Implementation of onsite, rapid ART initiation among People Who Inject Drugs living with HIV at Syringe Services Program

Protocol Version 2
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1) **Protocol Title:** Implementation of onsite, rapid ART initiation among People Who Inject Drugs (PWID) living with HIV at Syringe Services Program (SSP)

2) **Objectives***

Aim 1: To evaluate/assess the effectiveness and feasibility of same-day rapid initiation of ART for PWID living with HIV who utilize the SSP *(SSP Rapid Initiation)*.
Aim 2: To identify barriers to success of HIV care retention and treatment adherence among PWID preparing for entry into long-term HIV care.
Aim 3: To compare adherence of patients in *SSP Rapid Initiation* after transition to a traditional healthcare clinic.

3) **Background***

PWID experience extensive barriers to engagement in HIV care. Challenges in linkage to care, retention in care, and viral suppression in PWID are well documented, with estimates that less than half of PWID living with HIV in the U.S. are virally suppressed[5,6]. In the 2018 Miami outbreak investigation and public health response in PWID, we were able to support 100% of newly infected individuals in achieving viral suppression through a test-and-treat approach with intensive patient navigation and medication management; but faced challenges in initiating ART in previously diagnosed PWID, with only 53% achieving suppression. Reasons for this sub-optimal result could include recognized barriers to HIV care and retention within the Miami community, including drug use, mental illness, stigma and transportation issues[7,8]. Although Miller et al.[9] recently reported that intensive and flexible patient navigation with psychosocial counseling was central to increased initiation of ART and viral suppression, the literature on evidence-based approaches to initiation of ART and retention in care for PWID is lacking.

Why Test and Treat? Early HIV diagnosis and immediate ART initiation are essential to rapidly decrease viral load, reduce the impact of outbreaks, and improve quality of life among PWID[10,11,12]. Established Test and Treat paradigms have shown decreased time to virologic suppression, the ultimate goal of controlling HIV transmission among PWID and their sexual partners[13]. However, traditional healthcare systems may not be the ideal environment to initiate HIV care in PWID, a population so stigmatized by the healthcare system and society at-large that they often avoid care due to profound distrust and structural barriers. ART initiation at an SSP is potentially an ideal venue, bringing services to the patient and making healthcare easily accessible. With SSPs just beginning in Florida, an *SSP Rapid Initiation* approach developed at the Miami IDEA SSP will enable new programs to rapidly implement pathways to rapid ART initiation.

4) **Inclusion and Exclusion Criteria***

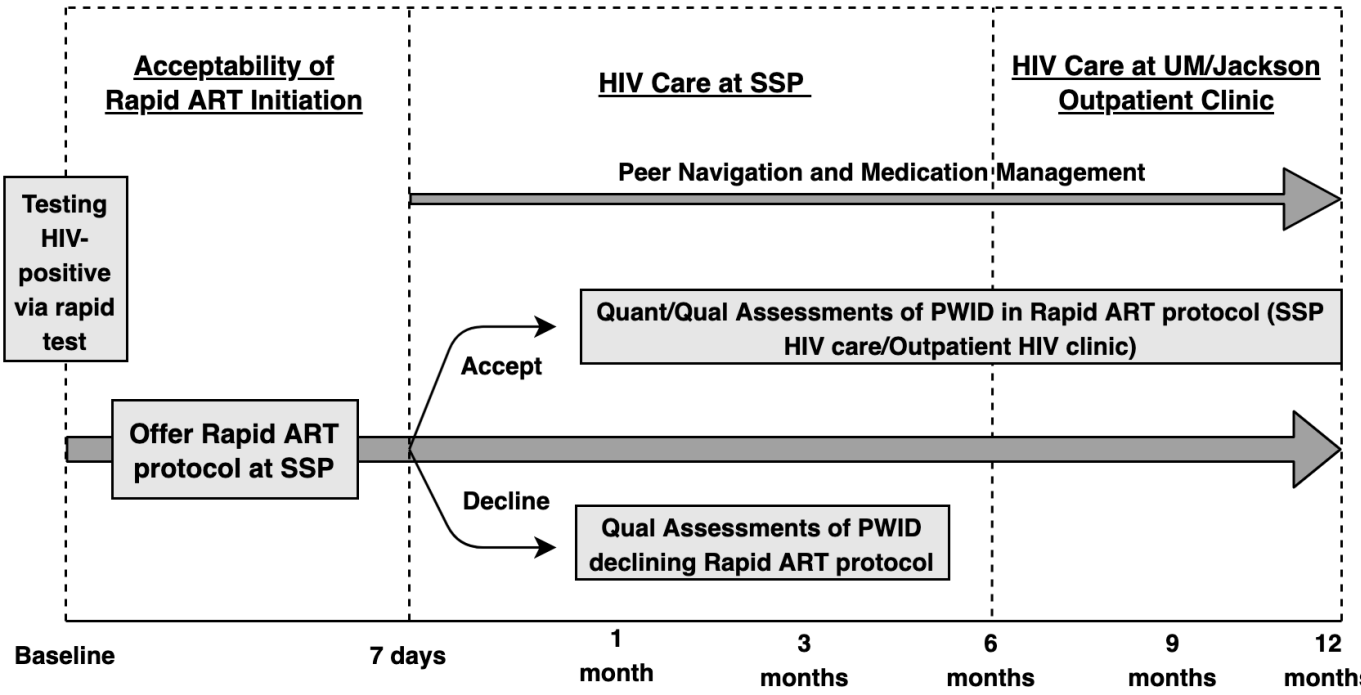
1) Adult (age>18 years); 2) positive rapid HIV test; 3) ability to provide informed consent; 4) HIV RNA > 200; 5) creatinine clearance > 30 as measured by serum creatinine; 6) no allergy to bictegravir/emtricitabine/tenofovir alafenamide (BFTAF) as indicated by patient history and self-reported allergies. *Any other comorbidities that at the discretion of the investigator would prevent the participant from participating in the study*.

