Promoting Pre-Exposure Prophylaxis Among People Who Inject Drugs Accessing Syringe Exchange Programs

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PROMOTING PRE-EXPOSURE PROPHYLAXIS AMONG PEOPLE WHO INJECT
DRUGS ACCESSING SYRINGE EXCHANGE PROGRAMS

A Thesis Presented to
The Faculty of the School of Medicine
Yale University

In Candidacy for the degree of
Master of Medical Science

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<tr>
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<td>Antiretroviral treatment</td>
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<td>ARTAS</td>
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<td>BTS</td>
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<td>RCT</td>
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<td>SBCM</td>
<td>Strengths-Based Case Management</td>
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<td>SEP</td>
<td>Syringe Exchange Program</td>
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<td>STI</td>
<td>Sexually Transmitted infection</td>
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<tr>
<td>TAF</td>
<td>Tenofovir Alafenamide</td>
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<tr>
<td>TDF</td>
<td>Tenofovir Disoproxil Fumarate</td>
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<td>USPSTF</td>
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Abstract

People who inject drugs are at increased risk of acquiring HIV and accounted for 10% of all new diagnoses in 2018. Pre-exposure prophylaxis has been shown to reduce HIV acquisition among at-risk populations, including people who inject drugs. However, pre-exposure prophylaxis is underutilized by people who inject drugs due to limited knowledge about its existence and purpose. The objective of this study is to determine the effectiveness of a patient navigation intervention in increasing initiation of pre-exposure prophylaxis among people who inject drugs. Specifically, we will carry out a randomized controlled study to compare the rates of pre-exposure prophylaxis initiation among individuals receiving an informational pamphlet or a multi-session intervention with a PrEP navigator. The results of this study will serve to determine whether an in-person patient navigation intervention is an effective strategy to improve pre-exposure prophylaxis initiation among people who inject drugs.
CHAPTER 1: INTRODUCTION

1.1 Background:

1.1.1 HIV among People Who Inject Drugs

In the United States, people who inject drugs (PWID) are disproportionately affected by HIV—constituting about 3% of adults in the general population but accounting for 10% of all new HIV diagnoses in 2018.\textsuperscript{1,2} The current national opioid epidemic has led to greater numbers of PWID, thereby putting new populations at higher risk for contracting HIV.\textsuperscript{3} Of the nearly one million people in the United States living with a diagnosed HIV infection in 2016, 10% of infections in males and 21% of infections in females were attributed to injection drug use.\textsuperscript{4}

Pre-exposure prophylaxis (PrEP) has been shown to reduce the risk of HIV acquisition in at-risk populations, including PWID.\textsuperscript{5,6} PrEP is a medication that comes in two formulations, consisting of tenofovir (TDF or TAF) and emtricitabine (FTC) in a fixed-dose combination that is taken orally once a day.\textsuperscript{5} The Centers for Disease Control and Prevention (CDC) recommends PrEP as one HIV prevention option in adult PWID based on the risks associated with sharing injection equipment and sexual behaviors such as unprotected sex.\textsuperscript{5,7,8} The indications for PrEP in adult PWID are that they must be (1) HIV-negative, (2) have injected non-prescription drugs in the last six months, and either a) have shared injection or drug preparation equipment in the past six months or b) are at risk for sexual acquisition.\textsuperscript{5} Sexual risks include sex without condoms, sexual partners of unknown or positive HIV status, or a bacterial sexually transmitted infection (STI) in the past 6 months.\textsuperscript{5} Despite the CDC’s recommendations that PrEP be provided to PWID at substantial risk for HIV, there has been limited uptake.\textsuperscript{2}
While it can be challenging to engage PWID in preventive services within routine medical settings, community-based harm reduction agencies are sites regularly accessed by PWID and may offer a potential solution.\(^9\) Harm reduction refers to patient-centered programs and practices that seek to reduce the potential adverse health consequences of illicit drug use. For example, syringe exchange programs (SEPs) provide sterile injection equipment and syringes to people actively using drugs and serve to decrease the transmission of infectious diseases, such as HIV.\(^10\) Harm reduction programs thus can be used as avenues for PrEP delivery due to their common goal of limiting HIV acquisition.

Despite the key role that harm reduction services play in risk reduction, their presence alone is not sufficient to prevent HIV. From 2015-2017, approximately 11% of HIV-positive PWID engaged in distributive syringe sharing, which means that they gave their used syringes to another person for use.\(^11\) Additionally, compared to HIV-positive people who do not inject drugs, HIV-positive PWID were more likely to have a detectable viral load (48% vs. 35%, \(p=0.008\)) and more likely to engage in high risk sex (\(p<0.001\)).\(^11\) This demonstrates that HIV-positive PWID are contributing to the spread of HIV among their HIV-negative peers.

According to the National HIV Behavioral Surveillance (NHBS) 2015 data, 27% of HIV-negative PWID receptively shared syringes, 49% receptively shared injecting equipment, and 67% had condomless vaginal sex in the previous 12 months.\(^8\) Overall, 72% had engaged in condomless heterosexual sex or receptive needle sharing during the surveillance period, which are factors strongly associated with HIV infection.\(^3,7,8\) During that same time frame, 58% received HIV testing and 52% received syringes from a SEP.\(^8\) These various HIV risk behaviors make PWID up to 22 times more likely to acquire HIV
compared to the general population in the United States. These statistics demonstrate that despite the presence of harm reduction services such as SEPs, PWID are still at risk for acquiring HIV through injection practices and sexual behaviors. This emphasizes the need for further harm reduction efforts and the opportunity for the introduction of PrEP as part of the range of services offered to PWID who are already accessing SEPs.

1.1.2 Current Trends in PrEP Use Among People Who Inject Drugs

The need for PrEP promotion and uptake among PWID has been strongly encouraged by organizations such as the CDC, the National Institutes of Health (NIH), and the United States Preventive Services Task Force (USPSTF). In 2015, the CDC estimated that 18.5% of PWID had substantial risks for acquiring HIV consistent with indications for PrEP use. In a study looking at real-world eligibility for PrEP among Canadian PWID, 37% of participants were eligible for PrEP according to CDC guidelines. Despite PrEP eligibility, systematic review and meta-analysis describing PrEP use among key populations has found that PWID reported the lowest PrEP use compared to other key populations such as men who have sex with men (MSM), Hispanics/Latinos, and transgender women.

To date, there has only been one efficacy trial evaluating PrEP among PWID. Results of this randomized, double-blind, placebo-controlled Bangkok Tenofovir Study (BTS) showed a 49% reduction in HIV incidence (95% CI 9.6-72.2; p=0.01) in 2,413 PWID from methadone clinics taking once daily PrEP compared to placebo. The reduction rate increased to as high as 83% (95% CI 40-98) for those with the highest amounts of medication adherence (97.5% adherence). However, even moderate adherence of five or more of days per week without missing more than two consecutive
doses showed a 73.5% reduction in HIV acquisition (95% CI 16.6-94.0; p=0.03). These findings publicized the efficacy of PrEP and led the CDC to endorse PrEP to prevent HIV acquisition in PWID in 2013.\textsuperscript{18} In a one-year open label extension to the BTS study, returning participants were offered one year of daily tenofovir for PrEP.\textsuperscript{19} Of the 1,315 eligible participants, 61% chose to start PrEP.\textsuperscript{19} This high participation rate indicates that a majority of PWID who are knowledgeable about PrEP may be interested in taking it once they are aware of its role in preventing HIV. Additionally, participants who injected heroin (OR 1.5, 95% CI 1.1-2.1, p=0.007) or had been in prison (OR 1.7, 95% CI 1.3-2.1, p<0.0001) were more likely to choose PrEP than participants without those characteristics.\textsuperscript{19} This suggests that participants may have based their decision to initiate PrEP on their perceived risk of HIV infection.\textsuperscript{19}

Despite the demonstrated success of PrEP in PWID, available data suggest that PrEP awareness and use are low among PWID.\textsuperscript{2,13} According to the 2015 NHBS data on injection drug use patterns in 20 U.S cities, only 9.7% of the 9,675 HIV-negative PWID surveyed had ever heard of PrEP.\textsuperscript{20} Even more striking is that only 0.3% had taken PrEP at any point during the 12 months before the interview.\textsuperscript{20} According to interviews with a number of key informants and HIV-negative PWID, limited PrEP knowledge and misperceptions about the risk of acquiring HIV act as barriers for eligible PWID to receive recommended PrEP care.\textsuperscript{21,22} These low rates of PrEP use can be attributed in part to the limited awareness about PrEP in PWID, which ranges from 3-56% depending on the subpopulations of PWID surveyed.\textsuperscript{2,9,21,23-33} However, once informed about it, PWID’s interest in taking PrEP can range from 47-79%.\textsuperscript{22-26,33,34} Notably, the 56% PrEP awareness finding came from a qualitative study of 397 PWID in San Francisco after a
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vigorous PrEP promotion campaign. The sample included PWID who were also MSM, and all seven male PWID who had used PrEP in the last year also identified as MSM. The researchers also found that PrEP awareness and use did not differ based on frequency of injection or by whether the respondent had used a needle used by someone else at any time in the last 12 months. This highlights that intersectional identities surrounding sexuality and gender identity can overlap to increase PrEP awareness, perhaps irrespective of PWID status.

In a cross-sectional survey sample of 265 HIV-negative PWID, 90% of PrEP eligible participants said they believed that it would be easy to take PrEP every day, suggesting that PrEP adherence may be feasible. However, medical providers serving PWID may not be currently well prepared to prescribe PrEP due to their limited knowledge about PrEP, perception of challenges to patient access, and uncertainty about adherence. These provider-level barriers demonstrate the need for PWID to become empowered about PrEP as they may not necessarily be getting offered PrEP by their providers. Therefore, strategies to reach PWID and introduce PrEP in settings serving PWID, such as syringe exchange programs, may be effective in overcoming this barrier.

1.1.3 Potential for Syringe Exchange Programs as Sites for PrEP

To date, there have been few PrEP interventions developed for actively injecting PWID. It has been well established that syringe exchange programs are a harm reduction strategy that can significantly reduce HIV prevalence and incidence among PWID. Individuals who acquire needles exclusively from SEPs are also significantly less likely to report syringe sharing (AOR 0.46, 95% CI 0.27-0.76). Evidence from a systematic review and meta-analysis demonstrates that the use of SEPs
is associated with a 44-58% decrease in HIV transmission rates among PWID.\textsuperscript{39} SEPs are an essential source of sterile needles, but are also valuable settings that can offer services such as condom provision, drug treatment referral, overdose prevention, and HIV testing.\textsuperscript{7,40}

About 52% of U.S PWID report having access to syringes via SEPs.\textsuperscript{8} Research has shown that having conversations about HIV prevention in SEPs leads to increased awareness of PrEP among PWID.\textsuperscript{41} Additionally, PWID that obtain needles primarily from harm reduction services such as SEPs were nearly twice as likely to have awareness about PrEP than those who did not access these programs in the past year.\textsuperscript{2} A study comparing injection behaviors among PWID before and after the introduction of SEPs found that they led to a decrease in overall receptive/distributive syringe sharing (75% before vs. 21% after, \( p < 0.05 \)), particularly among HIV-positive persons (90% vs. 9%, \( p < 0.05 \), respectively).\textsuperscript{42} This suggests that SEPs are an effective harm reduction tool that can decrease the HIV transmission risk among PWID by increasing PrEP awareness and promoting safer injection drug practices.

Previous studies have recommended the integration of educational efforts about PrEP into existing services for PWID, such as SEPs, along with facilitated access to PrEP.\textsuperscript{24,33,34,43-45} Qualitative research also suggests that PWID have high levels of trust in SEPs, due to the ways in which they create a stigma-free environment.\textsuperscript{46,47} In a cross-sectional study of 138 PWID evaluating PrEP eligibility and access among SEP users, 86% of participants reported that they would prefer to access HIV screening from a SEP rather than a STI clinic, indicating that SEPs may be a viable access point to connect PWID to PrEP.\textsuperscript{34} Despite utilization of SEPs where participants presumably go to access
harm reduction supplies, this same study reported that 45% of PWID still engaged in high-risk injection behaviors, such as needle sharing. In another cross-sectional study of 1,445 PWID recruited from California SEPs, researchers found that a sizeable majority of the sample was sexually active, had multiple sexual partners, and did not use condoms consistently for anal, vaginal, or oral sex. These risky sexual behaviors tended to co-occur with high levels of syringe sharing behaviors, despite participation in SEPs.

These overlapping patterns of sexual and injection related HIV risk behaviors have also been well described in a qualitative study of Northeast PWID. This study found that the three predominant contexts in which these high risk behaviors occur are through multiple concurrent sexual partnerships, injecting drugs with sexual partners, and exchanging sex for money. Since sexual risk behaviors are also an important driver of HIV infections among PWID, SEPs alone are not enough to protect PWID who are also engaging in HIV sexual risk behaviors. This highlights that the introduction of PrEP into SEPs could be a valuable supplemental strategy in the goal of reducing HIV infections among PWID.

1.2 Statement of the Problem:

PWID are a population at increased risk for HIV acquisition due to risk factors such as injection drug practices and unprotected sexual intercourse. PrEP is a medication that can significantly reduce the risk of contracting HIV in PWID by as much as 83%. Despite the benefits of PrEP, as little as 3% of PWID may know about its existence and purpose in preventing HIV, leading to underutilization among PrEP-eligible PWID. There have been a number of qualitative studies evaluating PWID’s perceptions and interest in PrEP, but to date there have been a limited number of studies evaluating
interventions to increase PrEP uptake among PWID.\textsuperscript{2,9,21-26,50} This lack of research has resulted in a gap in the literature about effective strategies to increase PrEP initiation among PWID. Patient navigation has emerged as a potentially effective strategy applied separately to PWID to increase linkage to HIV care and promote PrEP uptake among diverse HIV-negative populations.\textsuperscript{51,52} However, to the best of our knowledge, there have not been any published studies evaluating the effect of patient navigation on PrEP initiation in populations of PWID.\textsuperscript{13} Furthermore, despite PWID’s preferences and utilization of harm reduction programs, there is a lack of studies which have specifically sought to engage PWID accessing harm reduction programs for PrEP education and intervention.\textsuperscript{10,34} Therefore, we propose a randomized controlled trial (RCT) in four SEPs to evaluate the effect of a patient navigation intervention on PrEP initiation rates among PWID after 12 weeks. The results gained by this novel study have the potential to provide a framework for future interventions to promote PrEP initiation among PWID.

