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Phase 1 and 2 Title (Aims 1 and 2): Development and pilot testing of a PrEP communication intervention and integration into an existing HIV testing service for female IV drug using clients of a needle exchange

Phase 3 Title (Aim 3): PEACE Project: PrEP Empowerment Achieved by Counseling and Education

NCT Number: 03541642

Attached are:

1. Protocol for clinical trial

2. Informed Consent for clinical trial

3. Statistical Analysis Plan for clinical trial

Protocol Number:
27206

Protocol Title:
PEACE Project: PrEP Empowerment Achieved by Counseling and Education

Principal Investigator:
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Introduction

Women who inject drugs (WWIDs) have a high risk of becoming infected with human immunodeficiency virus (HIV) due to both needle sharing and sexual behaviors,[1,2] especially if they participate in female sex work.[3] WWIDs also experience stigma, discrimination, poverty, homelessness, and gender-based socio-cultural factors that exacerbate HIV risk.[3,4] Even when risk-reduction resources are available, they utilize services less, including HIV testing and prevention counseling.[5,6] Clearly, risk reduction interventions are warranted.[2,6] Pre-exposure prophylaxis (PrEP) shows significant promise for reducing risk of HIV acquisition. In the first clinical trial "Preexposure Prophalaxis Initiative" ('iPrEX'), PrEP reduced the risk of HIV acquisition by 44% on an intention to treat basis.[7] However, in subsequent trials that included women[8,9] and people who inject drugs (PWIDs)[10], the number of WWIDs was too small to assess efficacy[10] and little research exists on how best to address PrEP in this group. Evidence suggests they are more at risk (i.e. "second in the needle") than their male counterparts. Research is needed to understand how WWIDs perceive HIV and PrEP, and whether a targeted intervention that is embedded in an existing and trusted syringe exchange program is feasible and holds promise in addressing structural barriers to accessing PrEP and increasing its use in this at-risk population.

To address this gap, we have conducted extensive formative evaluation combining in-depth qualitative methods with larger quantitative surveys, utilizing a unique and innovative marketing evaluation technique called perceptual mapping and vector message modeling. This technique produces graphic 3-D models, resulting in highly targeted and effective messages that are not possible with conventional survey methods. It is used widely in marketing research, and data strongly support its utility for influencing health decision making. In a review of social science approaches, the RAND Corporation notes that it is a superior approach to understanding perceptions and creating highly targeted message strategies that can be implemented into interventions.[11] Previous work by the Principal Investigator (PI) has shown significant results in interventions targeting decision making in various health domains,[12–18]

including a current NIMH funded study on PrEP barriers in transgender women. To address psycho-social barriers, we propose using these methods to inform the development of highly targeted messages that will be used in an intervention utilizing print materials, PrEP counseling, and supportive text messaging. To address societal and structural barriers we will then embed the intervention in Prevention Point Philadelphia, a large social service agency that does syringe exchange and provides trusted medical personnel by using existing services and distributing PrEP through their medical clinic. We will examine the feasibility and acceptability of the intervention components. We will examine preliminary data regarding its potential efficacy in engaging WWIDs in initiating and adhering to PrEP when compared to more traditional physician-based PrEP counseling and materials

This study will use results found from protocol # 25028 and test in a randomized controlled trial the acceptability, feasibility and potential efficacy of a PrEP intervention. The specific aim for this randomized controlled trial (RCT) is:

SPECIFIC AIM: To pilot test the intervention in engaging HIV- WWIDs in PrEP by integrating it into the health care services of a syringe exchange to assess promise of efficacy. To address Aim three we will: 1. Conduct a pilot test with WWIDs (n=68) randomized to an "Enhanced" intervention that includes targeted PrEP messages in counseling, materials, and text messages compared to a "Basic" intervention that includes general messages in counseling, materials, and text messages. To assess promise of efficacy, we will compare PrEP adherence (biomedical testing, self-report) at one month, end and three-month follow-up and assess differences in self-reported PrEP attitudes, self-efficacy and decisional conflict.

Role of Principal Investigator

Sarah Bauerle Bass - Dr. Bass is the PI for the project and will oversee all operations. She is responsible for designing instruments, overseeing research assistants, conducting analysis for perceptual mapping and vector analysis, modeling messages and applying them in order to assess for cultural salience and receive insight into potential intervention strategies with women who inject drugs. She will oversee recruitment, data collection, monitor safety and human subject issues and facilitate communication between and among study staff and study site. She will also monitor the study budget and expenditures. As PI she will oversee all aspects of the project to ensure successful completion.

Study Objectives

The main objective of this study is to pilot test a randomized intervention to increase uptake and adherence to PrEP in women at risk of HIV who are clients of Prevention Point Philadelphia, a needle exchange program.

If successful, the proposed pilot study will significantly contribute to HIV prevention by examining the unique perceptions of PrEP in WWIDs and the acceptability, feasibility, and

potential impact of using health communication strategies in adjunct with existing services in a social service agency.

Background

Despite significant knowledge of how HIV is transmitted and the availability of effective preventive methods, over 2 million new cases are reported globally each year.[19] Injection drug use (IDU) is a significant route of transmission. In the US, 10% of new HIV infections are caused by IDU[20] and while overall prevalence due to IDU has declined, it still represents the third most common mode of transmission.[21,20] Significantly, IDU often occurs in conjunction with risky sexual behavior, compounding HIV risk.[21] The CDC reports that among PWIDs without HIV, 34% reported sharing syringes in the last year, 58% shared injection equipment, 69% had condomless vaginal sex, and 23% reported male-female anal sex.[22] Clearly this group is at significant HIV risk, especially WWIDs who also have added gender-based societal and structural barriers to accessing HIV prevention services.