5) **Study Design**

We plan to utilize a hybrid quasi-experimental design to test the effectiveness and implementation outcomes of successful delivery of rapid ART initiation intervention in an SSP (Figure 1). In addition, we will use a multi-method approach, collecting both quantitative and qualitative data on patients (n=50) accepting the rapid ART initiation protocol at the SSP, patients declining to engage in the rapid ART initiation protocol, and patients after transition to a traditional Ryan White clinic. To assess the effectiveness of the *SSP Rapid Initiation*, we will compare the percentage of PWID virally suppressed at 6 months post baseline at the SSP compared to at 6 months post transition to UM/Jackson Adult Outpatient HIV Clinic. Since this proposed study is in its pilot phase, this study will not be examining differential effects in treatment groups in the study, but rather provide preliminary data to support a future randomized-controlled trial. Represented in the figure below, participants at the SSP will be tested for HIV using a rapid test, which when reactive will be confirmed using a second rapid HIV test from another manufacturer following a CDC-approved dual rapid HIV testing algorithm. If a patient tests positive, the patient will be offered immediate initiation onto ART at the SSP. Baseline labs (4^{th} Generation HIV test, HIV viral load, CD4, HIV genotype, CBC, CMP, Gonorrhea/Chlamydia, RPR, HCV Antibody, HCV RNA, HbsAg, HBsAb, HAV Total) will be obtained and sent to the Miami-Dade County Health Department. Patients will have up to 7 days post HIV-positive test to start on ART (per definition of rapid ART initiation). The community advisory board and peer navigators at the SSP will assist in the *SSP Rapid Initiation* protocol design, execution, and process improvement. Peers will work between the SSP and the Ryan White clinics. Our experience with the 2018 HIV cluster in PWID in Miami taught us that medication management (i.e., pill lockers at the SSP, third party pickup of ART at ADAP by SSP staff, weekly medication drops to participants unable to access medications at the fixed site) was highly effective at supporting adherence in PWID living with HIV. Peer navigators will conduct outreach to *SSP Rapid Initiation* participants, monitor appointments, and provide transport to healthcare services. This intensive linkage and active follow-up delivered by peer PWID living with HIV is essential to delivery of care to this population. Peers will be tasked with helping participants with eligibility (e.g., Ryan White, Medicaid) and ADAP enrollment when they transition to the transitional HIV clinic. This grant will enable them to have ongoing support in clinic after transition to the traditional healthcare environment for long-term care.

Patients who decline engagement in ART after one week will be asked to partake in semi-structured interviews. Patients who accept will be initiated onto ART at the SSP. A medication adherence plan will be developed for each patient by SSP staff to optimize medication adherence. Quantitative and qualitative assessments exploring barriers and facilitators of HIV treatment adherence will be given at 1, 3, 6 and 12 months post treatment start date. In addition, HIV viral load will be measured at 1, 3, 6, 9 and 12 months post treatment start date to assess viral suppression.

