IRB Study Number: 20210017

Mobile delivery of PrEP at a Syringe Services Program—A Pilot Study

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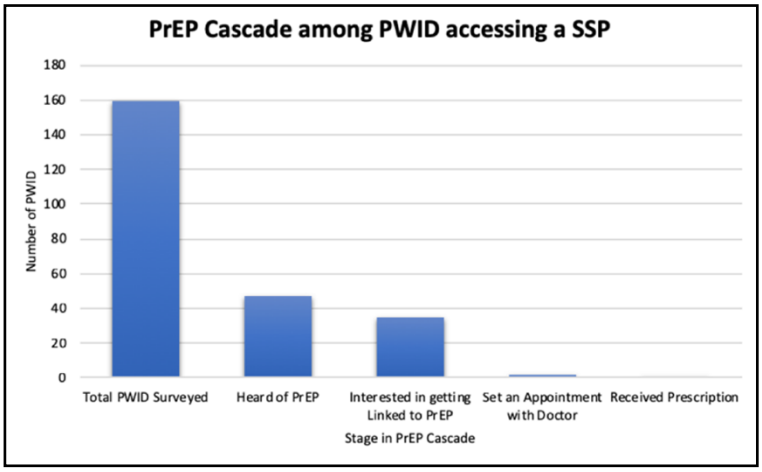
1) **Protocol Title:** Mobile delivery of PrEP at a Syringe Services Program—A Pilot Study

2) **Objectives***

Aim 1: To develop a sustainable protocol for *Rapid Mobile PrEP* initiation at the IDEA Syringe Services Program (SSP).
Aim 2: To assess the acceptability and feasibility of *Rapid Mobile PrEP* for People Who Inject Drugs (PWID) who utilize the Miami IDEA SSP.

3) **Background***

PrEP is an understudied and underutilized HIV prevention strategy for PWID. PrEP has been widely studied in MSM. The evidence for daily oral PrEP is compelling; clinical trials have demonstrated risk reduction of 44-86% in HIV infections for those receiving PrEP with efficacy >90% for those taking the medication more than 4x/week (6-11). The Bangkok Tenofovir Study showed a 48.9% decrease in HIV incidence in PWID who took daily tenofovir compared to those who took placebo, as well as significant interest among PWID in continuing PrEP after the trial. However, there has been a large gap in the literature about PrEP in PWID since that trial. In Miami, our preliminary data from the National HIV Behavioral Surveillance (NHBS) IDU4 cycle showed that of 434 participants, 88.5% would take an HIV prevention pill if it were available to them at no cost. Through our recent CFAR pilot award, we assessed knowledge and interest in PrEP at the IDEA SSP among HIV negative clients (n=159). Of PWID surveyed, 70% were not aware of PrEP. Of those with knowledge about PrEP, 75% were interested in linkage to PrEP and received a referral for PrEP services. However, only 6% made an appointment with a provider to be evaluated for PrEP, and ultimately no one surveyed received a prescription for PrEP. These findings suggest willingness to use PrEP among PWID at the IDEA SSP, yet overwhelming barriers to PrEP use including low PrEP awareness and the same structural and economic barriers that we have documented in MSM populations (cost, transportation, language issues, stigma, and immigration status).



4) **Inclusion and Exclusion Criteria***

Inclusion criteria for this study are: 1) over the age of 18, 2) speak either English or Spanish, 3) ability to provide informed consent, 4) currently enrolled in the SSP and have exchanged at least two times in the past three months, 5) have a negative HIV rapid test result, 6) estimated creatinine clearance > 30 ml/minute for Descovy and >60 for Truvada. Individuals will be excluded from this study if they 1) do not meet the above criteria of inclusion, 2) decline to participate, 3) test positive for HIV via rapid test, 4) are pregnant or plan on becoming pregnant 5) have symptoms acute HIV. *Any other comorbidities that at the discretion of the investigator would prevent the participant from participating in the study.*

