PROTOCOL

Combination primary care and prevention services for women who inject drugs and exchange sex in Seattle, Washington

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Version 3.0

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STUDY TEAM

University of Washington
Maria Corcorran, MD, MPH (MPI)

Lauren Violette, MPH (Research Coordinator)

Shireesha Dhanireddy, MD (co-I)

Sara Glick, PhD (co-I)

Emily Williams, PhD (co-I)

Elizabeth Austin, MPH (qualitative data analyst)

Hennepin Healthcare
Jenell Stewart, DO, MPH (MPI)

University of California San Francisco
Monica Gandhi, MD, MPH (key personnel)

Study Organizations

UW
Dr. Maria Corcorran, MPI, is an Assistant Professor in the Division of Allergy and Infectious Diseases and oversees grant management with the Division's grant management team. Data management and use of the REDCap Database are through University of Washington. Additionally, the co-investigators and the project manager are University of Washington employees.

SHE Clinic
Dr. Maria Corcorran, MPI, and Dr. Shireesha Dhanireddy, co-I, are physicians and clinical directors of collocated clinics at the Aurora Commons, our community partner. For this project, medical record encounters for clinical visits will be extensions of SHE Clinic. Participants can follow up at SHE Clinic for any clinical care and/or test results on days when the SHE Mobile intervention is not available.

Aurora Commons
A nonprofit organization located in north Seattle on Aurora Avenue. Participants for formative work, informing this intervention, were recruited from Aurora Commons.

Public Health Seattle & King County (PHSKC)
PHSKC has agreed to use of a medical van for this research project. Additionally, the PHSKC will supply rapid HIV/syphilis tests and naloxone.

Hennepin Healthcare Research Institute (HHRI)
Dr. Jenell Stewart, MPI, is an Assistant Professor in the Division of Infectious Diseases at Hennepin Healthcare and the University of Minnesota, and is assisting in protocol development, project oversight, and analysis.

SUMMARY

Combination primary care and prevention services for women who inject drugs and exchange sex in Seattle, Washington

Design: Pilot of novel care model for low-barrier care and adherence support for uptake and sustained use of biomedical HIV prevention and medications for opioid use disorder for women who inject drugs

Study Population: 50 female-identifying people ≥18 years of age and older who have ever injected drugs and are not known to be HIV-positive

Study Site: Community-based clinic on north Aurora Avenue in Seattle, WA

Primary Study Objectives:

1. Evaluate uptake of PrEP and MOUD
2. Evaluate sustained use of PrEP and MOUD
3. Evaluate treatment completion rate and time to completion after POC STI testing
4. Assess acceptability of pilot community-based care model
5. Assess acceptability of POC STI testing at community-based site.

Approach: We will conduct a pilot study of a community-based novel care model developed with community feedback and a community advisory board (CAB) co-design process during phase I of this project. We will enroll 50 female-identifying people and follow them for 6 months. We will assess uptake of PrEP and buprenorphine; POC STI testing and treatment completion rates; sustained use of PrEP and buprenorphine at months 3 and 6 (n=50). We will conduct surveys, guided by CFIR, to assess and characterize the acceptability and feasibility of venue-based primary and HIV prevention care among women who inject drugs (WWID).

Background and rationale

Women who inject drugs (WWID) experience frequent barriers to receiving primary care, especially sexual health and addiction services, because of perceived stigma, competing needs, and structural inequities within the healthcare system. Barriers to care among WWID are often exacerbated by the additional social chaos of unstable housing and engagement in transactional sex. These structural realities promote exclusion from traditional primary care systems, increase risk of HIV acquisition, and have led to rising rates of syphilis infections and overdose deaths among WWID in recent years. PrEP, buprenorphine, and STI control are key components of the End the HIV Epidemic prevention pillar and proven tools for reducing risk of HIV acquisition and opioid overdose, but uptake and sustained use of these interventions are low among WWID.

A recent HIV outbreak among WWID in Seattle exposed the ongoing HIV risk faced by this population and highlighted major gaps in access to care. In response to this substantial, unmet need for combination primary care and prevention services, in 2018 we established the Safe. Healthy. Empowered. (SHE) Clinic, a weekly pop-up clinic for WWID. Operating only 4 hours per week, this walk-in primary care clinic, co-located with a day shelter, was able to engage over 190 socially and medically marginalized women in care. Preliminary data demonstrated a significant reduction in nonemergent emergency department visits among SHE Clinic patients as well as high initial uptake of HIV prevention and addiction treatment interventions, including PrEP, buprenorphine, and STI testing. Nevertheless, the impact of these interventions has been limited by poor adherence and follow-through, and preliminary needs assessment data indicate that many WWID would find an evening clinic, closer to where they sleep and work, more accessible and desirable.

Despite being at high risk for HIV acquisition, WWID face multiple barriers to accessing primary care. Common structural barriers, such as poverty, unstable housing, limited transportation, and the cost of medical care are compounded by a multitude of competing needs related to drug use and general safety and survival that impede WWIDs ability to access both traditional and non-traditional healthcare settings. These structural and individual-level barriers are exacerbated by the perceived stigma associated with injection drug use and exchange sex, and by the fact that harm reduction services are often targeted towards men and fail to incorporate gender-specific care for women. This gender disparity not only results in limited availability of reproductive healthcare, childcare services, and other services focusing on women's needs within harm reduction structures, but it also results in a lack of trauma-informed care for WWID. Furthermore, WWID lack access to much needed reproductive services, with prior studies in Seattle showing low rates of contraceptive use and high rates of unplanned pregnancies among this marginalized population. **Engaging WWID in combination primary care and HIV prevention is a challenge, and acceptability and reduced stigma are essential components to successful uptake and sustained use of evidence-based interventions.**