There are an estimated 2 million WWIDs in the US.[23] Compared to males who inject, WWIDs have a measurable increased risk of HIV Infection[2] due to biological, behavioral and socio-structural factors.[24] Despite these factors, comparatively little has been done to develop and evaluate efficacy of HIV prevention in this group.[24] Most systematic reviews and reports by both UNAIDS and WHO discuss women's risks based on childbearing and sexual risk rather than IDU.[24] Importantly, IDU and sexual behavior are concomitantly intertwined, since WWIDs often engage in sex work[25,26] for money or in exchange for drugs, thus increasing their chance for infection.[27–30] Even if in a relationship with a primary male partner, women may have no control over a partner's condom use and injection equipment, despite their wide availability[31] in the US, and are often injected by their partners ("second on the needle") and after their partners inject themselves.[32] They are also often victim to violence from partners and sex trade clients, are homeless, and have psychiatric comorbidities, making HIV risk reduction a low priority for them.[33] These risks can be further enhanced by discrimination and stigma, and a propensity for hiding their addiction from others.[34–36] Despite these significant risks, WWIDs are often not prioritized as an accessible population, falling through the cracks of existing HIV prevention programs that do not address their specific needs. A multi-pronged approach is important to address WWIDs and their HIV risk,[6] but drug treatment, harm reduction, and HIV prevention programs specifically for women are not often available, despite evidence of efficacy.[35,37]

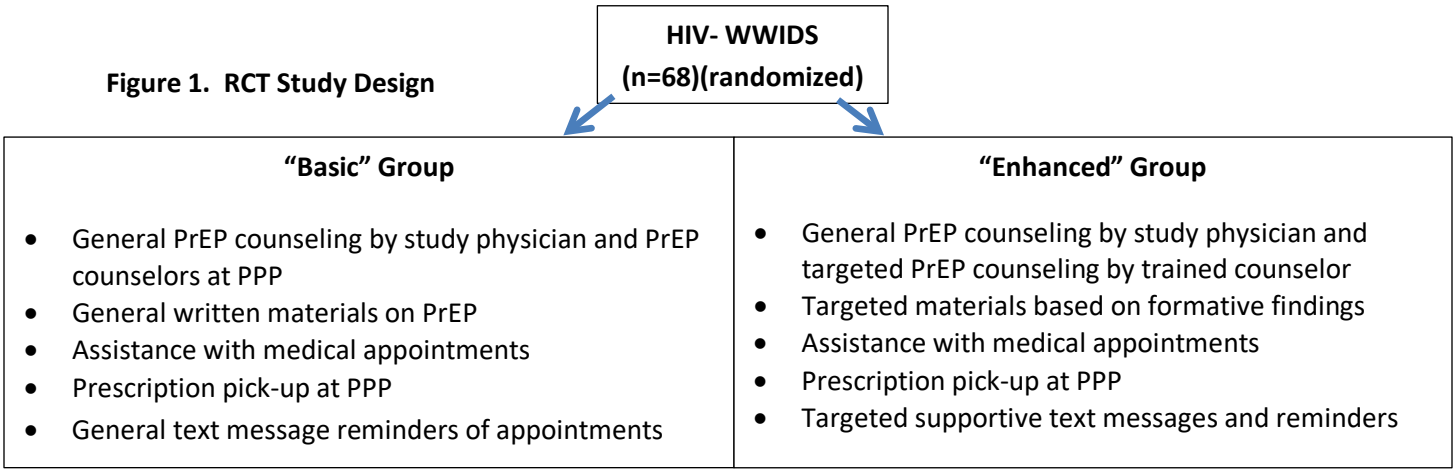
HIV prevention strategies are important to address risk in WWIDs, including PrEP. HIV risk reduction strategies for WWIDs should include individual-focused strategies (e.g. negotiation skill building, condom use, HIV testing), social strategies (e.g. couple-based counseling, peer support, syringe exchange) and biomedical prevention (e.g. PrEP). PrEP medication, the latest HIV prevention tool, has been most extensively tested in men who have sex with men (MSM; e.g. iPrEX trial).[7] With initial findings indicating significantly lower risk of HIV acquisition, subsequent studies have focused on other at-risk groups. Of those that have included women, the FEM-PrEP study[8] (at-risk women in Africa) and the Partners PrEP[38] (HIV discordant couples) trial were specifically aimed at addressing risk associated with heterosexual transmission. The only trial to address IDU risk specifically occurred in Thailand involving 2,413 PWIDs.[10] Results

indicated an HIV risk reduction of 48.9% in intervention PWIDs, which increased to 74% when limited only to patients with good adherence. While women overall had better PrEP adherence, there were not enough women enrolled to specifically look at barriers or facilitators to PrEP use in WWIDs. In fact, little research exists on WWIDs and their barriers to accessing and using any HIV prevention services, indicating a key area of research to stop the HIV epidemic[2] in this at-risk population.

Study Design

During this study we will: 1) Conduct a pilot test with WWIDs (n=68) randomized to either a "Basic" or "Enhanced" intervention. Women randomized to the "Basic" group will receive general PrEP counseling from the study physician and PrEP counselor at Prevention Point, general written materials, as well as "general" reminder text messages for appointments. Those in the "Enhanced" group will receive targeted counseling by a trained PrEP counselor who will emphasize the targeted messages, doctor counseling, customized written materials, as well as supportive targeted text messages and reminders. Targeted messages and materials are informed by our formative findings. Both groups will get assistance with making their doctor appointments and will have PrEP dispensed at Prevention Point's medical clinic. 2) To assess promise of efficacy, we will compare PrEP adherence (biomedical testing, self-report) as primary outcomes at one month, end, and three-month follow-up. We will compare changes to self-efficacy, decisional conflict, and PrEP perceptions as secondary outcomes. To assess feasibility and acceptability we will compare attitudes about the intervention, prescription pick up, and number of text messages opened. Figure 1 illustrates the study design:

Figure 1. RCT Study Design



Randomized Pilot

We will recruit and enroll 68 WWIDs from syringe exchange who consent to participate in the intervention and will be randomly assigned to either the "Enhanced" or "Basic" group. Both groups will participate for six months (three months in the intervention and a three month follow-up), receiving PrEP counseling at Prevention Point (intervention monthly; control as requested by the participant), educational materials (targeted vs. general) and PrEP reminders via text messages (intervention also receives supportive messages about PrEP use). They will

also complete surveys at the start of the study, at the one-month mark (mid intervention), the three month mark (end of intervention) and three months after the intervention is complete (follow up). Demographic information will be collected along with perceptions of PrEP, decisional conflict, and self-efficacy. Other moderators will also be collected. Compliance with PrEP will be assessed through self-report (in person and via text) and through either blood test or urine sample at one month, three months and six months. For recruitment and study timeline, see attachment A.