1.3 Goals and Objectives:

The overall objective of this study is to educate and link participants to PrEP to increase the amount of eligible PWID who have initiated PrEP medication within 12 weeks of the intervention. This RCT will compare two PrEP education delivery formats, a PrEP information pamphlet (control) vs. a PrEP pamphlet plus patient navigation (intervention), to assess if there is a significant difference in PrEP initiation rates between the two groups. To address the lack of PrEP uptake among PWID, all participants regardless of group allocation will receive the PrEP pamphlet. The pamphlet will discuss the risk behaviors associated with acquiring HIV, risk reduction techniques, the role of PrEP in HIV prevention, information on local PrEP providers, and financial resources for
covering the costs associated with PrEP. The intervention group will additionally receive a patient navigation intervention based on motivational interviewing and strengths-based case management (SBCM) models to explore interest and perceived barriers to initiating PrEP. The intervention will consist of a 45-60 minute one-on-one session with a PrEP navigator within a SEP. These participants will be offered up to four follow up sessions with the PrEP navigator to address any additional PrEP related concerns. The control group will only receive the PrEP pamphlet as the enhanced standard of care condition. In addition, assessments at baseline and 12-week follow-up will examine PrEP awareness, HIV risk behaviors, perception of HIV risk, and likelihood of starting PrEP.

The primary outcome will be the rates of PrEP initiation within 12 weeks of the intervention among both groups of participating PWID in the SEP setting. PrEP initiation rates will be assessed using self-report and confirmatory tenofovir urine testing. Secondary outcomes include the comparison of results from pre and post intervention assessments. An exploratory outcome will be sustained adherence to PrEP, measured via self-report and tenofovir dried blood spots (DBS) confirmation, 18 weeks after randomization. The results of this study will determine the added impact of patient navigation to a PrEP educational pamphlet to promote PrEP initiation among PWID accessing syringe exchange programs.

1.4 Hypothesis:

Among PWID accessing syringe exchange programs, we hypothesize that the intervention group with PrEP discussion facilitated by a PrEP navigator will result in a 12-week PrEP initiation absolute rate difference of 15% compared to the enhanced standard of care control group.
1.5 References:


CHAPTER 2: REVIEW OF THE LITERATURE

2.1 Introduction:

We conducted a thorough review of the literature between December 2019-May 2020 using Ovid (Medline), Pubmed, Scopus, and Web of Science. Only articles in English were evaluated. Review of titles and abstracts determined their relevance to the proposed study. Key terms used in each database to extract articles pertaining to the study population and intervention were: people who inject drugs (injection drug use, persons who inject drugs, intravenous drug use, PWID, IDU, IVDU), and pre-exposure prophylaxis (preexposure prophylaxis, PrEP). Terms used to identify any overlap between the study setting and intervention were: syringe exchange program (needle exchange program, needle syringe program, syringe services program) and pre-exposure prophylaxis (preexposure prophylaxis, PrEP). Terms used to identify model PrEP navigation studies included: pre-exposure prophylaxis (preexposure prophylaxis, PrEP) and navigator (navigation, educator, coordinator) or “case management” (“case manager”) or “PrEP navigator.” We used combinations of keywords for PWID and navigation to find studies that applied a patient navigation strategy in populations of people who inject drugs. Terms used to find articles on PrEP initiation combined the terms describing PrEP and PWID with initiation OR uptake. Controlled vocabulary terms included a combination of (drug users or substance abuse, intravenous or people who inject drugs) and (pre-exposure prophylaxis or anti-HIV agents) and (syringe exchange program or needle-exchange programs or harm reduction).

2.2 Review of Empirical Studies:

2.2.1 Patient Navigation as an Intervention in HIV Care
Patient navigation is a patient-centered healthcare strategy increasingly applied to HIV care in order to promote access and reduce barriers to services that improve health outcomes.\textsuperscript{1,2} This model of care shares some commonalities with the roles of health educators, case managers and social workers.\textsuperscript{2} In a qualitative meta-synthesis by Roland et al., clients reported that navigators provided support for HIV and social service needs, increased engagement and adherence in care, and promoted self-efficacy.\textsuperscript{3} While there is no single definition for the role of a patient navigator nor a protocol for how their services should best be applied, patient navigation shows promise in improving HIV care continuum outcomes.\textsuperscript{1} In a systematic review performed by Mizuno et al., five out of the six studies reported a positive association between patient navigation and linkage to HIV care.\textsuperscript{1} When translated into HIV-prevention, patient navigation can be evaluated in the context of the PrEP care continuum, which includes three main categories (Figure 1).\textsuperscript{4,5} Similarly to HIV patient navigators, PrEP navigators have emerged as an intervention to increase mobility through the PrEP continuum and improve PrEP implementation.\textsuperscript{6} In a prospective study of 187 transgender women and MSM, approximately 90\% were linked to PrEP via a peer navigator program over a 90-day intervention period.\textsuperscript{7}

\textbf{Figure 1:} PrEP Care Continuum\textsuperscript{4,5}
Additionally, a pilot study of 61 adults interested and eligible for PrEP randomized participants to either a patient navigation intervention or a passive referral for PrEP, with the goal of increasing PrEP linkage and initiation. Overall 40% of the intervention group and 29% of the control group initiated PrEP by 12 weeks (p=0.37). The patient navigation intervention used a strengths-based case management model in which the navigator supported the participants’ abilities and assets and helped them identify PrEP resources in the community. The goal of this strategy was to counter indifferent attitudes regarding linkage to prevention services and encourage positive engagement in the process. While this study only included two participants who had engaged in injection drug use in the last 90 days, it is a model of an intervention used to increase PrEP initiation through patient navigation. It is important to note that this study began with a small sample size and then had a 50% loss to follow up in both the intervention and control groups. All individuals who were randomized were included in the analysis and those lost to follow up were assumed to have not reached the study endpoints. This huge loss is likely the reason why the difference in PrEP initiation between both groups was not statistically significant. This pilot study highlights the need for further research with a more substantial study sample and recruitment of PWID to determine the impact of patient navigation on PrEP initiation.

One patient navigation study that has been operationalized across diverse settings is the Antiretroviral Treatment Access Study (ARTAS). ARTAS was a RCT of 316 recently diagnosed HIV-infected persons randomized to either the standard of care (passive referral) or SBCM for linkage to nearby HIV clinics. The primary outcome was self-reported attendance at an HIV clinic at least twice over a 12-month period. The
results of the study showed a higher proportion of participants in the intervention group visited an HIV clinician at least twice within 12 months (64% vs. 49%, RRadj 1.41, p=0.006). This study showed that offering a brief patient navigation intervention of five sessions or fewer is a tangible and promising strategy in promoting treatment uptake.

While PWID made up approximately 10% of each group, the rates of treatment linkage in each subgroup were not described. Notably, ARTAS did not specifically address PWID’s needs, and found less effectiveness for those injecting drugs, suggesting the need for accommodations to support PWID. Despite ARTAS’s limited application to the target population of our study, the intervention is a marker for the potential success of patient navigation in linkage to care. Using linkage to care as an outcome, this intervention can also be applied to PrEP care and initiation. ARTAS has been adapted in a number of other studies and applied to increase the engagement of PWID in care and promote PrEP linkage and initiation. All studies demonstrated success in their patient navigation interventions and reached their respective primary objectives.

A key study that challenged the efficacy of patient navigation was a multi-site RCT of 801 hospitalized participants with comorbid substance use and elevated HIV viral loads. Researchers evaluated the effect of a structured patient navigation intervention with or without financial incentives to improve HIV viral suppression rates. Patient navigation included up to 11 sessions of care coordination with SBCM and motivational interviewing. Financial incentives of up to $1,160 were provided for achieving target behaviors aimed at reducing substance use and improving HIV outcomes. The control group received the standard practice of the respective 11 hospitals for linking hospitalized patients to HIV care and substance use treatment. Results of the study showed no
differences in rates of HIV viral suppression versus non-suppression among the 3 groups at 12 months.\textsuperscript{12} However, the study had a number of limitations in the context of our proposed intervention. First, the study did not focus primarily on PWID and only 18.4% of participants reported injection drug use in the prior year. While participants did have substance use disorders, a majority used stimulants, which is associated with a lower likelihood of becoming virally suppressed compared to those who use opiates, alcohol or both.\textsuperscript{12} Additionally, several study sites were not located in areas with harm reduction services and there were inconsistent addiction treatment options for participants.\textsuperscript{12} These limitations highlight the need for the patient navigation to be targeted towards specific groups of people who use drugs, along with appropriate access to treatment services.

Multiple studies involving a patient navigation intervention have focused on overcoming barriers to care. To do so, they have utilized patient-centered approaches such as SBCM and motivational interviewing as part of the patient navigator role.\textsuperscript{2,7-9} They have also worked to directly address financial concerns of PrEP and ancillary service needs such as referrals to substance use treatment or mental health counseling.\textsuperscript{7,13} These various components of the patient navigation strategies demonstrate the diversity in approaches and feasibility of adapting the intervention to meet the needs of specific populations, such as PWID.

\textbf{2.2.2 Patient Navigation in PWID}

Patient navigation has shown success in populations of PWID and been adapted to achieve various outcomes. While there are no studies modeling the use of patient navigation to promote PrEP uptake in PWID, there are a number of studies assessing other health care connection outcomes, such as entry into drug treatment and
antiretroviral treatment (ART) initiation. In an uncontrolled prospective study in Greece of 45 recently HIV diagnosed PWID, 87% entered care within 2 months of the patient navigation intervention and 77% of those then initiated ART. The patient navigator had consistent contact with participants, assisted with appointment scheduling, helped to address ART access and insurance coverage, and connected participants to medical facilities for additional care. This intensive case management approach was adapted to meet the needs of PWID, particularly in addressing structural and administrative barriers such as health insurance access, legal issues, and social issues. While one major limitation to this study is its small sample size and uncontrolled design, its results report the role of patient navigation on the continuum of care for PWID with recent HIV infection. It therefore holds promise as an adaption for HIV-negative PWID at substantial risk for HIV who can benefit from PrEP initiation.

Similarly, a RCT in Russia of 349 HIV-positive PWID not on ART studied the effect of a peer-led SBCM intervention compared to usual care (resource card with harm reduction and HIV care information). The results showed that within 6 months of enrollment, 51% of the intervention group and 31% of the controls were linked to HIV care, defined by one or more visits to an HIV medical provider (AOR 2.34, 95% CI: 1.49-3.67, p<0.001). It also showed that participants who attended two or more case management sessions or all five sessions had greater rates of linkage to HIV care when compared to the control group (AOR 2.57, 95% CI 1.59-4.16, p<0.0001 and 2.91, 95% CI 1.68-5.07, p<0.0002, respectively). Ninety-one percent of intervention group participants were very much or somewhat satisfied with the case management intervention. Notable limitations to the generalizability of this study include that
participants were screened for eligibility while in an inpatient addiction hospital 1-5 days after admission and after treatment of withdrawal symptoms. Therefore, participants were in a controlled setting during their first intervention session and were not actively injecting drugs. While subsequent case management sessions were conducted in the community after hospital discharge, the intervention did not reach people who did not receive treatment at the narcology hospital. While both of these previously described studies included HIV-positive participants rather than HIV-negative, they both studied PWID and demonstrated the feasibility and effectiveness of applying a patient navigator approach to increase linkage to care.\textsuperscript{11,14}

In a vanguard RCT conducted in three cities in Ukraine, Vietnam and Indonesia, 502 HIV-infected PWID were randomized in a 1:3 ratio to a brief case management and individually tailored psychosocial counseling session versus standard of care (referrals to ART and substance use treatment).\textsuperscript{15} The case management component included systems navigation, which helped participants manage logistical barriers to treatment such as scheduling ART or medication for addiction treatment (MAT) initiation appointments, assisting with medical paperwork, and answering health related questions. The systems navigators met with the intervention arm participants at least twice, with subsequent sessions tailored to the needs of the participants.\textsuperscript{15} The initial encounters with systems navigators were brief, with 84\% lasting 30 minutes or less and a median of 3 encounters per person in the first 8 weeks.\textsuperscript{15} The psychosocial counseling component used motivational interviewing, problem solving, skills building, and goal setting to promote initiation of ART and MAT.\textsuperscript{15} Intervention arm participants received a minimum of two psychosocial counseling sessions, where the first session focused primarily on ART, and
the second targeted ART adherence and MAT. Participants were also offered booster sessions which were tailored to individual needs. A majority (58%) of initial counseling encounters were 31-60 minutes long, and 83% of participants completed two or more sessions within 60 days, with a median of 7 sessions per person.\textsuperscript{15}

In all three sites, one person served as both the systems navigator and psychosocial counselor. After 26 weeks, 73% of the intervention group and 36% of the control group reported being on ART (95% CI 1.6-2.3), and 38% of the intervention group and 24% of the control reported being on MAT (95% CI: 1.2-2.2).\textsuperscript{15} Overall, these results demonstrate the positive and significant impact that a navigation and motivational interviewing approach can have on treatment linkage and initiation in PWID. A notable caveat to these results was the lack of uniformity in the effect of the intervention across all three sites. There was a positive intervention effect for ART and MAT initiation in Ukraine and Vietnam, but limited effect in Indonesia.\textsuperscript{15} This limitation could be due to underlying sociocultural differences among these countries, which further emphasizes the need for such intervention in American PWID.

One study that targeted PWID in our setting of a SEP evaluated the effect of a SBCM intervention versus passive referral to drug treatment in 245 PWID seeking addiction treatment.\textsuperscript{16} Passive referral included a voucher with the date and time of the participant’s intake appointment at the drug treatment program. All participants were given a treatment voucher prior to their participation in the study, therefore the role of the case manager was primarily to facilitate treatment entry among those who had already received a referral. The SBCM intervention built upon each participant’s strengths by promoting goal setting and helping to manage their needs to achieve those goals. Being
each participant was already practicing harm reduction by attending a SEP, the strategy was to expand on this motivation. The duration and frequency of each session was based on the individual needs and desires of the participants. The case managers addressed barriers to treatment entry by assisting with transportation to the facility, childcare, social services, and referrals to health services. Treatment entry was defined as having attended the intake appointment for opioid agonist therapy within 7 days of the baseline interview. Within 7 days, 40% of the intervention group versus 26% of the control group entered treatment (p=0.03). The median duration of case management sessions were 25 minutes, but participants who received 30 minutes or more of case management within 7 days were 33% more likely to enter treatment. There was a median of two contacts with the case manager per participant. Factors significantly associated with entering treatment included: having two or more contacts with a case manager prior to the intake visit (OR 2.46, 95% CI:1.33-4.59), spending more time with the case manager, or being driven to treatment by a case manager (OR 4.94, 95% CI: 2.19- 11.4).