Pre-exposure prophylaxis (PrEP), buprenorphine, and sexually transmitted infection (STI) control are proven interventions for reducing risk of HIV acquisition, but their use among WWID remains low. PrEP reduces HIV acquisition among women, including WWID, and the Centers for Disease Control and Prevention (CDC) recommend the use of PrEP in PWID who share injection equipment and/or have overlapping sexual risk factors. Nevertheless, multiple U.S. cities report extremely low rates of PrEP use among PWID, ranging from 0 – 3%. Similarly, results of a recent systematic review revealed that PrEP uptake among PWID was low, between 0 – 3% across 23 studies, despite this populations' high willingness to use PrEP. Despite this, there are currently no recommendations or guidelines for how to best support PWID, in particular WWID, with PrEP use and adherence. Most domestic studies on PrEP for PWID characterized awareness

of, interests in and determinants of PrEP use, but lack novel interventions to improve PrEP uptake and sustained use. Medications for opioid use disorder (MOUD), including buprenorphine, similarly reduce the risk of HIV acquisition in WWID through a reduction in both needle-sharing and sexual risk behaviors. However, women are under-represented in both inpatient and outpatient substance use treatment programs, and, in comparison to their cisgender male counterparts, women delay treatment until further on in their addiction. The provision of low-barrier buprenorphine can improve uptake; however, sustained use of buprenorphine, and rates of adherence and retention in care may be less than 50% at 6 months across all genders of PWID. In addition to PrEP and MOUD, robust data supports the use of STI control in HIV prevention, due to the substantial increased risk of HIV acquisition associated with STI coinfection. Despite the existence of proven interventions, comprehensive sexual and reproductive healthcare tailored to WWID is lacking, even among those who exchange sex and experience high rates of STIs. Point-of-care (POC) testing provides an important opportunity to leverage venue-based healthcare to provide comprehensive services on a walk-in basis. The use of rapid POC STI testing nearly eliminates issues with patient loss to follow-up and incomplete or missing treatment, which continues to be a problem for STI case-detection based public health efforts.

In 2018, our team at the University of Washington established a weekly clinic, the Safe. Healthy. Empowered. (SHE) Clinic, to provide care for WWID and exchange sex. SHE Clinic is co-located and operated in collaboration with Aurora Commons, a not-for-profit drop-in center that provides basic needs and day-shelter for unhoused individuals in Seattle. HIV prevalence is approximately 10% among SHE Clinic patients, with 80% of patients engaging in injection drug use and 69% reporting exchange sex; although internal, unpublished estimates suggest the prevalence of exchange sex may be >90% in the SHE Clinic population. Initially operating only four hours per week, SHE Clinic, under the direction of Dr. Dhanireddy (co-I), has provided care to over 190 socially and medically marginalized women in Seattle. Nonemergent emergency department visits among SHE Clinic patients significant declined over a six-month period when compared with similar visits among WWID in north Seattle who had never received care at SHE Clinic. Uptake of PrEP (33%) and buprenorphine (49%) among SHE Clinic patients has improved significantly. Significant barriers to care remain for these socially and medically marginalized women. Despite the availability of PrEP and the high prevalence of HIV and HIV-risk factors in this population, sustained use of PrEP is exceedingly low (0-5%) among SHE Clinic patients after six months, as is sustained use of buprenorphine (12%) (**Preliminary Results**).

Addressing the gap in prevention and addiction services for PWID is a priority for reducing HIV incidence in King County, particularly in the wake of the recent cluster of linked infections among PWID. Through funding received from Ending the HIV Epidemic (EHE): A Plan for America, Public Health – Seattle and King County (PHSKC) plans to collaborate with SHE Clinic to expand daytime clinical services at the Aurora Commons drop-in center. The expansion of clinical care at Aurora Commons will add further opportunity for referral and linkage to care for WWID; however, it will not reach WWID who are unable to seek care during the day and are staying in exchange-sex venues even further north from Aurora Commons. **Furthermore, how to best optimize HIV prevention services, specifically for WWID, remains an unanswered question and a top research priority for PHSKC (Letter of Support)**. The PHSKC HIV/STD Program is looking to researchers and partner organizations (e.g., SHE Clinic) for guidance and support on evidenced-based practices and has a long history of collaboration with University of Washington (UW) researchers, with several dually-appointed researchers, including Dr. Sara Glick, a UW faculty member, PHSKC epidemiologist, and a study co-investigator.

WWID in north Seattle favor evening clinic hours at a location closer to where they sleep and exchange sex (Preliminary Results). These preferences highlight key accessibility and opportunity challenges created by traditional models of care within the United States – models that are not conducive to socially and medically marginalized populations. Although not yet

adopted in U.S. cities, there is considerable international experience providing care for female sex workers (FSWs) in venues for exchange sex. This form of co-located care helps to break down accessibility and opportunity challenges and has been shown to reduce the incidence of sexually transmitted infections (STIs), increase HIV prevention behaviors, improve linkage to care, and reduce the incidence of HIV among FSWs in countries across South America and sub-Saharan Africa. Leveraging lessons learned through the provision of venue-based care in the international setting, our multidisciplinary team will use a global to local approach to expand SHE Clinic through the creation and implementation of an evening pop-up clinic near venues for exchange sex and drug use in Seattle. Informed by a formative evaluation of the barriers, facilitators, and client-centered approaches to sustained PrEP and buprenorphine use, **this novel venue-based clinic aims to increase uptake and sustained use of proven HIV prevention interventions, including PrEP and buprenorphine, improve rates of STI testing and treatment among WWID, many of whom exchange sex, and serve as a model that can be further tested at scale.**