Study Timeline

We plan to begin the pilot RCT as soon as Institutional Review Board (IRB) approval is granted. We anticipate enrollment to take place between July through November, 2020 with follow-ups completed by March, 2021.

Inclusion/Exclusion Criteria

All participants must be self-identified women, 18 years of age or older, able to read and speak English, be HIV negative, self-report HIV risk behavior, report never taking PrEP, have a cell phone that accepts text messages, and must be a client of Prevention Point Philadelphia. They will also have to have health insurance (i.e. Medicaid). Individuals with mental illness that interferes with cognitive understanding or ability to provide informed consent will be excluded, with researchers trained to identify participants who exhibit signs of inability to meaningfully participate.

Inclusion Criteria

1. Woman-identified HIV negative client of Prevention Point Philadelphia
2. 18 of years of age or older
3. Self-report either sharing needles or having unprotected sex in the last 3 months
4. Speak and read English
5. Not have used PrEP previously
6. Have a working cell phone that receives text messages
7. Have health insurance

Recruitment

For this phase, we will recruit participants who are self-identified female clients of Prevention Point Philadelphia. Because Prevention Point received funds from the city, this protocol has also gone through review at the City of Philadelphia and been approved (see attached).

Prevention Point Philadelphia **(PPP)**. PPP is the only syringe exchange in Philadelphia. They promote health, empowerment and safety for communities affected by drug use and poverty by offering case management, syringe exchange, medical services, HIV and Hepatitis C (HCV) testing, addiction services, housing services, free meals, legal clinic and overdoes prevention and reversal training. PPP serves hundreds of people throughout the week, many of whom attend almost daily.

Sampling

Subjects will be screened for their interest in and eligibility for participating. We aim to enroll 68 women, assuming a 75% retention rate at the end of the intervention, leaving us a final study sample of 50. Treatment allocation will be accomplished using randomization through REDCap, a HIPAA approved research management software.

PROCEDURE PHASE 3

For graphic representation of study Procedure, see attached. Participants will be asked to participate after or while waiting for services at the study site. If they are interested, research staff will take participants into a designated private room and ask eligibility questions and be HIPAA consented. If they report that they meet the eligibility requirements, they will be taken to an HIV tester at Prevention Point Philadelphia for confirmation of status. If a woman tests positive for HIV, she will be provided regular counseling through PPP's testing program and given access to resources and services to link her to immediate care. If the woman does not have HIV and is eligible to be in the study, she will be consented into the study.

Once confirmed to be HIV-, participants will be randomized to a group using REDCap's randomization tool and a baseline survey will be conducted by research staff. All survey assessments will be orally administered to participants to address any literacy or cognitive issues. Responses will be entered into REDCap by a research staff member.

After the baseline survey is complete, research staff will introduce the participant to the appropriate PrEP counselor. Individuals in the "Basic" group will be introduced to the current PrEP counselors at Prevention Point. Those in the "Enhanced" group will be introduced to a study counselor that will be providing the targeted messages and counseling. Initial counseling will be about PrEP and importance of adherence. The PrEP counselors will also make an appointment for the participant to meet with a doctor at Prevention Point to be assessed for whether PrEP is appropriate for the participant to take.

When the participant meets with the doctor at Prevention Point, they will use the Centers for Disease Control's diagnostic criteria for PrEP prescription (see Table 1). The doctor will not know whether the participant is in the control or intervention group. Once a participant has met with a doctor, completed testing, and is determined to be a good candidate for PrEP, their prescription will be sent to a participating pharmacy that provides medications to Prevention Point Philadelphia through their 340B clinic. 340B is a federal drug pricing program that Prevention Point Philadelphia is a member of.

Table 1. CDC Diagnostic Criteria for Prescribing PrEP

Physician will Provide at First Visit:	Physician will Provide at all visits
Assessment of possible Acute HIV infection	Assessment of HIV status
Lab screenings to determine indications (gonorrhea/chlamydia, P23+ HIV ½, RPR, HCV antibody with reflex to HCV viral load, HBV antigen and antibody, BMP for creatinine)	Assessment of side effects and advice on management

HIV risk assessment to determine PrEP indication	Assessment of adherence and counseling to support it
Medication fact sheet to patients with dosing, side effects	Assessment of STI symptoms, HIV risk behavior, counseling for risk reduction
Counseling on HIV risk reduction methods	Information on anything new regarding PrEP and respond to questions
Advice on adherence	
Advice on PrEP use with contraception and pregnancy	
Prescription for Truvada (a brand name of PrEP)	

After the appointment, PrEP medication will be delivered to Prevention Point in weekly packets. Each participant will be assigned a small locked locker and study staff will place a week's worth of medication in the locker every Monday. Participants can then pick up the medication when it's convenient for them and study staff can keep track of whether medication has been picked up. This information will be provided to the PrEP counselors so they can follow up with the participant if medication has not been picked up.

It is expected that participants will meet with their PrEP counselor at least four times during the intervention. For the "Enhanced" group, the PrEP counselor will reach out, emphasize study messages, and set up at least monthly appointments after the initial appointment. For the "Basic" group, PrEP counselors will meet with women at initial appointment and for the next three weeks. They will then be available as needed and will meet with participants when they request, but they will not actively reach out to participants which is how PrEP counseling is currently taking place. For an example of how targeted messages would be delivered in the "Enhanced" group, see table 2.

