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Effect of HIV Self-Testing on PrEP Adherence Among Gender-Diverse Sex Workers in Uganda: A Randomized Trial

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Background: HIV self-testing (HIVST) and pre-exposure prophylaxis (PrEP) are complementary tools that could empower sex workers to control their HIV protection, but few studies have jointly evaluated PrEP and HIVST in any setting.

Methods: The Empower Study was an open-label randomized trial in Uganda. Sex workers were offered F/tenofovir disoproxil fumarate and randomized 1:1 to monthly HIVST and quarterly in-clinic testing (intervention) or quarterly in-clinic HIV testing alone (standard of care) and followed up for 12 months. PrEP adherence was measured using electronic adherence monitoring and tenofovir diphosphate (TFV-DP) levels in dried blood spots. Adherence outcomes and sexual behaviors were compared by arm using generalized estimating equation models.

Results: We enrolled 110 sex workers: 84 cisgender women, 14 transgender women, 10 men who have sex with men, and 2 transgender men. The median age was 23 years. The 12-month retention was 75%. Nearly all (99.4%) used ≥1 HIVST kit. The proportion with TFV-DP levels ≥700 fmol/punch in the HIVST and standard of care arms at the 3-, 6-, 9-, and 12-month visits was 2.4%, 2.3%, 0%, and 0% and 7.9%, 0%, 0%, and 0%, respectively, with no differences by randomization arm ($P > 0.2$). Self-reported condomless sex acts with paying partners was similar by arm [adjusted incidence rate ratio 0.70; 95% confidence interval (CI): 0.42 to 1.17; $P = 0.18$]. One seroconversion occurred (HIV incidence, 0.9/100 person-years); TFV-DP was not detected at any visit.

Conclusions: A gender-diverse sample of sex workers in Uganda used HIVST but not daily oral PrEP for HIV protection. Alternate approaches to promote PrEP use, including long-acting formulations, should be considered in this population.

Key Words: HIVST, PrEP, adherence, sex worker, Africa

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INTRODUCTION

Globally, cisgender women, cisgender men, and transgender sex workers (TGSWs) are 49, 21, and 14 times as likely, respectively, to be living with HIV as other adults in the general population.[1] Yet sex workers are less likely than the general population to engage with HIV services because of concerns about sex work criminalization, entrenched social stigma, and discrimination from health workers.[2,3] In addition, condom use is often difficult to negotiate or results in less income generation,[4] highlighting the need for additional HIV prevention approaches. Empowering sex workers to use combination HIV prevention interventions could help decrease HIV acquisition in this vulnerable population. HIV self-testing (HIVST) and tenofovir (TFV)-based oral pre-exposure prophylaxis (PrEP)

are evidence-based, self-controlled HIV prevention tools, but they are currently not well used by sex workers.[5,6] Moreover, these tools could be used with their paying and nonpaying (intimate) sexual partners to maximize impact.

Several features of HIVST and PrEP may be particularly attractive for sex workers. HIVST, a process in which an individual performs an HIV rapid diagnostic test and interprets the result independently,[7] is highly acceptable with users appreciating its convenience and discretion[7–9] and is recommended by the World Health Organization.[10] HIVST can empower those who may otherwise not test, or test as frequently, by providing autonomy, freedom, and control over testing decisions.[11] Moreover, HIVST reaches people at high risk of HIV and may be an important entry point for PrEP, which may similarly empower the user.[10] The effectiveness of PrEP, however, is highly dependent on adherence, which has been challenging for many, including sex workers.[12,13] HIVST and PrEP are potentially complementary tools that could be combined to empower sex workers to prevent HIV acquisition, but few studies have jointly evaluated PrEP and HIVST in any setting.

Limited data are available regarding whether joint HIVST and PrEP delivery could increase PrEP adherence and reduce sexual risk behaviors among sex workers. Although variable by population, condom use increased, and diagnoses of sexually transmitted infections (STIs) decreased in previous PrEP studies, suggesting PrEP use can be synergistic with other prevention methods.[14] To test whether combination HIVST and PrEP influenced uptake and use of each prevention intervention, we conducted a randomized trial among HIV-negative cisgender women, cisgender men, and TGSWs initiating PrEP in Uganda. We hypothesized that joint HIVST and PrEP delivery could be empowering through combined use of both interventions.