Study Design

General Overview

We will implement a pilot clinic one evening per week, with the primary goal of measuring a community-based extension of SHE Clinic's impact on uptake and sustained use of HIV pre-exposure prophylaxis (PrEP) and medications for opioid use disorder (MOUD). The clinic will be dispatched with a driver, nurse, physician, and research assistant. The van clinic will be outfitted with space to obtain a confidential history and physical exam and include a space for sample collection. Similarly, the van clinic will be equipped with a WiFi hotspot with a laptop linked to University of Washington's EMR system for clinical documentation, orders, and referrals. In addition to standard of care, (Table 1), we will provide participants with rapid point-of-care HIV and STI testing. All people presenting for a walk-in clinic visit who do not enroll will be offered laboratory-based testing and prescription medications, which are subject to insurance/billing. Women enrolled in the research study will be instructed on self-collection of vaginal swab specimens, which will be tested for *C. trachomatis* and *N. gonorrhoeae* using the 30-minute Binx Health rapid PCR platform. OSOM swabs for trichomonas will be placed into a sterile tube and processed on site with rapid testing kits (Sekisui Diagnostics) along with POC HIV and syphilis testing via finger prick (Chembio Diagnostic Systems). Any samples that cannot be tested using point-of-care methods will be transported to Harborview Medical Center laboratory following clinic sessions. Results will be delivered to participants, either immediately, via cell phone for lab-based tests or when a participant follows up at the mobile clinic or at SHE Clinic. STI treatment will be given per clinical guidelines. Treatment of gonorrhea will consist of intramuscular ceftriaxone 500mg x1. Participants who test positive for chlamydia will be recommended to take doxycycline 100mg PO BID for 7 days; however, azithromycin 1g PO x1 will be offered as an alternative if participants are unable to complete a 7-day course of antibiotics. Similarly, participants who test positive for trichomonas will be recommended to take metronidazole 500mg PO BID for 7 days; however, metronidazole 2g PO x1 will be offered as an alternative if participants are unable to complete 7 days of antibiotics. Early syphilis will be treated with 2.4 million units of benzathine penicillin x1 or oral doxycycline 100mg BID for 14 days, pending benzathine penicillin availability. Late latent syphilis will be treated with 2.4 million units of benzathine penicillin weekly for 3 weeks or oral doxycycline 100mg BID for 28 days, pending benzathine penicillin availability.

Results will be noted in participants' EMR for improved continuity of care across the healthcare system. Study participants who return for results (or receive them via phone) and undergo appropriate treatment, if necessary, will be eligible for a $15 travel reimbursement, as per SHE Clinic standard of care. This novel venue-based clinic will be integrated within the larger

University of Washington (UW) healthcare system, and necessary referrals will be made to UW facilities, including a large UW medical campus located two miles north of Aurora Commons. Participants not already registered in the UW system will receive a medical record number and clinical portions of study visits will be documented in electronic medical records to improve overall continuity of care. Referrals for syringe services will similarly be made to a local syringe service program. Additional dedicated research activities taking place in this care model will include surveys and adherence monitoring via dried blood spot (DBS), as detailed below. Adherence support will be incorporated into this model using established evidence-based approaches in response to the analysis of formative qualitative work and recommendations of the community advisory board.

Data Collection Overview

Clinical study visits will occur at enrollment, a follow-up study visit at month-3, and an exit visit at 6-months post-enrollment. For participants who are prescribed buprenorphine, additional brief refill visits will occur at monthly intervals. All assessments will occur during in-person visits in the pilot clinic. Each study visit will consist of a short survey, an eligibility assessment for oral PrEP and MOUD, standard clinical care, and biological sample collections (i.e., DBS sample collection for research only, self-collected vaginal swabs for point-of-care STI testing, and blood samples for blood born infection testing). To test the impact of this pilot clinic model on improving uptake and sustained use of HIV prevention services, we will utilize medical record data and DBS drug (buprenorphine and tenofovir) levels. Prior to enrollment, participants will be asked to provide consent for participation in the study, review of electronic medical record (EMR) data, and review of pharmacy records. Consent will be collected using electronic data capture (REDCap) and participant data will be collected by medical record number (MRN) utilizing an EMR querying technology (Leaf) generated by the University of Washington as well as manual chart review. Participants meeting CDC eligibility criteria for PrEP will be counselled on HIV risk, offered HIV testing, and if negative and interested, oral PrEP will be prescribed per clinical guidelines. Additionally, participants with active self-reported use of opioids will be counselled on options for opioid use disorder treatment, and those interested in MOUD, will be provided with a prescription for buprenorphine-naloxone or buprenorphine, per clinical guidelines. Uptake of PrEP and buprenorphine will be measured by review of pharmacy and EMR records and will be defined by filling a prescription for PrEP or buprenorphine. In collaboration with Dr. Monica Gandhi and the University of California San Francisco (UCSF) Hair Analytical Laboratory (HAL), we will measure sustained use of PrEP and buprenorphine via tenofovir disoproxil fumarate (TDF) and buprenorphine levels in samples of 150 hairs. The UCSF-HAL can simultaneously test for buprenorphine, fentanyl, and tenofovir from the same specimen, and we will measure these drug levels at 3- and 6- months to evaluate adherence to PrEP and buprenorphine. Additionally, dried blood spots (DBS) will be collected and archived to ensure that drug levels are collected during this study in the event there are any complications with hair testing.

At each visit, brief demographic and behavioral surveys will be administered to women enrolled in the study via tablets, with responses recorded in REDCap. At the end of each visit an additional survey assessing acceptability of venue-based care will be administered to each participant. Questions will be informed by the CFIR and designed to assess the acceptability and relative priority of venue-based primary and HIV prevention care among women seeking services. *As part of an assessment of* acceptability, questions will also focus on the perceived stigma associated with receipt of care at the pop-up van clinic near a venue for drug use and exchange sex. Following completion of the intervention, information on feasibility, implementation barriers and facilitators will be collected using semi-structured interviews with

clinical staff to contextualize logistical and structural barriers faced by venue-based service delivery.

Screening and Recruitment

Overview of screening and recruitment

Flyers advertising the venue-based clinic will be posted at local harm-reduction and social service sites: the Aurora Commons, People's Harm Reduction Alliance, Mary Pilgrim Inn, The Gateway, WeCare Methadone Clinic, and at other locations within the community, based on the suggestions of the community advisory board. All women who present to the venue-based clinic will be screened for possible enrollment using a brief survey programed into REDCap. Screening surveys will be self-administered, unless the participant requests that a clinic team member assist them in filling out responses to screening questions. Women who meet inclusion criteria will be provided with brief information about the study and asked if they would like to learn more. Women who express interest in the study will then be connected to the research assistant, who will explain the study in more detail and go through the informed consent process. Women who agree to participate will provide informed consent via REDCap on a study tablet housed within the clinic. Women who are ineligible for the study, or those who do not wish to participate, will still be allowed to access standard of care medical services within the venue-based clinic.

Screening questions

1. How old are you?
2. What's your gender identity?
3. Have you ever injected drugs, even just once, in your lifetime?
4. Have you ever been tested for HIV?
    a. If yes, when and what was the result?