Figure 1. Conceptual Framework of *SSP Rapid Initiation* Pilot Study



Quantitative Assessments of those accepting rapid ART

Baseline assessment of participants will include socio-demographics, drug and sexual risk behaviors, HIV knowledge, and SSP utilization. If re-engaging: date of HIV diagnosis, previous HIV clinic attendance, previous ART exposure, and reason(s) for discontinuing ART. Follow-up assessments will include a side effect inventory, mental health screening, timeline follow-back on ART adherence, timeline follow-back on drug use.

Qualitative Assessment of those accepting rapid ART

Qualitative assessments will include patient perspectives on HIV diagnosis and living with HIV, including both HIV and PWID stigma. The interviews will explore which symptoms are most important to the patient, their experience with ART in the past and experience on BFTAF in the current study, and facilitators and barriers to ART adherence in the past and in the current study. These assessments will also include formative feedback on ART initiation at the SSP, medication management at the SSP, follow-up HIV care at the SSP, and barriers and facilitators to transition to a more traditional HIV clinic for long-term care. Those who are eligible for the study will be consented and asked to participate in a 30-minute interview conducted at the IDEA SSP for which they will receive $50

Qualitative Assessment of those declining rapid ART

In-depth interviews with PWID living with HIV who do not engage in treatment with 7 days of HIV test result will be conducted. We anticipate conducting 10 interviews, which is sufficient to achieve data saturation and will be conducted within 3 months post HIV test result. Inclusion criteria are: 1) 18 years of age or older; 2) enrolled in the IDEA SSP; 3) HIV positive rapid test result; 4) English or Spanish speaking, 5) declined rapid ART initiation at the SSP. Those who are eligible for the study will be consented and asked to participate in a 30-minute interview conducted at the IDEA SSP for which they will receive $25.

These semi-structured interviews will explore: 1) the role of key personal and structural barriers to engagement in HIV care (e.g., transportation, poverty, and stigma); 2) perceived benefit of engaging in rapid initiation of HIV care on personal health outcomes (i.e., viral

suppression); 3) reasons for declining rapid ART initiation protocol (e.g., prior clinic experience, previous ART side effects), 4) recommendations for structuring the intervention to maximize participant engagement (e.g., physical location, hours of operation, duration, and frequency); 5) recommendations for intervention facilitator demographics and training; and 6) current knowledge, attitudes, and awareness regarding HIV treatment in PWID. All interviews will be audio-recorded and transcribed verbatim by an external transcription company.

6) **Arms and Interventions**

This single arm pilot study will assess the effectiveness of on site initiation of HIV care 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 HIV care outside of a traditional healthcare clinic. The medication offered will be BFTAF, 50/200/25mg tablet to be administered orally. 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***

	Screening	**0**	**1**	**3**	**6**	**9**	**12**
Lab Assessments	HIV Rapid	HIV Ag/Ab Test HIV RNA CD4 count HIV genotype CBC CMP GC/CT RPR HCV Ab HCV RNA HBsAg anti-HBs Anti-HAV Total	HIV RNA CD4 count CBC CMP	HIV RNA CD4 CBC CMP GC/CT RPR	HIV RNA CD4 CBC CMP GC/CT RPR	HIV RNA	HIV RNA
Assessments	Eligibility	Baseline		Quant/Qual	Quant/Qual		Quant/Qual

Participants at the SSP will be tested for HIV using a rapid test, which when reactive will be confirmed using a second rapid HIV test from another manufacturer following a CDC-approved dual rapid HIV testing algorithm. Confirmatory testing no longer requires venipuncture. A 4th generation test will be sent as indiated below. The initiation of care, however, will not be delayed. If a patient tests positive on dual rapids, the patient will be offered immediate initiation onto ART at the SSP. If accepted, they will provide informed consent. They will have an immediate HIV care visit with a provider in person or via encrypted Zoom technology. A prescription for BFTAF will be written and filed for the participant, and BFTAF will be provided on site. ART will be initiated immediately, and in the rare case that changes in dosing or ART based on lab values (e.g. creatinine) is needed,

they will made once lab results return. This is now standard of care nationwide for rapid initiation. The care visit will be documented in UChart. Baseline labs (4th Generation HIV test, HIV viral load, CD4, HIV genotype, CBC, CMP, Gonorrhea/Chlamydia, RPR, HCV Antibody, HCV RNA) will be obtained and sent to the Miami-Dade County Health Department. Patients will have up to 7 days post HIV-positive test to start on ART (per definition of rapid ART initiation).