Notably, this study population consisted of PWID already seeking drug treatment from the SEP, which means that these participants were already a motivated subgroup of PWID. However, rates of drug treatment entry were still low overall, demonstrating that entering treatment can still be difficult. This could have been due to the short 7-day window in which participants were considered to have entered treatment. It is possible that a longer timeframe could have allowed for more arrangements to be made for treatment entry. In an attempt to identify the mechanism through which the intervention facilitated treatment entry, the “intention to treat” and “as treated” models both found that transportation assistance was the most important factor (AOR 4.99, 95% CI 1.98-12.56,
and AOR 3.89, p=0.03, respectively). This suggests that transportation can be an enormous barrier for PWID seeking to access treatment and should be considered as a component in a patient navigation strategy. The findings of this study demonstrate that it is possible to implement a patient navigation strategy within the SEP setting in PWID. While the outcome of this intervention is not our primary outcome of increasing PrEP initiation in PWID, it showed that a similar intervention in our study population and setting are feasible and can show success. This suggests that there is a benefit to offering integrated treatment referrals and case management services from within a SEP.

Another iteration of this intervention is a RCT of 557 Hispanic PWID in Puerto Rico. Researchers implemented a combined counseling and case management behavioral intervention which used motivational interviewing strategies to engage participants in drug treatment, reduce drug use, and reduce injection-related HIV risk behaviors. Participants in the experimental arm were nearly twice as likely to enter drug treatment (OR=1.85, 95% CI 1.50-2.74) and half as likely to continue drug injection (OR=0.55, 95% CI = 0.34-0.88). Among those who continued to inject, participants in the experimental group were less than half as likely to share needles (OR=0.42, 95% CI = 0.18-0.91). These results further reinforce that implementing a patient navigation intervention with components such as motivational interviewing can help increase linkage to care and reduce high risk HIV behaviors like needle sharing.

Similarly, in another RCT case management intervention of 360 PWID, 98% of the case managed participants were admitted into substance use treatment programs, compared to only 57% of the intervention group (p<0.01). The case manager was cited by 87% of the intervention group participants as the major reason that access to treatment
was made easier.\textsuperscript{18} Case managers increased access to service providers, assisted with transportation to drug treatment, and provided continuity of care. Those assigned a case manager entered treatment in substantially greater numbers and more rapidly than clients who attempted to access treatment through usual routes.\textsuperscript{18}

The studies discussed throughout this section highlight the various ways in which patient navigation interventions have been used to connect PWID to various resources, such as MAT and ART. While there is no study that has directly focused on using patient navigation as a means of increasing PrEP initiation in PWID, current data demonstrate that patient navigation is feasible, well-studied, and particularly applicable to PWID and HIV-prevention initiatives. Therefore, our study will incorporate the successful aspects of the literature review into our study design to evaluate the rates of PrEP initiation in PWID accessing SEPs after the implementation a patient navigation intervention.

\textbf{2.3 Identifying Possible Confounding Variables:}

While reviewing related literature, we identified several confounding variables that we will address through our study design. First, we will use stratified randomization to randomize participants by insurance status and SEP site. Being uninsured has been consistently reported as a barrier to PrEP access, especially in PWID.\textsuperscript{19-21} Therefore, stratification based on insurance status (insured vs. uninsured) will ensure equal distribution of uninsured participants among the intervention and control groups. Stratification by SEP site is another important criterion because the services provided at each SEP can vary based on location and the resources that they have available.

Previous RCTs on patient navigation have sought to assess whether randomization was successful and identify any confounders by comparing the baseline
characteristics of participants in the intervention and control arms. Examples of characteristics recorded in these studies include: gender identity, sexual orientation, age, race/ethnicity, education level, previous knowledge of PrEP, income, employment status, insurance coverage, and the need for transportation assistance.

Qualitative studies exploring PrEP awareness and acceptability among PWID have consistently reported that willingness to use PrEP is associated with higher perceived HIV risk and PrEP knowledge. Studies have also reported that PrEP willingness is associated with younger age, no regular employment, engaging in sex work, multiple sexual partners, and being female. Given these findings, we will consider these demographic factors as potential confounders and measure them at baseline to ensure comparability across both groups.

A study of sociodemographic correlates of PrEP uptake in Tennessee with a heterogenous population that included PWID found a significant independent association between age, race/ethnicity, and transmission risk on PrEP uptake. Transmission risk included male to male sexual contact, injection drug use, and high risk heterosexual contact. All of these factors have the potential to impact participants’ desire and determination to initiate PrEP, independent of our patient navigation strategy. For this reason, we will be thorough in assessing these characteristics through our baseline assessment. If we do find any imbalances between the control and intervention groups, we will adjust for any differences in our statistical analyses.

2.4 Review of Relevant Methodology:
This section of the literature review discusses the methodology that is relevant to the proposed study. A more detailed description of the proposed study methods is discussed in Chapter 3.

2.4.1 Study Setting and Design

We will conduct a multi-site study which will include participants from four SEP sites in Connecticut: The Greater Hartford Harm Reduction Coalition, the New Haven Syringe Exchange, Apex Community Care in Danbury, and the Bridgeport Health Department Syringe Exchange Program. The proposed study has a multi-center design to ensure adequate recruitment and expand our generalizability. According to Connecticut Department of Public Health (DPH) surveillance data, these are cities that have high levels of drug overdose and HIV incidence among PWID.\textsuperscript{25,26} This data is suggestive of active injection drug use and the spread of HIV among PWID in Connecticut, demonstrating the potential for PrEP implementation within these areas. PrEP delivery is best optimized when provided as a part of a multicomponent package that includes safety monitoring, behavioral intervention, and the integration of PrEP as part of a comprehensive care platform.\textsuperscript{27} Our study will deliver this bundle through our PrEP navigation intervention, connection to PrEP services, and integration into SEPs.

Our study will target HIV-negative PWID and help them move along the continuum of PrEP delivery. The key steps in the PrEP continuum include: 1) identifying individuals at highest risk for HIV and increasing awareness, 2) facilitating access and linkage to care to enhance PrEP uptake, and 3) adherence to PrEP and retention in care \textbf{(Figure 1)}.\textsuperscript{3} Our focus is on the second step of this continuum, as the study inclusion criteria will already serve to identify PWID at risk for HIV acquisition. The steps in PrEP
initiation include linking individuals to a site of PrEP delivery with a PrEP provider, obtaining baseline laboratory testing, identifying how it will be paid for, and actually starting the medication.\textsuperscript{5} Connecting the participants to a PrEP provider who can perform the necessary baseline testing will be part of the information pamphlets provided to both the control and intervention groups.

Previous studies have shown that cost can be a barrier to access of PrEP.\textsuperscript{5,28-31} Therefore, our study design will seek to reduce this burden by providing all participants with information regarding the copayment assistance program offered by Gilead Sciences, the company that produces Truvada®, which is the brand name for the FTC/TDF fixed dose formulation of PrEP. Gilead’s Medication Assistance Program provides PrEP at no cost to individuals who earn <500% of the federal poverty level.\textsuperscript{5} Additionally, the Connecticut DPH has a comprehensive PrEP Program Resources guide which outlines how to pay for PrEP.\textsuperscript{32} It highlights that Gilead offers up to $7,200 per year of medication co-pay assistance, regardless of financial need.\textsuperscript{32} The Connecticut DPH has also stated that all major health insurance companies and state-provided insurance in Connecticut will cover PrEP medication and the necessary medical care associated with it.\textsuperscript{32} Providing these resources to all participants will help minimize individual cost as a barrier to accessing HIV prevention services and PrEP medication.

\textbf{2.4.2 Review of Recruitment Techniques}

This study will recruit among individuals accessing services from four syringe exchange programs in Connecticut, as well as from peer referral. Upon review of recruitment and sampling techniques, the most viable option that emerged is a form of convenience sampling known as snowball sampling. This is a method used to engage “hard-to-reach” populations such as PWID.
Iterations of snowball sampling have been used in a number of previously referenced studies to recruit PWID.\textsuperscript{33-35} Snowballing taps into the social networks of PWID by recruiting initial small groups of participants and asking each one of them to identify other members who will then be contacted and asked to identify other potential participants, and so on.\textsuperscript{35,36} The process continues until a sufficient number of participants have been recruited to meet sample size requirements. The ideal initial participants are people with diverse demographic characteristics known to belong to a large network of PWID.\textsuperscript{34} One necessary condition for successful snowballing is that members of this hidden population know each other.\textsuperscript{36} A limitation of this method is those missing from the recruitment frame are likely to be those socially isolated from other members of the rare population.\textsuperscript{36} While we will only enroll participants who have accessed one of the SEP sites in the last month, a strength of our approach is that we will recruit directly from the SEP and complement this with peer referral to maximize outreach.

\textbf{2.4.3 Inclusion and Exclusion Criteria}

The CDC-recommended indications for PrEP use by PWID include: being >18 years old, without acute or established HIV infection, with any injection of drugs not prescribed by a clinician in the past 6 months, AND at least one of the following: any sharing of injection or drug preparation equipment in the past 6 months or risk of sexual acquisition.\textsuperscript{37} Risk for sexual acquisition includes: any anal sex without condoms, a bacterial STI in the last 6 months, infrequent condom use with one or more partners of unknown HIV status or who are known to be at substantial risk for HIV infection, or an ongoing relationship with an HIV-positive partner.\textsuperscript{37} In addition to the CDC criteria above, inclusion criteria for the Doblecki-Lewis et al. study included: ability to meet the navigator at the research site, ability to give informed consent, willingness to provide
contact information, and ability to be contacted by phone. All participants were informed that they would be responsible for the cost associated with the provider visit and associated HIV testing per the health center’s policies. We will utilize both the CDC guidance and this prior study to inform our inclusion criteria. An additional inclusion criterion specific to our study is that participants must have accessed services from a SEP at least once in the past month.

In previous studies, HIV-negative status has been evaluated at baseline with HIV antibody testing using the OraQuick Rapid HIV-1 antibody test. The CDC recommends that if a rapid antibody test is used (as opposed to antigen testing), clinicians should assess for nonspecific signs or symptoms of viral infection during the preceding month or on the day of evaluation. Symptoms include: fever, fatigue, myalgia, skin rash, headache, pharyngitis, cervical adenopathy, arthralgia, night sweats, or diarrhea. Prior to PrEP initiation, participants must receive an assessment of their renal function and a test for hepatitis B virus (HBV) infection, because decreased renal function (i.e., CrCl <60 ml/min) and HBV infection are potential safety issues for the use of PrEP. As all participants in our study will need to see a PrEP provider to get a PrEP prescription, these additional tests will be conducted at the discretion of the PrEP provider.

Our exclusion criteria will be modeled from a study that trialed same-day PrEP initiation in an STI clinic. Criteria includes: any known renal dysfunction, being HIV positive, a history of chronic HBV infection, pregnancy, indications for HIV post-exposure prophylaxis, or any signs or symptoms consistent with an acute HIV infection (as listed above). On-site point of care urine pregnancy tests can be obtained upon enrollment in our study, along with the OraQuick antibody HIV test.
2.4.4 Randomization Techniques

In the protocol for a study seeking to increase linkage of HIV-positive PWID already in addiction treatment to HIV care through a patient navigation intervention, researchers used stratified randomization. Randomization into intervention or control was stratified based on whether participants had seen an infectious disease clinician in the last 12 months prior to enrollment and on reported history of hospitalization due to HIV infection. The goal of stratified randomization was to ensure balance with respect to these potential confounders. The researchers also used a computer-generated randomization table to achieve blocked randomization with random block sizes for each stratum. This method ensures a balance in sample size across both groups and minimizes selection bias. Due to the nature of the intervention, participants and patient navigators could not be blinded to group assignment. The study sought to minimize measurement bias by having the baseline assessment administered prior to randomization and by concealing randomization assignment from the follow up assessors.

Similarly, Doblecki-Lewis et al. had participants complete an interviewer-administered baseline survey following enrollment but prior to randomization. Participants were then immediately randomized to either the patient navigation intervention or the enhanced standard of care control. Randomization was stratified by subgroups of MSM and transgender women and heterosexual men and women. Randomization occurred via computer-generated block randomization with randomly selected block sizes. Both the control and intervention groups received the first step of their intervention immediately after randomization, which meant that all intervention
participants received at least one in-person patient navigation session and all members of the control group received their PrEP information pamphlets.\(^8\)

In contrast, Strathdee et al. used cluster randomization.\(^16\) At the beginning of the study, each SEP site was randomized to receive either the case management intervention or the passive referral to drug treatment. About halfway through the recruitment period, there was a 1-month washout period in which no participants were recruited. After washout, the sites originally randomized to case management received the control condition and vice versa, until the end of enrollment. The goal of this design was to limit contamination of the control participants. However, this method led to an unequal number of subjects in each group (52% in the intervention vs. 48% in the control). Despite this, there were no baseline differences between the intervention and control groups with respect to any sociodemographic or behavioral characteristics or self-reported barriers to access to treatment.\(^16\) While minimizing contamination is an important concern, for the purposes of our study design we will randomize our participants by individual, rather than by SEP site. This is because our study only includes four SEP sites and we will need to stratify participants based on potential confounders. Lastly, it is important to note that for all of these studies of patient navigation interventions, it was not possible to blind the participants given the nature of the intervention.

**2.4.5 Review of Successful Patient Navigation Components**

Comprehensive reviews of HIV prevention strategies in PWID have recommended combination prevention packages that include behavioral, structural, and biologic interventions in order to have the greatest impact on preventing new HIV
infections.\textsuperscript{41-43} According to Degenhardt et al., combining strategies such as behavioral interventions and SEP services to address HIV risk have the highest level of evidential support in reducing sexual and injection risk behaviors when compared to single interventions.\textsuperscript{42} With these recommendations in mind, our proposed study incorporates all of these criteria by designing an intervention that combines the use of evidence-based HIV prevention strategies of PrEP, syringe exchange programs, and patient navigation.