Inclusion Criteria

- ≥18 years of age
- Female identifying
- Ever injected drugs
- Not known to have HIV
- Willing and able to provide informed consent to participate in the study

Exclusion Criteria

- <18 years of age
- Never injected drugs
- HIV positive
- Medical or psychological co-morbidities that prevent participation per study team assessment.
- Non-English speaking

Informed Consent

Consent will be obtained by trained research staff from participants who meet all inclusion criteria. Care will be taken to ensure that the treating physician and nurse do not obtain consent from potential participants and that the informed consent conversation can occur in a private space. The study will be thoroughly described by research staff to potential participants. The research staff will give the subjects adequate time to look at and read the electronic consent form, summarize each section, and ask the subjects if they understand. Potential participants

will have the opportunity to ask questions about the study and study procedures. Individuals who choose to participate and are deemed able to provide informed consent will fill out and sign an electronic informed consent document in REDCap (via a study tablet).

After the participant has signed, the research staff will have the opportunity to review the form to ensure that it is correctly signed and dated. A copy of the consent form will be given to the participant in print or via email, per their preference. Completed consent forms will be stored electronically in the UW REDCap account.

Study Visits

Enrollment study visit

Enrollment will occur at the time the informed consent document is electronically signed. Following enrollment, each participant will be given a unique study ID to prevent duplicate enrollments. The study ID will consist of the patient's last initial, first initial, and the day they were born. The baseline study visit will occur immediately following enrollment and will consist of completing a baseline health questionnaire, counseling for HIV risk reduction, counseling for treatment of opioid use disorder (if applicable), point of care (POC) STI testing, POC HIV testing, offering oral PrEP for HIV risk reduction (if applicable), and offering buprenorphine for treatment of opioid use disorder (if applicable). All participants will also be offered laboratory-based STI testing of the oral and rectal sites. Participants who consent for PrEP will also have phlebotomy performed for serum creatinine, hepatitis B serologies, and a 4th generation HIV antigen/antibody assay. Clinic staff will also address any immediate medical concerns of the participant and treat as able per standard of care. At the enrollment study visit, each participant will be given a $25 Visa gift card for their participation.

In addition to reimbursement for each study visit, participants will receive a financial incentive of $15 for returning to receive any test results that required off-site lab testing, as is standard of practice at our community partner, Aurora Commons/SHE Clinic. Participants on buprenorphine will also receive $15 each time they return for monthly refills. Financial incentives will be paired with low-barrier, walk-in care and adherence counseling at each visit

Baseline study visit data collection

An electronic health questionnaire will be filled out by participants in REDCap using a clinic tablet. Research staff will be allowed to assist the participant in filling out the electronic health questionnaire, if the participant chooses. The questionnaire will assess for risk factors for HIV, PrEP eligibility, prior use of PrEP, history of substance use, prior use of medications for opioid use disorder (MOUD), and current use of MOUD. At the end of the study visit, each participant will complete a brief electronic survey in REDCap. This survey will assess the patient's overall experience receiving care at the venue-based clinic and assess the level of acceptability and perceived stigma associated with venue-based care.

During or immediately following the visit, the clinic staff will fill out a visit summary report in REDCap, indicating the results of POC STI and HIV testing, any STI treatment given, if the participant was prescribed PrEP or reasons they were not prescribed PrEP, and if the participant was prescribed buprenorphine or reason the participant was not prescribed buprenorphine.

Follow-up study visits, Month 3 and Month 6 (Exit visit)

All patients will be asked to return to the clinic 3 months and 6 months following enrollment. At these follow-up study visits, patients will undergo additional counseling for HIV risk reduction

and treatment of opioid use disorder, as indicated based on their individual risk and substance use behaviors. At both the Month 3 and Month 6 visits, all patients will fill out a brief questionnaire self-reporting substance use and sexual behavior in the past three months. Participants who were previously prescribed PrEP through the venue-based clinic will fill out questions about their adherence to PrEP and barriers/facilitators to taking PrEP. Participants who were previously prescribed buprenorphine will similarly fill out questions about their adherence to buprenorphine and barriers/facilitators to taking buprenorphine. All participants who received a prescription for PrEP or buprenorphine will be asked to provide a 150-strand hair sample and a DBS sample for tenofovir and/or buprenorphine drug level checking. Any participant not previously initiated on PrEP or buprenorphine will be offered PrEP and/or buprenorphine at the follow-up study visits, as indicated per practice guidelines. Participants will be tested for STIs using POC testing, and any participant diagnosed with an STI will received prompt treatment prior to leaving clinic, as outlined in the "Study Design: General Overview" section of this protocol. Additionally, participant will be offered laboratory-based STI testing of the oral and rectal sites. Participants who initiated PrEP will have phlebotomy performed for a 4th generation HIV antigen/antibody assay. Participants who did not initiate PrEP at baseline but initiate PrEP at month 3 or 6 will also have phlebotomy for serum creatinine and hepatitis B virus (HBV) serologies. Clinic staff will similarly address any immediate medical concerns of the participant, as per standard of care. At the end of each follow-up study visit, participants will be given a $25 Visa gift card for their participation.

In addition to reimbursement for each study visit, participants will receive a financial incentive of $15 for returning to receive any test results that required off-site lab testing, as is standard of practice at our community partner, Aurora Commons/SHE Clinic. Financial incentives will be paired with low-barrier, walk-in care and adherence counseling at each visit.

Hair samples and DBS samples will be placed in individual, labeled small plastic bags and returned to study facilities at Harborview Medical Center for safe, secure storage following each clinic session.

Follow-up study visit data collection

An electronic follow-up health questionnaire will be filled out by participants in REDCap using a clinic tablet. This will occur at both the 3 and the 6-month follow-up visits. Research staff will be allowed to assist the participant in filling out the electronic health questionnaire, if the participant chooses. The questionnaire will assess sexual practices and substance use behaviors in the prior 3 months, as well as self-reported adherence to PrEP (if prescribed), barriers and facilitators to taking PrEP (if prescribed), self-reported adherence to buprenorphine (if prescribed), and barriers and facilitators to taking buprenorphine (if prescribed). At the end of the study visit, a short survey will be complete to assess the patient's overall experience receiving care at the venue-based clinic and assess acceptability and the level of perceived stigma associated with venue-based care.