5) **Study Design**

To create a sustainable protocol for dissemination of our *Rapid Mobile PrEP* initiation at future Florida SSP expansion sites (Aim 1):
Firstly, we will develop a protocol for initiation of *Rapid Mobile* PrEP at the Miami IDEA SSP site. Throughout the grant period, we will continuously update our protocol through rapid feedback and implementation of new approaches to overcome encountered problems as they arise. In addition to academic dissemination of our work, we will produce an adaptable protocol for new SSPs as they expand throughout the state. We will enroll a prospective, open-label cohort, similar to the PrEP Demonstration Project at the Miami-Dade County Health Department, assessing uptake, adherence, and retention.

Acceptability and feasibility of *Rapid Mobile PrEP* among SSP clients (Aim 2):
We will pilot test mobile PrEP at the IDEA SSP (N=100), conducting ongoing brief qualitative assessments and process improvement and developing sustainable protocol for adaptation at Florida's SSP expansion sites in geographic hotspots. We will report the proportion of eligible PWID who elect to initiate *Rapid Mobile PrEP* to understand acceptability among at-risk PWID. Likewise, we will report correlates of initiation and retention. We hypothesize that coupling PrEP services with the provision of syringes and harm reduction equipment will increase retention in this *Rapid Mobile PrEP* initiation study.

We will conduct detailed interviews including demographics, drug and sexual risk behaviors, and medical history. Labs will include: HIV via 4th generation test, HBsAg, gonorrhea/chlamydia (urine, rectal, pharyngeal), syphilis, creatinine, and HCV RNA. Participants will be offered immediate FTAF at the IDEA SSP on the first encounter and will meet with the peer navigator for a medication management and adherence plan that may include on-site storage of medications and deliveries of PrEP coupled with provision of injection supplies.

If a participant becomes ineligible for PrEP during follow up based on renal function, other adverse events, or HIV infection, they will be contacted and discontinued from the study. Participants who test positive for HIV during study follow up will be linked to HIV care. Participants with chronic hepatitis B virus infection will be contacted immediately by the clinician for a discussion of the risks and benefits of FTAF in the context of chronic hepatitis B. Finally, PWID who decline study enrollment will be asked to participate in a brief survey that will include demographics, reason for declining, PrEP awareness and knowledge, and perceived HIV risk. Those who decline the study will receive $25 cash payment for this brief, 30 minute interview.

The effectiveness of PrEP requires that it be taken every day minimizing missed doses as well as continuing PrEP over time during periods of potential HIV exposure. Follow up visits will occur at 1, 3, 6, 9 and 12 months. At each study visit participants will complete surveys about PrEP use since their last visit including semiqualitative/open-ended questions about reasons for use or non-use. We will use this combination of quantitative and qualitative data to determine individual and structural contributors to non-adherence and discontinuation of PrEP among PWID. For each study visit including baseline, participants will receive $50 cash payment.