\textit{Number and Length of Sessions}

In the Strathdee et al. study, factors significantly associated with a greater odds of entering drug treatment were randomization to the case management intervention (OR 1.84; 95\% CI 1.07-3.16), having two or more contacts with a case manager prior to the intake visit at the drug treatment program (OR 2.47; 95\% CI 1.33-4.59), having spent an average of 15 minutes or more with a case manager (OR 1.94; 95\% CI 1.05-3.60), and being driven to treatment by a case manager (OR 4.94; 95\% CI 2.19-11.4).\textsuperscript{16} While the primary outcome of this study (entering drug treatment) is not the same as our objective of PrEP initiation, the patient navigation intervention and SEP setting are the same as in our study. These findings demonstrate the added value of offering a patient navigation intervention for PWID from within a SEP, which we will apply in our study to promote PrEP initiation among PWID. Therefore, we will adopt the successful components of their case management approach in our study design, including multiple contacts with the PrEP navigator, visits greater than 15 minutes, and transportation assistance.

The methodology previously described in the ARTAS trial has been closely replicated in at least four other studies.\textsuperscript{7-11} While the key populations and outcomes assessed across the five studies varied, the adapted patient navigation interventions were
successful in meeting each study’s primary objectives. Therefore, the ARTAS model is as an ideal framework to design our PrEP navigator intervention. The intervention will be adapted to meet the needs PWID in SEPs to promote our goal of increasing PrEP initiation within this population. All five studies offered a minimum of one patient navigation session with a maximum of five sessions. After the first session, participants had the option to attend four additional follow-up visits with the patient navigator to review personal strengths, reevaluate available resources, and focus on the remaining elements of the SBCM model. In ARTAS, all patient navigation contacts had to occur within 90 days of randomization. The length of each session varied between studies, ranging from 5 to 60 minutes. However, in the Strathdee et al. study, researchers found that participants who received 30 minutes or more of case management within 7 days from the baseline visit were 33% more likely to initiate treatment than those with sessions lasting less than 30 minutes. Given this finding, our initial session will be 45-60 minutes in length, modeled after the duration used in Doblecki-Lewis et al.

**Timeframe for Measuring Outcomes**

We will use a period of 12 weeks from the start of the PrEP navigation intervention as our timeframe for initiating PrEP. Studies by Reback et al. and Doblecki-Lewis et al. used 12 week periods in their respective studies to evaluate linkage to PrEP and PrEP initiation. In an uncontrolled pilot trial of 19 MSM receiving a 2-session motivational interviewing intervention, 37% of participants obtained PrEP within one month. In a retrospective study evaluating time to PrEP initiation in primary care clinics in San Francisco, researchers found that PrEP users initiated PrEP after a median of only 7 days, but there was a large minority of 29% that initiated PrEP between 30-90 days
after the patient navigation intervention. Given these findings, we would like to maximize the amount of time participants have to navigate the PrEP care continuum and initiate PrEP. Therefore, we will use 12 weeks as our cutoff point for determining successful PrEP initiation among our samples of PWID.

**Specifications of the PrEP Navigators**

The role of the patient navigator in previous studies has been occupied by community case managers, nurses, and study staff. Despite variations in the patient navigator identity, all studies provided specific training to personnel on how to deliver the patient navigation services. In Strathdee et al., all case managers underwent a 3-day training workshop on SBCM and the local resources available. Case managers were supervised by experienced social workers and each case manager held a case load of about 20 clients. The quality of the case management sessions was assessed via review of strength assessments, action plans, case logs, and group supervision checklists. On a monthly basis, case managers participated in group supervision sessions led by the Project Director, which involved presentation and discussion of challenging cases. The goal of all of these activities was to ensure a high degree of fidelity across the case management team. Each of the 10 SEP sites had one to three case managers. In Robles et al., the case management intervention was conducted by a registered nurse with intensive training in motivational interviewing strategies. A case manager with a bachelor’s degree in social work and training in the intervention protocol met with participants after each session to review lessons learned and provide assistance with overcoming any perceived barriers.
Similarly, in the ARTAS trial, case managers were trained as a group prior to participant enrollment through an intervention manual. This is in contrast to Doblecki-Lewis et al., which used trained study staff as patient navigators to deliver their SBCM intervention. For our purposes, the patient navigators will be community case managers with a minimum of a bachelor’s degree. They will undergo a multi-day training on how to apply strengths-based case management principles and motivational interviewing to their participant interactions, as modeled through multiple patient navigator studies.

2.4.6 Content of the Patient Navigation Intervention

The core components of a SBCM intervention are engagement, strengths assessment, personal case planning, and resource acquisition. Engagement begins by developing a collaborative partnership between the patient navigator and the client, while reviewing the purpose of SBCM. The strengths assessment occurs at the first visit, where the navigator uses open-ended questions to record specific skills, talents, abilities, and behaviors of the participant. Personal care planning is the process of identifying short- and long-term goals for the participant, as well as referring them to community resources that address their identified needs and case management goals. In the resource acquisition component, the navigator will use information from the baseline needs assessment to identify client goals and help connect the client to services that address these goals.

Doblecki-Lewis et al. applied these same core principles to their patient navigation strategy. Following initial assessment, providers discussed available resources in the community for HIV prevention while supporting and motivating participants’ efforts to engage in these strategies. Navigators also took notes based on each participant’s encounter to record any barriers or facilitators to PrEP uptake. The
navigator then discussed strategies to overcome these barriers with the participant. There were also interviewer-administered assessments taken at baseline, 6 weeks, and 12 weeks of follow up. Measures included socio-demographics, experiences with PrEP, risk perception, risk behaviors, current prevention strategies, experiences with providers and clinics for HIV prevention care, perceived barriers and facilitators to obtaining PrEP, knowledge, beliefs and attitudes towards PrEP, adherence self-efficacy, health literacy/numeracy, depression, quality of life, and social support. Participants were asked at 4, 6, 8, and 12 weeks after the initial intervention if they had made an appointment with a PrEP provider or initiated PrEP.8

The motivational interviewing patient navigation strategy used by Robles et al. addressed goal setting, decision making, reinforcement, and attitude change.17 Counselors would involve the participants in the decision process and explore discrepancies to reduce ambivalence towards drug treatment and HIV risk behavior change. Each of the 6 sessions had a specific outline and design, focusing on topics such as participants’ plans for behavior change, drug use patterns, relapse prevention, and obstacles to change. Throughout the study, counselors and case managers followed a protocol for documenting all intervention sessions and completed monthly appraisals of participants’ progress. Six months after the baseline interview, participants were contacted by outreach workers and given a follow up assessment similar to the baseline survey.17

The aforementioned studies describe the core structure of SBCM and motivational interviewing principles as they pertain to patient navigation approaches. Both components have shown success in PWID and can work synergistically to increase PrEP initiation as part of the patient navigation package.
2.4.7 Content of Control Condition

The control condition, also known as the “enhanced standard of care,” includes a PrEP pamphlet with PrEP information and HIV prevention tools for participants. In Doblecki-Lewis et al., contents of this condition included a list of PrEP providers in the area, HIV testing sites, STI clinics, recommendations regarding initiating discussion with the provider regarding PrEP, and information regarding available financial assistance to assist with the cost of PrEP. This package ensured that participants in the control group received the same key information regarding PrEP access as the intervention group.

In a PrEP implementation study targeting MSM, participants were provided with a one-page informational sheet which included clinical indications for PrEP, a description of PrEP treatment, common side effects, and compliance guidelines. In another PrEP uptake study among MSM, the control group participants received the same PrEP information listed in the study above plus printed educational materials from the CDC, a list of local PrEP providers, and PrEP copay assistance cards from the manufacturer. A review of these studies indicates that the key features of the PrEP pamphlet should include a PrEP overview, local PrEP providers, and the available financial resources.

2.4.8 Outcomes

The primary outcome of our study is PrEP initiation within 12 weeks of the intervention. This has been assessed in previous studies through periodic check-ins with participants to evaluate their progress in obtaining PrEP during the study. In Doblecki-Lewis et al., participants were contacted at 4, 6, 8, and 12 weeks after randomization and asked if they had made an appointment with a PrEP provider or initiated PrEP. We will adapt this model to periodically track the progress of our participants at 4, 8, and 12
weeks. Once participants report PrEP initiation, they will be asked to come into the SEP within a week for confirmatory urine tenofovir metabolite testing, which will be able to detect both TDF and TAF formulations of PrEP. A urine tenofovir concentration of greater than 10ng/mL is suggestive of PrEP dosing within the last 7 days.47

Secondary outcomes will assess HIV risk behaviors (needle sharing, sexual practices), awareness of PrEP and its function, likelihood of starting PrEP and perception of personal risk for HIV acquisition by group, before and after the intervention. These outcomes will be assessed with self-reported measures at baseline and post-intervention at week 12. Self-reported HIV risk behaviors regarding drug use and sexual intercourse during the past 30 days will be assessed using an adapted version of the HIV Risk-Taking Behavior Scale (HRBS).20 This 11-question scale has been shown to be a valid and reliable instrument for PWID and is designed for administration by an interviewer, which takes 10 minutes.48 The higher the score, the greater risk the subject has of contracting and/or transmitting HIV.48 Questions regarding PrEP awareness will be adapted from McFarland et al. (Appendix C).49 Likelihood of PrEP initiation will include “How likely are you to take a pill for PrEP each day to prevent HIV infection?” This question is adopted from a study seeking to increase PrEP uptake among black MSM.46 A Likert scale from 1 (very unlikely to take PrEP) to 5 (very likely to take PrEP) will be used. Perception of personal risk of HIV will be adopted from a PrEP implementation program for MSM in a STI clinic and asked as “How would you rate your risk for contracting HIV?” A Likert scale from 1 (extremely unlikely) to 5 (extremely likely) will be used.29 These assessments will be collected at baseline through a structured 1-hour interview
with a trained study staff member. The same assessment will be repeated 12 weeks after the baseline interview. Appendix C contains the full assessment with all components.

For those participants who initiate PrEP, an exploratory outcome will be sustained adherence evaluated at 18 weeks. Sustained adherence will be assessed via self-report and confirmatory testing, with participants indicating how consistently they took the medication (number of doses per week). In the landmark BTS, adherence criteria was defined as self-report of taking PrEP at least five days a week, with no more than two consecutive days off. The BTS also found that adherence is a key factor in determining the efficacy of PrEP in PWID. Sustained adherence can be confirmed via a tenofovir biomarker level with dried blood spots. Tenofovir is a component of the PrEP medication and persists in red blood cells with a half-life of approximately 17 days. Blood is collected via a fingerstick and a threshold of 700 fmol/punch in DBS indicates cumulative dosing of four or more doses of PrEP per week over the prior 6-8 weeks.

2.4.9 Review of Sample Size Calculation and Power

Our sample size calculation was determined based on an appraisal of results from the randomized controlled trials of Gardner et al., Doblecki-Lewis et al., Samet et al., and Strathdee et al. In ARTAS, researchers assumed an absolute difference of 15-20% in linkage to care rates would be scientifically meaningful, and further assumed a 20% loss to follow up to perform their sample size calculation. Through their patient navigation intervention, they found a 15% absolute increase in linkage to HIV care at 6 and 12 months compared to the standard of care passive referral group. While the linkage to care described in this study refers to connecting HIV-positive people who were not on...
ART medications to HIV clinics, we can parallel their outcome of linkage to care with linkage to PrEP, which is part of the PrEP initiation process.

In Doblecki-Lewis et al., researchers calculated sample size to detect a 25-30% absolute risk difference between their patient navigation and passive referral control groups.\(^8\) Overall, their results showed an absolute rate difference of 11% in PrEP initiation between both groups.\(^8\) While their study did not specifically look at PWID, it used a similar patient navigation intervention and specifically looked at the primary outcome of PrEP initiation. In Samet et al., researchers used a patient navigation intervention to link HIV-positive PWID to HIV care.\(^11\) They calculated sample size to provide 80% power to detect an absolute difference of 15% in proportions liking to HIV care.\(^11\) Results showed a 20% absolute rate difference between the intervention and control groups.\(^11\) While the study outcome of linkage to HIV care is not the same as ours, it was conducted in our target population of PWID, using patient navigation.

Lastly, Strathdee et al. studied the effect of patient navigation on entry into drug treatment among PWID referred from SEPs.\(^16\) They found that the absolute rate difference in treatment entry within 7 days was 14% between the intervention and control groups.\(^16\) This study used PWID as the population, recruited from SEPs, and evaluated the effect of a patient navigation intervention. While treatment entry is not the same as PrEP initiation, it is a comparable outcome. Taking the results from all four of these studies, the average absolute rate difference seen is 15%, which has become our target difference in PrEP initiation rates between our intervention and control groups.

Given this 15% absolute difference of effect, we must predict the initiation rates in the intervention and control group. Based on an extensive review of the literature, we
know that knowledge and use of PrEP in PWID is very low at baseline.\textsuperscript{50} Therefore, we predict that the rate of PrEP initiation in the control group that receives the PrEP information pamphlet and harm reduction standard of care will be 3%. Given the absolute rate difference of 15\%, the rate of initiation in the intervention group with patient navigation is estimated to be 18\%. When performing our sample size calculation, we will use a 2-tailed alpha of 0.05 and a power of 80\%, while accounting for an estimated 20\% loss to follow up.

\textbf{2.5 Conclusion:}

While knowledge of PrEP is critical to enable successful implementation, the mere provision of information about PrEP efficacy and access may not be enough to influence PrEP uptake in PWID.\textsuperscript{51} This emphasizes the need for an additional intervention such as patient navigation which utilizes subjective information such as perceived barriers to encourage participant action.\textsuperscript{51} The information presented in the literature review supports the promise of a patient navigation intervention to increase PrEP initiation among PWID. Our study design combines PrEP promotion and a patient navigation approach within a SEP to target the biobehavioral and structural environments of PWID. While there is data supporting the various components of our study design, there has yet to be a published study that introduces patient navigation in a SEP as a means of increasing PrEP initiation in PWID. Through our review of the literature, we have described the models that will inform use our study design, as well as the previous research demonstrating the need for this intervention. This project will add to the literature regarding the best approaches to increase PrEP uptake among PWID.

\textbf{2.6 References:}


CHAPTER 3: STUDY METHODS

3.1 Study Setting and Design:

We will conduct an effectiveness study in the context of a multi-center, randomized controlled trial. We will be evaluating the effect of a PrEP navigation intervention on PrEP initiation rates among PWID. Our multi-site study will include PWID from four syringe exchange program sites in Connecticut: The Greater Hartford Harm Reduction Coalition, the New Haven Syringe Exchange, Apex Community Care in Danbury, and the Bridgeport Health Department Syringe Exchange Program. We will use a 1:1 randomization to assign participants to the intervention and control groups and stratify based on SEP site and insurance coverage. Due to the nature of the intervention, the participants and PrEP navigators cannot be blinded to group assignment. However, randomization assignment will be concealed from the follow-up assessors.

