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Contingency Management and Pre-Exposure Prophylaxis Adherence Support Services (CoMPASS): A Hybrid Type 1 Effectiveness-Implementation Study to Promote HIV Risk Reduction among People who Inject Drugs

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Abstract

Background: HIV disproportionally affects persons who inject drugs (PWID), but engagement with HIV pre-exposure prophylaxis (PrEP) is low. We describe the rationale and study design for a new study, "**Co**ntingency **M**anagement and **P**re-Exposure Prophylaxis (PrEP) **A**dherence **S**upport **S**ervices (CoMPASS)," a hybrid type 1 effectiveness-implementation trial to promote HIV risk reduction among PWID.

Methods: In four community-based programs in the northeastern United States, PrEP-eligible PWID (target n=526) are randomized to treatment as usual or **C**ontingency **M**anagement (CM) and, as indicated, stepped up to **P**rEP **A**dherence **S**upport **S**ervices (CoMPASS) over 24 weeks. During CM sessions, participants receive timely tangible rewards for verifiable activities demonstrating 1) PrEP initiation and adherence, and 2) engagement with medications for opioid use disorder (MOUD) and other OUD-related care. Participants who do not have high levels of biomarker-confirmed PrEP adherence at week 12 will be stepped up to receive **P**rEP **A**dherence **S**upport **S**ervices (PASS) consisting of strengths-based case management over 12 weeks. Interventions are delivered by trained PrEP navigators, staff embedded within the respective sites. The primary outcome is sustained PrEP adherence by dried blood spot testing at 24 weeks. To inform future implementation, we are conducting implementation-focused process evaluations throughout the clinical trial.

Conclusions: Results from this protocol are anticipated to yield novel findings regarding the impact and scalability of CoMPASS to promote HIV prevention among PWID in partnership with community-based organizations.

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Keywords

HIV; opioid use disorder; injection drug use; HIV pre-exposure prophylaxis; contingency management; stepped care

1. Introduction

In the United States, persons who inject drugs (PWID) are disproportionately impacted by HIV, accounting for 1 in 10 new cases in 2018.[1] To reduce HIV risk, leading international

and national organizations, such as the World Health Organization, and Centers for Disease Control and Prevention (CDC), recommend a range of HIV prevention interventions for PWID, including access to syringe service programs (SSP), medications for opioid use disorder (MOUD), and HIV pre-exposure prophylaxis (PrEP).[2–4] PWID, however, often do not receive such interventions, likely due to limited knowledge about PrEP, healthcare system mistrust, and competing priorities.[5]

To address these challenges, there have been efforts to link PWID accessing SSPs to MOUD[6] and to integrate HIV testing and counseling with OUD-related care.[7] Yet few efforts to date have provided PWID accessing such services comprehensive HIV prevention interventions that include PrEP.[5] Further, limited attention has been paid to integrating interventions to enhance motivation to take PrEP, such as contingency management (CM).[8] Among PWID, CM improves substance use outcomes,[9] prevention and treatment of infectious diseases,[10] and medication adherence.[11] For some, CM alone may be an insufficient strategy to improve PrEP uptake, necessitating additional interventions, such as strengths-based case management,[12,13] to overcome individual and structural barriers. To date, no studies have evaluated the impact of CM on PrEP uptake and adherence nor used a stepped care model to promote HIV prevention among PWID.[14]

Thus, with the overall goal of promoting HIV risk reduction and improved health among PWID, we are conducting a randomized controlled trial to evaluate the impact of **CM** with, as indicated, **P**rEP **A**dherence **S**upport **S**ervices (PASS) (CoMPASS) compared to treatment as usual (TAU) on promoting PrEP initiation and adherence.