During or immediately following the visit, the clinic staff will fill out a visit summary report in REDCap, indicating the results of POC STI / HIV testing, if the participant was prescribed PrEP, reason they were not prescribed PrEP (if applicable), if the participant was prescribed buprenorphine, and reason the participant was not prescribed buprenorphine (if applicable).

Refill visits

Due to prescribing laws, participants who initiate buprenorphine-naloxone or buprenorphine will be given a maximum of one month of therapy at a time. As such, they will be asked to come

back for brief refill visits every month. No additional research data collection will occur during these refill visits. Participants will receive a $15 incentive for returning for buprenorphine refills.

Standard of Care

All female identifying persons who present to the venue-based clinic will be eligible for receipt of HIV and STI testing, as well as oral PrEP and MOUD, regardless of participation in the research study. Similarly, study participants will be eligible for care if they visit the venue-based clinic for interim visits outside of their designated study visits (e.g., baseline, 3-months, 6-months, montly refills for buprenorphine). Standard of care will include checking vital signs, addressing any immediate health concerns as able/feasible within the van clinic, laboratory-based HIV screening, laboratory-based STI testing, and prescription of oral PrEP and/or MOUD, though many services will require billing and insurance claims through the healthcare system and women will be made aware of these prior to initiating these services (e.g., laboratory-based testing, prescription drugs) (Table 1).

Table 1. Study Procedures

Study Visit Month	0	3	6	Refill visits and Interim non-study visits
General Research Activities				
Obtain informed consent	X			
Screen for inclusion/exclusion	X			
Collect updated contact information	X	X	X	X
Reimbursement	X	X	X	
Research Questionnaires				
Demographic information	X			
Behavior (sexual and drug use and risk perception)	X	X	X	
Adherence to PrEP and/or MOUD		X[b]	X[b]	
Acceptability of venue-based care	X	X	X	
Health and acute healthcare need	X	X	X	X
Provider clinical summary report	X	X	X	X
Standard of care				
Medication review	X	X	X	X
General symptom assessment	X	X	X	X
Blood pressure checks	X	X	X	X
Supply condoms	X	X	X	X
Contraception counseling and provision/referral	X[ab]	X[ab]	X[ab]	
Laboratory Pregnancy testing	X[ab]	X[ab]	X[ab]	X[ab]
Narcan prescription	X[a]	X[a]	X[a]	X[ab]
Laboratory HIV test	X[ab]	X[ab]	X[ab]	X[ab]
Laboratory STI (CT/GC and TV) genital testing	X[ab]	X[ab]	X[ab]	X[ab]
Laboratory STI (CT/GC) pharyngeal and rectal testing	X[ab]	X[ab]	X[ab]	X[ab]
Laboratory Syphilis testing (IgG and/or RPR)	X[ab]	X[ab]	X[ab]	X[ab]

	Laboratory Hepatitis B serologies	X[ab]			
	Laboratory Creatinine check	X[ab]		X[ab]	
	Laboratory Hepatitis C testing	X[ab]			X[ab]
	Suboxone prescription	X[ab]	X[ab]	X[ab]	X[ab]
	PrEP prescription	X[ab]	X[ab]	X[ab]	X[ab]
	STI treatment	X[ab]	X[ab]	X[ab]	X[ab]
	Referral to specialty care	X[ab]	X[ab]	X[ab]	X[ab]
Research Clinical Care					
	POC HIV/Syphilis testing (rapid test)	X	X	X	
	POC Trichomonas screening (self-collected vaginal swab)	X	X	X	
	POC CT/NG testing (self-collected vaginal swab)	X	X	X	
	Hair sample collection (for TFV and Bupe levels)	X	X	X	
	Dried Blood Spot (for TFV and Bupe levels)	X	X	X	
	Financial Incentive for Returning for Results (following study visits)	X[b]	X[b]	X[b]	X[b]
[a]only for those who consent to billing/insurance claim **[b]If clinically indicated**					

Lab Processing and Results Delivery

Study specific labs will include hair sample and DBS collection for detection of tenofovir and buprenorphine levels, as well as self-collected vaginal swabs for POC STI testing and POC fingerstick HIV and syphilis testing.

Hair testing:
Hair samples will be sent to the Hair Analytical Laboratory (HAL) at the University of California San Francisco (UCSF-HAL). The HAL uses liquid chromatography-tandem mass spectrometry (LC-MS/MS) for testing. The HAL has found high rates of acceptability and feasibility (>95%) of collecting hair samples among U.S. adolescents and women. Our group has experience with hair collection across studies and has found it acceptable.

HAL will test hair sample for tenofovir and buprenorphine levels, as indicated based on medications prescribed to each participant. Results of hair sample testing will be used for research purposes only to determine adherence to prescribed medications, and results will not be returned to the individual participant.

DBS testing:
Dried blood spots will be obtained at baseline and at quarterly follow-up visits (Month 3 and Month 6) using a lancet finger stick to express drops of blood onto a 5-spot DBS card. This will be done following collection of a blood droplets from finger for the HIV/syphilis rapid test. The card will be labeled with participant ID and transported to PI's locked office where they will be securely stored for possible TFV and buprenorphine testing.

POC STI testing:
Chlamydia and Gonorrhea testing
Participants will give their self-collected vaginal swab specimen to clinic staff prior to survey completion. Participants will collect a vaginal swab in a private space in the study clinic. POC STI tests for *C. trachomatis* and *N. gonorrhoeae* will be available within 30 minutes using a small, FDA approved, CLIA waived PCR machine supplied by Binx Health. POC STI samples

will be processed in real time, with results delivered to participants during the study visit, and no samples stored.

Trichomoniasis testing
POC STI test for *T. vaginalis* will be available within 10 minutes using individual FDA approved, CLIA waived lateral flow OSOM tests. This trichomonas rapid antigen test does not require equipment or a machine to process and is an immunochromatographic capillary-flow enzyme immunoassay based on trichomonas membrane proteins. Women will be instructed on self-collection of vaginal swab specimens. OSOM swabs will be placed into a sterile tube and processed on site. Results will be delivered in real-time and no samples will be stored.