METHODS

Trial Design

The Empower Study was an open-label randomized trial conducted in Kampala, Uganda (NCT03426670). Cisgender women [female sex workers (FSWs)], cisgender men who have sex with men (MSM), and TGSWs (N = 110) were offered oral PrEP (coformulated emtricitabine/tenofovir disoproxil fumarate) and individually randomized 1:1 to receive monthly HIVST and quarterly in-clinic testing (intervention) or quarterly in-clinic HIV testing alone (standard of care; SOC). Blinded allocation to study arm was performed by research nurses using REDCap electronic data capture tools.[15,16] Study participants and research staff were not blinded to intervention assignment. There were no significant protocol changes after trial commencement. The study objectives were to test the effect of HIVST in addition to clinic-based testing alone on: (1) PrEP adherence and (2) sexual behaviors. In addition, we qualitatively explored how HIVST and PrEP influenced prevention uptake among sex workers and their partners.[17] Study data were reviewed by an independent data monitoring committee. Intervention design was informed by protection motivation theory.[18,19] This trial is reported in accordance with the Consolidated Standards of Reporting Trials statement.[20]

Population and Procedures

The Empower Study involved sex workers; estimated HIV prevalence among FSWs in Kampala was 37% in 2016.[21] Data for MSM and TGSWs are not available. Participants were enrolled using peer recruiters between June 7, 2018, and January 10, 2019, and followed up for 12 months. The trial ended on January 31, 2020. Participant sex was self-identified. At study entry, sex workers were aged 18 years or older, received money or goods in exchange for sexual services, tested negative for HIV and Hepatitis B virus, were willing to take PrEP, were willing and able to comply with study procedures, and had adequate renal function (creatinine clearance $\geq$60 mL/minute). Research nurses taught sex workers in the HIVST arm how to use OraQuick rapid HIV-1/2 self-test kits (OraSure Technologies). At each quarterly visit, they received 4 HIVST kits; 2 for own use and 2 for testing sexual partners. At the time of the study, HIVST kits were only available through research studies. All study participants received quarterly in-clinic HIV rapid testing as SOC. Oral PrEP was provided to all participants, who received 3 bottles each with a 1-month supply of coformulated 200 mg of emtricitabine/300 mg of tenofovir disoproxil fumarate. Participants in the HIVST arm were instructed to self-test before starting each monthly course of PrEP, during the two-month period between scheduled quarterly study visits. Adherence to PrEP was measured using Wisepill devices for electronic adherence monitoring (EAM) (Wisepill Technologies, South Africa); these devices are smart pill containers that record a date-and-time stamp for each opening as a proxy for pill ingestion. Dried blood spot samples (DBS) were also collected quarterly for detection and quantification of tenofovir diphosphate (TFV-DP) levels.[22] Data on PrEP adherence and sexual risk behaviors were collected during monthly live phone interviews and quarterly in-person visits, including validated sociobehavioral scales for stigma (HIV stigma scale[23]) and problematic alcohol use (RAPS-4 scale[24]). Participants were screened for depression using the Patient Health Questionnaire[25]; those with Patient Health Questionnaire-9 scores $\geq$10 were escorted to the Infectious Diseases Institute mental health clinic, if desired. Study interactions occurred in English or Luganda (local language). All participants were offered additional HIV prevention services, including individualized HIV and PrEP counseling, condoms, and lubricants; other forms of contraception (FSWs only); and free STI screening and treatment (as SOC per national guidelines).[26] All participants were clinically monitored for adverse events. Each received an IRB-approved reimbursement of UGX 30,000 (USD 7.86).

Laboratory Methods

Sex workers were tested for HIV using serial rapid tests according to national guidelines.[27] Hepatitis B virus testing was performed using Pal HBsAg rapid tests (Healgan Scientific, Houston, TX). Serum creatinine testing was performed using a Cobas Integra 400 biochemistry analyzer (Roche, Germany). Creatinine results were available within 72 hours; abnormal values were flagged and participants contacted for clinical management. Intracellular TFV-DP

concentrations were quantified from DBS tested in batch at the University of Cape Town Clinical PK Laboratory, South Africa, using validated liquid chromatography/tandem mass spectrometry methods.[28]