3.2 Study Population, Sampling, and Recruitment:

This study will recruit among PWID accessing services from four SEPs in Connecticut. We will use snowball sampling to identify PWID from the various SEPs, who will then be contacted and screened for the presence of inclusion and exclusion criteria. For individuals who meet criteria, study participation will be offered, and informed consent will be obtained. Upon informed consent, participants will complete interviewer-administered baseline assessments, which will include sociodemographic factors, PrEP awareness, risk perception, risk behaviors, and likelihood of starting PrEP.

The ideal initial participants are people with diverse demographic characteristics known to belong to a large network of PWID. These individuals will be identified by employees of the SEP who are familiar with the individuals accessing its harm reduction
services. There will also be flyers within each SEP site for individuals to self-identify if interested (Appendix A). The initial participants will then be asked to recruit peers from their injecting networks who also identify as PWID that have access to the SEP. These peers are then screened for eligibility and consented to join the study and provide baseline data. The newly identified participants will then be asked to recruit more potential participants, and the process continues until a sufficient number of participants have been recruited to meet sample size requirements. All participants will receive $20 USD as a cash incentive for each peer that they successfully refer into the study. Through our sampling process, we will obtain a population of HIV-negative PWID with qualifying risk factors for HIV who access a SEP. The inclusion and exclusion criteria are listed below in Table 1.

**Table 1: Inclusion and Exclusion Criteria**

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
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<tbody>
<tr>
<td><strong>CDC Criteria:</strong></td>
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<tr>
<td>- Age ≥ 18 years old</td>
<td>- Any known renal dysfunction (CrCl &lt;60 ml/min)</td>
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<tr>
<td>- Without acute or established HIV infection</td>
<td>- History of HIV-positive test</td>
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<td>- Illicit drug injection within the past 6 months</td>
<td>- Self-report of taking PrEP at baseline</td>
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<tr>
<td>AND at least one of the following:</td>
<td>- Indications for post-exposure prophylaxis (PEP):</td>
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<td>- Any sharing of injection or drug preparation equipment in the past 6 months</td>
<td>- Exposure to bodily fluids within 72 hours that is known to be HIV-positive or at substantial risk for HIV</td>
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<td>- Risk of sexual acquisition:</td>
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<tr>
<td>- Anal sex without condoms</td>
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<td>- Bacterial STI in the last 6 months</td>
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<tr>
<td>- Infrequent condom use with 1 or more partners of unknown HIV status or known to be at substantial risk for HIV</td>
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<td>- Ongoing relationship with an HIV-positive partner</td>
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<tr>
<td><strong>Study Specific Criteria:</strong></td>
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<tr>
<td>- Must have accessed SEP services at least once in the last month</td>
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<td>- Able to meet with a navigator at the syringe exchange program</td>
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<td>- Ability to give informed consent</td>
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<tr>
<td>- Willing to provide contact information and be contacted by phone</td>
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<tr>
<td><strong>Exclusion Criteria:</strong></td>
<td>- History of chronic HBV infection</td>
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<td>- Pregnancy</td>
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<tr>
<td>- Signs or symptoms of acute HIV infection:</td>
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<tr>
<td>- Fever</td>
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<td>- Fatigue</td>
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<td>- Myalgia/arthralgia</td>
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<td>- Skin rash</td>
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<td>- Headache</td>
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<td>- Pharyngitis</td>
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<td>- Cervical adenopathy</td>
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<td>- Night sweats</td>
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<td>- Diarrhea</td>
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HIV negative status will be evaluated at baseline with HIV antibody testing using the OraQuick Rapid HIV-1 antibody test in the absence of any signs or symptoms of acute HIV infection in the preceding month (see Table 1). Prior to PrEP initiation, participants must receive an assessment of their renal function and a test for HBV infection. As all participants in our study will need a visit with a PrEP provider to get a PrEP prescription, these additional tests will be conducted at the discretion of the respective PrEP provider.

3.3 Participant Protection and Confidentiality:

Prior to recruitment, we will obtain Yale Institutional Review Board (IRB) approval by submitting an application for approval of study design and safety. This application must be approved prior to the initiation of the study. In compliance with the Yale IRB application requirements, we will include an Authorization and Consent for Participation in Research Project 200 FR. 1 form. This form includes an invitation to participate in the study, description of the research project and procedures, potential risks and benefits, economic considerations, treatment alternatives, confidentiality and privacy agreements, and guidance on voluntary participation and withdrawal (Appendix B). All participants must be able to provide written, informed consent.

All research investigators must complete a Health Insurance Portability and Accountability Act (HIPAA) training session and provide evidence of certification to the Yale IRB. All participants’ personally identifiable health information will remain protected under strict HIPAA compliance. Records collected throughout our study will be secured on an encrypted web-based data management system, only accessible by approved researchers requiring direct access to the information. To protect personal health information, each
participant’s file will be de-identified and codified. Once the analyses are complete, we will destroy all personal participant data.

3.4 Study Variables and Measures:

The independent variable is a standardized PrEP navigation intervention with a trained PrEP navigator. This intervention will include motivational interviewing and SBCM. The control variable will be an enhanced SEP harm reduction standard of care with a PrEP information pamphlet. The typical standard of care for a SEP is to provide sterile syringes and injection equipment to its clients. The dependent variable and primary outcome will be PrEP initiation rates in both groups, 12 weeks after randomization. PrEP initiation will be confirmed via self-report and a urine tenofovir concentration of greater than 10ng/mL. Secondary outcomes, assessed by self-report at baseline and week 12, include HIV risk behaviors (needle sharing, sexual practices), awareness of PrEP and its function, likelihood of starting PrEP, and perception of personal risk for HIV acquisition before and after the intervention (Appendix C). We will assess the average change in scores in these pre and post assessment measures between the control and intervention groups.

For those participants who initiate PrEP, an exploratory outcome will be sustained adherence evaluated at 18 weeks after randomization. Adherence will be evaluated via self-report and confirmatory DBS testing, with participants indicating how consistently they took the medication (number of doses per week). By collecting blood from a fingerstick, we will use a threshold of 700 fmol/punch to represent a cumulative amount of four or more doses of PrEP per week over the last 6-8 weeks.

3.5 Methodology:
3.5.1 Assignment of Intervention

All participants will be assigned to either the intervention or control group through stratified randomization. The participants will be randomized using computer-generated block randomization with randomly selected block sizes. Stratification will be by SEP site and insurance status. There will be a 1:1 allocation to intervention and control groups. Immediately following randomization, the control and intervention groups will receive their respective interventions. This ensures that all participants in the PrEP navigation group receive at least one in-person PrEP navigation session and that all members of the control group receive their PrEP information pamphlets.

3.5.2 Intervention Design

The PrEP navigation will include a minimum of one session, with the option to attend up to five sessions total. All PrEP navigation sessions must be completed within 90 days of randomization. The mandatory initial session will be 45-60 minutes in length and the duration of subsequent sessions will vary based on participant needs. In the initial session, the PrEP navigator will utilize a structured and standardized manual that explores various SBCM concepts such as engagement, strengths assessment, personal case planning, and resource acquisition. The motivational interviewing component will weave in goal setting, decision making, positive reinforcement, and attitude change. The focus on this initial session will be to help participants explore identified risk behaviors and motivations towards initiating PrEP. The additional sessions will provide assistance with connecting to providers, transportation, scheduling appointments, and accessing prescriptions. Each PrEP navigator will have a copy of the baseline assessment as a reference during this session.
The PrEP navigators will be case managers from the community with a minimum of a bachelor’s degree. All PrEP navigators will attend a multi-day mandatory training on the principles and application of motivational interviewing and strengths-based case management. They will also learn how to deliver the standardized intervention manual objectives for the initial PrEP navigation session. The quality of the PrEP navigation sessions will be assessed by the project director via review of strengths assessments, action plans, and case logs. Participants in the PrEP navigation intervention group will also receive the PrEP pamphlet that the control group gets.

3.5.3 Control Design

Participants in the control group will receive a PrEP pamphlet and the SEP harm reduction standard of care. The PrEP pamphlet will be based on CDC materials regarding the risk of HIV in PWID, use of PrEP in PWID, local providers, prescription access, and financial assistance for PrEP (Appendix D).

3.6 Data Collection:

Data on the primary outcome of PrEP initiation rates will be collected at intervals of 4, 8, and 12 weeks after the time of the initial intervention in each group (PrEP navigation session vs. PrEP pamphlet). The research coordinators will ask participants whether they have made an appointment with a PrEP provider or initiated PrEP. This information will be collected by telephone calls made to each participant and their self-reported answers. If participants report that they have initiated PrEP, they will be asked to come into the SEP site within a week for confirmatory urine tenofovir testing.

An interviewer-administered baseline assessment that includes sociodemographic factors, PrEP awareness, risk perception, HIV risk behaviors, and likelihood of starting
PrEP will be collected at the beginning of the study after informed consent. This same assessment will be re-administered at the completion of the study, 12 weeks after randomization to assess secondary outcomes.

Data for the exploratory outcome of sustained adherence will be collected at week 18 weeks. This will be evaluated by self-report and a confirmatory DBS testing threshold of 700 fmol/punch. See Appendix E for the data collection form.

### 3.7 Sample Size Calculation:

Based on the review of the literature and adaptation of previous study results to our study setting, outcome, and population, the resulting absolute difference we predict between the intervention and control groups for PrEP initiation is 15%. From this data, we estimate the initiation rates in the intervention and control groups will be 18% and 3%, respectively. For the given effect size (population proportions of 0.03 vs. 0.18), sample sizes would have to be 65 in each group (total 130) to reach a 2-tailed alpha of 0.05 and a power of 80%. The justification for these values is informed by very low levels of PrEP initiation in PWID, especially in the SEP setting. As a baseline of PrEP initiation in the control group, we predict a 3% initiation rate through the PrEP pamphlet and harm reduction standard of care. Therefore, our predicted effect size for the intervention group is an 18% rate of PrEP initiation in participants receiving PrEP navigation. To maintain the ability to detect this effect size, we will also account for an estimated 20% loss to follow up which will increase our desired sample size to 156 participants. See section 2.4.9 for a full justification of the calculation, and Appendix F for the calculation.

### 3.8 Analysis:
Statistical analyses will be carried out by researchers blinded to group allocation. All data will be analyzed in an intention to treat approach, based on participants’ original group allocation. Statistical significance is defined as $p<0.05$ for all measurements. The primary outcome will be PrEP initiation by 12 weeks, reported as a dichotomous variable. Results will be compared via a chi square test for two unpaired samples. The PrEP adherence evaluation at 18 weeks will assess whether or not participants took the pill at least 4 days of the week in the preceding 6 weeks. Therefore, adherence will be operationalized as a dichotomous variable and compared via chi square.

Baseline characteristics will be compared to ensure limited variation between the intervention and control groups. Continuous variables (age, mean HRBS score) will be reported as a mean and standard deviation and compared via student t-test. Categorical variables (gender, sexual orientation, education etc.) will be compared using a chi square test and reported as a proportion of the population. If we do find any differences between the control and intervention groups, we will adjust for any differences with a multiple logistic regression. The pre and post assessment will compare overall PrEP awareness, HIV risk behaviors, perception of HIV risk, and likelihood of starting PrEP, before and after the respective interventions in the treatment and control groups. We will assess the average change in these pre-post assessment measures between the control and intervention groups. These results will be analyzed using a Wilcoxon signed rank test for non-parametric paired samples and report the level of statistical significance.

3.9 Timeline and Resources:

The proposed study will be completed within the allotted two-year timeframe. We will allocate 3 months for the IRB approval process. All PrEP navigators will attend a
multi-day mandatory training on the principles and delivery of the standardized
intervention manual objectives for the initial PrEP navigation session. This training will
occur immediately after IRB approval, before enrollment begins. Participant recruitment
and enrollment will begin at month 4 and will occur on a rolling basis over the course of
12 months. After the 12 months, enrollment will stop but data collection will continue for
an additional 5 months. This ensures that we obtain the 12-week PrEP initiation rates for
the last participants recruited plus the additional 6 weeks needed to evaluate sustained
adherence. There will be a 5-month period at the end of the study for data analysis. Table
2 illustrates the proposed timeline.

The study will take place at four SEP sites throughout the state of Connecticut.
The personnel requirement for each study site will include: a research coordinator to
enroll patients, two PrEP navigators to implement the intervention, a research assistant to
follow up with patients and collect confirmatory labs, a project director to oversee the
work of the PrEP navigators, and a research analyst to gather and organize the data. Each
SEP site will have an office space reserved for the PrEP navigator to conduct the
intervention visits. At the end of the study, the research analysts will help with data entry
and statistical calculations.

All participants will receive a $50 gift card as compensation for completion of the
baseline and 12-week assessments. They will also receive $10 for giving their
confirmatory urine sample and $25 for their confirmatory DBS fingerstick sample.
### Table 2: Proposed Timeline

| Specific Steps          | Month | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  | 11  | 12  | 13  | 14  | 15  | 16  | 17  | 18  | 19  | 20  | 21  | 22  | 23  | 24  |
|-------------------------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| IRB Approval            |       | X   | X   | X   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Staff Training          |       |     |     |     | X   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Enrollment/Recruitment  |       | X   | X   | X   | X   | X   | X   | X   | X   | X   | X   | X   | X   |     |     |     |     |     |     |     |     |     |     |     |     |
| Data Collection         |       | X   | X   | X   | X   | X   | X   | X   | X   | X   | X   | X   | X   |     |     |     |     |     |     |     |     |     |     |     |     |
| Data Analysis           |       |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

### 3.10 References:

CHAPTER 4: CONCLUSION

4.1 Advantages and Disadvantages:

Our proposed study design has a number of advantages. The effectiveness design delivers the PrEP navigation intervention in SEP settings that are already being utilized by PWID. Providing PrEP education and implementing PrEP navigation in the real-world settings of SEPs increases the generalizability of the intervention. Additionally, the PrEP navigation sessions are tailored to individual needs to help facilitate participants’ access to PrEP. This individualization provides a high degree of external validity with indications for broader implementation in other SEPs in the future. Lastly, the RCT design and use of stratified randomization limits bias, mitigates known and unknown confounders, and will describe the overall relationship between PrEP navigation and rates of PrEP initiation among PWID.