Syphilis testing:
A rapid combination HIV/syphilis test (Chembio Diagnostic Systems) will be used to evaluate for *Treponema pallidum* antibodies. Any positive syphilis antibody test will be followed by laboratory-based confirmatory testing. Using shared decision making empiric treatment may be given (or initiating depending on stage of syphilis) prior to receiving confirmation of diagnosis.

HIV testing:
A rapid combination HIV/syphilis test (Chembio Diagnostic Systems) will be used to evaluate for incident HIV infections. Samples will be processed using the Chembio microreader kit. Any positive HIV test will be considered a possible seroconversion. Participants will be counseled on unconfirmed possible HIV diagnosis, the need to stop taking PrEP, and the need for laboratory-based confirmatory testing, which can be drawn on-site. All questions on HIV and HIV testing will be answered. Laboratory-based 4th generation HIV Ab/Ag test and HIV viral load will be drawn with samples sent to Harborview Medical Center, and participants will be linked to the SHE Clinic for next day follow-up.

Laboratory studies for clinical care:
Phlebotomy samples for standard of care labs will be centrifuged (as indicated), labeled, and transported back to Harborview Medical Center (HMC) on ice, where they will be delivered directly to the HMC lab for processing. Results will be reported out in the electronic medical record (EMR). The research team medical provider will call patients to deliver critical and urgent results. If the patient/participant is not reachable by phone, the research team medical provider will enlist the assistance of SHE Clinic staff to help in locating the patient/participant. Patients/participants will be asked to return the venue-based clinic the following week, or they can present to SHE Clinic during daytime hours, to follow-up on results.

Management of new diagnoses
Participants found to have a diagnosis of chlamydia, gonorrhea, trichomoniasis, or syphilis will be offered prompt treatment. Treatment of gonorrhea will consist of intramuscular ceftriaxone 500mg x1 provided in clinic. Participants who test positive for chlamydia will be recommended to take doxycycline 100mg PO BID for 7 days; however, azithromycin 1g PO x1 will be offered as an alternative if participants are unable to complete a 7-day course of antibiotics. Similarly, participants who test positive for trichomonas will be recommended to take metronidazole 500mg PO BID for 7 days; however, metronidazole 2g PO x1 will be offered as an alternative if participants are unable to complete 7 days of antibiotics. Early syphilis will be treated with 2.4 million units of benzathine penicillin x1 or oral doxycycline 100mg BID for 14 days, pending benzathine penicillin availability. Late latent syphilis will be treated with 2.4 million units of benzathine penicillin weekly for 3 weeks or oral doxycycline 100mg BID for 28 days, pending benzathine penicillin availability. Single dose medications will be available in clinic. Otherwise

prescriptions will be sent to the Harborview Long-term Care Pharmacy for delivery to SHE Clinic within 48 hours. Participants with clinical concern for complicated STI (i.e., PID) will be offered prolonged treatment (single dose IM ceftriaxone and 2-week course of doxycycline and metronidazole) and referred for prompt follow up in SHE Clinic, another primary care clinic, or urgent care as indicated. Participants will be encouraged to tell partners to also be treated and made aware that these are reported by the lab to public health department. Should patients develop signs or symptoms of an STI at any point in the study they may come to the study clinic for additional laboratory-based testing (including for BV or candida infections) and treatment if needed.

Management of HIV

Patients who test positive for HIV on rapid or follow-up laboratory-based testing will be counseled on strategies to prevent transmission and referred to SHE Clinic for urgent evaluation and initiation of antiretroviral therapy, per clinical guidelines.

Management of pregnancy

Participants found to be pregnant will be counseled on referral options and supported as needed with rapid referral for OB care at the UW Northgate Family Medicine Clinic, as well as follow up at SHE Clinic. Participants will be counseled on PrEP and MOUD safety and efficacy during pregnancy.

Management of viral hepatitis

Participants diagnosed with hepatitis B virus (HBV) and/or hepatitis C virus (HCV) will be counseled on strategies to prevent transmission and referred to SHE Clinic for further evaluation and management.

Management of acute opioid overdose or severe intoxication

In the event that participant presents to the research clinic and is found to be severely intoxicated or experiencing an acute opioid overdose, emergency medical personnel will be called for transport to a local emergency department. In the case of an opioid overdose, the individual will be given intranasal Narcan by research clinic staff.

Research Reimbursement and Incentives

Participants will receive up to a total of $75 in reimbursement for participating in this study. They will be reimbursed $25 for the baseline study visit, $25 for the 3-month study visit, and $25 for the 6-month study visit. Reimbursement will be provided in the form of a Visa gift card, that will be giving to the participant at each study visit. Participants who return to the venue-based clinic between study visits for clinical care will not be reimbursed for interim visits. Participants who return to the research clinic to receive results of laboratory tests will receive an additional $15 incentive for follow-up. Persons who are not participants in this study but access the venue-based clinic for standard of care will not receive any reimbursement or financial incentive. Study team members will retain a log of each reimbursement provided, and participants will be asked to sign their initials on the log to confirm receipt of each $15 Visa gift card.

Protection of Human Subjects

Involvement of Human Subjects

This is a prospective observational cohort study, which aims to enroll 50 women who inject drugs in a venue-based clinic. Study participants will be offered HIV PrEP and buprenorphine for treatment of opioid use disorder, as indicated by national guidelines. The main objective is to

assess the impact of venue-based care on uptake and sustained use of PrEP and buprenorphine for the prevention of HIV and treatment of opioid use disorder, respectively.

Research Material Obtained from Participants

Individuals who are eligible and enroll in venue-based care will complete a baseline, 3-month and 6-month study visit. Data to be collected at those visits include information on demographics, risk factors for HIV, PrEP eligibility, prior use of PrEP, history of substance use, prior use of medications for opioid use disorder (MOUD), current use of MOUD, and self-reported adherence to PrEP and/or MOUD, as indicated. Participants will also provide information on their experience accessing venue-based care, including acceptability and perceived stigma associated with accessing venue-based care. POC HIV testing, POC STI testing, and standard of care labs for PrEP will be obtained at baseline, 3-months and 6-months. Hair samples and DBS samples to test for tenofovir and buprenorphine will be obtained at 3-month and 6-month visits. A review of the participants medical and pharmacy records will be conducted.