2. Methods

2.1. Overall design

Funded by NIDA,[15] CoMPASS is a hybrid type 1 effectiveness-implementation trial[16] enrolling PWID at one of four participating community-based sites. CoMPASS includes a 24-week intervention period with 12-month follow-up to evaluate the intervention's impact on PrEP initiation and adherence and OUD-related care and behaviors (Figure 1) among 526 PrEP-eligible PWID. The primary outcome is sustained PrEP adherence at 24 weeks, assessed using dried blood spot (DBS) testing defined as a tenofovir-disoproxil diphosphate (TFV-DP; Truvada®) level >700fmol/punch or emtricitabine/tenofovir disoproxil fumarate (FTC-TDF; Descovy®) level >175fmol/punch, reflecting cumulative dosing over 6-8 weeks and consistent with 4 or more doses per week.[17] Secondary outcomes include HIV risk behaviors; engagement in OUD-related care (SSP, MOUD) and extra-medical opioid use; and (exploratory) sexually transmitted infection (STI) and HIV acquisition. Additionally, we will evaluate the impact of the intervention on PrEP adherence based on alternative measures of adherence (i.e., point-of-care urine testing at week 12), self-report, and pharmacy data.

We will also generate data regarding factors that impact implementation.[18] Consistent with community-engaged research principles,[19] all aspects of this project from original concept through design choices and implementation have been conducted with community partners with the goal of optimizing its potential for promoting HIV prevention among PWID in a sustainable fashion. To examine whether treatment effects vary among subgroups, we will

conduct exploratory and hypothesis generating analyses. We will study whether treatment effects differ by demographic and clinical characteristics known to be common in this population and impact medication adherence, including housing status and depression. In addition, we will examine whether treatment effects differ by site of recruitment.

2.2. Rationale for study design

The rationale for our study design is guided by several principles. First, given existing data,[10,11,20] CM holds promise for promoting PrEP initiation and adherence among PWID.[10] Second, the use of PrEP navigators to promote PrEP uptake has largely ignored PWID.[21,22] Patient navigation has demonstrated efficacy to help patients with HIV navigate complexities of the medical system and retain them along the HIV care continuum and may also help patients navigate along the PrEP care continuum.[23–26] Third, stepped care strategies, the graded implementation of interventions for a given condition based on individual response, serve to optimize resources while being responsive to individual needs; such approaches are especially appropriate when a single intervention approach may not be uniformly adequate and resources are constrained.[27,28] Fourth, informed by prior work[18] and our own experiences,[29,30] implementation science frameworks, including RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance)[31] and Promoting Action on Research Implementation in Health Services (PARiHS), help guide the collection and evaluation of data in the context of ongoing randomized clinical trials to inform future implementation efforts.[32] We also use the PARiHS framework in addition to RE-AIM as it is commonly used as a determinant framework, focusing on understanding factors that impact the delivery of an intervention. For example, to assess “implementation” of the intervention, we will track the types of trainings and supports that are needed to enhance fidelity to intervention delivery among PrEP navigators. Similarly, guided by the PARiHS framework, to assess factors that would be necessary to support “maintenance” beyond the research infrastructure, we are evaluating clinician and staff perspectives on the “evidence” for PrEP among individuals with OUD pre- and post-RCT conduct.

2.3. Study aims and hypotheses

Among PrEP-eligible PWID, our study aims to compare effectiveness of CoMPASS vs. TAU on sustained PrEP adherence at 24 weeks. We hypothesize CoMPASS will be associated with a higher proportion of biomarker-confirmed and self-reported PrEP adherence compared to TAU. Second, we will compare the effectiveness of CoMPASS vs. TAU on HIV risk behaviors; engagement in OUD-related care and extra-medical opioid use; and exploratory STI and HIV acquisition. We hypothesize that CoMPASS will be associated with improvements in risk behaviors and OUD-related outcomes. Lastly, we will conduct an implementation-focused process evaluation of CoMPASS among PrEP navigators, front-line providers, staff, and leadership at each site.