Table 2. Targeted messages for "Enhanced" group

Potential Construct from Vector Modeling	In-clinic PrEP Counseling	Written/Visual Materials	Text Message
Staying HIV- is worth taking a daily medication for.	HIV is no joke. The best way to stay HIV- is to be on PrEP. It's just one pill a day and it can significantly lower your risk of getting it.	We know you have a lot going on but if you set up a time to take the pill every day, it will get easier. We can help you think about how to add this to your day. Ask us!	Remember, it's only 1 pill a day. U can do it and we can help!
Worry about being able to take medication every day	It can be a pain to take medication every day but it's worth the effort because you can be sure that you stay free from HIV.	You may not want to take medication every day because of the time and effort it takes. But it is worth it. It can give you the peace of mind to know that you are HIV free.	Get peace of mind! Take your medication every day. Call XXX-XXX-XXXX if you have ??
Worry that taking medication will interfere with drug use.	I know you might worry that taking PrEP might interfere with your daily life, especially if you are	There is no evidence that taking PrEP will interfere with taking other substances.	Getting your medication is easy and doesn't interfere with other use.

	using substances. But there is no reason to worry. PrEP is safe and easy to take and because you are getting it here at Prevention Point, it is easy to talk.		Call XXX_XXX_XXX if you have ?s!
Don't believe doctors will want to treat WWIDs or care about them staying HIV-	I know sometimes it's hard to go to the doctor, but we have doctors who really care about our clients and who want you to stay HIV negative.	Some people do not like to go to the doctor, but using PrEP can help you stay HIV-. We only send our clients to doctors we know will work with you and who care about your health.	Remember…UR doc wants you to keep taking your medication every day! Call XXX-XXX-XXXX if you have ??

All participants will receive study text messages throughout the study. "Enhanced" group participants will receive weekly text messages. These texts will include supportive messages about taking PrEP that emphasize why they should continue to take their PrEP as prescribed, as well as reminders to pick up their medication. "Basic" group participants will receive bi-monthly text message reminders to pick up their medication. We will work with Mosio, which provides text messaging services and has experience working with studies funded by the National Institutes of Health. Temple University has signed a contract with Mosio for this service. In that contract is a data sharing agreement that states that any data collected for the study will be shared with Dr. Bass, the Principal Investigator, and cannot be used for any other purpose.

Mosio will have no identifying information other than a participant's phone number. Mosio will collect user data on the number of participants who open the text messages and will also re-send text messages if they remain unopened for more than two days to assess feasibility. In addition, participants will be provided the opportunity to engage with study personnel if they have questions. A phone number will be provided in every text and study personnel will be available to take participant's phone calls and answer their text messages. All messages/calls are sent to the study coordinator's email and we will provide language that indicates that if questions are after business hours of 9 am to 5 pm we will answer the question the next morning. There will also be an opportunity to provide feedback. At mid-intervention participants will be asked to text back an answer to an adherence question. This provides an opportunity for participants to be actively engaged and to assess feasibility and acceptability. We will receive weekly reports from Mosio on which participants have opened text messages to assess feasibility.

At the end of the first month, all participants will also receive a text asking about their adherence to PrEP. They will respond with a 1 or 0 to indicate they have or have not taken PrEP the previous day. To help alleviate any problems with running out of cell phone minutes, every participant will receive a $25 gift card to help pay for minutes needed. If they lose or have their cell phone stolen, we will assist them in getting a new one through the current services at PPP.

PPP has a current service that provided assistance to clients and we will work with them to help the study participant.

At the end of the first month we will also contact participants about completing a quick assessment of adherence and acceptability of the intervention. This will be done in person at Prevention Point. Similarly, at the end of the three-month intervention study staff will contact participants about completing a post-test assessment. We will attempt to correspond assessments to be at a time when they are already at Prevention Point and ideally meeting with their PrEP counselor or there for other services.

Participants will also continue to be monitored by the physician at Prevention Point. It is expected that a blood test or urine sample measuring PrEP levels and an HIV screening test would be done at the beginning, mid-point and the end of the intervention. It will also be done three months after the intervention is over. This will provide biomedical adherence data and ensure that participants have remained HIV negative.

After the intervention is over, all study participants may continue their PrEP prescription and have it administered out of the medical clinic at Prevention Point. In addition, PrEP counselors will remain available for participants should they have any further questions. Specialized counseling and text messages will no longer be provided. Three months after the intervention is over, we will contact participants to complete the last study assessment. This will be done at Prevention Point when the participant is there.

Instruments

There are five study assessments (See attachments). They include:

1. Eligibility Screener
2. Baseline Assessment
3. Mid-Intervention Assessment (in person and one question via text)
4. Post-Intervention Assessment
5. Three month follow-up Assessment

Analysis Plan

General - All data will be graphed and tabulated by treatment group for review of distributional properties and anomalous values prior to the main analyses. Continuous and normally distributed variables will be summarized with means and standard deviations. All parameter estimates will be bound by 95% confidence intervals and tests for differences in means and proportions will be deemed statistically significant $p < 0.05$. Post-hoc tests of significance will be based on adjustments for alpha to protect family-wise error rates at 5% using the method of Benjamini & Hochberg. For all analyses described in this study, we will use Statistical Analysis Software (SAS, version 9.4,Cary, N.C.).

Primary Outcome. The study's intent is to provide directional insight into the design of subsequent programmatic studies. As such, univariate group comparisons will be accomplished using an independent two-sample t-test for continuous measures (or non-parametric Wilcoxon

statistic if the data is non-normally distributed) and chi-square test for categorical measures (or Fisher's Exact test if appropriate). Blood test results will also be compared to adherence benchmarks for Tenofovir-Emtricitabine and categorized as a binary variable (yes/no) based upon the mean value observed by all patients, with data at one month, three months and three months post intervention. We will use ANCOVA to assess differences betweenself-reported adherence and adherence as measured by blood test in the treatment group. Primary efficacy analyses will be a comparison of experimental to control group at one month, three months and three months post intervention, while other subgroup analyses based on race/ethnicity or age, for instance, as well as potential mediators and moderators, will be considered post-hoc exploratory analyses. In addition, logistic regression modeling will be used for binary adherence measures to assess group differences. Model assumptions will be tested, including linearity between the logit of the independent variables and the dependent, multicollinearity, and model misspecification.