In terms of limitations, we know that the pathway from PrEP navigation to PrEP initiation requires several steps. While the purpose of the PrEP navigators is to help participants overcome barriers and increase access, previous studies have had high losses to follow up in PWID.\textsuperscript{1,2} While we account for loss to follow up in our sample size calculation and try to reduce it by ensuring participants are accessible by phone, it is hard to completely prevent and predict this challenge. Additionally, PrEP initiation does not always result in sustained PrEP adherence. However, given the low baseline uptake of PrEP in PWID and data supporting continued use after initiation, we hope that this can be an important first step for future studies.\textsuperscript{3} Lastly, our study’s SEPs are located solely within Connecticut in primarily urban areas where access to PrEP providers is relatively high.\textsuperscript{4} As a result, our
findings may not generalize to rural PWID or geographic areas where these services are not as accessible.

4.2 Clinical and Public Health Significance:

Research is urgently needed to understand how to package PrEP as a harm reduction tool that might be efficacious and make PWID more likely to engage in harm reduction techniques. The proposed study may help in addressing this critical gap in the literature about how best to reach PWID to promote PrEP initiation. Our study uses the evidence-based successes of patient navigation for PWID and applies them in the community-based setting of SEPs to increase PrEP initiation. The overall clinical and public health significance of increasing PrEP initiation among PWID is a resulting reduction in HIV incidence. This public health benefit is consistent with the goals of current national initiatives to reduce the number of new HIV infections in the United States by 90% by 2030. If this intervention is successful, it can provide insight on how PrEP navigation can be incorporated as part of the standard of care in SEPs in the future. The results of this study can also be a basis for future studies to target long-term PrEP use and adherence among PWID.

4.3 References:


Appendix A: Recruitment Flyer

Yale SCHOOL OF MEDICINE

Volunteers Needed for a Research Study

Are you a person who injects drugs and uses services from a syringe exchange?

We are conducting a research study to investigate whether a patient navigation intervention can help connect people who inject drugs to an HIV-prevention medication called pre-exposure prophylaxis or PrEP.

Who is eligible?
- People who inject drugs accessing a syringe exchange
- Age 18+
- HIV-negative

What will you have to do?
- Receive education about a medication called pre-exposure prophylaxis or PrEP
- Provide personal information regarding your HIV risk behaviors and knowledge/attitudes about PrEP
- Be willing to meet with a PrEP navigator for at least 1 session

Compensation:
- Up to $135 as reimbursement for completion of assessments and collection of urine and blood samples

To learn more or to see if you are eligible to participate:
Call us at 203-555-1234 or email prepnavstudy@yale.edu
Appendix B: Compound Consent and Privacy Rule Authorization Form

CONSENT FOR PARTICIPATION IN A RESEARCH STUDY
200 FR. 1 (2016-2)

YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: Promoting Pre-exposure Prophylaxis Among People Who Inject Drugs Accessing Syringe Exchange Programs

Principal Investigator: E. Jennifer Edelman, MD, MHS

Invitation to Participate and Description of Project
We are inviting you to participate in a research study designed to look at the effects of a standardized patient navigation intervention on pre-exposure prophylaxis (PrEP) initiation among people who inject drugs accessing syringe exchange programs. You have been asked to participate because you have met the inclusion criteria as an HIV-negative person who injects drugs with risk factors for HIV. PrEP is a medication that can significantly reduce the risk of HIV acquisition in people who inject drugs by as much as 83%.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the research study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, possible benefits and possible alternative treatments. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Description of Procedures
If you agree to participate in this study, our research coordinator will ask you questions regarding your beliefs, risk behaviors and demographics. These will include questions on your PrEP awareness, risk behaviors, likelihood of starting PrEP, and HIV risk beliefs. We will also collect demographics such as age, gender identity, sexual orientation, race/ethnicity, education, income, employment status, insurance coverage, past PrEP use, medication use, history of sex work, and transportation needs.

You will then be randomly assigned to receive (a) a patient navigation intervention with a PrEP navigator OR (b) a PrEP information pamphlet and the usual standard of care from the syringe exchange program. All participants will receive the PrEP information pamphlet regardless of group allocation. Randomization occurs through a computer-based system in which you have equal chances of being assigned to the intervention or control group. Once you have been assigned to a group, you will be assigned a unique study code that will be used to identify you throughout the study.
If you are assigned to the PrEP navigation intervention, you will be asked to attend an initial session with a PrEP navigator, lasting 45-60 minutes. During the first session, the navigator will use a standardized manual to explore your strengths and perceived motivations or barriers towards PrEP initiation. You will have the option to attend up to five PrEP navigation sessions total and the length of each subsequent session will vary based on your needs. The additional sessions can provide assistance with connecting to providers, transportation, scheduling appointments, and accessing prescriptions.

Research staff will contact you by phone at 4, 8, and 12 weeks after being randomized to receive either the intervention or control condition. At this time, you will be asked if you have made an appointment with a PrEP provider or initiated PrEP. If you report that you initiated PrEP, you will be asked to come into the syringe exchange within a week for confirmatory urine testing. At the 12-week mark after your intervention, we will repeat the assessment on your beliefs about PrEP and risk behaviors that you took at the beginning of the study. If you are confirmed to have initiated PrEP, you will be contacted again at 18 weeks to assess if you are still taking PrEP and how many times a week you take the medication. We will ask you to come into the syringe exchange program again to get a confirmatory fingerstick blood test.

A description of this study is available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time. You will be told of any significant new findings that are developed during the course of your participation in this study that may affect your willingness to continue to participate. If research results are published, your name and personal information will not be given.

**Risks and Inconveniences**

We identify very few physical risks, discomforts or inconveniences associated with the study. Some questions regarding your HIV risk behaviors ask for personal details about your sexual history and injection drug use, which might make you feel uncomfortable. These questions are not meant to judge you. They will be used to understand your risk behaviors that could potentially expose you to HIV. Other risks from participating in the study include the breach of confidentiality about your health status and participation in the study. This is very unlikely to occur, as all study investigators are trained and certified in research privacy. A minor inconvenience may be the monthly phone calls with a representative from the study. We also ask that you provide blood, urine and oral swab samples during the study to confirm HIV-negative status and PrEP use. The blood will be collected via fingerstick, which uses a sterile lancet to obtain a small quantity of capillary blood for testing. There are no major risks associated with this technique.

**Benefits**

The potential benefits of this study are connection to PrEP services and the initiation of PrEP medication, which can significantly reduce your risk of acquiring HIV as a person who injects drugs.

**Economic Considerations**
There are no costs associated with participation in the study. However, you will be responsible for the costs associated with the PrEP medication and PrEP provider visit per the health center’s policies. To mitigate these potential barriers, we have provided information on how to acquire PrEP at low cost or even free of charge. Depending on your insurance provider, you may be eligible for full coverage of these costs. Additionally, many of the medical providers listed on the PrEP provider guide will be able to offer assistance in signing up for health insurance and applying for payment assistance programs. As compensation for your participation in the study, you will receive $50 for each assessment you complete, $25 for a fingerstick sample, and $10 for a urine sample.

Treatment Alternatives
If you choose not to participate in this study, there are no alternative treatments available. If you are interested in PrEP but do not want to participate in this study, you may ask for more information from your primary care provider.

Confidentiality and Privacy
We understand that information about your health is personal, and we are committed to protecting the privacy of that information. Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as required by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases, such as HIV or hepatitis. Information will be kept confidential by using only identification numbers on study forms, storing signed forms in locked cabinets, and password protecting data stored on a computer. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific permission for this activity is obtained.

The information about your health that will be collected in this study includes:
- Research study records
- Records about phone calls made as part of this research
- Records about your study visits

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes. All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine are required to comply with HIPAA and to ensure the confidentiality of your information.

Voluntary Participation and Withdrawal
Participating in this study is voluntary. You are free to choose not to take part in this study. Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this
research study and will not receive study interventions as a study participant if you do not allow use of your information as part of this study.

If you do become a subject, you are free to stop and withdraw from this study at any time during its course. To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. This will cancel any future phone calls. The researchers may also withdraw you from participating in the research if necessary. When you withdraw from the study, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to ensure the integrity of the study and/or study oversight. There are no penalties involved with withdrawal from the study.

Questions
We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the permission form carefully – as long as you feel is necessary – before you make a decision.

Authorization
I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

Name of Subject:_____________________________
Signature:___________________________________
Date:______________________________________

___________________________________________ ___________________
Signature of Principal Investigator Date

or

___________________________________________ ___________________
Signature of Person Obtaining Consent Date

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator.

If, after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at 203-432-5919. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.
Appendix C: Baseline and Post Intervention Assessment

Baseline and Post Intervention Assessment

This assessment will be administered by a trained interviewer. It should take about 30 minutes to complete.

Participant Study ID: ________________

Section 1: Baseline Demographics
1) What is your age? ______
2) What is your gender identity? (self-described)
   □ Male □ Female □ Transgender Woman □ Transgender Man □ Other: ______
3) What is your sexual orientation? (self-described)
   □ Heterosexual/straight □ homosexual/gay/lesbian □ bisexual □ Other: ______
4) What is your ethnicity/race? (check all that apply)
   □ White/Caucasian □ Black/African American □ Hispanic/Latino □ Other:_____
5) What is your education level?
   □ Less than high school □ High school graduate □ More than high school
6) What is your annual income?
   □ <10k □10-19,999 □>20k
7) What is your employment status?
   □ Employed □ Unemployed
8) Do you have health insurance?
   □ Yes □ No
9) Have you ever used PrEP before?
   □ Yes □ No
10) Do you take any prescription medications daily?
    □ Yes □ No
11) Would you need assistance with transportation in order to get to a PrEP provider appointment?
    □ Yes □ No

Section 2: HIV Risk Taking Behavior Scale (HRBS)¹

A. Drug Use Section:
“I am going to ask you a few questions about your drug use over the last month…”

1) How many times have you injected any drugs in the last month?
   None……………………………0
   Once a week or less…………1
   More than once a week………2
   (but less than once a day)
   Once a day……………………3
   2-3 times a day…………………4
   More than 3 times a day………5
IF SUBJECT HASN'T INJECTED IN THE LAST MONTH, SCORE ZERO FOR THE DRUG USE SECTION, AND GO TO QUESTION 7.

2) How many times in the last month have you used a needle after someone else had already used it?
   No times................................. 0
   One time................................. 1
   Two times............................... 2
   3-5 times............................... 3
   6-10 times......................... 4
   More than 10 times........... 5

3) How many different people have used a needle before you in the last month?
   None........................................0
   One person............................. 1
   Two people.......................... 2
   3-5 people............................ 3
   6-10 people........................... 4
   More than 10 people............ 5

4) How many times in the last month has someone used a needle after you have used it?
   No times................................. 0
   One time................................. 1
   Two times............................... 2
   3-5 times............................... 3
   6-10 times......................... 4
   More than 10 times........... 5

5) How often, in the last month, have you cleaned needles before re-using them?
   Doesn't re-use.......................... 0
   Every time............................. 1
   Often................................. 2
   Sometimes............................ 3
   Rarely................................. 4
   Never................................. 5

6) Before using needles again, how often in the last month did you use bleach to clean them?
   Doesn't re-use.......................... 0
   Every time............................. 1
   Often................................. 2
   Sometimes............................ 3
   Rarely................................. 4
   Never................................. 5

Drug subtotal: ________
**B. Sexual Behavior Section:**

“I am going to ask you a few questions about your sexual behaviors over the last month…”

7) How many people, including clients, have you had sex with in the last month?
   - None........................................0
   - One.........................................1
   - Two..........................................2
   - 3-5 people.................................3
   - 6-10 people.................................4
   - More than ten people...............5

IF NO SEX IN THE LAST MONTH, SCORE ZERO FOR SEXUAL BEHAVIOR

8) How often have you used condoms when having sex with your regular partner(s) in the last month?
   - No regular partner ..........................0
   - Every time....................................1
   - Often..........................................2
   - Sometimes..................................3
   - Rarely.........................................4
   - Never.........................................5

9) How often did you use condoms when you had sex with casual partners?
   - No casual partners ..........................0
   - Every time....................................1
   - Often..........................................2
   - Sometimes..................................3
   - Rarely.........................................4
   - Never.........................................5

10) How often have you used condoms when you have been paid for sex in the last month?
   - No paid sex..................................0
   - Every time....................................1
   - Often..........................................2
   - Sometimes..................................3
   - Rarely.........................................4
   - Never.........................................5

11) How many times did you have anal sex in the last month?
   - No times.................................0
   - One time....................................1
   - Two times.................................2
   - 3-5 times.................................3
   - 6-10 times.................................4
More than 10 times..................... 5

Sexual Behavior Sub-total: __________

TOTAL SCORE: _________________
(drug use subtotal + sexual behavior subtotal)

Section 3: Assessing PrEP Awareness^{2}

1) Pre-exposure prophylaxis or PrEP is an antiretroviral medicine, such as Truvada®, taken for months or years by a person who is HIV negative to reduce the risk of getting HIV. Before today, have you ever heard of PrEP?

2) Before today, did you know that PrEP can prevent the transmission of HIV from sharing injection equipment?

3) In the past 12 months, have you had a discussion with a health care provider about taking PrEP?

4) In the past 12 months, have you taken PrEP to reduce the risk of getting HIV?

Section 4: Likelihood of Initiating PrEP^{3}

1) How likely are you to take a pill for PrEP each day to prevent HIV infection?
   1- Very unlikely to take PrEP
   2- Unlikely to take PrEP
   3- Unsure
   4- Likely to take PrEP
   5- Very likely to take PrEP

Section 5: Belief of one’s own risk of HIV^{4}

1) How would you rate your risk for contracting HIV?
   1- Extremely unlikely
   2- Unlikely
   3- Neutral
   4- Likely
   5- Extremely likely
References:


Appendix D: PrEP Pamphlet Information

HIV and Injecting Drugs 101

Sharing needles, syringes, or other drug injection equipment like cookers puts people who inject drugs at high risk for getting HIV.

Can I get HIV from injecting drugs?

Yes, if you share needles, syringes, or other injection equipment with someone who has the virus. Sharing can transfer blood from person to person, and blood can carry HIV.

Also, when you’re high on drugs, you’re more likely to take risks with sex, which can increase your risk for getting HIV.

How can I lower my risk of getting HIV?

The best way is to stop injecting drugs. To find a treatment program to help you quit, visit findtreatment.samhsa.gov or call 1-800-662-HELP (4357).