Statistical Analysis

The primary outcome was PrEP adherence, as measured by EAM (number of days with recorded device openings divided by number of days with device detected as active)[29] and TFV-DP levels in DBS ($\geq$700 fmol per punch). We restricted device openings to 1 per day to avoid misclassification of adherence from multiple openings (eg, due to curiosity or device use for other medications). A secondary adherence measure was pharmacy refill (proportion of expected pills taken). The χ^2 test and 1-way analysis of variance models were used to compare outcomes by randomization arm. Correlations of adherence measures were calculated using paired sample t tests, and tests of significance were performed using the Fisher exact test. We used an intent-to-treat approach (analyzed all participants regardless of PrEP refills) to compare adherence outcomes by randomization arm using a generalized estimating equations model using repeated measures with identity link, exchangeable correlation structure, and robust variance estimates. The trial had 80% power to detect a 17%–23% increase in PrEP adherence resulting from the use of HIVST with a sample size of 110 sex workers assuming an SD of 30%–40%, a 10% loss to follow-up, and a 2-sided alpha of 0.05. Secondary outcome measures were self-reported: (1) condomless sex acts and (2) acceptability of HIVST (assessed by HIVST kit usage and experiences). We used zero-inflated Poisson regression to assess condom use with paying and nonpaying partners because the distribution of sex acts was overdispersed relative to the Poisson distribution (ie, conditional variance was larger than the conditional mean).[30] Covariates included baseline demographics, including age, sex, marital status, level of education, duration of sex work, and problematic alcohol and drug use, and were independently tested for associations with outcomes. Analyses were adjusted a priori for gender. We used the Spearman correlation to evaluate the relationship between EAM and TFV-DP levels in DBS. Statistical analyses were performed using Stata 14 (StataCorp, College Station, TX).

Ethics Approval

The study was approved by the Higher Degrees Research Ethics Committee, Makerere University School of Public Health (HDREC 500), Partners Human Research Committee/Massachusetts General Hospital (2017/P001951/PHS), Uganda National Council for Science and Technology (SS 4467), and National Drug Authority (CTA 0046). Each participant provided written informed consent.

RESULTS

Population Characteristics

We screened 136 sex workers and enrolled 117 of them; reasons for nonparticipation are shown in Figure 1.

Seven participants who emigrated or lost interest in the study within 1 month of study entry were disenrolled (3 in the HIVST arm and 4 in the SOC arm). The final study sample comprised 110 sex workers (57 in the HIVST arm and 53 in the SOC arm) with <10% difference in sociodemographic characteristics between arms (Table 1). Of them, 84 were FSWs, 14 were transgender women (TGW), 10 were MSM, and 2 were transgender men. The median age was 23 years [interquartile range (IQR) 20–28]. Eighty-eight participants (80%) were single; sex work was the main source of income for 75 participants (68%). Sixty-nine participants (63%) had at least 1 child. The median age at onset of sex work was 19 years (IQR 17–23); the median monthly income was UGX 400,000 (USD 104.77). The median charge for vaginal and anal sex acts were UGX 20,000 and UGX 125,000 (USD 5.18 and USD 32.38) without a condom, and UGX 5000 and UGX 50,000 shillings (USD 1.30 and USD 12.95) with a condom, respectively. At baseline, 95 participants (86.4%) had heard about PrEP. Most of the participants (n = 88; 80.0%) were worried about getting infected with HIV, 87 (79.1%) believed that PrEP could prevent them from getting infected with HIV, and 66 (60.0%) were worried about PrEP side effects. Participation retention (completed study visits) was 67% and 75% at 6 and 12 months, respectively. The 12-month visit completion was 81% and 70% in the HIVST and SOC arms, respectively, with no differences by arm ($P = 0.19$). Overall, the 12-month retention was 90% for MSM, 81% for TGSWs, and 73% for FSWs.

HIVST

In a visit-level analysis among intervention participants (n = 161/228 possible visits), the proportion of sex workers in the HIVST arm who self-reported using $\geq$1 kit was 99.4% (160/161) overall, with 97.4% (38/39), 100% (40/40), 100% (39/39), and 100% (43/43) at the 3-, 6-, 9-, and 12-month visits, respectively. In addition, 158 participants (98.1%) believed that the kit gave an accurate result, 154 (95.7%) said the kit was very easy to use, and 133 (82.6%) preferred to self-test at home by themselves compared with clinic-based testing. A minority (n = 45; 27.9%) tested at least once with someone else, including paying partners (n = 22; 48.9%), nonpaying partners (n = 16; 35.6%), and family members (n = 3; 6.7%). At the 161 visits, 99 (61.8%) reported using the HIVST kit before opening a new PrEP bottle and 93 (57.8%) reported HIVST use before sex act with a paying partner. All (100%) said they felt confident enough to show somebody else how to use HIVST kits, and 159 (98.8%) said they would recommend HIVST to friends and relatives. Secondary distribution of HIVST kits to paying and nonpaying partners of sex workers in the intervention arm was reported at 71 (44.1%) and 51 (31.7%) visits, respectively.