Secondary outcomes. Secondary outcomes include self-efficacy, PrEP attitudes and decisional conflict. These measures are all continuous. Following evaluation of the primary outcome, we will explicitly examine the association between treatment adherence characteristics and extent of change among individuals in the treatment conditions in order to evaluate dose-response associations. Multiple linear models will be used to examine relationships between the groups and decisional conflict scale items, self-efficacy, and PrEP attitude scales at month three and three months post intervention. In these models, baseline outcome measures will be adjusted as covariate in the model development. PrEP attitudes will also be assessed through perceptual mapping analysis and compared from baseline to three month and three month follow-up for each group to assess "movement" toward adherence and away from negative perceptions of PrEP use. Promise of efficacy would indicate more movement by those in the "Enhanced" group compared to the "Basic" group. We will also explore potential mediators and moderators (HIV stigma, depression, level of drug use, social support). Outliers will be assessed using standardized residuals; if necessary, analyses will be accomplished for all data as well for non-outlying cases only.

Acceptability and feasibility will be analyzed using survey items and objective measures (opened text messages, prescription pick-up). Quantitatively we will assess each feasibility and acceptability measure in both groups by inspecting trajectory plot of mean levels of satisfaction over time. No formal testing is proposed except for the descriptive statistics summarized at each follow-up assessment. We will also explore associations between participant characteristics and acceptability in order to identify subgroups of participants for whom the intervention may be less acceptable. Qualitative data will be collected via open-ended answers on the mid-intervention, post intervention and three month follow-up survey. This data will be analyzed using the Krueger method of analyzing narrative data. A thematic framework will be developed to create categories and quotes will be indexed according to categories to reduce data. Charting of quotes to enable analysis will then occur. These quotes, along with items with low mean ratings and those with the highest proportion of disagree and strongly disagree responses, will be used to assess acceptability and feasibility to inform development of a full-scale intervention.

Power calculations are not provided because we will be pilot testing a new intervention, and its effect size is not known. We have not fully powered the randomized test due to the study's size and purpose, which is to assess the feasibility, acceptability and promise of efficacy of the intervention, however with a projected n=25 in each group comparing adherence we have 80% power to detect an effect size of 0.79 (if it is a continuous measure) or an OR or 2.56 (if binary). Positive results will aid in our ability to further test the intervention in a fully powered randomized controlled trial and whether it is feasible in the context of offering it in a community-based, clinical setting.

Procedures Involved in Human Research

Description of Protocol

Consent Process

HRP-802=-Investigator Guidance Informed Consent will be followed to obtain informed consent. Before all assessments, a research staff member will review the written informed consent with the participants. Participants will have time to review the material and will be reminded that their participation is voluntary.

All participants will give informed consent to participate in the project and HIPAA consent to have access to health-related information. They will sign a PPP HIPAA consent that allows Project PEACE study staff to have access to their HIV test result, adherence information, and other medical information pertinent to the study. The research staff will read, review, and discuss consent forms with all potential participants prior to asking them to acknowledge the consent. If the potential participant appears confused or indicates she does not understand the consent, the moderator will attempt to identify the misunderstanding and to explain the consent again. If the potential participant still does not comprehend the consent, she will be excluded from the study. We will confirm that potential participants understand the material covered in the consent procedure by asking questions prior to asking the person to sign the consent form. These will include open-ended (e.g., "Could you tell me what's going to happen if you enroll in the study?") and closed questions (e.g., Will you get free medications as part of this research study?"). Responses that suggest confusion or inaccuracies that staff cannot successfully clarify will result in exclusion from the study and direction to appropriate outside referrals. If the participant agrees to participate, we will indicate this willingness on the REDcap project on a wireless tablet. We will provide a paper copy of the consents to the participant to take with her.

Provisions to Maintain the Confidentiality of Data

Assessment responses and all other data (e.g. % prescription pickups) will be entered into REDCap, which is protected behind Temple's firewall and HIPAA compliant. Each participant will be auto-populated with a study ID and no identifying information will be linked to the study record. Only the research staff will have access to, or be able to open, the REDCap database.

Risk to Participants

1. **PrEP use** - There are some risks to taking PrEP, including nausea, dizziness, headache and fatigue. These usually subside after a few weeks of taking the medication. The physician will assess each participant for appropriateness of taking PrEP and anyone who has counter indications will not be prescribed PrEP. They will also be monitored throughout the intervention by the medical staff at PPP to ensure that no one whose side effects may be damaging continues to take PrEP.

2. **Breach of confidentiality -** All data from study phases will be coded to protect the confidentiality of participants and only the Principal Investigator, study coordinator, and the PrEP Counselor will have access to the list of participants' names and cell phone numbers. That list will be kept in a locked file (hardcopy only) in the office of Dr. Bass. The dataset with the coded data, with names removed, will be kept in her locked Laboratory, on a computer that is password protected. Research assistants will only have access to de-identified data.

Participants will be informed during the consent process that if they reveal information about an elder or a child being abused (including sexual abuse), about their intent to commit physical violence against an identifiable person, or about their intent to harm themselves, the study staff member will be required to determine if the information is reportable to law-enforcement or child-protection authorities. We believe it is highly unlikely that such information would be revealed during the course of study participation for two reasons. First, we will not seek this type of information in our study survey or interview guide. Second, as noted, the participants will be informed during the consent process that disclosure of such information could result in a report being made to the authorities.

3. **Discomfort with questions** - Because assessments and counseling may cover sensitive issues, such as social stigma, drug use and sexuality, participants may experience embarrassment and/or distress. The plan for ensuring necessary medical or professional intervention in the event of any social or psychological discomfort is to ensure that a subject who appears distressed to the research staff or PrEP counselors will be able to communicate with a medical or counseling staff member on a same day basis. Prevention Point has processes in place to assess and deal with clients who are having problems and we will use the same process. The recruitment and research staff will also have access to a Temple University Hospital mental health professional at Episcopal Hospital (a Temple affiliate that offers mental health services) and Co-Investigator Dr. Gina Simoncini, a staff physician at Temple University Hospital and Episcopal will be on call 24 hours a day.

4. **Mobile phones** – It is possible that someone other than the participant will read study text messages. In addition to reviewing this potential risk as part of the informed consent procedure, we will advise participants in the pilot RCT that everyone should enable password protection on their mobile phones. We will assist participants in learning how to use password protection on their mobile phones and also explain how

some phones (e.g., Androids) have the capability to hide text message threads in a private inbox that is password protected. To this end, we can assist participants with enabling password protection for their phones, and if possible given their devices, for messages sent from our identity as a text-message sender. We can also assist them in learning how to delete text messages. We will work with Mosio, the contracted text-messaging company, to ensure that these strategies are employed for the text-messaging component of the proposed research. This company is highly experienced with research protocols and is HIPAA certified.