If you choose to inject drugs, here are some ways to lower your risk for HIV:

• Use new, sterile needles and syringes every time you inject, and never share injection equipment.
• If you do share needles and syringes, always clean used needles and syringes with bleach. Cleaning your needles and syringes can greatly reduce your risk for HIV and hepatitis C.
• Bleach can’t be used to clean water or cotton. New, sterile water or cotton should be used each time.
• Take daily medicine to prevent HIV called pre-exposure prophylaxis (PrEP). When taken daily, PrEP is highly effective for preventing HIV from sex or injection drug use.
• If you think you’ve been exposed to HIV within the last 3 days, ask a healthcare provider about post-exposure prophylaxis (PEP) right away. PEP can prevent HIV, but it must be started within 72 hours.
• Use condoms the right way every time you have anal or vaginal sex, or choose activities with little to no risk like oral sex. Abstinence (not having sex) is always an option.

Where can I get new, clean needles and syringes?

• Many communities have syringe services programs that give out new, clean needles, syringes, bleach kits, and other supplies. To find one near you, visit nasen.org/directory.
• Some pharmacies sell new, clean needles and syringes.
• In some places, doctors can write prescriptions for new, clean needles and syringes.

For more information please visit www.cdc.gov/hiv

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of HIV/AIDS Prevention

July 2019
How does PrEP help prevent HIV infection?

- The two medications that make up PrEP block the virus’s ability to start infections.
- If you take PrEP daily, the presence of the medication in your blood and tissues can stop the virus from establishing itself in your body.
- PrEP is highly effective as long as you take it every day. Condoms provide additional protection against HIV, as well as most sexually transmitted diseases (STDs) and unintended pregnancy.

How should this medicine be used?

- You must take one tablet by mouth every day.
- Do not stop taking PrEP without talking to your doctor. When your supply of medicine starts to run low, contact your doctor or pharmacy to get more.
- You will be at higher risk of becoming infected with HIV if you miss multiple doses or stop taking PrEP than if you take it every day.

PrEP medications are very safe

Some people in clinical studies of PrEP had early side effects, such as an upset stomach or loss of appetite, but these were mild and usually went away in the first month. Some people also had a mild headache. No serious side effects were observed. You should tell your health care provider if these or other symptoms become severe or do not go away.

What side effects can this medication cause?

- Most people do not have side effects while taking PrEP. However, you might experience some of the following when you begin taking the medication:
  - upset stomach
  - headache
  - vomiting
  - loss of appetite
- These side effects usually fade during the first month of taking PrEP. Tell your doctor if any of these symptoms are severe or do not go away.

Is PrEP all you need?

Even though PrEP is one important tool for protecting yourself from HIV, no method offers 100% protection. While taking your PrEP medicine, you can further reduce your chance of getting HIV by:

- Using condoms during sex
- Cleaning injection equipment if you inject drugs

Plus, while PrEP greatly reduces your risk for contracting HIV, it won’t protect you from other sexually transmitted infections. Together, these methods offer more complete protection.
If you believe you were exposed to HIV in the past 72 hours (3 days), go immediately to an emergency room or urgent care clinic and ask for HIV Post-Exposure Prophylaxis (PEP).

What is Pre-exposure Prophylaxis (PrEP)?

“PrEP” stands for Pre-Exposure Prophylaxis. The word “prophylaxis” means to prevent or control the spread of an infection or disease. Pre-exposure prophylaxis is the use of antiretroviral (ARV) medication by HIV-negative individuals at high risk of HIV infection to reduce their risk.

As of December, 2016 the single FDA-approved option for PrEP is once-daily dosing of a medicine called Truvada® (emtricitabine/tenofovir). Truvada was approved for use as PrEP in 2012 but has been used successfully as a component of HIV treatment since 2005. When a negative person is exposed to HIV through sex or injection drug use, these medicines can work to keep the virus from establishing a permanent infection – keeping the individual HIV-negative. PrEP is currently recommended for certain sexually active gay, bisexual and other men who have sex with men (MSM), heterosexual active men and women, and intravenous drug users (IDU). The Centers for Disease Control and Prevention (CDC) estimates that 1 in 4 MSM and 1 in 5 IDU might be good candidates for PrEP. More information on PrEP is available on the CDC website.

Why take PrEP?

With 50,000 new HIV infections each year in the United States, and no cure or vaccine available, prevention is key. PrEP has been shown to be highly effective and when taken every day may reduce a person’s risk of getting HIV by more than 90%. PrEP can be used in combination with condoms and other risk-reduction methods for even greater protection. Most people experience few if any side effects when taking PrEP.

How do I get PrEP?

PrEP is only available by prescription. If you are interested in PrEP and do not have somewhere you regularly receive medical care or have had difficulty discussing PrEP with your doctor or nurse practitioner, please refer to the following list. These facilities all have at least one provider experienced with PrEP and offer respectful medical care to populations including MSM, IDU, and LGBT individuals. Some providers have indicated they have weekend and evening hours.

How do I pay for PrEP?

- **Uninsured:** You may qualify for free or low-cost health insurance. View your options at [www.accesshealthct.com](http://www.accesshealthct.com).
- **Insured:** The maker of Truvada offers up to $7,200/year of medication co-pay assistance, regardless of financial need (no application required, just enter your information): [www.gilead.com](http://www.gilead.com). There are also other resources such as the Patient Access Network or the Patient Advocate Foundation that may be able to assist with the cost of Truvada. Speak with any medical providers below for more info.
- **Not eligible for Insurance:** Choose a federally qualified health center (FQHC) – these clinics will see undocumented and other patients ineligible for insurance on a sliding-scale fee basis. The maker of Truvada can provide PrEP medication free of cost (application required, needs doctor’s signature): [www.gileadadvancingaccess.com/get-started-advancing-access](http://www.gileadadvancingaccess.com/get-started-advancing-access).

All major health insurance companies and state-provided insurance in CT will cover PrEP medication and the necessary medical care. Depending on your plan, you may be responsible for co-pays, co-insurance, and/or deductibles. A number of resources are available to help with these costs and can reduce or even eliminate what you pay out of pocket. Project Inform has an excellent flow-chart that explains your options for affording PrEP: [http://www.projectinform.org/pdf/PrEP_Flow_Chart.pdf](http://www.projectinform.org/pdf/PrEP_Flow_Chart.pdf).

Many of the medical providers listed on the following page will be able to offer assistance in signing up for health insurance and applying for payment assistance programs. If a site convenient to you cannot offer you such assistance, or you have other questions about whether PrEP may be right for you, please contact Luis Diaz at the CT Department of Public Health @ 860-509-7418 or [Luis.Diaz@CT.Gov](mailto:Luis.Diaz@CT.Gov).

More Information:

- **CDC Website:** [http://www.cdc.gov/hiv/basics/prep.html](http://www.cdc.gov/hiv/basics/prep.html)
- **Project Inform PrEP information and educational materials:** [www.projectinform.org](http://www.projectinform.org)
- **Gilead Website:** [https://start.truvada.com/](https://start.truvada.com/)
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<th>Telephone</th>
<th>Program Contact</th>
<th>Program Email</th>
<th>Additional Information</th>
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<tr>
<td>Community Health Center, Inc.</td>
<td>5 North Main Street, Enfield, CT 06082</td>
<td>860-266-0257</td>
<td>Maria Lorenzo Or Nicole Morgan, LPN</td>
<td><a href="mailto:LorenzM@CHC1.com">LorenzM@CHC1.com</a> Or <a href="mailto:MorganN@chc1.com">MorganN@chc1.com</a></td>
<td>Primary care available on site</td>
</tr>
<tr>
<td>Planned Parenthood of Southern New England (PPSNE)</td>
<td>111 Hazard Avenue, Enfield, CT 06082</td>
<td>860-741-2197</td>
<td>Tyrell Cooper, APRN and Jennifer Bouley, Health Center Manager</td>
<td><a href="mailto:PrePnowPP@ppsne.org">PrePnowPP@ppsne.org</a></td>
<td><a href="http://WWW.PPSNE.ORG">WWW.PPSNE.ORG</a> OR ZIPPER® in APP Store lists all services, locations &amp; appointments</td>
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<tr>
<td>Community Health &amp; Wellness Center</td>
<td>469 Migeon Avenue, Torrington, CT 06790</td>
<td>860-489-0931</td>
<td>Provider: Paul Anthony, MD</td>
<td></td>
<td>Primary care available on site</td>
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<tr>
<td>Planned Parenthood of Southern New England (PPSNE)</td>
<td>249 Winsted Road, Torrington, CT 06790</td>
<td>860-489-5500</td>
<td>Tyrell Cooper, APRN and Tammy Hreba, Health Center Manager</td>
<td><a href="mailto:PrePnowPP@ppsne.org">PrePnowPP@ppsne.org</a></td>
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<tr>
<td>University of Connecticut Health Center</td>
<td>263 Farmington Avenue, Farmington, CT 06032</td>
<td>860-679-4225</td>
<td>Juliana Mantey, RN</td>
<td><a href="mailto:mantey@uchc.edu">mantey@uchc.edu</a></td>
<td></td>
</tr>
<tr>
<td>CCMC/UCONN Pediatric, Youth + Family HIV Program</td>
<td>CT Children’s Medical Center 282 Washington St., 21 Hartford, CT 06106</td>
<td>860-545-9400, option 3</td>
<td>Gail Karas, RN</td>
<td><a href="mailto:Gkaras@connecticutchildrens.org">Gkaras@connecticutchildrens.org</a></td>
<td>Youth 14 and up</td>
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Connecticut Department of Public Health
HIV Prevention Program • 860-509-7807
www.ct.gov/dph

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<tr>
<td>Community Health Services</td>
<td>500 Albany Avenue, Hartford, CT 06120</td>
<td>860-808-8749</td>
<td>Nitza Agosto HIV/EIS Program Manager</td>
<td><a href="mailto:Nitza.agosto@chshartford.org">Nitza.agosto@chshartford.org</a></td>
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<td>Planned Parenthood of Southern New England (PPSNE)</td>
<td>1229 Albany Avenue, Hartford, CT 06112</td>
<td>860-728-0203</td>
<td>Tyrell Cooper, APRN and Stephanie Blanchard, Health Center Manager</td>
<td><a href="mailto:PrePnowPP@ppsne.org">PrePnowPP@ppsne.org</a></td>
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<td>Planned Parenthood of Southern New England (PPSNE)</td>
<td>1030 New Britain Avenue, West Hartford, CT 06110</td>
<td>860-953-6201</td>
<td>Tyrell Cooper, APRN and Jane Yousman, Health Center Manager</td>
<td><a href="mailto:PrePnowPP@ppsne.org">PrePnowPP@ppsne.org</a></td>
<td><a href="http://WWW.PPSNE.ORG">WWW.PPSNE.ORG</a> OR ZIPPER® in APP Store lists all services, locations &amp; appointments</td>
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<tr>
<td>First Choice Health Center</td>
<td>94 Connecticut Blvd, East Hartford, CT 06108</td>
<td>860-528-1359</td>
<td>Haimavathi Bhat, DO</td>
<td></td>
<td>Primary care available Saturday Hours: 8am-1:30pm <a href="http://www.chc.org">www.chc.org</a></td>
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<tr>
<td>Planned Parenthood of Southern New England (PPSNE)</td>
<td>319 Main Street, Manchester, CT 06040</td>
<td>860-643-1607</td>
<td>Tyrell Cooper, APRN and Caitlin Murphy, Health Center Manager</td>
<td><a href="mailto:PrePnowPP@ppsne.org">PrePnowPP@ppsne.org</a></td>
<td><a href="http://WWW.PPSNE.ORG">WWW.PPSNE.ORG</a> OR ZIPPER® in APP Store lists all services, locations &amp; appointments</td>
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<tr>
<td>Planned Parenthood of Southern New England (PPSNE)</td>
<td>1548 West Main Street, Willimantic, CT 06226</td>
<td>860-423-8426</td>
<td>Tyrell Cooper, APRN and Beth Murana, Health Center Manager</td>
<td><a href="mailto:PrePnowPP@ppsne.org">PrePnowPP@ppsne.org</a></td>
<td><a href="http://WWW.PPSNE.ORG">WWW.PPSNE.ORG</a> OR ZIPPER® in APP Store lists all services, locations &amp; appointments</td>
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<th>860-774-0533</th>
<th>Tyrell Cooper, APRN and Jessica Davila, Health Center Manager</th>
<th><a href="mailto:PrEPnowPP@pspne.org">PrEPnowPP@pspne.org</a></th>
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<td>The Waterbury Hospital</td>
<td>140 Grandview Avenue, Suite L-01 Waterbury, CT 06708</td>
<td>203-573-7250 ext. 6349</td>
<td>William Rosa</td>
<td>William.Rosa@wthlyhos p.org</td>
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<tr>
<td>Community Health Center, Inc.</td>
<td>51 North Elm Street Waterbury, CT 06702</td>
<td>860-266-0257</td>
<td>Maria Lorenzo Or Nicole Morgan, LPN</td>
<td><a href="mailto:LorenM@CHC1.com">LorenM@CHC1.com</a> Or <a href="mailto:MorganN@chc1.com">MorganN@chc1.com</a></td>
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<td>Planned Parenthood of Southern New England (PPSNE)</td>
<td>969 West Main Street, Waterbury, CT 06708</td>
<td>203-753-2119</td>
<td>Tyrell Cooper, APRN and Antonietta Schaalman, Health Center Manager</td>
<td><a href="mailto:PrEPnowPP@pspne.org">PrEPnowPP@pspne.org</a></td>
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<td>675 Main Street Middletown, CT 06457</td>
<td>860-266-0257</td>
<td>Maria Lorenzo Or Nicole Morgan, LPN</td>
<td><a href="mailto:LorenM@CHC1.com">LorenM@CHC1.com</a> Or <a href="mailto:MorganN@chc1.com">MorganN@chc1.com</a></td>
<td>Primary care available on site Open until 7pm M-Th, Open Saturday</td>
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<tr>
<td>Planned Parenthood of Southern New England (PPSNE)</td>
<td>26 Woman’s Way, Meriden, CT 06451</td>
<td>203-238-0542</td>
<td>Tyrell Cooper, APRN and Novia Butler, Health Center Manager</td>
<td><a href="mailto:PrEPnowPP@pspne.org">PrEPnowPP@pspne.org</a></td>
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<td>134 State Street Meriden, CT 06450</td>
<td>860-266-0257</td>
<td>Maria Lorenzo Or Nicole Morgan, LPN</td>
<td><a href="mailto:LorenM@CHC1.com">LorenM@CHC1.com</a> Or <a href="mailto:MorganN@chc1.com">MorganN@chc1.com</a></td>
<td>Primary care available on site Open until 7pm M-Th, Open Saturday</td>
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<p>| Community Health Center, Inc. | 85 Lafayette St. New Britain, CT 06450 | 860-266-0257 | Maria Lorenzo Or Nicole Morgan, LPN | <a href="mailto:LorenM@CHC1.com">LorenM@CHC1.com</a> Or <a href="mailto:MorganN@chc1.com">MorganN@chc1.com</a> | Primary care available on site Open until 7pm M-Th, Open Saturday |
| Planned Parenthood of Southern New England (PPSNE) | 100 Grand Street, New Britain, CT 06052 | 203-238-8097 | Tyrell Cooper, APRN and Novia Butler, Health Center Manager | <a href="mailto:PrEPnowPP@pspne.org">PrEPnowPP@pspne.org</a> | <a href="http://www.pspne.org">www.pspne.org</a> or ZIPPER® in APP Store lists all services, locations &amp; appointments |
| Community Health Center, Inc. | 395 North Main Street Bristol, CT 06010 | 860-266-0257 | Maria Lorenzo Or Nicole Morgan, LPN | <a href="mailto:LorenM@CHC1.com">LorenM@CHC1.com</a> Or <a href="mailto:MorganN@chc1.com">MorganN@chc1.com</a> | Primary care available on site Open until 7pm M-Th, Open Saturday |
| STD/Infectious Disease Clinic of Norwich | 107 Lafayette St. Norwich, CT 06360 | 860-823-6545 | Ann Hartman, RN, BSN Provider: Clifford Stobø, MD | Ann.hartman@hhhealth c.org | Primary care available on site Open until 7pm M-Th, Open Saturday |
| Planned Parenthood of Southern New England (PPSNE) | 12 Case Street, Norwich, CT 06360 | 860-889-5211 | Tyrell Cooper, APRN and Jeneen Ortzi, Health Center Manager | <a href="mailto:PrEPnowPP@pspne.org">PrEPnowPP@pspne.org</a> | <a href="http://www.pspne.org">www.pspne.org</a> or ZIPPER® in APP Store lists all services, locations &amp; appointments |
| Community Health Center, Inc. | 481 Gold Star Hwy, Suite 100 Groton, CT 06340 | 860-266-0257 | Maria Lorenzo Or Nicole Morgan, LPN | <a href="mailto:LorenM@CHC1.com">LorenM@CHC1.com</a> Or <a href="mailto:MorganN@chc1.com">MorganN@chc1.com</a> | Primary care available on site Open until 7pm M-Th, Open Saturday |
| Community Health Center, Inc. | 1 Shawn Cove New London, CT 06320 | 860-266-0257 | Maria Lorenzo Or Nicole Morgan, LPN | <a href="mailto:LorenM@CHC1.com">LorenM@CHC1.com</a> Or <a href="mailto:MorganN@chc1.com">MorganN@chc1.com</a> | Primary care available on site |
| Planned Parenthood of | 45 Franklin Street, New London, CT 06320 | 860-443-5820 | Tyrell Cooper, APRN or Jessica Johnson, | <a href="mailto:PrEPnowPP@pspne.org">PrEPnowPP@pspne.org</a> | <a href="http://www.pspne.org">www.pspne.org</a> or ZIPPER® in APP Store |</p>
<table>
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<tr>
<th>Southern New England (PSPNE)</th>
<th>Health Center Manager</th>
<th>Lists all services, locations &amp; appointments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Health Center, Inc.</td>
<td>263 Main St. #202 Old Saybrook, CT 06475</td>
<td>860-266-0257</td>
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</table>