Peer navigators will conduct outreach to *SSP Rapid Initiation* participants, monitor appointments, and provide transport to healthcare services. This intensive linkage and active follow-up delivered by peer PWID living with HIV is essential to delivery of care to this population. A medication adherence plan will be developed for each patient by SSP staff to optimize medication adherence. Quantitative and qualitative assessments exploring barriers and facilitators of HIV treatment adherence will be given at 1, 3 and 6 months post treatment start date. In addition, HIV viral load will be measured at 1, 3, and 6 months post treatment start date to assess viral suppression**.** Peers will be tasked with helping participants with eligibility (e.g., Ryan White, Medicaid) and ADAP enrollment when they transition out of the trial to a traditional care environment.

For each 30-minute interview conducted at the IDEA SSP, participants will receive $50.

Qualitative Assessment of those declining rapid ART

In-depth interviews with PWID living with HIV who do not engage in treatment with 7 days of HIV test result will be conducted. We anticipate conducting 10 interviews, which is sufficient to achieve data saturation and will be conducted within 3 months post HIV test result. Participants will be consented and asked to participate in a 30-minute interview conducted at the IDEA SSP for which they will receive $25.

8) **Primary Endpoints**

Study Aim	Primary Outcome (Patient-Level)	Definition	Primary Outcome (Implementation)	Definition
Aim 1	Viral Suppression	HIV viral load <200 copies/ml at 6 months post baseline	Acceptability of Rapid Initiation of ART	Number and percentage of PWID living with HIV that enter *SSP Rapid Initiation*
Aim 2	Treatment Adherence	HIV Viral Load <200, pill counts, medication log, appointment attendance	Barriers to Adherence	Exploration of challenges to HIV treatment management at SSP
Aim 3	Viral Suppression	HIV Viral Load <200, pill counts, medication log, appointment attendance	Feasibility of peer navigation	Exploration of challenges to HIV treatment management at traditional HIV clinic

For this proposed study, we expect that ongoing, peer-driven patient navigation based at the SSP will result in patients' remaining virally suppressed after transition to the UM/Jackson Adult Outpatient HIV Clinic. More importantly, based on the hybrid design, this study will lay the foundational groundwork to provide a proof of concept for HIV care at SSPs, including pertinent implementation information for future expansion sites in the state of Florida. We expect to uncover barriers and facilitators to implementation of rapid ART initiation at an SSP, including patient-level perspectives on improving delivery of care developed in the *SSP Rapid Initiation among PWID Living with HIV* protocol.

Secondary outcomes: Time to viral suppression, or viral suppression at 1 month, will be assessed. Treatment adherence will be assessed both by follow-up viral load results (1, 3, 6, 9, 12 months) as well as by medication management measures (e.g., PWID accessing meds weekly, pill counting by SSP staff) and attendance at clinic visits. Successful transition to HIV care at a Ryan White clinic will also be assessed. The clinic-based peer patient navigator will assist in transition of patients to long-term care within six months of ART initiation. Ryan White clinic appointment attendance and successful re-enrollment in Ryan White/ADAP will be assessed.

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 present pilot data on rapid ART initiation at an SSP. Data will be presented as frequency tables, and viral suppression will be reported as a percentage suppressed at each time-point (1, 3, 6, 9, 12 months). 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). Categorical data will be analyzed using frequency of responses and continuous variables will be analyzed using means and standard deviations.

Qualitative Data Analysis: Qualitative data collected from the in-depth interviews will be analyzed using general inductive methodology[31], 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.

11) **Risks to Subjects***

Study procedures: there is risk of discomfort to phlebotomy, but no risk above routine HIV care

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

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.

13) **Potential Benefits to Subjects***

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

14) **Vulnerable Populations***

This study will exclude children because the provider is board certified in Internal Medicine and only sees adult patients. Children will be rapidly referred to University of Miami Department of Pediatrics Test and Treat program.

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 and HIV physician with expertise in treating HIV among PWID. 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, internist and addiction medicine physician. 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.

Local Number of Subjects

We intend to recruit 50 PWID living with HIV and currently not engaged in ART treatment to assess the SSP Rapid Initiation pilot program. Since this is a pilot, there were no statistical considerations made with determining sample size. We expect that 20% of those approached to participate will decline. Those who decline will be asked to participate in a brief qualitative assessment to explore patient-level factors for declining treatment (N=10).

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.