Integrating HIV Preexposure Prophylaxis With Community-Based Syringe Services for Women Who Inject Drugs: Results From the Project SHE Demonstration Study

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Introduction: To guide future preexposure prophylaxis (PrEP) implementation for women who inject drugs (WWID), a population increasingly represented in new HIV cases in the United States, we present results from a demonstration project integrated within a syringe services program (SSP) in Philadelphia, PA.

Methods: WWID ≥18 years were educated about and offered 24 weeks of daily PrEP. Participants completed surveys and clinical assessments at baseline and at weeks 1, 3, 12, and 24. We used descriptive statistics to estimate feasibility/acceptability, engagement in the care cascade, HIV/sexually transmitted diseases (STI) and pregnancy, issues of safety/tolerability, and preferences/satisfaction with PrEP services. Multivariable logistic regression with generalized estimating equations was used to identify factors associated with PrEP uptake and retention.

Results: We recruited 136 WWID. Of those, 95 were included in the final sample, and 63 accepted a PrEP prescription at week 1. Uptake was associated with greater baseline frequency of SSP access [adjusted odds ratio (aOR) = 1.85; 95% confidence interval (CI): 1.24 to 2.77], inconsistent condom use (aOR = 3.38; 95% CI: 1.07 to 10.7), and experiencing sexual assault (aOR = 5.89; 95% CI: 1.02, 33.9). Of these 95, 42 (44.2%) were retained at week 24. Retention was higher among women who reported more frequent baseline SSP access (aOR = 1.46; 95% CI: 1.04 to 2.24). Self-reported adherence was high but discordant with urine-based quantification of tenofovir. Baseline STI prevalence was 17.9%; there were 2 HIV seroconversions and 1 pregnancy. Safety/tolerability issues were uncommon, and acceptability/satisfaction was high.

Conclusions: Integrating PrEP with SSP services is feasible and acceptable for WWID. This suggests that daily PrEP is a viable prevention tool for this vulnerable population.

Key Words: preexposure prophylaxis, HIV prevention, women, injection drugs, syringe exchange, harm reduction

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INTRODUCTION

HIV is of increasing public health concern among persons who inject drugs (PWID) in the United States. Since the early 1990s, HIV diagnoses among PWID had dropped dramatically from 40% to 6% in 2017.[1] However, cities across the United States have recently reported HIV outbreaks within this population.[2,3] Additionally, the Centers for Disease Control and Prevention (CDC) estimates that 220 counties in 26 states have the potential for HIV outbreaks attributable to opioid use.[4] In Philadelphia, there has been a 115% increase in new HIV infections among PWID between 2016 (33 new cases) and 2018 (71 new cases), which prompted the Health Department to declare an HIV outbreak.[5]

The rise of new HIV infections stems from (1) the increasing size of the population that uses injection drugs[6]; (2) saturation of illicit fentanyl into drug markets which increases the potential for parenteral exposure as a result of more frequent injecting (fentanyl has a shorter half-life than heroin)[7]; (3) densely connected injection networks among PWID[8]; and (4) limited investment, compared with

community needs, in evidence-based interventions to prevent HIV in this population. For example, 10 US states have no sanctioned syringe service programs (SSP)[9] despite decades of evidence documenting the benefits of this intervention.[10] The potential for HIV to quickly escalate among PWID across the US signals an urgent need to increase evidence-based prevention strategies. Among PWID, women who inject drugs (WWID) are disproportionately represented in new cases of HIV by a magnitude of 1.5-fold to 2.5-fold.[11,12] Research has demonstrated that women experience greater vulnerability to HIV than male counterparts for a multitude of reasons related to structural, interpersonal, and biological factors.[12] Despite this, WWID are understudied within the larger drug-using population,[13] and as a consequence, gender-specific needs of WWID are frequently overlooked in HIV prevention and treatment services.[12]

Preexposure prophylaxis (PrEP) is an effective biomedical prevention intervention that could reduce HIV incidence among PWID. The Bangkok Tenofovir Trial demonstrated a 49% reduction in HIV acquisition and up to 74% among PWID with the highest adherence to once daily PrEP.[14] Studies have also demonstrated that once educated about PrEP, PWID find PrEP acceptable.[15] However, PWID may face barriers to uptake, including low utilization of preventive health care[16] and provider biases that impede prescribing to this population.[12,17] Barriers experienced by WWID may differ from those experienced by men because of gender and power inequity.