| Planned Parenthood of Southern New England (PSPNE) | 263 Main Street, Old Saybrook, CT 06475 | 860-388-4459 | Tyrrell Cooper, APRN and Jasmin Oooco, Health Center Manager | PreEPnowFP@ppsne.org | Tuesday, Wed 9-5; Thurs 12-7 | www.ppsne.org or ZIPPER® in APP Store lists all services, locations & appointments |

| Community Health Center, Inc. | 114 East Main Street Clinton, CT 06413 | 860-266-0257 | Maria Lorenzo Or Nicole Morgan, LPN | LorenzM@CHC1.com Or MorganM@chc1.com | Primary care available on site |

| Anchor Health Initiative | 2200 Whitney Ave., Suite 290 Hamden, CT 06518 | 203-903-8308 | Iliana Velez ilevez@anchorhealthinitiative.org | | Tuesday, Wed 9-5; Thurs 12-7 | www.anchorhealthinitiative.org |

| Yale New Haven Hospital (YNHH)-PreP Services | 20 York Street, CB84 New Haven, CT 06510 | 203-688-3184 | Kelly Moore and Damaris Navarro | Kelly.Moore@ynnh.org & Damaris.navarro@ynnh.org | www.ppsne.org or ZIPPER® in APP Store lists all services, locations & appointments |

| Planned Parenthood of Southern New England (PSPNE) | 345 Whitney Avenue, New Haven 06511 | 203-503-0450 | Tyrrell Cooper, APRN and Lauren Pereira, Health Center Manager | PreEPnowFP@ppsne.org | www.ppsne.org or ZIPPER® in APP Store lists all services, locations & appointments |

| Nathan Smith Clinic-YNHH PreP Services | 15 York Street, New Haven, CT 06510 | 203-688-3184 203-688-5303 | Kelly Moore Provider: Dr. Onyema Oguzua | Kelly.Moore@ynnh.org Onyema.Oguzua@yale.edu | |

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| Connecticut Department of Public Health HIV Prevention Program | 860-509-7807 | www.ct.gov/dph |

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| Haelen Infectious Disease/YNHH PreP Services | 1450 Chapel Street New Haven, CT 06511 | 203-688-3184 203-789-4135 | Kelly Moore Provider: Dr. Michael Virata | Kelly.Moore@ynnh.org Michael.virata@ynnh.org | Open until 8pm M-F, 9:30a-12:30p Saturday |

| Cornell Scott Hill Health Corp | 428 Columbus Avenue New Haven, CT 06519 | 203-503-3550 | Delores Greensee dgreenee@cornellscott.org | | |

| Yale University AIDS Program-Community Health Care Van | 270 Congress Avenue New Haven, CT 06519 | 203-996-0161 | Rodolfo Lopez Provider: Sharon Joslin, APRN | | |

| Fair Haven Community Health Care (FHCHC) | 374 Grand Ave. New Haven, CT 06513 | 203-777-7411 203-503-0505 | Kelly Rivera Dr. Kristin Wagner | k.wagner@fhchc.com | Primary care available on site |

| Community Health Center, Inc. | 8 Delay Street Danbury, CT 06810 | 860-266-0257 | Maria Lorenzo Or Nicole Morgan, LPN | LorenzM@CHC1.com Or MorganM@CHC1.com | Primary care available on site |

| Planned Parenthood of Southern New England (PSPNE) | 44 Main Street, Danbury, CT 06810 | 203-743-2446 | Tyrrell Cooper, APRN and Jennifer Tommasini, Health Center Manager | PreEPnowFP@ppsne.org | www.ppsne.org or ZIPPER® in APP Store lists all services, locations & appointments |

<p>| Planned Parenthood of Southern New England (PSPNE) | 4697 Main St. Bridgeport, CT 06606 | 203-366-0664 | Tyrrell Cooper, APRN and Isolina Cole, Health Center Manager | <a href="mailto:PreEPnowFP@ppsne.org">PreEPnowFP@ppsne.org</a> | <a href="http://www.ppsne.org">www.ppsne.org</a> or ZIPPER® in APP Store lists all services, locations &amp; appointments |</p>
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<th>Clinic Name</th>
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<th>Phone</th>
<th>Provider/Coordinator</th>
<th>Email</th>
<th>Availability</th>
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<tr>
<td>Southwest Community Health Clinic (SCHC)</td>
<td>46 Albion Street, Bridgeport, CT 06605</td>
<td>203-332-3518</td>
<td>Luis Magana, PA</td>
<td><a href="mailto:imagana@swhc.org">imagana@swhc.org</a></td>
<td>Primary care available on site</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Deanne Walsh, APRN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimus Health Care, Inc.-PreP Services</td>
<td>471 Barnum Ave, Bridgeport, CT 06608</td>
<td>203-696-3260 X3435</td>
<td>Raphael Muniz, RW Programs Administrator/Coordinator</td>
<td><a href="mailto:rmuniz@ogothc.org">rmuniz@ogothc.org</a></td>
<td>Primary care available on site</td>
</tr>
<tr>
<td>Circle Care Center, World Health Clinicians, Inc.</td>
<td>618 West Avenue, Norwalk, CT 06850</td>
<td>203-852-9525 Ext. 309</td>
<td>Trish Garten</td>
<td><a href="mailto:tgarton@wwhcc.org">tgarton@wwhcc.org</a></td>
<td>Primary care available on site</td>
</tr>
<tr>
<td>Community Health Center, Inc.</td>
<td>49 Day Street, Norwalk, CT 06854</td>
<td>860-266-0257</td>
<td>Maria Lorenzo Or Nicole Morgan, LPN</td>
<td><a href="mailto:LorenzM@CHC1.com">LorenzM@CHC1.com</a> Or <a href="mailto:MorganM@chc1.com">MorganM@chc1.com</a></td>
<td>Primary care available on site</td>
</tr>
<tr>
<td>Stamford Infectious Diseases</td>
<td>166 W Broad St Suite 202, Stamford, CT 06902</td>
<td>203-353-1427</td>
<td>Lori Conklin, Providers: Lynda S. Street, M.D., Asha Shah, M.D.</td>
<td><a href="mailto:Lstreet@stamhealth.org">Lstreet@stamhealth.org</a> &amp; <a href="mailto:AShah1@shipnids.org">AShah1@shipnids.org</a></td>
<td>Primary care available on site</td>
</tr>
<tr>
<td>Anchor Health Initiative</td>
<td>30 Myano Lane, Suite 16, Stamford, CT 06902</td>
<td>203-674-1102</td>
<td>Idiana Velez, Director of PreP Navigation</td>
<td><a href="mailto:ivelez@anchorhealthinitiative.org">ivelez@anchorhealthinitiative.org</a></td>
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<th>Phone</th>
<th>Provider/Coordinator</th>
<th>Email</th>
<th>Availability</th>
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<tbody>
<tr>
<td>Planned Parenthood of Southern New England (PPSNE)</td>
<td>35 Sixth Street, Stamford, CT 06905</td>
<td>203-327-2722</td>
<td>Tyrell Cooper, APRN and Doris Walden, Health Center Manager</td>
<td><a href="mailto:PrePnow@pprne.org">PrePnow@pprne.org</a></td>
<td><a href="http://www.ppsne.org">www.ppsne.org</a> or ZIPPER® in APP Store lists all services, locations &amp; appointments</td>
</tr>
<tr>
<td>Community Health Center, Inc.</td>
<td>141 Franklin St, Stamford, CT 06901</td>
<td>860-266-0257</td>
<td>Maria Lorenzo Or Nicole Morgan, LPN</td>
<td><a href="mailto:LorenzM@CHC1.com">LorenzM@CHC1.com</a> Or <a href="mailto:MorganM@chc1.com">MorganM@chc1.com</a></td>
<td>Primary care available on site</td>
</tr>
<tr>
<td>Stamford Hospital</td>
<td>166 W Broad St #202, Stamford, CT 06905</td>
<td>203-276-5510</td>
<td>Brenice Duroseau, Provider</td>
<td><a href="mailto:BDuroseau@stamhealth.org">BDuroseau@stamhealth.org</a></td>
<td>Open only 7am-5pm M-Th, Open Saturday</td>
</tr>
<tr>
<td>StayWell Health Center</td>
<td>80 Phoenix Ave, Waterbury, CT 06702</td>
<td>203-756-8021</td>
<td>Kathy Pitzer</td>
<td><a href="mailto:Kpitzer@staywellhealth.org">Kpitzer@staywellhealth.org</a></td>
<td></td>
</tr>
<tr>
<td>APNH</td>
<td>1302 Chapel St, New Haven, CT 06511</td>
<td>475-441-7020</td>
<td>Brittany Trnka</td>
<td><a href="mailto:Trnka.Brittany@APNH.org">Trnka.Brittany@APNH.org</a></td>
<td></td>
</tr>
<tr>
<td>Waterbury Health Department</td>
<td>185 S Main St, Waterbury, CT 06706</td>
<td>203-574-6883 ext. 7216</td>
<td>Jackie Robertson</td>
<td><a href="mailto:Jrobertson@waterburycare.org">Jrobertson@waterburycare.org</a></td>
<td></td>
</tr>
<tr>
<td>APEX Community Care</td>
<td>85 West St, Danbury, CT 06810</td>
<td>203-778-2437</td>
<td>Jason Egbert</td>
<td><a href="mailto:jegbert@apexcare.org">jegbert@apexcare.org</a></td>
<td></td>
</tr>
</tbody>
</table>
References:


Appendix E: Data Collection Sheet

Outcomes Tracking Form

Participant Study ID: ________________

**PrEP Initiation Record**

Date of Intervention: ________________

<table>
<thead>
<tr>
<th>Follow up:</th>
<th>Contact made with participant?</th>
<th>Appointment made with PrEP provider?</th>
<th>Initiated PrEP?</th>
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</thead>
<tbody>
<tr>
<td>4 weeks</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
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<tr>
<td>8 weeks</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
</tr>
<tr>
<td>12 weeks</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
</tr>
</tbody>
</table>

Date of Reported PrEP Initiation: ____________

Confirmatory Urine Tenofovir Testing Results: ____________

**Sustained Adherence Record**

*Recorded 18 weeks after randomization*

<table>
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<tr>
<th>Follow up:</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Does the participant report that they have been taking the medication an average of 4 or more times a week?</td>
<td>Y/N</td>
</tr>
<tr>
<td>Confirmatory DBS Testing &gt;700 fmol/punch?</td>
<td>Y/N</td>
</tr>
</tbody>
</table>
Appendix F: Sample Size Calculation

The following calculation was made using the Power and Precision Version 4 tool:

Two-tailed test:
Alpha (level of significance) = 0.05
B (type II error) = 0.20, corresponding to a power of 80%

For a given effect size (population proportions of 0.030 vs. 0.180), sample sizes (65 and 65), and alpha (0.05, 2-tailed), power is 0.804. This means that 80% of studies would be expected to yield a significant effect, rejecting the null hypothesis that the two population proportions are equal.

Factoring in an expected 20% loss to follow up, the total N = 156, with 78 participants in each group.
BIBLIOGRAPHY


56. Moitra E, van den Berg JJ, Sowemimo-Coker G, Chau S, Nunn A, Chan PA. Open pilot trial of a brief motivational interviewing-based HIV pre-exposure