5. **HIV Stigma/Discrimination** - Women who inject drugs may have experienced stigma or discrimination from healthcare providers due to their drug use. This experience may influence their illness perceptions, interest in initiating or adhering to PrEP and/or cause anxiety for those who wish to seek healthcare but feel too stigmatized. By design, this study addresses a group at disproportionate risk for HIV. As such, we will provide all women with the following information during informed consent (regardless of whether they choose to consent and participate in the study): (1) an up to date resource list which includes information for local agencies and clinics providing medical care, HIV testing, housing, food, mental health and substance abuse treatment, crisis hotlines, and case management; and (2) safe sex and drug use information, including materials specifically designed for the HIV and STI prevention needs of WWIDs. To build trust, we have developed the intervention so that women will be tested, seen by a physician, and have medication distributed at Prevention Point, a trusted organization in their community. We will also use existing Prevention Point PrEP counselors to deliver the intervention, who will already be known by the study populations.

Potential Benefits to Participants

Participation may contribute to increasing participants' initiation and adherence of PrEP, which will lower their HIV risk. Participation also may help participants consider how perceived stigma impacts their feelings about PrEP and help "normalize" the use of HIV prevention within the IDU community. The risks of discomfort or embarrassment discussing HIV and PrEP are reasonable in relation to the anticipated direct benefits to the subjects and the contribution subjects can make to society by reducing HIV stigma among WWIDs and encouraging HIV prevention efforts among their peers.

Privacy

As noted, all data will be coded to protect the confidentiality of participants. Only the Principal Investigator and the study coordinator will have access to the list of actual participant names and cell phone numbers. That list will be kept in a locked file (hardcopy only) in the office of Dr. Bass. The REDCap dataset with the coded data, with names removed, will be stored behind the firewall of Temple University. Medical information (adherence, HIV tests etc.) in medical charts will not be removed from Prevention Point. The study coordinator will access this through Prevention Point's electronic health record and note findings in the de-identified REDCap

database that will assign an ID number for each participant. Information will be entered into REDCap as coded data (i.e. adherence is coded 0 as no, 1 as yes). The PrEP counselors will know the names of the participants, but they will not have access to the REDCap database or participant medical records. The research assistant will only have access to de-identified data.

Compensation

Participants will receive up to a total of $175 in gift cards. These incentives will be provided for different steps of the research study. Compensation will not be provided to those who drop out of the study or do not complete the step. Compensation will be broken down as follows:

- $5 for conducting the eligibility screener and HIV test
- $15 for completing the baseline test
- $40 for meeting with the PrEP counselor (Up to four times, $10 each time)
- $15 for doctor visits (three times, $5 each time)
- $10 for completing one-month survey
- $20 for completing three month survey
- $50 for completing three month follow up survey
- $20 for cell phone minutes

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ATTACHMENTS

A – STUDY TIMELINE AND IMPLEMENTATION

B – ELIGIBILITY QUESTIONNAIRE

C- HIPAA CONSENT

D- STUDY CONSENT

E- BASELINE SURVEY

F- MID INTERVENTION ADHERENCE SURVEY

G- END OF INTERVENTION SURVEY

H- THREE MONTH FOLLOW UP SURVEY

I – OUTCOMES AND SOURCE

TEMPLE UNIVERSITY

College of Public Health

Temple IRB Approved

05/17/2021

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PARTICIPANT INFORMED CONSENT

Title of research: P.E.A.C.E. Project: *PrEP Empowerment Achieved by Counseling and Education*

Protocol Number: 27206

Principal Investigator and Department: Sarah Bauerle Bass, PhD, MPH – Temple University Department of Social and Behavioral Sciences

Sponsor: This research has been funded by the National Institutes of Health, National Institute of Drug Abuse, grant number 1R34DA046305-01.

Why is this research being done? The purpose of this research is to see if a communication intervention that addresses the needs of women at Prevention Point Philadelphia (PPP) who are at risk for HIV helps them to start and keep using PrEP (Pre-Exposure Prophylaxis). PrEP is an HIV prevention medication and is taken as a once daily pill that can reduce one's chances of contracting HIV by over 90%. We will compare participants between two groups. One group will receive tailored messaging and one will receive usual messaging about PrEP. All women will be provided PrEP. Approximately 68 women will participate in this study.

Why am I being invited to take part in this research? We invite you to take part in a research study being conducted by Temple University researchers because you are a female client of PPP. If you are eligible and participate in this program, we will offer a counseling program and access to PrEP. To take part in the program you will participate in counseling sessions with a PrEP counselor, see the doctor at PPP and be prescribed PrEP if you are eligible, get educational materials about PrEP, receive reminder text messages, and be able to pick up your PrEP medication weekly at PPP.

Who is eligible to be in this research? To be eligible for this study you must be a self-identified female, be 18 years of age or older, not have HIV, be at risk for HIV because of drug use or sexual activity, speak and read English, are not currently taking PrEP, are able to take PrEP based on a blood test conducted by a PPP doctor, have a working cell phone that accepts text messages, and have some type of health insurance, including Medicaid. We will confirm your HIV status through testing and look at your cell phone to confirm it can receive text messages. If you do not have health insurance and are not on Medicaid, we can assist with helping you see if you are eligible.

What should I know about this research?

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you.

- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

How long will I be in this research? You will be asked to participate in the study for six months. For three months you will participate in at least four one-on-one PrEP counseling sessions, lasting approximately 20 minutes each, get reminder text messages and get your PrEP medication at PPP. For the remaining three months you can still get your PrEP medication at PPP but you will no longer have to attend counseling or get text messages.