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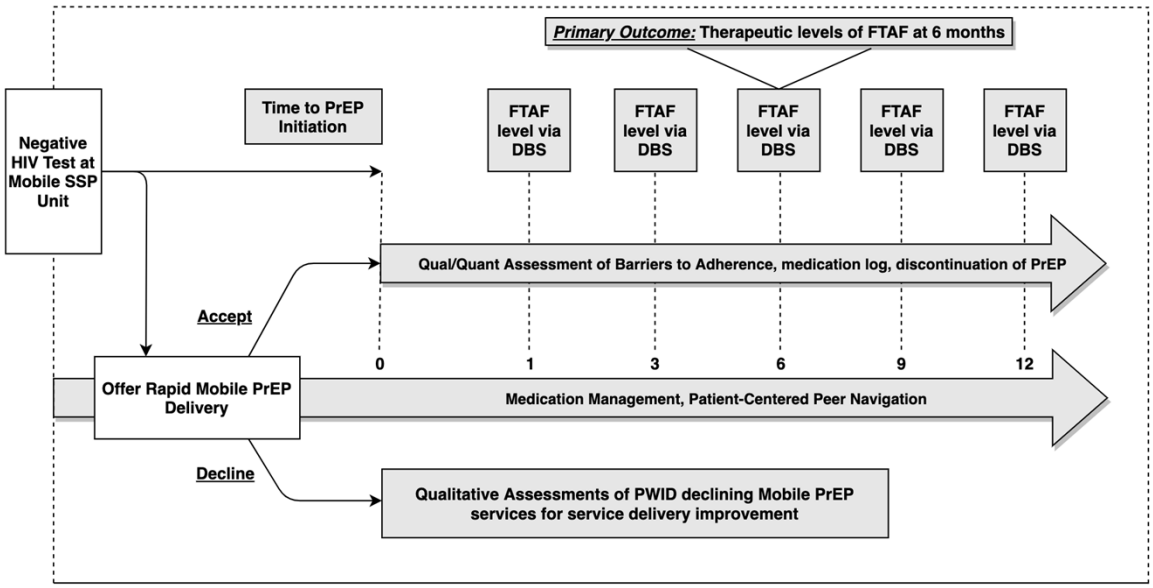
6) **Arms and Interventions**

This single arm pilot study will assess the effectiveness of on site initiation of PrEP and followup at an SSP (fixed site or mobile exchange on outreach). The study is 1 year duration, and study visits are conducted at at 0, 1, 3, 6, 9 and 12 months as outlined above. The intervention is delivery of PrEP outside of a traditional healthcare clinic. The principal medication offered will be FTAF 200/25mg tablet to be administered orally. In this study, we will offer Descovy to men and trans women due to decreased risk of side effects. If the participant is a assigned female at birth, Truvada will be prescribed instead of study drug per FDA approval. **It is noted that signigicant risk for HIV among PWID is sexual.** The intervention will include wraparound support by the peer navigator. Study visits will be conducted either at the IDEA Exchange fixed location, or on the mobile unit in the community (e.g. homeless encampments). The fixed site and mobile unit are equipped with private rooms for medical encounters. Medical visit with a provider and phlebotomy will be provided on site.

7) **Procedures Involved***

Figure 1. Conceptual Framework for *Rapid Mobile PrEP*



8) **Primary Endpoints**

Patient-Level Outcomes	Definition	Implementation Construct Domain	Definition
PrEP levels at 6 month follow up (primary)	Intracellular levels of tenofovir diphosphate (TFV-DP) by dried blood spot (DBS).	Acceptability/feasibility of Rapid Initiation of PrEP	Number of PWID at risk for HIV that enter *Rapid Mobile PrEP*
Time to PrEP initiation post negative HIV	Number of days between receiving negative HIV test	Acceptability/feasibility of Rapid Initiation of PrEP	Mean time to PrEP initiation among PWID.

rapid test (secondary)	result and initiating PrEP, by self-report		
PrEP Persistence	TFV-DP levels on DBS, pill counts, medication log, appointment attendance	Barriers to persistence	Exploration of challenges to PrEP persistence

9) **Data and Specimen Banking***

For clinical data, we will use the UHealth's electronic health record, UChart, which is locked under dual authentication.

All data collected will be housed in the REDCap database system, which is locked under dual authentication by University of Miami Information Technology and then extracted for analysis by the principal investigator. Only study staff will have access to survey results.

As for the in-depth interviews, sessions will be audio-recorded, transcribed by an external company, de-identified for analysis and stored on a password-protected computer in a secured office in the Don Soffer Clinical Research Center. Only study staff will have access to results.

