP among men and transgender women who have sex with men^{9,23} and also with serodiscordant couples.⁷ Shorter duration in receiving PrEP was also shown to be associated with higher adherence.⁶ The finding that adherence decreased by 31% after every 6 months of follow-up may reflect that initial enthusiasm for a novel prevention method can be difficult to maintain with time and strategies to preserve adherence over time may be necessary.⁷

We did not find any association between adherence and the sexual behavior variables that we assessed. These results add up to the lack of evidence of condom migration (decrease in condom use as a result of being substituted by another preventive intervention) or risk compensation (increase in HIV risk-taking behavior) reported in this cohort of FSWs despite concerns raised on increasing risky sexual behaviors and sexually transmitted infections (STIs) among PrEP users.²⁴ In addition, a significant decrease in

STIs episodes was also reported in the cohort of interest.^{17,24} This is encouraging because it seems that in this context, PrEP is acting as a supplementary STI prevention intervention rather than an alternative to condom use. However, because FSWs enrolled in the study may have had more opportunities to get counseling, screening, and treatment of STIs than in the routine care offered to them, such enhanced services could also have contributed to the decrease in STIs in this cohort.

Limited data on heavy alcohol drinking and PrEP adherence among FSWs in the West African region are available. In our study, we did not find an association between heavy alcohol use and PrEP adherence. However, a study conducted among high-risk women in Kenya reported alcohol use as a reason for PrEP suboptimal adherence.²⁵ Another study in Zimbabwe reported that women who had alcohol 2 to 3 times per week were less likely to adhere to PrEP compared with those who never drank.²⁶ The lack of association between adherence and alcohol in our study suggests that the participants may take their PrEP medication at a time other than when alcohol is being consumed (e.g., in the morning, whereas alcohol consumption mainly occurs at night).

Intention to use PrEP was measured because it has been shown to be a strong predictor of adherence according to the TPB.¹⁵ Our results showed that participants with higher intention to adhere at baseline were more likely to be actually adherent. Assessing PrEP intention early in the study is thus important to provide adequate counseling and service planning to increase intention to adhere to PrEP. It would have been also interesting to explore the barriers and facilitators to translate intention to actual PrEP adherence.

Our results also indicate that TPB constructs of affective attitude and perceived behavioral control should be taken into account when planning interventions to improve PrEP adherence. Both affective attitude and perceived behavioral control had an effect on intention to adhere to PrEP, and intention to adhere directly affected adherence to PrEP. It is noteworthy that perceived behavioral control did not affect adherence directly but only through intention. As mentioned earlier, according to the TPB, perceived behavioral control is thought to influence behavioral performance

TABLE 4. Factors Associated With Optimal Daily Adherence Measured by Blood Drug Concentration Using the Planned Behavior Theory

Factors	OR _{adherence} Not Adjusted (95% CI)	P	OR _{adherence} Adjusted (95% CI), Full Model	P	OR _{adherence} Adjusted (95% CI), Final Model	P
Intention						
Less high	Ref		Ref		Ref	
High	2.31 (1.35–3.94)	0.0022	2.99 (1.48–6.02)	0.0022*	2.65 (1.46–4.81)	0.0013
Perceived behavioral control	1.06 (0.82–1.37)	0.6632	0.91 (0.64–1.32)	0.6308		
Affective attitude	1.17 (0.95–1.44)	0.1342	1.02 (0.71–1.46)	0.9250		
Cognitive attitude	1.22 (0.94–1.59)	0.1367	1.13 (0.76–1.69)	0.5476		
Behavioral beliefs	0.94 (0.80–1.10)	0.4349	0.89 (0.68–1.16)	0.3887		
Social roles	0.97 (0.81–1.18)	0.7610	0.94 (0.73–1.21)	0.6222		
Subjective norms	0.93 (0.86–1.01)	0.1064	0.98 (0.86–1.11)	0.7145		
Normative beliefs	0.91 (0.79–1.03)	0.1383	0.95 (0.76–1.17)	0.6124		
Moral norms	1.01 (0.87–1.18)	0.8952	1.03 (0.84–1.26)	0.8065		
Age, y		0.0195		0.0431*		0.0083 [†]
<25	Ref		Ref		Ref	
25–34	2.02 (0.99–4.14)		2.25 (0.94–5.38)		2.41 (1.01–5.74)	
35–44	3.17 (1.47–6.80)		3.95 (1.50–10.36)		4.38 (1.79–10.75)	
≥45	2.81 (1.22–6.48)		3.12 (1.07–9.09)		3.70 (1.32–10.35)	
Nationality		0.2134		0.3797		
Beninese	Ref		Ref			
Others	1.31 (0.85–2.02)		1.28 (0.73–2.25)			
Stayed until the end of the study?		0.4818		0.6528		
Yes	Ref		Ref			
No	1.18 (0.75–1.85)		0.88 (0.52–1.51)			
Follow-up visit		<0.001		<0.001*		<0.001 [‡]
Day 14	Ref		Ref		Ref	
Month 6	0.41 (0.28–0.59)		0.32 (0.21–0.51)		0.33 (0.21–0.52)	
Month 12	0.28 (0.17–0.46)		0.23 (0.13–0.40)		0.24 (0.14–0.42)	
Month 18	0.24 (0.14–0.42)		0.22 (0.11–0.42)		0.22 (0.12–0.42)	
Month 24	0.13 (0.06–0.31)		0.09 (0.03–0.25)		0.11 (0.04–0.28)	