Who can answer my questions about this research? If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed below. This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at (215) 707-3390 (irb@temple.edu) or 215-685-0869 (participantDPH@phila.gov) if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

If you have questions about:	**Please Contact**
This study, complaints, or think the study has hurt you.	Dr. Sarah Bass, Temple University (215) 204-5110, sbass@temple.edu, 1301 Cecil B. Moore Ave., Philadelphia, PA 19122. 24 Hour phone number: (215) 204-0377
If you have a concern or complaint, or question about your rights as a research participant while you are in this study or after the study ends.	Institutional Review Board at Temple University (215) 707-3390 or email them at irb@temple.edu OR Research Participant Coordinator, Philadelphia Department of Public Health Institutional Review Board, (215) 685-0869, research participantDPH@phila.gov

If you take part in this research, you will be responsible to:

- Meet with PPP staff and doctors as directed, including for HIV, STI testing and other tests
- Take medication as prescribed
- Maintain a cell phone that can receive text messages
- Come to PPP during regular business hours (9am-5pm) to pick up your prescription
- Meet at least four times with your PPP PrEP counselor for individual counseling sessions at PPP during regular business hours over the course of the first three months of the study
- Meet with Temple University study staff at PPP during regular business hours to complete surveys lasting approximately 25 minutes each, at the beginning, middle and end of the project, and then three months after the study is over
- Participate in most activities of the study, totaling approximately eight hours over the course of six months

What happens to me if I agree to take part in this research? We will ask for your signature to confirm that you consent to participant in the study. A Temple University study staff member will go over the consent document with you and answer any questions that you may have about the consent document and the study. If you indicate that you do want to take part in the study, we will refer you to an HIV tester at PPP to see if you are eligible. If you are eligible you will take a 25 minute survey and will then meet with the PPP PrEP counselor who will make an appointment for you with a doctor at PPP. The doctor will use a blood test to assess whether PrEP is appropriate for you to take. If it is, the doctor will provide a prescription for PrEP and we will assist you with filling that prescription so you can pick it up weekly at PPP. Over the course of the next three months you will meet approximately every two weeks with the PrEP counselor for the first month and will meet approximately every month after that for a total of four sessions. You will be provided educational materials about PrEP, receive weekly text messages reminding you to take your medication and pick it up, and be provided a weekly dosage of PrEP that you can pick up at PPP. You will also be expected to complete a survey one month into the study that will take 10 minutes, a survey at the end of the three-month study that will take 25 minutes, and a final survey three months after the study is over that will take 25 minutes. Over the course of six months, you will spend approximately 2 hours taking surveys, 3 hours in counseling sessions, and approximately one hour at doctor visits.

Could being in this research hurt me? There are side effects that have been reported by those who have taken PrEP, such as stomach aches or nausea, but they are usually minor and last a short time. The doctor will discuss these side effects with you. A cell phone with PrEP related messages may be a risk for some participants who would not want others to see those messages. We will help you lock your phone so that only you can open the messages.

Will being in this research benefit me? If taken daily, PrEP is over 90% effective at preventing HIV. Participating in this study could help you greatly decrease your likelihood of getting HIV. You will continue to have access to PrEP after this study and will continue to be able to pick up your prescription at Prevention Point. As long as you have insurance, PrEP is covered so you will not have to pay for PrEP during or after your participation in the study.

Will it cost me money to be in this research? Taking part in this research will not cost you anything. Medication, counseling and doctor visits associated with this study will be provided to you for free. You will not be reimbursed for travel or child care.

What other choices do I have besides taking part in this research? This study is not a part of the PrEP projects that have already taken place at PPP. You do have access to PrEP and PrEP counseling at PPP, even if you do not choose to participate in this research. If you choose not to be in this study but would still like to discuss PrEP further, you can ask a PPP staff member to connect you with a PrEP counselor.

What happens to the information collected for this research? We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy. Participation in this study will not identify you though we cannot ensure absolute confidentiality. The IRB, Temple University, Temple University Health system, Inc. and its affiliates, and other representatives of these organizations, may inspect and make copies of the information you provide for their own records as part of their oversight on this project. Representatives from the National Institutes of Health and the Office for Human Research Protections at the Department of Health and Human Services may also inspect data. The Philadelphia Department of Public Health Institutional Review Board may also review the data. Survey level data will be collected by Temple University study staff and will not be shared with PPP staff, including doctors and PrEP counselors. HIV test results and urine and blood tests measuring PrEP adherence conducted by PPP staff will be shared with Temple University study staff, as this information is essential to conducting the study. Please note: Any

information about child abuse or intent to harm self or others will be reported to authorities, as required by law.

Data gathered in this study may be analyzed for years after it is collected. It is estimated that it will be stored for up to 10 years and will be destroyed after all analysis is complete. All data will be recorded in RedCap, a password protected online research database system, and will be labeled with an ID number, not your name or other identifying information. This information cannot be linked to your name. Your name will be kept separately and only Dr. Bass and her study staff will have access to this file. No PPP staff, including the co-Investigator Mr. Benitez, will have access to any study data. If you withdraw from the study, we will have your data and survey responses up to the point of you withdrawing. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be 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.

Federal law provides additional protections of your personal information. These are described in an attached document titled "Authorization to obtain and disclose confidential information."

Certificate of Confidentiality: This research is covered by a Certificate of Confidentiality from the National Institutes of Health. A Certificate of Confidentiality helps protect your identifiable information and biological samples. Researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of child abuse and neglect or harm to self or others. The Certificate of Confidentiality will also not be used to prevent disclosure for any purpose you have consented to in this informed consent document, including data from your medical record that is related to study outcomes, including blood test results.

What if I am injured because of taking part in this research: If you are injured as a result of taking part in this research, immediately notify the research team and they will arrange for you to get immediate medical care. There is no commitment by Temple University, Temple University Health System, Prevention Point or its subsidiaries to provide monetary compensation or free medical care to you in the event of a research-related injury. Dr. Gina Simoncini is a co-Investigator on the study and is a medical provider at Temple University Hospital with experience working with women who inject drugs. If you have a research-related injury, please

contact Dr. Gina Simoncini at (215) 707-1800 during either regular hours or after hours and on weekends and holidays.