One strategy that may mitigate barriers among WWID is integrating PrEP within SSP. Many SSP provide long-term treatments that require prescriptions and medical monitoring, such as medications for opioid use disorder. It stands to reason that PrEP interventions, delivered in settings already used and trusted by PWID, are more likely to be acceptable and could increase PrEP uptake and retention. For example, buprenorphine maintenance[18] and antiretroviral medication adherence[19] have been higher among PWID receiving care in an SSP compared with traditional medical settings. Research has yet to assess the feasibility and acceptability of SSP-based PrEP care for PWID, and in particular, WWID. To address this gap, we conducted Project Sexual Health Equity (Project SHE), a community-based PrEP demonstration project for cisgender WWID incorporated into the SSP at Prevention Point Philadelphia (PPP), Pennsylvania.

METHODS

Study Setting and Recruitment

Project SHE was conducted between April 2018 and June 2019 at PPP, one of the busiest SSP in the United States distributing over 3.2 million syringes in 2018 (Andres Freire, Director of Prevention Services, personal communication, September 9, 2019). Recruitment and eligibility screening were conducted face to face during PPP's *Ladies Night*, a weekly drop-in program that provides food, showers, clothing, and monthly social support programming (ie, free haircuts, self-defense classes, etc.). Marketing included hanging flyers throughout PPP, word of mouth from PPP staff to clients, and informal peer referral. Table 1 shows the schedule of research activities that occurred over 24 weeks of follow-up. The study was approved by the Drexel University Institutional Review Board and PPP Executive Board. Participants provided written informed consent before study activities and could receive up to $155 in compensation for their time if they completed all visits.

Participant Eligibility

Eligible women were HIV seronegative, reported nonprescription injection drug use within 30 days, and at least one behavior associated with elevated HIV risk (eg, syringe sharing, sex exchange, or inconsistent condom use) in the past 6 months, consistent with 2017 CDC PrEP prescribing guidelines (see Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B568).[20] Women who were pregnant, breastfeeding, or expressed intention to become pregnant within 12 weeks were excluded based on scientific evidence available at that time.

PrEP Provision

Procedures were intended to reflect real-world PrEP access and use. At baseline, a phlebotomist experienced working with PWID would attempt to draw blood up to 3 times to establish creatinine clearance. After the third failed attempt, a blood draw would be scheduled for the first follow-up appointment. Participants interested in PrEP were assisted in using their own health insurance or assistance programs to secure coverage of emtricitabine/tenofovir disoproxil fumarate as PrEP. Uninsured and underinsured participants were referred to PPP case managers for assistance in applying for insurance. Study staff completed prescription assistance applications for the drug manufacturer's copay assistance program (Gilead Pharmaceuticals, Foster City, CA). Participants accepting a PrEP prescription could choose to either receive a paper prescription to take to their own pharmacy or have their medications delivered to PPP through a partnership with Philadelphia Pharmacy. Importantly, participants were allowed to switch between paper prescription and medication delivery and were able to initiate or terminate PrEP at any point in the study. At their final study visit, participants who were interested in continuing PrEP were given a list of local PrEP providers, including study staff.

Retention and Withdrawal Procedures

To increase retention, a member of the research team was positioned by the front door of the SSP to greet women, remind participants of their scheduled visits, and ensure those needing an ad hoc visit (ie, participants reporting medications were lost or stolen) were seen. The staff member was also provided with a list of names of participants who had missed appointments or were lost to follow-up with the goal of reengaging them in the study if they wanted to continue. WWID with an available mobile phone could also choose to receive a reminder call/text before each visit. Participants could be withdrawn for the following reasons: inability to

TABLE 1. Schedule of Demonstration Project Procedures

Procedure	Baseline	Follow-up 1	Adherence Check-in*	Follow-up 2	Follow-up 3
Timeline		Week 1	Week 3	Week 12	Week 24
Informed consent	x				
RA-administered quantitative questionnaire†	x	x	x	x	x
Clinical interviews‡					
Relevant medical history	x				
Current/concomitant medication	x			x	x
Self-report PrEP adherence			x	x	x
PrEP distribution		x		x§	x§
HIV/STI testing‡					
HIV screening	x			x	x
Syphilis	x			x	x
Gonorrhea/chlamydia‖	x			x	x
Hepatitis B virus	x				
Pregnancy testing‡	x			x	x
Safety assessment‡					
Renal functions test	x				x
Persistent side effects			x	x	x
PrEP-related AE/SAE		x	x	x	x
Adherence laboratory assessment‡					
FTV concentration in urine¶				x	x
Qualitative interview#		x		x	x

*Adherence check in was only for participants who initiated PrEP.
†Data stored in Qualtrics.
‡Data stored in Redcap.
§Treatment given +1 wk after appointment if relevant.
‖Oropharyngeal, rectal, and vaginal swabs were self-collected.
¶Only among those reporting PrEP adherence within 7 days.
#Purposive sample of those declining PrEP and/or various levels of adherence.
AE/SAE, adverse event/serious adverse event; FTV, tenofovir disoproxil fumarate.

obtain blood samples via venipuncture to establish creatinine levels at both the baseline and week 1 follow-up, pregnancy, HIV seroconversion, missing an appointment and failing to reengage within 12 weeks, or for being disruptive or threatening to staff.