Effect of HIVST on PrEP Adherence

The median follow-up was 11.1 months (IQR 11.0, 11.3) per participant. We evaluated 1072 person-months in the intent-to-treat analysis. Eight participants (14%) in the HIVST arm and 18 (34%) in the SOC arm told research staff
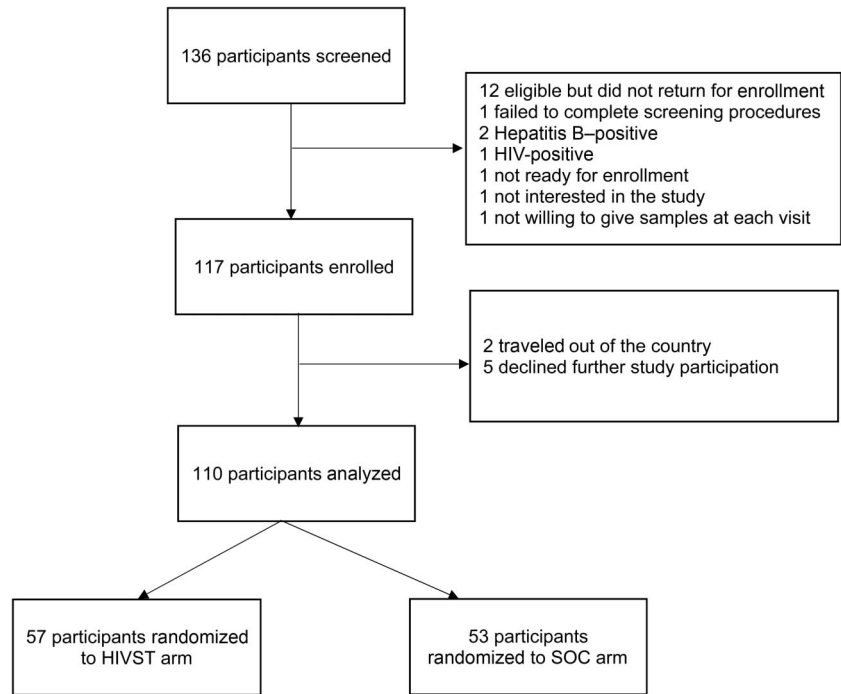
FIGURE 1. Trial profile.

they had permanently stopped taking PrEP during the study. Overall, the mean adherence by EAM was 25.9% (30.9% and 20.6%; $P = 0.047$) at 6 months and 17.2% (22.1% and 11.5%; $P = 0.052$) at 12 months in the HIVST and SOC arms, respectively (Fig. 2). The TFV-DP detection was 21% and 21% at the 3-month visit, 21% and 25% at the 6-month visit, 14% and 11% at the 9-month visit, and 20% and 10% at the 12-month visit ($P > 0.2$ for all comparisons) for the HIVST and SOC arms, respectively. The proportion with TFV-DP levels ≥700 fmol per punch in the HIVST and SOC arms at the 3-, 6-, 9-, and 12-month visits was 2.4%, 2.3%, 0%, and 0% and 7.9%, 0%, 0%, and 0%, respectively, with no differences by randomization arm ($P > 0.2$). Similar findings were observed when adherence was measured by pharmacy refill at the 3-, 6-, 9-, and 12-month visits ($P > 0.1$ for all comparisons). As shown in Figure 3, the correlation between EAM and DBS had a rho of 0.212 overall (0.240 in the HIVST arm and 0.193 in the SOC arm; $P = 0.04$ for the randomized groups). No intervention effect was observed on PrEP adherence by randomization arm over the 12-month period as measured by EAM (adjusted odds ratio [aOR]: 3.32; 95% CI: −5.3 to 11.9; $P = 0.45$) or DBS TFV-DP levels [aOR 1.01; 95% confidence interval (CI): 0.91 to 1.97; $P = 0.98$] (Table 2).

Effect of HIVST on Sexual Risk Behaviors

At baseline, the mean number of sexual partners in the previous month was 72 (range 30–120). Most of the participants (n = 67; 61%) had intimate partner(s) and 51 (76%) reported never using condoms with intimate partners. Sixty-eight percentage of participants did not disclose sex work to their intimate partners. Overall, we observed no

difference in self-reported condomless sex acts with paying partners by randomization arm (adjusted incidence rate ratio [aIRR]: 0.70; 95% CI: 0.42 to 1.17; $P = 0.18$).