Assessment data will be collected directly onto iPads used by research team members. We will utilize the Research Electronic Data Capture (REDCap) system through the University of Washington's Institute of Translational Health Services (ITHS) to log and store data.

Women who are started on buprenorphine therapy will also return for monthly refill visits, during which time no additional study data will be collected.

Risks to Human Subjects

There are limited physical risks to study subjects beyond what is incurred during standard primary care. Participants may experience mild bruising or pain at the site of point of care finger prick testing (e.g., POC HIV and syphilis testing, DBS sampling), or at the site of phlebotomy draws. Participants who choose to initiate on oral PrEP and/or buprenorphine will be at risk of experiencing established side effects, as outlined in each drugs' prescribing materials.

Participants may experience psychological distress associated with discussing confidential topics such as sexual and drug use practices. Research medical team staff will be trained in trauma-informed care and to address psychological distress with a calm, non-judgmental attitude. We will take steps to minimize any psychological discomfort by ensuring confidentiality as described below. We will only enroll patients who understand the study procedures and are willing to participate.

Participants may also experience loss of confidentiality related to study visits, which is likely the most serious risk of the study. We take this risk seriously, and we will take steps to protect participants' confidential data and anonymity. All subjects will be informed of risks and provide their consent prior to enrollment.

Adequacy of Protection Against Risks

Risks of psychological distress from the research assessments will be minimized by using research medical staff that are trained in how to provide trauma-informed care. Participants may choose to leave the study visit at any time. If consequences arise due to research procedures (e.g., distress, anxiety, suicidal thoughts), then the physician investigators will be available to assess subjects in real time and make appropriate interventions or referrals based on the clinical circumstances.

Loss of confidentiality is very unlikely given the structures that will be put in place to avoid inadvertent disclosure. These structures to assure confidentiality include the following: each subject will receive a unique identification number, and research data collection and data entry forms will be electronic and identified only with this number. Only the master enrollment list and electronic informed consent forms will have identifying information on them. These documents will be kept on secure University of Washington servers / in REDCap, accessible only to principal investigators, the research assistant and research coordinator. Tracking information will be kept similarly. Computer data will be password protected and accessible only to research staff needing the information for follow-up and monitoring purposes. Files stored on UW servers will be protected by electronic firewalls that restrict access to designated users.

Another possible threat to confidentiality could arise if a participant indicates an imminent danger to self or others or if a participant discloses abuse of vulnerable persons such as children, the elderly, or the disabled. Ethical and legal requirements may force us to disclose this type of information to relevant authorities. We will attempt to minimize this threat to confidentiality by clearly informing participants of the risks involved during the informed consent process.

Potential Benefits

Participants may benefit from access to research POC STI testing, which is not generally commercially available. Participants may similarly benefit from the reimbursement provided for attending study visits and returning for lab results.

Importance of Knowledge to be Gained

The study will inform us about the ability of venue-based care to improve and support uptake and sustained use of critical HIV prevention interventions, including PrEP and buprenorphine, for women who inject drugs, many of whom also engage in exchange sex. It will also inform us about the acceptability and feasibility of providing venue-based care for women who inject drugs. If the study demonstrates benefit of venue-based care, this would provide evidence that this type of intervention should be studied at scale.

Electronic Health information

This novel venue-based clinic will be integrated within the larger University of Washington (UW) healthcare system, and necessary referrals will be made to UW facilities, including a large UW medical campus located two miles north of Aurora Commons. Participants not already registered in UW system will receive a medical record number and clinical portion of study visits will be included in electronic medical records to improve overall continuity of care. Participants will consent to a review of their health information in the UW Epic EHR system and review of local pharmacy records.

Incarcerated Participants

As per NIH guidance, research participants who become incarcerated during the study will be temporarily withdrawn from the study until OHRP guidelines are met. When subjects are incarcerated their buprenorphine and PrEP treatment may not be continued, and they do not have access to cell phones, so they cannot continue participation for these reasons. When subjects become released from incarceration, we will resume study procedures. If research staff members are unable to contact a participant who has missed an appointment or cannot be reached to remind them of an upcoming research visit, research staff should check the local law enforcement databases to determine if the study participant is incarcerated.

Important Definitions

Adverse Event (AE)

Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure.

Serious Adverse Event (SAE)

Any adverse event that results in any of the following outcomes:

- Death
- Life-threatening
- Event requiring inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability/incapacity
- Results in birth defect

Unanticipated problems/events

They must meet all of the following criteria (per UW definition):

1) Unexpected-- The harm (or potential harm) is inconsistent with risk information previously reviewed and approved by the Institutional Review Board (IRB) in terms of nature, severity, or frequency as well as the characteristics of the study population

2) Related or probably related to participation in the research. Probably related: there is reasonable (more likely than not) that the incident, experience or outcome may have been caused by the procedures involved in the research, or that it is associated with the use of any drug, biologic, or medical device that is part of the research.

3) Suggests that the research placed (or did place) one or more subjects or other a greater risk of harm than was previously know or recognized. This includes physical, psychological, economic, educational advancement, or social harm.

Classifying adverse events

Adequate review, assessment, and monitoring of adverse events require that they be classified as to ***severity***, ***expectedness***, and potential ***relatedness*** to the study intervention. Study protocols will include a description of how adverse events will be classified in these terms and the appropriate course of action.

Severity

Classifications often include the following:

- ***Mild:*** Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.
- ***Moderate:*** Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning
- ***Severe:*** Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating

Severity is not synonymous with seriousness. A ***severe*** rash is not likely to be an ***SAE.*** Likewise, a ***severe*** headache is not necessarily an ***SAE.*** However, ***mild*** chest pain may result in a day's hospitalization and thus is an ***SAE.***

Expectedness

AEs must be assessed as to whether they were expected to occur or unexpected, meaning not anticipated based on current knowledge found in the protocol, investigator brochure, product insert, or label. Categories are:

• ***Unexpected -*** nature or severity of the event is not consistent with information about the condition under study or intervention in the protocol, consent form, product brochure, or investigator brochure.