2.4. Study context

The study is being conducted in the context of the Yale Center for Interdisciplinary Research on AIDS-supported New England HIV Implementation Science Network.[33] The coordinating center is at Yale School of Medicine; the Yale Center for Analytical Sciences coordinates data management and statistical support. The participating organizations include

Apex Community Care, Inc., Connecticut Harm Reduction Alliance, Recovery Network of Programs, Inc., and Stanley Street Treatment And Resources, Inc. (Table 1). Diverse in their mission and infrastructure, these organizations serve individuals in areas highly impacted by injection drug use and HIV.[34,35]

2.5. Inclusion and exclusion criteria

Individuals are eligible for study entry if they: 1) receive or are willing to receive services at one of the participating sites; 2) have a recent HIV negative test without concern for acute HIV;[36] 3) are ≥18 years old; 4) report injection drug use in the past 6 months; 5) meet PrEP eligibility criteria by reporting either a) sharing of injection or drug preparation equipment; or b) sexual risk behaviors (i.e. condomless sex or STI) in the past 6 months;[3,4] 6) meet Diagnostic and Statistical Manual (DSM)-5 criteria for OUD; 7) have a cell phone or access to a cell phone of a household member; and 8) provide written informed consent. Individuals are excluded for: 1) being currently prescribed PrEP; 2) self-report or urine testing confirming pregnancy, are breastfeeding, or trying to conceive; 3) any plans that would preclude study completion (e.g. surgery, major medical treatments such as chemotherapy, incarceration, travel out of state/country); 4) inability to provide at least one collateral contact; 5) non-English speaking (for sites without Spanish-speaking staff); or 6) have kidney disease (as PrEP is contraindicated). While the CDC's 2021 PrEP guidelines[37] highlight the safety of PrEP among pregnant individuals and on the developing fetus, previous guidelines noted the lack of available data on fetal safety and most trials discontinued PrEP use upon discovery of pregnancy. As this study and intervention were developed prior to the release of the 2021 guidelines, we established and maintain pregnancy, intent to become pregnant, and breastfeeding as exclusion criteria.

2.6. Recruitment and randomization

Participants are recruited with a multi-pronged recruitment approach involving: 1) recruitment flyers and self-referral; 2) front-line staff and peer referral and 3) research team outreach. Potentially eligible individuals are asked for verbal consent to complete a brief screener to determine whether they have injected drugs and are PrEP eligible by reporting either a) sharing of injection or drug preparation equipment or b) engaging in sexual risk behaviors in the past 6 months.[4] Individuals meeting inclusion/exclusion criteria and providing written informed consent to participate will complete baseline assessments and are randomized 1:1 to either CoMPASS or TAU, stratified by site. To ensure concealment of intervention allocation, a random permuted block sequence has been generated and intervention assignments distributed through Research Electronic Data Capture (REDCap).[38,39] Randomized participants receive $50 gift cards upon completion of each of the baseline, week 12, and week 24 assessments.

2.7. Intervention overview

2.7.1. Treatment as Usual (TAU)—Participants randomized to TAU receive a health handout with information on how to access PrEP, MOUD and harm reduction services with options for where such services may be obtained. As none of the study sites are otherwise actively engaging PWID for PrEP receipt, this is in addition to current standard practices

at each of the participating sites. All participants may be referred to any additional services as deemed appropriate based on interactions they have with site clinicians and staff; such treatment services are catalogued by self-report as part of the follow-up assessments.

2.7.2. CoMPASS—CoMPASS involves an introductory session with provision of a health handout followed by nine sessions of prize-based CM over 12 weeks to encourage participation in HIV prevention interventions in a flexible manner to promote progress towards engagement in HIV prevention-related care. Participants who do not have evidence of biomarker confirmed PrEP adherence by week 12 (non-responders) will be stepped up to five sessions of PASS.