Optimal daily adherence means all pills were taken in the last week. The outcome variable intention to adhere to PrEP was measured on a scale of 1 (not likely at all) to 7 (very likely) using 3 questions from the theory of planned behavior. The variable was then dichotomized into high intention (7) or less high intention (<7). For the other constructs, mean scores were computed from the questions composing the constructs and the continuous variables were evaluated in the models. All the constructs were measured on a scale of 1 (not likely at all or very low) to 7 (very likely or very high). The number of participants who have completed the behavioral questionnaire is 169. The number of observations on adherence during follow-up for this analysis was 404.

*Significant variables with $P < 0.05$ in univariate models were included in a multivariate model.

[†] P for trend = 0.0037 when including age as a continuous variable in the model.

[‡] P for trend < 0.001 when including duration of follow-up as a continuous variable in the model.

Ref indicates reference category.

(adherence to PrEP in this case) in 2 ways: first, by influencing intentions to perform the behavior, and second, by directly affecting the behavioral performance.^{15,20} Our results thus imply that FSWs who perceived that they were in greater control of being adherent to PrEP may have had stronger intentions to adhere compared with FSWs who perceived less control over adherence to PrEP. Optimal adherence measured by blood drug concentration reported in this cohort of FSWs was low, and our results suggest that support is needed for FSWs with associated factors. Potential strategies to increase and support adherence may be structured around affective attitude and perceived behavioral control. Indeed, these constructs may serve to guide counseling messages. Barriers to adherence need to be identified, and individuals need to overcome these barriers to increase self-efficacy and thus adherence to PrEP. Adherence could also be made a more enjoyable experience. For example, more flexible PrEP delivery methods and less frequent dosing regimen should be investigated in this high-risk population. Recent research has shown that PrEP is not intended for life-long use and is only needed during periods of potential HIV exposure. Adherence to PrEP should therefore be aligned with this high-risk period.²⁷ It is important to note, however, that 4 PrEP doses a week may be sufficient to achieve 96% efficacy among men,²⁸ whereas women may need more doses per week to achieve comparable levels of protection against HIV infection.²⁹

A number of limitations need to be taken into account when interpreting the findings and planning future research. First, attrition was high in our study, which led to an important decrease in statistical power over the course of the study and may have limited our ability to correctly detect factors associated with PrEP adherence. Second, of the 225 FSWs who had blood drug measurements at D-14, only 75.1% ($n = 169$) FSWs completed the TPB and TIB questionnaire. An explanation for these missing data is that FSWs had some difficulties understanding the Likert scale used on the behavioral questionnaire and thus did not want to answer the questions. This suggests that it is essential to integrate and validate the behavioral theoretical constructs based on the study population context to allow participants to better understand the questionnaires and respond accurately. Third, the TPB and TIB were administered at D-14, and thus, the behavioral data were simultaneously collected with the drug measurement data. Ideally, behavioral data should have been collected before the drug measurement data. However, measuring intention to adhere to treatment when participants have already started using the medication may be an advantage because the behavioral beliefs would be more realistic. Moreover, although intention to adhere was measured at the same time as actual adherence, we still found that high intention was significantly associated with the behavior. Fourth, we used self-report assessments. The accuracy of these assessments may have been

limited by recall and/or social desirability biases. Participants received intensive promotion of consistent condom use and adherence counseling and were therefore well aware of the importance of adherence to PrEP. In addition, for the behavioral questionnaire, subjective norm was measured by a single construct. Measurement of this construct could have been improved. Fifth, we did not explore in detail the reasons why participants were or were not adherent to PrEP, and a qualitative analysis might therefore be helpful. Finally, this study was specific to high-risk FSWs, and our results may not be generalizable to other populations in other settings and with different PrEP adherence levels such as women in serodiscordant couples. Despite these limitations, our study has several strengths including the use of behavioral and demographic factors to assess PrEP adherence, and a biologically measured adherence outcome. Indeed, drug concentrations that were used in this study are reported to be one of the most accurate adherence measures.³⁰ Finally, this is the first study using the TPB and TIB to evaluate the behavioral factors associated with PrEP adherence among FSWs in West Africa.

In conclusion, as in previous studies, younger age and longer duration of PrEP use were associated with poorer adherence among FSWs in Benin.^{6,9,23} Our use of theoretical behavioral models, such as the TPB and the TIB, showed that intention was also associated with higher levels of adherence. This observation opens the door to the development of interventions addressing the determinants of intention, namely, in the case of our study population, the affective attitude, and the perceived control toward PrEP adherence behavior.

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