Subgroup Analyses

We observed an apparent intervention effect on PrEP adherence in the small subset of 16 TGSWs: EAM (aOR 3.86; 95% CI: 1.15 to 12.9 $P = 0.006$) and DBS TFV-DP levels (aOR 3.99; 95% CI: 1.58 to 10.05; $P = 0.003$). An intervention effect on sexual risk behaviors was observed among MSM (aIRR 0.11; 95% CI: 0.06 to 0.20; $P < 0.001$), and TGSWs (aIRR 0.18; 95% CI: 0.10 to 0.32; $P = 0.001$) were less likely to report condomless sex acts with paying partners than FSWs regardless of randomization arm. Similar findings were observed for condom use with nonpaying partners with no difference by arm (aIRR 0.98; 95% CI: 0.70 to 1.39; $P = 0.93$), but with MSM less likely to report condomless sex acts (aIRR 0.01; 95% CI: 0.00 to 0.05; $P < 0.001$) than FSWs (Table 3).

Adverse Event Profile and HIV Acquisition

No serious adverse events were identified as related to study participation or PrEP. We detected 1 seroconversion in the HIVST arm at the 9-month visit (HIV incidence, 0.9 per 100 person-years). Tenofovir was not detected in DBS at the 3-, 6-, or 9-month visits, and drug resistance testing was not performed because the FSW participant did not return for her postser-oconversion visit. She was encouraged to start antiretroviral treatment but repeatedly declined (see Fig., Supplemental Digital Content, http://links.lww.com/QAI/B779).

TABLE 1. Baseline Characteristics by Randomization Arm

Characteristic	HIVST (N = 57), N (%) or Median (IQR)	SOC (N = 53), N (%) or Median (IQR)
Sex		
Female	39 (68.4)	45 (84.9)
Male	7 (12.3)	3 (5.7)
Transgender	11 (19.3)	5 (9.4)
Age	23.1 (20.9–28.9)	22.2 (20.4–25.1)
18–24	32 (56.1)	33 (62.3)
25–29	14 (24.6)	12 (22.6)
30–34	7 (12.3)	4 (7.6)
older than 35	4 (7.0)	4 (7.5)
Completed yr of education	7 (3–10)	9 (6–11)
0	3 (5.3)	11 (20.7)
1–7	19 (33.3)	18 (34.0)
8–11	25 (43.9)	17 (32.1)
≥12	10 (17.5)	7 (13.2)
Marital status		
Divorced/separated/widowed	10 (17.5)	9 (17.0)
Married	1 (1.8)	2 (3.8)
Single with a nonpaying partner	20 (35.1)	21 (39.6)
Single without nonpaying partner	26 (45.6)	21 (39.6)
No. of children		
None	26 (45.6)	15 (28.3)
1–2	19 (33.3)	29 (54.7)
≥3	12 (21.1)	9 (17.0)
Average monthly income (UGX)	300,000 (150,000–500,000)	300,000 (200,000–600,000)
Sex work main source of income		
Yes	37 (64.9)	38 (71.7)
No	20 (35.1)	15 (28.3)
Age at onset of sex work [n = 108]	19 (17–25)	19 (17–22)
Sexual partners in previous mo	60 (20–140)	80 (30–100)
Average charge for vaginal sex act with a condom [n = 84]	5000 (5000–10,000)	8000 (5000–10,000)
Average charge for vaginal sex act without a condom [n =49]	30,000 (10,000–50,000)	20,000 (20,000–30,000)
Average charge for anal sex act with a condom [n = 30]	50,000 (20,000–70,000)	30,000 (30,000–50,000)
Average charge for anal sex act without a condom [n = 26]	50,000 (20,000–150,000)	50,000 (32,500–90,000)
Currently smoking tobacco	6 (10.5)	5 (9.4)
Currently using other recreational drugs	10 (17.5)	9 (17.0)
Possible depression*	24 (42.1)	21 (39.6)
Problematic alcohol use†	32 (56.1)	30 (56.6)
Sex work stigma‡	52 (91.2)	48 (92.5)

*The Patient Health Questionnaire (PHQ-2), which has been validated in Uganda,[25] was used to assess depression; a response of yes to either question is considered possible depression.

†Alcohol use was assessed using the RAPS-4 scale[24]; a response of yes to 1 or more questions is considered problematic alcohol use in the previous yr.

‡Stigma was assessed using the HIV stigma scale[23]; data indicate a response of agree or strongly agree.