2.7.2.1 Contingency management: After the introductory session, CM visits are designed to occur weekly for the first 6 weeks and then every other week until week 12 for a total of 9 sessions during which participants are eligible to receive rewards. Since CM interventions are most effective when they involve frequent monitoring, we designed the CM intervention frequency based on the goals of optimizing the balance between: 1) need for regular monitoring to support behavior change; 2) expected timeline during which target behaviors could be reasonably completed; 3) participant burden (e.g., aligning an individual's visit frequency with that of their routine utilization of services); and 4) organizational resources. Rewards are earned upon verified completion of the planned activities for the week (e.g., attending an appointment with a PrEP prescriber, pick up PrEP prescription) through "draws" of paper slips from a fishbowl with preset probabilities of rewards (Table 2). Rewards are tailored to the preferences of the community-based programs, such as gift cards to local stores and personal care items.[8]

The multi-target nature of the CM intervention allows for promotion of progression in the two domains of PrEP and MOUD engagement to best support stability over time, while the individualized and flexible approach allows a high level of tailoring to individual patient needs and ability. The reinforcement schedules for each target behavior are independent, promoting participants' access to reinforcers even if progress is limited to one of the two domains (Tables 3–4). The schedules escalate over time if targeted behaviors are consistently met. A weekly bonus is provided when both activities are completed and verified in a given week. When a target behavior is not completed and verified, zero draws are awarded and the draw schedule resets.

Over the course of the nine sessions, participants may earn up to 168 draws equivalent with an average maximum earning of $608.[58] The CM counseling is designed to be approximately 20 minutes in duration, manual-guided, and provided by trained PrEP navigators.[59]

Rewarding PrEP.: The ultimate goal is to move the participant quickly toward high levels of PrEP initiation and adherence (i.e., missing fewer than 3 doses of PrEP in the past week by self-report[40,41]) with confirmation by point-of-care urine testing for presence of tenofovir metabolites.[42] We used these thresholds given high levels of PrEP adherence are particularly important for HIV prevention among PWID[43,44] and biomarker testing is an objective and routine method to validate self-reported adherence.

Rewarding engagement in MOUD and other OUD-related care.: Participants are also independently rewarded for objectively verified progress in engaging in OUD-related care, with tailored sessions to the individual with a focus on promoting MOUD (e.g., attending intensive outpatient programs, Opioid Treatment Program intake, pharmacy fill of buprenorphine/naloxone, urine toxicology screen negative for opioids).

2.7.2.2 Determining response for stepped care: Our intention is to have a low threshold to offer additional support when participants do not have evidence of high levels of PrEP adherence.[28] Participants who either: 1) did not present for the final CM visit by week 14; 2) have not initiated PrEP by week 12; 3) report ≥3 missed doses of PrEP in the past week;[17,40] 4) report <3 missed doses of PrEP in the past week but decline point-of-care urine testing; or 5) report <3 missed doses of PrEP in the past week and agrees to point-of-care urine testing but no tenofovir metabolites are detected,[42] will be stepped up to PASS (Figure 2).

2.7.2.3 PrEP Adherence Support Services (PASS): PASS sessions are informed by the AntiRetroviral Treatment and Access to Service (ARTAS)[12] intervention, which demonstrated that 5-session community-based strengths-based case management, informed by Social Cognitive Theory, was successful in linking patients recently diagnosed with HIV to care.[12] We integrated ARTAS[12] content to be relevant to PrEP using the Project Inform PrEP navigation manual,[45] which has been endorsed by the CDC and AIDS Education Training Centers. The core elements of these sessions include: 1) strengthening an effective, working relationship between the PrEP Navigator and the participant; 2)) assessing the participant's strengths and encouraging them to use their skills to engage in PrEP and OUD-related care; 3) facilitating the participant's ability to identify and pursue their own goals and develop a step-by-step plan to accomplish these goals by completing a PASS action plan; and 4) maintaining a participant-driven approach by conducting up to five structured sessions of active, community-based case management.[46] Grounded in motivational interviewing principles, these sessions are designed to enhance participant readiness to engage in PrEP and achieve other goals.[47] Sessions conclude with completion of the PASS action plan.