Measures

Feasibility and Acceptability

Feasibility was defined as the proportion of women with successful venipuncture for creatinine clearance testing among eligible participants. Acceptability was defined as the proportion of women who meet eligibility criteria and elected to enroll into the study.

Participant Characteristics

Participant characteristics were measured at baseline, including sociodemographic characteristics; frequency of SSP access in the past 6 months; drug-related and sexual behaviors within the previous 6 months; perceived HIV risk; and PrEP awareness (see Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B568).

HIV, Sexually Transmitted Diseases, and Pregnancy

As part of PrEP clinical care, the following diagnostic procedures were performed at baseline, week 12 and week 24: Insti rapid HIV1/HIV2 antibody test (bioLytical, BC, Canada)[21]; self-collected swabs for gonorrhea and chlamydia at genital, oropharyngeal, and rectal sites; rapid plasma reagin for syphilis screening; hepatitis B surface antigen (baseline only); and urine-based pregnancy tests. All positive tests for notifiable diseases were reported by the laboratory and PPP per local regulations. Diagnostic procedures are presented in Supplemental Digital Content (see Table 2, http://links.lww.com/QAI/B568).

Engagement in the PrEP Care Cascade

Engagement in care measures included the following: (1) intention to initiate PrEP at baseline: "*We are going to offer you a prescription for PrEP today. Do you plan to take that prescription?*"; (2) PrEP uptake was defined as the proportion of WWID who accepted a paper prescription or bottle of Truvada among those returning to care at weeks 1, 12, and 24; (3) proportion retained in care, estimated as the number of participants who attended weeks 1, 12, and 24 appointments divided by the baseline sample size; (4) the proportion of participants who planned to continue PrEP care after completing the study; (5) self-reported PrEP adherence, assessed at weeks 12 and 24 was assessed with the following question: "*How many PrEP pills have you missed in the past 7 days?*". Participants who reported 100% adherence at weeks 12 and 24 (ie, missed no PrEP doses in the past 7 days) also

provided a self-collected urine sample to quantify tenofovir levels into 3 categories of adherence: (1) adherent within previous 48 hours (>1000 ng/mL), (2) partially adherent within the previous week but not in the previous 48 hours (10–1000 ng/mL), (3) and nonadherent within the previous week (<10 ng/mL).[22]

Safety and Tolerability

Safety of PrEP was assessed at baseline and week 24 using creatinine clearance (CrCl; normal threshold ≥ 60 mL/min).[20] A detailed medical history was collected at all visits and included an assessment of side effects that were recorded by the clinician. Clinical records were reviewed to identify persistent side effects (eg, headaches, nausea, or fatigue lasting longer than 12 weeks), and PrEP-related serious adverse events (eg, hospitalization or death).

Care Preferences and Satisfaction

We measured (1) women's preferences for future sexually transmitted disease (STI) testing (SSP versus mobile clinic, ER, private doctor's office, and STD clinic) at week 1; (2) women's preference for receiving PrEP at the SSP versus taking a paper script to be filled elsewhere, determined based on clinical records indicating which option participants chose at each follow-up; and (3) agreement with the following statement, "*I would prefer to receive PrEP care at Prevention Point Philadelphia*," asked at the week-24 visit. Related to satisfaction, participants were asked the following from the Client Satisfaction Questionnaire at week 24:[23] "*How satisfied are you with the services you received?*" (answer choices were "quite dissatisfied," "indifferent or mildly dissatisfied," "mostly satisfied," or "very satisfied") and "*To what extent has our program met your needs?*" (answer choices were "none of my needs have been met," "only a few of my needs have been met," "most of my needs have been met," or "almost all of my needs have been met"). For analyses, we dichotomized these outcomes to "very satisfied/mostly satisfied," and "most or all of my needs have been met" compared with all other responses.

Statistical Analysis

Descriptive statistics were calculated for participant characteristics and behaviors, engagement in care, clinical assessments and diagnostic procedures, care preferences, and satisfaction. Logistic regression models were used to assess baseline factors associated with retention in care at week 24. Longitudinal PrEP uptake was modeled using logistic generalized estimating equations, with an exchangeable correlation structure, to account for repeated measures[24] Factors associated with each outcome ($\alpha = 0.05$) were entered into separate models each adjusted for age, race/ethnicity, and current housing status. Statistical analysis was conducted in R version 3.6.2[25] using *geepack*.[26]

RESULTS

Feasibility and Acceptability

We screened 136 WWID for eligibility between April 2018 and March 2019; 100 met the inclusion criteria and were enrolled into the study. Of those, 100% elected to participate in the study and completed the baseline survey. We successfully obtained a blood sample from 96 participants for creatinine testing; 4 were excluded after the third failed attempt to draw blood at week 1. These participants were provided with a list of local clinics providing PrEP. One participant was also withdrawn because of concerns about staff safety during follow-up. Thus, the final sample included 95 participants.