• ***Expected -*** event is known to be associated with the intervention or condition under study.

Relatedness
The site investigator assesses the potential event relationship to the study intervention and/or participation. A comprehensive scale in common use to categorize an event is:
• *Definitely Related*: The adverse event is clearly related to the investigational agent/procedure – i.e. an event that follows a reasonable temporal sequence from administration of the study intervention, follows a known or expected response pattern to the suspected intervention, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the subject's clinical state.
• *Possibly Related:* An adverse event that follows a reasonable temporal sequence from administration of the study intervention follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors.
• *Not Related:* The adverse event is clearly not related to the investigational agent/procedure. - i.e. another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible.

Data Safety Monitoring Plan
The principal investigators (MPIs) will be responsible for ensuring participant safety on a day-to-day basis. The MPIs (Dr. Maria Corcorran and Dr. Jenell Stewart) along with the Data Safety Monitoring Board (DSMB) will oversee the safety of participants and the validity and integrity of the data. Drs. Corcorran and Stewart will be responsible for selecting the DSMB members and ensuring they have no conflicts of interest with the current study or principal investigators.

DSMB Responsibilities
The DSMB will be responsible for reviewing and evaluating the study protocols, plans for participant safety, and data monitoring plan prior to study enrollment. The DSMB will also evaluate the study progress, including participant recruitment, enrollment, and retention, data collection, and general operations of the venue-based clinic. The DSMB will evaluate for treatment harm or benefit, including individual AEs and SAEs, and make decisions regarding the continuation, modification or termination of the study based on these data. The DSMB will also review external information, if relevant to the study, that might affect the ethics of study continuation (e.g., new therapeutic advances that impact standard of care).

Cadence of DSMB meetings
The DSMB will meet remotely with study MPIs:

1. Prior to enrollment
2. Once the study has reached 50% enrollment (n=25)
3. At least every 6 months thereafter while the study is active.

Following each meeting, the DSMB will make recommendations on continuation, modification, or termination of the study. Aside from these regular meetings, an unanticipated AE may prompt an ad hoc report to be distributed and may result in an ad hoc teleconference for the entire DSMB. Upon study completion no additional meetings will be required of the DSMB.

DSM Reporting

Following each meeting the DSMB will produce a report that will be sent to the UW IRB within 10 days and to NIDA within 30 days of the DSMB meeting. The report will include a meeting summary, DSMB recommendations regarding the continuation, modification, or termination of the research project, and any other specific recommendations put forth by the DSMB.

Analysis Plan

1. Evaluate uptake of PrEP:
    a. Defined as the proportion of participants who accept a prescription for PrEP from the study team at any point (i.e., baseline, Month 3, and/or Month 6 visit) during study participation. The denominator will be all participants (N=50) enrolled in the study.
    b. Participants who accept prescriptions for PrEP at multiple points throughout the study will only be counted once when calculating uptake.
    c. Final analysis will present uptake as a percentage (proportion).
2. Evaluate uptake of MOUD
    a. Defined as the proportion of participants who accept a prescription for MOUD from the study team at any point (i.e., baseline, Month 3, and/or Month 6 visit) during study participation. The denominator will be all participants (N=50) enrolled in the study.
    b. Participants who accept prescriptions for MOUD at multiple points throughout the study will only be counted once when calculating uptake.
    c. Final analysis will present uptake as a percentage (proportion).
3. Evaluate sustained use of PrEP
    a. PrEP: Dried blood spot (DBS) samples were obtained at each visit to assess PrEP adherence via tenofovir-diphosphate (TFV-DP) concentrations. Sustained use was defined as >4 doses/week, resulting in a DBS TFV-DP concentration of >700 fmol/sample at 3 and/or 6 months post-enrollment among those prescribed PrEP at a preceding study visit.
    b. Final analysis will present sustained use for both PrEP as a percentage (proportion).
4. Evaluate sustained use of MOUD
    a. MOUD: DBS samples were obtained at each visit to assess MOUD adherence via buprenorphine and norbuprenophrine concentrations, both measured in ng/mL. Sustained use was defined as any buprenorphine and/or norbuprenophrine detected, resulting in a DBS >0 ng/mL concentration of buprenorphine and/or norbuprenophrine at 3 and/or 6 months post-enrollment among those prescribed MOUD at a preceding study visit.
    b. Final analysis will present sustained use for MOUD as a percentage (proportion).
5. Evaluate STI treatment completion rate and time to completion after POC STI testing
    a. Treatment completion will be defined as documented treatment following a reactive POC STI test (chlamydia, gonorrhea, syphilis, and/or trichomonas). Treatment will either be indicated in the Visit Clinical Summary from the study visit or noted during medical record chart review by a study provider. If treatment

was not provided on the same day as the visit, the date of treatment will be documented in the study database.

b. Final analysis will present the treatment completion rate as the proportion of STIs where treatment was documented, by all STIs and by type.
c. Final analysis will present the time to treatment completion as the proportion of STIs treated same-day. Of the STIs not treated same-day, time to treatment will be presented as median number of days with an interquartile range.

6. Assess acceptability of pilot community-based care model
    a. Participants completed an acceptability survey following each study visit. Acceptability will be presented by study visit (i.e., enrollment, Month 3, and Month 6) as a proportion of all enrolled participants (N=50) who responded to the following questions:
        i. “I feel confident that my health is improved by getting care in a mobile clinic.” (Agree, Somewhat agree)
        ii. “I feel safe getting care in a mobile clinic.” (Agree, Somewhat agree)
        iii. “I am worried about how people will react if they see me getting care at a mobile clinic.” (Disagree, Somewhat disagree)
7. Assess acceptability of POC STI testing at community-based site.
    a. Participants completed an acceptability survey following each study visit. Acceptability will be presented by study visit (i.e., enrollment, Month 3, and Month 6) as a proportion of all enrolled participants (N=50) who responded to the following questions:
        i. “I felt comfortable getting rapid STI testing in the mobile clinic.” (Agree, Somewhat agree)
        ii. “I prefer getting rapid tests for sexually transmitted infections (STI) more than getting traditional STI tests.” (Agree, Somewhat agree)