2.7.4 Intervention training and monitoring—Designated as "PrEP Navigators," existing staff (i.e., harm reduction specialist, drug counselor, PrEP navigator) at each site are trained to deliver the intervention. Training in our manualized intervention was led by experts in CM, motivational interviewing, harm reduction, PrEP navigation, and internists certified in HIV and/or Addiction Medicine. Initial training consisted of six hours of content delivered virtually in two sessions with follow-up monthly videoconference and a booster training on the PASS intervention components as the first participants approached 12-week follow-up. Content included CM, motivational interviewing principles, HIV risk reduction with a focus on PrEP as well as MOUD and SSP, harm reduction, and stigma reduction strategies for working with PWID. Facilitated by structured visit forms, the PrEP navigators are trained to monitor and track target behaviors and implement the reward schedule. Following the start of CoMPASS enrollment, subject matter experts on the research team began rating audio recordings of sessions using an adapted CM Competence Scale[48] and a

corresponding scale developed to assess fidelity to PASS components and provide ongoing feedback.

2.8. Data collection protocol

Assessments are collected by research coordinators at baseline, week 12, and week 24, with participant interview and objective measures to assess PrEP adherence (Table 3). Additionally, at month 12, PrEP adherence will be assessed by pharmacy fill/refill data and incident STI and HIV infections will be assessed by surveillance data. These assessments are designed to ensure the participant meets eligibility criteria, assess important predictor variables, and study outcomes. The primary study outcome is sustained PrEP adherence at 24 weeks assessed by dried blood spot (DBS) testing for tenofovir metabolites processed by Molecular Testing Labs.[49] For participants not reporting taking PrEP, levels will be assumed to be zero and not confirmed by biomarker testing. Secondary study outcomes, assessed at 12 and 24 weeks, include biomarker-confirmed PrEP adherence by DBS and urine (week 12 only) testing; HIV risk behaviors; engagement in OUD-related care (SSP, MOUD) and opioid use; and exploratory STI and HIV acquisition at 52 weeks. Process outcomes include participation in CM intervention visits, activities completed and rewards earned, proportion who are stepped-up to PASS, participation of PASS visits, and time to initial PrEP fill.

Baseline assessments will facilitate exploratory and hypothesis generating analyses to examine whether the intervention's effectiveness differs based on baseline sociodemographic and clinical characteristics. The HIV Symptom Index[50] will assess bothersome symptoms and study-related and study-unrelated adverse events are recorded. For treatment services, we are tracking meetings with PrEP navigators, substance use and harm-reduction services, and medical services.[51] To facilitate future economic analyses, we are measuring health-related quality-of-life using the Patient-Report Outcomes Measurement Information System (PROMIS)-Preference score (PROPr)[52,53] and rewards earned from CM. To assess cost, we will track PrEP navigator time associated with delivering the intervention, costs of PrEP adherence monitoring (i.e., urine point-of-care test), and rewards earned per CM session.

2.9. Statistical considerations

2.9.1. Justification of sample size—The primary aim of this study is to compare the effectiveness of CoMPASS versus TAU on sustained PrEP adherence by DBS testing at 14 weeks. Based on prior research[54–56] and the vulnerability of the population under study, we hypothesize that 5% of participants randomized to TAU will demonstrate sustained PrEP adherence at 24 weeks. We believe that a 10% absolute increase (5% versus 15%) in sustained PrEP adherence represents a clinically meaningful improvement with CoMPASS over TAU and is consistent with treatment effects observed in studies evaluating the impact of CM.[10,11,20] With 90% power and a two-sided type I error rate of 5% using a two-sample test of proportions, we will need 368 total participants (184 per group) to detect the 10% absolute change. To account for participant attrition, we inflated our sample size by 30% and thus aim to recruit a total of 526 participants (263 per arm).

For secondary outcomes, we assume a conservative type I error rate of 1% to account for multiple testing. For self-reported adherence, if we assume a rate in the control group ranging from 5% to 10%, we will have at least 90% power to detect an absolute increase ranging from 14% to 16%, and at least 80% power to detect an absolute increase ranging from 12% to 14%. For HIV risk behavior, extra-medical opioid use, and engagement in OUD-related care, we anticipate being similarly powered. The sample size calculation was performed with PASS 2019 (Kaysville, Utah).