Participant Characteristics

The sample included predominately white women (n = 66; 69.5%) with a median age of 36 years (interquartile range: 32–44 years; Table 2). Most reported having unstable housing, including 63.4% who self-identified as currently homeless, earned less than $4999 a year, and had safety-net insurance. Despite reporting a variety of behaviors associated with HIV acquisition [eg, >70% reported engaging in transactional sex (n = 68) or inconsistent condom use (n = 75)], less than half perceived that they were likely to acquire HIV. Just more than half of the sample was aware of PrEP before enrollment.

HIV, STI, and Pregnancy

During the 29.6 person-years of follow-up among study participants, there were 2 HIV seroconversions (6.8 HIV diagnoses per 100 person-year; 95% confidence interval: 0.8 to 24.4). These participants tested positive at week 12 and week 24, respectively. Both reported either inconsistent or no PrEP adherence 2 weeks before their HIV diagnosis. At baseline, 17.9% (17 of 95) screened positive for bacterial STI at any site, and 2.1% (2 of 95) tested positive for hepatitis B: one of whom declined PrEP, whereas the other initiated PrEP. At week 12, urinalysis indicated that the participant with hepatitis B had tenofovir levels consistent with nonadherence in the past 2 weeks despite self-reports of not missing any PrEP doses in the past 7 days. However, there was no evidence of harms (eg, symptoms suggestive of hepatic inflammation) to this participant. There were 18.6% (11 of 59) and 9.5% (4 of 42) cases of incident STI detected at weeks 12 and 24, respectively. There was one pregnancy over the course of the study.

Engagement in the PrEP Care Cascade

Women's engagement in the PrEP care cascade varied over time as depicted in Figure 1. At baseline, 88.4% (84 of 95) WWID intended to accept a PrEP prescription, and over follow-up, 70.8% (63 of 89) accepted PrEP at week 1, 81.4% (48 of 59) at week 12, and 59.5% (25 of 42) at week 24. After adjusting for age, race/ethnicity, and housing status, 3 baseline factors were associated with increased odds of PrEP

TABLE 2. Sample Characteristics of Women Who Inject Drugs (n = 95) Enrolled in a PrEP Demonstration Project in Philadelphia

	n (%) or Median (IQR)
Median age (IQR)	36 (32–44)
Race/ethnicity	
White, non-Hispanic	66 (69.5)
Black, non-Hispanic	14 (14.7)
Hispanic/Latino	11 (11.6)
Mixed race, non-Hispanic*	4 (4.2)
Sexual orientation	
Heterosexual	59 (62.1)
Homosexual	6 (6.3)
Bisexual	30 (31.6)
Education (n = 94)†	
Less than high school	37 (39.4)
High school grad	32 (34.0)
Some college or higher	25 (25.1)
Annual income (n = 93)†	
$0–4999	53 (57.0)
$5000–9999	13 (14.0)
$10,000+	27 (29.0)
Insurance at baseline (n = 94)†	
Public/Safety Net insurance	84 (89.4)
Private insurance	2 (2.12)
No insurance	8 (8.51)
Current housing	
Own home	6 (6.3)
Staying with family/friends	25 (26.3)
Single room occupancy	11 (11.6)
Living in shelter/treatment facility	14 (14.7)
Living on street	39 (41.1)
Self-identified current homelessness (n = 93)†	59 (63.4)
Frequency of SSP access (n = 91)	
Never	8 (8.8)
Few times a year	1 (1.0)
Few times in the last 6 mo	2 (2.2)
Few times in a month	5 (5.5)
Once a week	24 (26.4)
Few times a week	36 (39.6)
Daily	15 (16.5)
Drug-related behaviors, past 6 mo	
Daily injection drug use	70 (73.7)
Median no. of daily injections (IQR) (n = 91)	5 (3–7)
Sharing syringes (n = 91)‡	42 (46.2)
Medication for opioid use disorder	15 (15.8)
Sexual risk factors, past 6 mo	
Median no. of sexual partners (IQR)	6 (2–21)
Inconsistent condom use‡	75 (78.9)
Transactional sex‡	68 (71.6)
Sex partner living with HIV‡	3 (6.4)
Sexual assault (n = 67)§	15 (22.4)
Self-perceived HIV risk (n = 94)†	
Extremely/very unlikely	51 (54.3)
Somewhat/very/extremely likely	43 (45.7)
Previously aware of PrEP	50 (52.6)

*Includes Asian, Pacific Islander, Native Hawaiian, and mixed race.
†Excludes participants for refusing to answer.
‡Behavior is a CDC indication for PrEP use by PWID.
§Excludes participants who did not receive the question on sexual assault.
IQR, interquartile range.

uptake, averaged over the 24 weeks of follow-up: inconsistent condom use, experiencing sexual assault, and frequency of SSP access within 6 months (Table 3, A). WWID who used condoms inconsistently (aOR = 3.38; 95% CI: 1.07 to 10.7), experienced sexual assault (aOR = 5.89; 95% CI: 1.02 to 33.9), and accessed the SSP more frequently (aOR = 1.85; 95% CI: 1.24 to 2.77), on average, had higher odds of PrEP uptake over follow-up compared with WWID who did not.