10) **Data Management***

Quantitative Data Analysis: Quantitative data will be analyzed using descriptive statistics and frequencies to examine the acceptability and feasibility characteristics of the PWID participants. Categorical data will be analyzed using frequency of responses and continuous variables will be analyzed using means and standard deviations. To assess barriers and facilitators to PrEP initiation (uptake), adherence, and retention, we will use Cox proportional hazard models to identify significant predictors for uptake, adherence, and retention on PrEP, and retention data will be presented as Kaplan-Meier survival plots. Multivariable models will be built to control for age, gender, race/ethnicity, insurance status, and income. Variables of association interest include: self-reported barriers to PrEP, sexual and injection risk behaviors, substance use, and social determinants of health (e.g., homelessness).
All quantitative data will be stored and managed in REDCap and all analyses will be performed using SAS statistical software (Version 9.4; SAS Institute, Cary, NC).

Qualitative Data Analysis: Qualitative data collected from the in-depth interviews will be analyzed using general inductive methodology, which allows for themes to be developed from the raw data based on a study objective/research question. A data codebook will be generated in an iterative process during transcript reading by the study team. All qualitative data analysis will be conducted using Dedoose (version 8.2.14, Sociocultural Research Consultants, Los Angeles, CA), a cross-platform software used for analyzing qualitative and mixed methods research.

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11) **Risks to Subjects***

Study procedures: there is risk of discomfort to phlebotomy, but no risk above a routine sexual health visit

Study Drug: Serious risks of taking Truvada and Descovy includes serious drug reactions such as lactic acidosis, hepatomegaly with steatosis, hepatotoxicity, hepatitis B virus exacerbation, pancreatitis, nephrotoxicity, bone density loss, neutropenia, immune reconstitution syndrome, autoimmune disordersand angioedema. Common adverse reactions include diarrhea, headache, fatigue, elevated CK, abnormal dreams, dizziness, insomnia, hypercholesterolemia, hyperamylasemia, neutropenia, LFTs elevated, nausea/vomiting, depression, rash, dyspepsia, abdominal pain, asthenia, increased creatinine, arthralgia/myalgia, cough, paresthesia, peripheral neuropathy, palmar-plantar hyperpigmentation, hypertriglyceridemia, hematuria, hyperglycemia, glycosuria, rhinitis and flatulence.

Risk of HIV acquisition in PWID is extremely complex. This study is to assess the acceptability on on-site iniation of PrEP and persistence over 1 year. Importantly, Descovy is preferred for PrEP due to decreased nephrotoxicity and bone toxicity. However, the initial studies were only in men who have sex with men and transwomen. Therefore, we will prescribe Descovy, the preferred medication to those who meet eligibility i.e. MSM or transwomen. We will prescribe Truvada to cis women while explaining the increased risk of loss of bone mineral density and renal function. Importantly, HIV outbreaks in this country among PWID, including in Miami, and their resultant investigations have all indicated that sexual risk, especially from sex work, plays a major role in HIV acquisition. Therefore we will offer different PrEP medications only because the studies for Descovy have not yet been conducted in women.

12) **Adverse Events and Serious Adverse Events**

AEs will be any of the common adverse reactions defined above. SAEs will include any hospitalization or death or disability that occurs with participants in the trial. AEs will be reported to the IRB in continuing reviews. SAEs will be reported to the IRB within 24 hours.

The following AEs of interest will be collected and reported: lactic acidosis, hepatomegaly with steatosis, hepatotoxicity, hepatitis B virus exacerbation, pancreatitis, nephrotoxicity, neutropenia, immune reconstitution syndrome, autoimmune disordersand angioedema.

13) **Potential Benefits to Subjects***

The potential benefit to the PWID is that they will be able to access rapid on-site PrEP initiation with few barriers, improving their overall health in the short and long term.

14) **Vulnerable Populations***

This study will exclude children because the providers are board certified in Internal Medicine and only see adult patients. Children will be rapidly referred to University of Miami Department of Pediatrics.

15) **Setting**

The IDEA Syringe Services Program of the University of Miami Miller School of Medicine is the study site.