DISCUSSION

In this randomized trial of HIVST codistributed with PrEP, PrEP adherence was low despite near-universal reported use of HIVST among cisgender women, cisgender men, and TGSWs in Uganda. The lack of intervention effect was consistent when PrEP adherence was assessed using electronically monitored adherence and TFV concentrations in DBS. EAM-assessed adherence was significantly higher in the HIVST arm at the 6-month visit, but this was not sustained during the 12-month study period. HIVST acceptability was high because nearly all sex workers used the kits to test themselves, and half of them distributed HIVST kits to paying and nonpaying partners. Self-reported condomless sex acts with paying and nonpaying partners decreased among MSM and TGSWs but not FSWs regardless of study arm. HIV incidence was low; only 1 seroconversion occurred (and this event occurred in the absence of PrEP use). In subgroup analyses, TGSWs were 4 times as likely to adhere to PrEP as FSWs, suggesting possible gender differences. However, the small numbers of TGSWs may result in an overestimation of the intervention effect.

Our results are consistent with those of other sex worker studies in sub-Saharan Africa in which oral PrEP
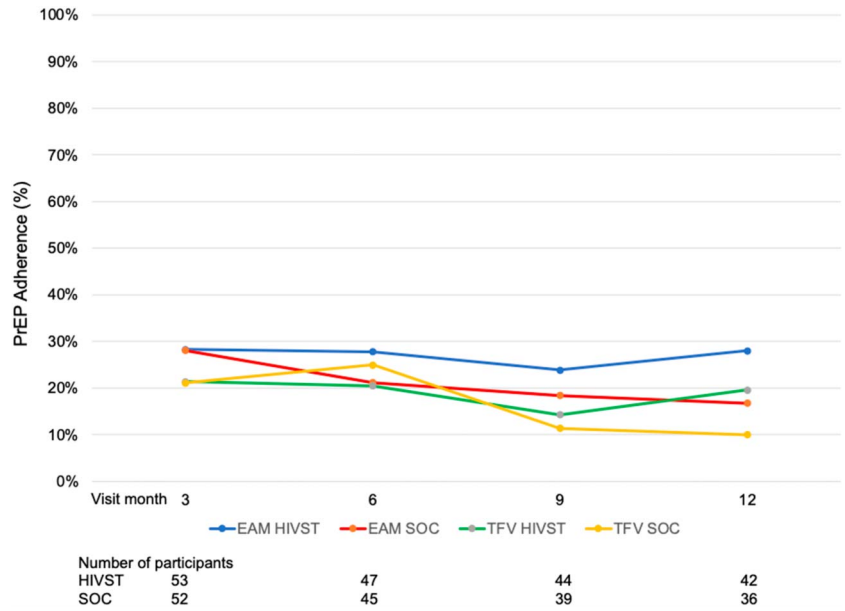
FIGURE 2. PrEP adherence by EAM and TFV-DP levels in DBS. full color online

was infrequently taken at levels sufficient to achieve HIV protection.[31–33] We found that despite continual engagement in sex work during the study, PrEP use was suboptimal during this risk period, suggesting a lack of prevention-effective adherence.[34] PrEP is an empowering self-controlled prevention tool that allows sex workers to control their HIV protection without requiring the consent of their partners.[35] Our published qualitative work in this cohort[17] found that combined HIVST and PrEP use enabled sex workers to overcome physical and emotional barriers to intimacy, preserve relationships with their intimate partners, and avoid the stigma and inconvenience experienced when testing at public health facilities, which empowered them to protect their sexual health. Recent work among young women in Kenya

found that HIV risk perception was dynamic, evolved as partnerships and sexual behaviors changed, and influenced PrEP and condom use over time.[36] The dynamic nature of HIV risk perception may have influenced PrEP persistence and could explain the misalignment between perceptions that PrEP was empowering and suboptimal PrEP adherence in our study.