Overall, retention was 93.7% (89 of 95) at week 1, 61.2% (59/95) at week 12, and 44.2% (42/95) at week 24. Of those accepting a prescription at week 1 (n = 69), 62.3% (n = 43) persisted on PrEP, 7.2% (n = 5) discontinued PrEP, and 30.4% (n = 21) were lost-to-follow-up (LTFU) by week 12. Of those declining a PrEP prescription at week 1 (n = 20), 30.0% (n = 6) remained off PrEP, 25.0% (n = 5) initiated PrEP, and 45.0% (n = 9) were LTFU up by week 12. Of the 48 women on PrEP at week 12, 47.9% (n = 23) persisted on PrEP, 29.2% (n = 14) discontinued PrEP, and 22.9% (n = 11) were LTFU by week 24. Of those declining a PrEP prescription at week 12 (n = 11), 27.3% (n = 3) remained off PrEP, 18.2% (n = 2) initiated PrEP, and 54.5% (n = 6) were LTFU by week 24. In our multivariable results (Table 3), WWID who accessed the SSP more frequently at baseline had greater odds of being retained in care at the end of follow-up compared with WWID who accessed the SSP less frequently (aOR = 1.46; 95% CI: 1.04 to 2.24). When the study ended, most women (37 of 42) indicated that they planned to continue PrEP.

About half of the sample self-reported taking all their medication at weeks 12 and 24 (Fig. 2A); this was not confirmed by urinalysis (Fig. 2B). Only 1 participant had prevention effective tenofovir levels (>1000 ng/mL) detected at weeks 12 and 24, although a sizeable proportion (15%–20%) had 10–1000 ng/mL of tenofovir detected, which is consistent with some level of adherence within the past week.

Safety and Tolerability

All participants had normal CrCl (≥60 mL/min) at baseline and week 24; 1 of 42 participants had decreased CrCl (33.3 mL/min), leading to PrEP discontinuation. No participants experienced side effects persisting for 12 weeks or longer or PrEP-related serious adverse events.

Care Preferences and Satisfaction

Most women preferred to receive future STI screening (54 of 89 at week 1) and their PrEP medications at the SSP as opposed to taking a paper prescription to fill elsewhere. Over the study period, 78.3% (54 of 69), 56.3% (27 of 48), and 60.0% (15 of 25) had medications delivered to PPP at weeks 1, 12, and 24, respectively (Fig. 1). At the final visit, most WWID reported preferring PrEP care at the PPP (32 of 36), satisfaction with services received (35 of 36), and most/all programmatic needs had been met (35 of 36).