16) **Resources Available**

Dr. Hansel Tookes (Contact PI) is a board-certified internist. Dr. Tookes was the driving force behind the establishment of the IDEA SSP and serves as the PI of the UM Harm Reduction Research Group. Dr. Tookes has extensive knowledge regarding HIV prevention among PWID and has utilized community-based research approaches to improve health outcomes among this vulnerable population.

Dr. David Serota (co-I) is a board-certified infectious disease specialist and internist. He specializes in the treatment of severe infections in PWID. He has extensive knowledge regarding HIV prevention in this high priority community, and a leader in harm reduction in our community.

Dr. David Forrest (co-I) is a medical anthropologist who brings expertise in advanced qualitative methods and research to inform HIV prevention among at-risk populations. Dr. Forrest is co-PI for the Miami-Dade site of the National HIV Behavioral Surveillance and has over 25 years of expertise conducting research among PWID.

Dr. Tyler Bartholomew (co-I) has expertise conducting HIV and HCV implementation research among PWID, including the implementation and evaluation of HIV/HCV testing and linkage to care at the IDEA SSP.

Dr. Katrina Ciraldo (co-I) is a board certified Family Medicine and Addiction Medicine specialist. She specializes in womens health with a focus on pregnant women with substance use disorders who are experiencing homelessness. Dr. Ciraldo has extensive knowledge in addiction medicine and innovator in the harm reduction community.

Dr. Teresa Chueng (co-I) is finishing her Infections Disease clinical fellowship at Jackson Memorial Hosptial and will start her appointment as Assistant Professor of Clinical Medicine in the Division of Infectious Diseases at the University of Miami Miller School of Medicine in July 2022. Dr. Chueng provides expertise in clinicial infectious disease, including HIV, hepatitis C, and infections related to injection drug use.

17) **Prior Approvals**

Funding agency approval: none

18) **Recruitment Methods**

Recruitment will be through the IDEA SSP participants with regular usage of SSP services (at least 1 visit per month). All PWID with a negative rapid HIV screen will be offered participation in this study. If they accept, SSP staff will refer to study research assistant for more information regarding this clinical trial. Study staff will be discrete from SSP staff to prevent possible undue influence.

Local Number of Subjects

The proposed study aims to pilot the *Rapid Mobile PrEP* protocol for 100 PWID at risk for HIV. We will ask 50 PWID who decline to participate in a brief qualitative assessment to explore reasons for declining treatment.

19) **Confidentiality**

The REDCap surveys will be anonymous and do not solicit protected health information or any identifying information. If results of this survey are reported to any agency, or in journals or at scientific meetings, data will be de-identified and presented in aggregate. In addition to the research staff, the following entities may review information collected as part of this survey activity: 1) Office of Human Research Protections (OHRP), 2) University of Miami Human Subjects Research Office, and 3) professionals who may be evaluating this survey activity

The in-depth interviews audios and transcripts will be stored in a password-protected file that will be stored on University of Miami secure network. Audio will be deleted immediately after transcription.

In order to secure the data, all staff will be trained on confidentiality via the CITI program including Human Subjects Research and Good Clinical Practice

20) **Provisions to Protect the Privacy Interests of Subjects**

All data will be stored on the PI's password protected computer and data will only be shared via secured access Sharepoint with other members of the research team. The computer is secured by UM IT, kept in a locked office in the Soffer Clinical Research Center. Qualitative data will be transcribed and stored on the PI's computer and shared only with the research team. Audio will be deleted immediately following transcription. Copies of the informed consent with patient signature will be stored in a locked filing cabinet within the PI's keycard secured office.

21) **Consent Process**

Written consent will be obtained at the IDEA SSP by study staff.

(See attached consent documents for reference)

22) **Process to Document Consent in Writing**

Writtten consent (provided both in English and in Spanish) will be obtained using e-consent in REDCap. REDCap e-Consent Framework provides standardized tools to obtain consent and store consent documentation with a certification screen and a storage function which automatically generates a "hard-copy" PDF of the signed form.