At least 4 doses per week are required to provide HIV protection after rectal exposure; higher adherence is likely required for vaginal exposure.[37,38] Second-generation PrEP drugs, including the dapivirine vaginal ring and injectable cabotegravir LA), are dosed at least monthly, which provides an adherence advantage over daily dosing.[39,40] However, concerns about side effects and HIV stigma may still limit
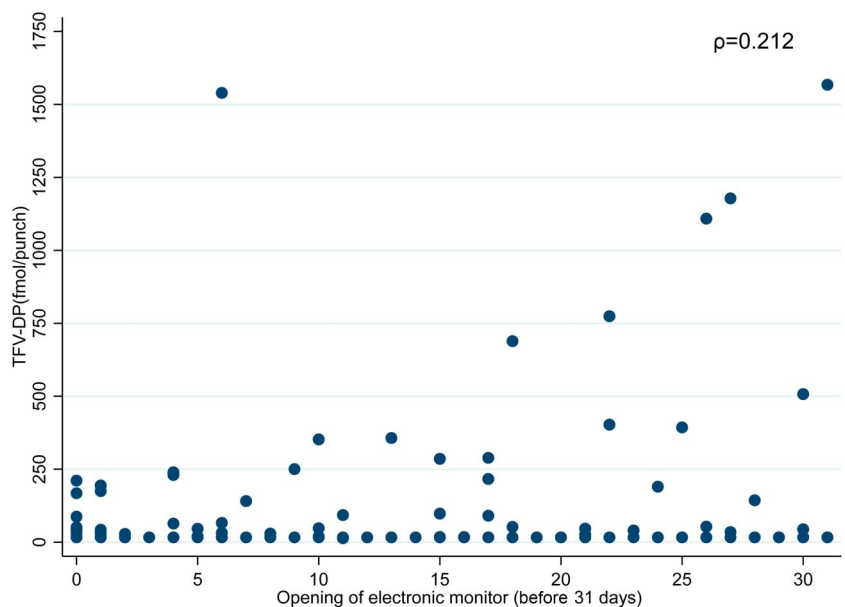
FIGURE 3. Correlation of PrEP adherence by electronic adherence monitoring and TFV-DP levels in DBS. full color online

TABLE 2. Effect of HIV Self-Testing on PrEP Adherence

PrEP Adherence	N (%)	OR; 95% CI	*P*	Adjusted OR 95% CI	*P*
EAM					
SOC	42 (54%)	Ref		Ref	
HIVST	36 (46%)	2.83 (−5.9 to 11.7)	0.53	3.32 (−5.3 to 11.9)	0.45
EAM (by gender)					
FSWs	58 (75)	Ref		Ref	
MSM	8 (10)	0.58 (−13.3 to 14.5)	0.94	−0.15 (−13.8 to 13.5)	0.98
TGSWs	12 (15)	−4.18 (−17.4 to 9.1)	0.54	−4.98 (−17.6 to 7.8)	0.45
TFV-DP levels in DBS (by arm)					
SOC	46 (53)	Ref		Ref	
HIVST	40 (47)	1.22 (0.52 to 2.89)	0.65	1.01 (0.44 to 2.35)	0.98
TFV-DP levels in DBS (by gender)					
FSWs	63 (74)	Ref		Ref	
MSM	9 (10)	1.36 (0.28 to 6.51)	0.70	1.35 (0.29 to 6.28)	0.69
TGSWs	14 (16)	4.00 (1.54 to 10.35)	0.004	3.99 (1.58 to 10.05)	0.003

uptake of long-acting PrEP. The HIV Prevention Trials Network 083 and 084 studies demonstrated that cabotegravir LA is a well-tolerated and effective injectable PrEP drug for cisgender women, MSM, and TGW.[39,41] Other long-acting PrEP agents, including islatravir and lenacapavir, are under evaluation.[42–44] Future studies should evaluate optimal approaches to motivate high uptake and sustained use of long-acting PrEP formulations among sex workers.

Nearly all sex workers in our study reported using HIVST, half gave kits to paying or nonpaying partners, and 1 in four self-tested with a partner. HIVST is a self-controlled prevention tool that could empower sex workers to negotiate condom use. Sex workers use point-of-sex testing (ie, using HIVST kits to screen paying partners) as a risk reduction strategy in settings where partners pay more for condomless sex acts.[17,45–47] Studies of FSWs, MSM, and TGSWs suggest that point-of-sex testing empowers and informs sexual decision-making such as avoiding sex act or insisting on condom use with paying partners who tested HIV-positive.[11,48–50] This ancillary benefit could motivate HIVST use among sex workers. However, some caution regarding the utility of HIVST for sexual decision-making is warranted; oral fluid self-test kits may be misinterpreted and have low sensitivity in acute HIV infection and in persons taking PrEP or antiretroviral therapy, which may result in false-negative results and a false sense of safety.[17,51,52]

We found no evidence of behavioral risk compensation among sex workers in agreement with previous reports.[53,54] In contrast with previous studies, we observed a lower likelihood of sex acts unprotected by condoms among MSM and TGSWs but not FSWs.[55] In our study, the median charge for anal sex act with a condom was 2.5-fold higher than that for condomless vaginal sex act, suggesting financial motivations to engage in condomless sex act may have been less compelling for MSM and TGSWs