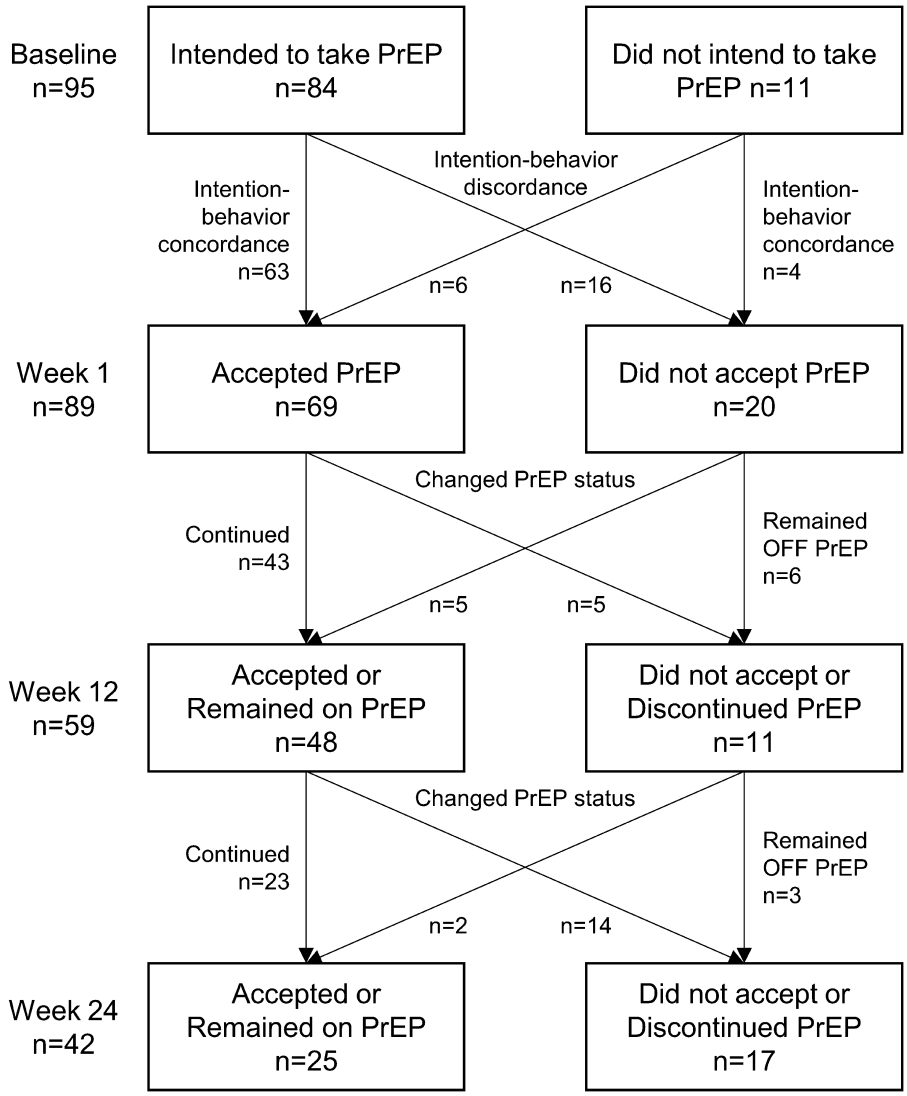

FIGURE 1. Flow diagram of PrEP intention, uptake, and retention in care at each study visit among women who inject drugs enrolled in a PrEP demonstration project in Philadelphia.

DISCUSSION

Our data demonstrate that WWID accessing SSP are at exceptionally high risk of HIV infection. The incidence rate during this small study of relatively short duration was higher than in other demonstration projects.[27–30] We also documented high rates of STI. This corroborates data from a pilot program based out of a mobile SSP in Camden (New Jersey, NJ) in which 1:4 women participants screened positive for STI.[31] These data confirm that WWID are a population among whom STI may be endemic, and sentinel surveillance is warranted. Identifying and treating acute infections can prevent deleterious health effects (eg, infertility) and reduce susceptibility to HIV.[32]

Once informed about PrEP, most of our participants expressed a desire to initiate it, and many went on to do so without additional intervention to increase uptake. Our results are consistent with survey work suggesting that PWID are interested in and willing to initiate PrEP.[15] Uptake was associated with 2 critical HIV risk factors, sexual assault and inconsistent condom use within 6 months of enrollment. Others have described the important role of sexual transmission of HIV in this population and suggested that sexual risk reduction strategies, delivered within the context of existing harm reduction programs, such as SSP, could help curb infections.[33] Our data suggest that women are interested in and willing to initiate PrEP. They also demonstrate the need to offer trauma-informed care for WWID and highlight the important role of SSP in providing postassault care to women. Findings from qualitative interviews with a subset (n = 25) of this sample suggest that experiences with sexual assault, a form of risk that women are susceptible to but unable to control, is an important motivating factor for PrEP uptake in this population.[34] Studies to better understand the role of trauma on PrEP uptake and persistence would be helpful for designing gender-specific prevention programs for WWID.

Engagement in later stages of the PrEP care continuum was more common than expected given the multitude of destabilizing factors reported by the participants (eg, high frequency drug use, homelessness, low income) known to

TABLE 3. Correlates of PrEP Uptake and Retention in Care Among Women Who Inject Drugs (n = 95) Enrolled in a PrEP Demonstration Project in Philadelphia