Can I be removed from this research without my approval? Dr. Sarah Bass, the principal investigator of the study, can remove you from the study without your approval. You may contact her at (215) 204-5110 or sbass@temple.edu. Possible reasons for removal include:

- It is in your best interest
- You have a side effect that requires stopping the research
- You need a treatment not allowed in this research, including HIV treatment
- The research is canceled by the FDA or the sponsor
- You are unable to take the research medication
- You are unable to keep your scheduled appointments

What happens if I agree to be in this research, but I change my mind later? If you decide to leave the research early, please contact Dr. Sarah Bass as soon as possible at (215) 204-5110 or sbass@temple.edu so that we have the potential to recruit others to be in the study. You can also contact any Temple study staff about your desire to leave the study at Prevention Point during regular business hours. If you stop being in this research, already collected data will not be removed from the research database.

Will I be paid for taking part in this research? If you are eligible, for taking part in this research you will be paid up to a total of $175 in gift cards. If you do not complete these steps or you withdraw from the study, you will receive gift cards for the steps you have completed. Your compensation will be broken down as follows:

- Edible snack for conducting the eligibility screener

If Eligible:

- $5 for completing HIPAA consent and HIV test
- $20 for completing the baseline test
- $40 for meeting with the PrEP counselor (4 times, $10 each time)
- $10 for doctor visit
- $10 for completing one-month survey
- $20 for completing 3 month survey
- $50 for completing 3 month follow up survey
- $20 for cell phone minutes

Federal tax law requires you to report this payment as income to the Internal Revenue Service if you are compensated more than $599.00 (in total) this year for participating in research. You may be asked to tell us your social security number or other identifying information (e.g., full name). If payments for this study are more than $599.00, we will report them to the Internal Revenue Service and send you a Form 1099-MISC.

This information will not be associated with the information or data you provide for this research. It will be stored separately from your data, it will not be linked in any way, and your identifying information will be destroyed within 1 year of study completion.

What else do I need to know about this research? Taking part in this research study is your choice. If you decide to take part in this study, you may leave it at any time without cost or penalty to you. Leaving the study will not affect your ability to receive services at Prevention Point Philadelphia.

Signature Block for Adult Subject Capable of Consent

Your signature documents your permission to take part in this research.

_____	_____
Signature of Subject	Date
_____	_____
Printed name of subject	Date
_____	_____
Signature of person obtaining consent	Date
_____	_____
Printed name of person obtaining consent	Date
_____	
Position of person obtaining consent	

Statistical Analysis Plan - Aim 3 Clinical Trial

General. All data will be graphed and tabulated by treatment group for review of distributional properties and anomalous values prior to the main analyses. Continuous and normally distributed variables will be summarized with means and standard deviations. All parameter estimates will be bound by 95% confidence intervals and tests for differences in means and proportions will be deemed statistically significant $p < 0.05$. Post-hoc tests of significance will be based on adjustments for alpha to protect family-wise error rates at 5% using the method of Benjamini & Hochberg. For all analyses described in this study, we will use Statistical Analysis Software (SAS, version 9.4,Cary, N.C.).

Primary Outcome. The study's intent is to provide directional insight into the design of subsequent programmatic studies. As such, univariate group comparisons will be accomplished using an independent two-sample t-test for continuous measures (or non-parametric Wilcoxon statistic if the data is non-normally distributed) and chi-square test for categorical measures (or Fisher's Exact test if appropriate). Blood test results will also be compared to adherence benchmarks for Tenofovir-Emtricitabine and categorized as a binary variable (yes/no) based upon the mean value observed by all patients, with data at one month, three months and three months post intervention. We will use ANCOVA to assess differences betweenself-reported adherence and adherence as measured by blood test in the treatment group. Primary efficacy analyses will be a comparison of experimental to control group at one month, three months and three months post intervention, while other subgroup analyses based on race/ethnicity or age, for instance, as well as potential mediators and moderators, will be considered post-hoc exploratory analyses. In addition, logistic regression modeling will be used for binary adherence measures to assess group differences. Model assumptions will be tested, including linearity between the logit of the independent variables and the dependent, multicollinearity, and model misspecification.

Secondary outcomes. Secondary outcomes include self-efficacy, PrEP attitudes and decisional conflict. These measures are all continuous. Following evaluation of the primary outcome, we will explicitly examine the association between treatment adherence characteristics and extent of change among individuals in the treatment conditions in order to evaluate dose-response associations. Multiple linear models will be used to examine relationships between the groups and decisional conflict scale items, self-efficacy, and PrEP attitude scales at month three and three months post intervention. In these models, baseline outcome measures will be adjusted as covariate in the model development. PrEP attitudes will also be assessed through perceptual mapping analysis and compared from baseline to three month and three month follow-up for each group to assess "movement" toward adherence and away from negative perceptions of PrEP use. Promise of efficacy would indicate more movement by those in the "Enhanced" group compared to the "Basic" group. We will also explore potential mediators and moderators (HIV stigma, depression, level of drug use, social support). Outliers will be assessed using standardized residuals; if necessary, analyses will be accomplished for all data as well for non-outlying cases only.

Acceptability and feasibility will be analyzed using survey items and objective measures (opened text messages, prescription pick-up). Quantitatively we will assess each feasibility and acceptability measure in both groups by inspecting trajectory plot of mean levels of satisfaction over time. No formal testing is proposed except for the descriptive statistics summarized at each follow-up assessment. We will also explore associations between participant characteristics and acceptability in order to identify subgroups of participants for whom the intervention may be less acceptable. Qualitative data will be collected via open-ended answers on the mid-intervention, post intervention and three month follow-up survey. This data will be analyzed using the Krueger method of analyzing narrative data. A thematic framework will be developed to create categories and quotes will be indexed according to categories to reduce data. Charting of quotes to

enable analysis will then occur. These quotes, along with items with low mean ratings and those with the highest proportion of disagree and strongly disagree responses, will be used to assess acceptability and feasibility to inform development of a full-scale intervention.

Power calculations are not provided because we will be pilot testing a new intervention, and its effect size is not known. We have not fully powered the randomized test due to the study's size and purpose, which is to assess the feasibility, acceptability and promise of efficacy of the intervention, however with a projected n=25 in each group comparing adherence we have 80% power to detect an effect size of 0.79 (if it is a continuous measure) or an OR of 2.56 (if binary). Positive results will aid in our ability to further test the intervention in a fully powered randomized controlled trial and whether it is feasible in the context of offering it in a community-based, clinical setting.