TABLE 3. Effect of HIV Self-Testing on Sexual Behaviors

Sexual Risk Behaviors	N (%) or Median (IQR)	IRR; 95% CI	*P*	Adjusted IRR (95% CI)	*P*
Age	22.8 (20.4–27.6)	1.00 (0.97 to 1.02)	0.82	0.99 (0.96 to 1.03)	0.70
Sex					
Female	84 (76)	Ref		Ref	
Male	10 (9)	0.06 (0.00 to 0.74)	0.03	0.11 (0.06 to 0.20)	<0.001
Transgender	16 (15)	0.16 (0.09 to 0.27)	0.01	0.18 (0.10 to 0.32)	<0.001
Duration of sex work	3.1 (1.7–4.8)	1.00 (0.97 to 1.03)	0.85	1.02 (0.97 to 1.07)	0.51
Problematic alcohol use	62 (56)	0.90 (0.48 to 1.67)	0.73	0.81 (0.46 to 1.45)	0.48
Condom use, paying partners (by arm)	70 (24–126)	0.78 (0.49 to 1.27)	0.29	0.70 (0.42 to 1.17)	0.18
Condom use, nonpaying partners (by arm)	11 (5–23)	1.07 (0.3 to 1.58)	0.73	0.98 (0.70 to 1.39)	0.93
Condom use, paying partners (by gender)					
FSWs	84 (76)	Ref		Ref	
MSM	10 (9)	0.06 (0.01 to 0.74)	0.03	0.11 (0.06 to 0.20)	<0.01
TGSWs	16 (15)	0.16 (0.09 to 0.27)	0.01	0.18 (0.10 to 0.32)	<0.01
Condom use, nonpaying partners (by gender)					
FSWs	84 (76)	Ref		Ref	
MSM	10 (9)	0.01 (0.00 to 0.07)	<0.01	0.01 (0.00 to 0.05)	<0.01
TGSWs	16 (15)	1.68 (1.38 to 2.04)	<0.01	1.55 (0.81 to 3.00)	0.19

than FSWs. A meta-analysis of 17 studies with 6671 MSM found that PrEP use was associated with a significant increase in condomless sex acts and STI diagnoses outside of sex work.[56] The association between PrEP and STI incidence is less clear for TGSWs, and programmatic data are lacking.

Subgroup analyses revealed a higher likelihood of PrEP adherence among TGSWs. This finding may be explained by motivation to access HIV prevention services for a marginalized population that had previously not participated in a clinical trial in Uganda. PrEP adherence among TGSWs in sub-Saharan Africa is poorly studied, offering few data for comparison. South African TGW reported a decreased HIV risk, HIV protection in the event of rape, and being in control of one's health as reasons for taking PrEP.[57] Other work in Kenya (n = 53) found that TFV-DP was detected in 62.5% of TGW vs 17.7% of MSM at the 6-month visit. In that study, PrEP use was motivated by unplanned or frequent risky sexual behavior and desire to remain HIV-negative.[58] Ongoing studies in Uganda (ClinicalTrials.gov NCT04328025, 04867798, and 04491422) will contribute to the knowledge base regarding HIVST and PrEP use in this population.

This study is the first, to the best of our knowledge, to evaluate HIVST and PrEP use among a gender-diverse sample of sex workers in sub-Saharan Africa. We achieved good retention among MSM and TGSWs in Uganda by establishing strong community linkages, leveraging peer support, and providing research staff with gender-sensitivity training. Of importance, no social harms related to research participation were identified. In addition to these strengths, our study has limitations. One-quarter of the study sample was lost to follow-up, but dropout rates did not differ by study arm. We enrolled a small sample of MSM and TGSWs; the gender differences we observed should thus be interpreted with caution. HIVST was only available through research programs at the time of the study, and intervention arm participants may have shared kits with the SOC group. Nevertheless, any such contamination would not have affected the null results of the trial because PrEP adherence was poor irrespective of randomization group. In addition, misclassification of device nonuse due to stigma may have occurred.[59] However, TFV-DP levels in DBS demonstrated similarly poor PrEP adherence.

In conclusion, our randomized trial found no benefit for HIVST in supporting PrEP adherence among sex workers in Uganda. Acceptability of HIVST was high with frequent use of this prevention tool for self-testing and testing with sexual partners. PrEP adherence was low and insufficient for HIV protection. Future studies should evaluate alternate strategies to promote sustained use of PrEP for sex workers in sub-Saharan Africa, including long-acting PrEP formulations.

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