	A. PrEP Uptake		B. Retention in Care	
	OR (95% CI)	aOR (95% CI)*	OR (95% CI)	aOR (95% CI)†
Age, yr	1.00 (0.95 to 1.05)		1.07 (1.02 to 1.13)	
Race/ethnicity				
White, non-Hispanic	Ref		Ref	
Black, non-Hispanic	0.89 (0.28 to 2.82)		0.88 (0.27 to 2.73)	
Hispanic/Latino	0.78 (0.21 to 2.84)		1.59 (0.44 to 6.01)	
Mixed race, non-Hispanic	2.68 (0.22 to 33.6)		1.32 (0.15 to 11.6)	
Education				
Less than high school	Ref		Ref	
High school grad	0.93 (0.35 to 2.45)		0.45 (0.16 to 1.17)	
Some college or higher	1.30 (0.45 to 3.72)		0.67 (0.24 to 1.85)	
Currently homeless	1.01 (0.42 to 2.42)		1.29 (0.55 to 3.07)	
Current housing				
Own home	1.20 (0.19 to 7.62)		1.29 (0.22 to 7.78)	
Staying with family/friends	0.74 (0.26 to 2.07)		0.73 (0.25 to 2.03)	
Single room occupancy	1.14 (0.28 to 4.67)		1.08 (0.27 to 4.18)	
Living in shelter/treatment facility	1.36 (0.38 to 4.98)		1.73 (0.51 to 6.16)	
Living on street	Ref		Ref	
Frequency of SSP access	1.56 (1.16 to 2.09)	1.85 (1.24 to 2.77)	1.44 (1.08 to 2.06)	1.46 (1.04 to 2.24)
Sharing syringes	0.75 (0.32 to 1.73)		0.50 (0.21 to 1.13)	
No. sexual partners	1.00 (0.99 to 1.01)		1.00 (0.99 to 1.00)	
Inconsistent condom use	2.79 (1.03 to 7.53)	3.38 (1.07 to 10.7)	0.66 (0.24 to 1.74)	
Transactional sex	0.74 (0.29 to 1.85)		0.80 (0.33 to 1.97)	
Baseline STI diagnosis	0.96 (0.32 to 2.84)		0.64 (0.20 to 1.85)	
Sexual assault (n = 67)‡	5.03 (1.14 to 22.2)	5.89 (1.02 to 33.9)	1.52 (0.47 to 4.89)	
Self-perceived HIV risk				
Extremely/very unlikely	Ref		Ref	
Somewhat/very/extremely likely	1.29 (0.56 to 3.02)		0.78 (0.34 to 1.76)	

*Model was adjusted for follow-up period, age, race/ethnicity, and current housing.
†Model was adjusted for age, race/ethnicity, and current housing.
‡Model was restricted to women who received the question on sexual assault at baseline.

decrease health care utilization.[35,36] Despite these challenges, most women attended their visit scheduled at week 1, although this dropped by more than half over the study follow-up period. Retention in the pilot project was comparable (ie, men who have sex with men in the United States)[37] or higher than those reported in numerous PrEP projects with women in sub-Saharan Africa.[29,30] We speculate that retention in care in our study was driven in part by streamlining PrEP programming into known and needed services (eg, SSP).[38] A recent study among ciswomen offering PrEP in a

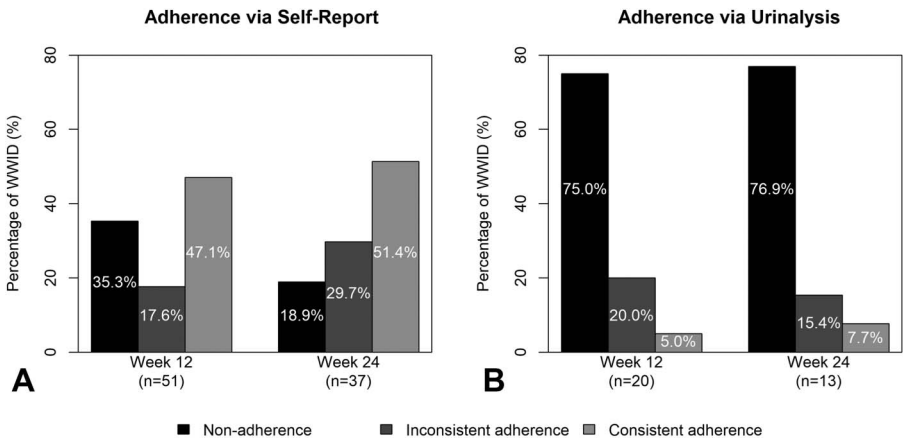

FIGURE 2. Self-reported adherence to PrEP (A) and tenofovir drug levels (B) at each study visit among women who inject drugs enrolled in a PrEP demonstration project in Philadelphia. The following categories describe adherence: nonadherent in the past 7–10 days (<10 ng/mL or taking 0 doses/week), inconsistent adherence in the past 7–10 days (10–1000 ng/mL or 1–5 doses/week), or consistent adherence in past 48 hours (>1000 ng/mL or 6–7 doses/week).

community sexual health setting reported retention of 61% at 3 months and 37.5% at 6 months.[39] A community university–affiliated PrEP program reported comparably lower retention (49%) among ciswomen and transgender men.[40] More focused research is needed to determine the implementation factors that may promote higher engagement in PrEP programs nested within high-value, existing services. Degree of trust, and mistrust of both the services providing PrEP and PrEP itself, community information, misinformation, and stigma are important to consider when positioning PrEP programs.[41,42]

In this vein, our findings highlight the need and potential domains for behavioral interventions to increase adherence in this population. Similar to other studies, self-reported adherence was overestimated compared with urine tenofovir levels, an objective biomarker of adherence.[43] This confirms the importance of collecting objective measures of adherence to validate self-report. These findings suggest that point of care tests that would allow for real-time and individualized delivery of intensive adherence counseling, or the provision of positive reinforcement, which would likely be beneficial for WWID, especially given the high threshold of adherence (6 of 7 doses/week) that women may need to achieve for maximal protection against HIV acquisition.[44] Other studies have also shown that women may initiate PrEP but quickly exhibit suboptimal adherence.[29,45,46] In future studies, it may be helpful to objectively measure adherence more frequently, especially during regimen initiation, and use this information to intensify support for women facing challenges to PrEP adherence.[47] Contingency management, an evidence-based intervention providing tangible rewards for behavior change, has been demonstrated to reduce substance use and improve HIV-related health behaviors, including treatment adherence among persons living with HIV.[48–52] Although there are concerns of the durability of intervention effects after incentives are discontinued, contingency management could provide unique opportunities for directly observed dosing to reinforce adherence.

From a safety perspective, all participants had normal baseline creatinine clearance. Although 1 of the 2 WWID who tested positive for hepatitis B surface antigen at baseline had suboptimal PrEP adherence, which can result in hepatitis B flares and liver injury,[53] no symptoms suggestive of liver injury were reported by this participant during his/her week-12 follow-up. These findings are consistent with reports from PrEP studies operating in categorical STD clinics[21,54] and may suggest that WWID are a population for whom PrEP is safe, as long as there is testing for renal function and careful monitoring of hepatitis B patients discontinuing PrEP, and ideally with laboratory measurement of biomarkers of liver injury. There is a growing body of literature demonstrating the effectiveness of same-day start programs to address challenges in traditional HIV treatment and prevention models.[54] Our data support the need for a pilot study to assess the impact of a same-day PrEP start program for WWID, a population for whom this approach has yet to be tested.

Finally, our team was experienced in drawing blood in this population, but phlebotomy remained challenging. Collapsed veins and scaring were common and are known complications of injection drug use. Programs for WWID should be prepared for these challenges, which are likely more common than for other PrEP populations and can impede PrEP monitoring.

Although this study provides preliminary data demonstrating the effectiveness of integrating PrEP and SSP services, our design has several limitations. First, we recruited a convenience sample from the SSP where clinical care was provided at no cost to a population with relatively high levels of insurance coverage (86 of 94). In other settings, cost might be a barrier to care that most of our participants did not face. Programs should plan to assist participants in enrolling in health insurance to ensure that they can access medications outside of a study. Second, we offered PrEP care during a weekly evening drop-in for women. Because many SSP have more male clientele than female clientele, it is likely that operating within a uniquely women's space had a positive impact on engagement, which might not generalize to programs without tailoring for women. Third, our sample consist predominately of white, cisgender women, and so our findings might not apply to racially and ethnically diverse populations. Our sample did reflect the demographic characteristics of women clients at PPP (Andres Freire, Director of Prevention Services, Oral Communication, September 3, 2020) and is similar to the larger population of PWID in Philadelphia.[55] Because Black and Latinx women are disproportionately burdened by HIV in the United States,[1] future studies should consider oversampling these women of color to culturally tailor interventions to maximize PrEP engagement. Given our small sample, we were unable to critically evaluate these potential nuances. Fourth, questions about acceptability and satisfaction were only captured at study exit, and because of a programming error, 6 of 42 survey responses were not recorded. Including these measures at exit could introduce bias because women retained in the study may have been more likely to hold more positive attitudes about their participation experience. Fifth, the lack of a comparison group limits the validity of our findings as do recall bias and social desirability bias, which are common in longitudinal, epidemiological studies. Finally, we acknowledge the limited generalizability of our results because SSP with less robust harm reduction services (ie, without existing clinical infrastructure) may face additional challenges to implementing PrEP as an additional service.

Together, our findings challenge the idea that daily PrEP is not a viable HIV prevention tool for PWID. Rather, we demonstrate that SSP are promising locations to reach WWID who would benefit from and are interested in receiving PrEP in this setting. Importantly, but not surprisingly, WWID will likely need additional supports to adhere and persist in care. Findings have implications for future interventions and programs to expand PrEP to WWID, a population increasingly burdened by HIV yet underrepresented in all phases of PrEP research and stigmatized in health care settings. Across settings research has shown that without adequate coverage of HIV prevention and treatment services, HIV outbreaks can escalate quickly through dense injection networks.[56] The emergence of HIV outbreaks during an unprecedented scourge of opioid-related overdose

deaths in the United States signals the need to aggressively scale-up evidenced-based interventions to prevent HIV to curb infections, including PrEP, among PWID. This first US-based demonstration project with WWID provides some key insight for programs and has implications for the delivery of longer acting formulations when they become commercially available.

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