2.9.2. Statistical analyses

Primary outcome.: The primary aim of this analysis is to determine if the proportion of individuals with sustained PrEP adherence differs at week 24 among those randomized to CoMPASS versus TAU. The primary outcome of sustained PrEP adherence is binary and will be modeled using generalized linear mixed models with a logit link with a random intercept adjusting for site. A contrast statement will be used to conduct the 24-week comparison. The use of mixed models allows all participants (even if they do not have the primary endpoint) to contribute information to the final model. Analyses will be conducted using intent-to-treat principles such that all randomized participants will be included in the denominator for calculating the proportion with sustained PrEP adherence except for unavoidable loss to follow-up (i.e., participants known to have died). Since mixed models assume the data are missing at random, we will also conduct sensitivity analyses (assuming those lost are all non-adherent, adherent, or a mixture). We will use multiple imputation techniques for missing data with sensitivity analyses using pattern-mixture and selection models to examine the robustness of the conclusions of the primary analysis to missing data. Additional exploratory and sensitivity analyses will be conducted, including per-protocol analyses and weighting based on adherence. In addition, if any baseline differences are found between treatment arms, we will conduct a sensitivity analysis employing covariate adjustment. We will set statistical significance at $p<0.05$ and use two-sided tests.

Secondary and exploratory outcomes.: For binary secondary outcomes of interest (e.g., self-reported adherence, extra-medical opioid use, HIV risk behaviors), we will similarly use generalized linear mixed models with a logit link with a random intercept adjusting for site. For continuous outcomes (e.g., tenofovir metabolite levels), we will use a linear mixed model with a random intercept adjusting for site. Methods for multiple comparisons (i.e., Bonferroni correction, false discovery) will be used to adjust for multiple comparisons in the secondary outcomes. We will set statistical significance at $p<0.01$ and use two-sided tests.

Exploratory analyses will be conducted for STI and HIV incidence by state health department surveillance data and PrEP persistence by pharmacy data will be assessed using a generalized mixed model with month 12 contrast. To examine whether treatment effects vary among subgroups, we will conduct exploratory and hypothesis-generating analyses. We will study whether treatment effects differ by demographic and clinical characteristics known to be common in this population that impact medication adherence by including analysis of treatment with covariate interactions as well as whether treatment effects differ by recruitment site.

2.10. Implementation-focused process evaluation

Our implementation-focused process evaluation of CoMPASS, grounded in RE-AIM[31] and PARiHS[18,32] frameworks, will include screening logs; minutes and logs from study team meetings; site visits; as well as data from enrolled participants (e.g., participant satisfaction). We will track any needed protocol modifications guided by the Framework for Reporting Adaptations and Modifications-Enhanced (FRAME).[57] These data sources are being complemented by a confidential online REDCap-based *CoMPASS Implementation Survey* within the first six months of launching the clinical trial as well as post-trial of clinicians, staff, and leadership at each site. We will assess the following domains: 1) demographic and practice characteristics; 2) perspectives and experiences regarding HIV prevention with PrEP; 3) potential barriers to promoting PrEP among PWID; 4) beliefs regarding CM; and 5) organizational readiness to implement and refer to CoMPASS (Appendix). The *CoMPASS Implementation Survey* was developed based on existing literature[58] and validated tools,[59] reviewed by our multidisciplinary team, and piloted prior to launch. Differences in pre- and post-trial responses will be assessed using appropriate parametric or non-parametric methods.

To grasp a richer understanding of the experiences and attitudes regarding HIV PrEP and CM, we will conduct a content analysis of open-ended responses in the participant and staff surveys.

2.11. Protection of participants

This HIPAA-compliant study is approved by the Yale School of Medicine Human Investigation Committee, the institutional review board of record for all participating sites. The study is also approved by the Connecticut Department of Public Health and the Massachusetts Department of Public Health. The Data Safety and Monitoring Board reviews study progress, experiences and adverse events, biannually.

2.12. Current status of CoMPASS

After completion of planning meetings, site visits (in-person and virtual as needed due to COVID-19), and trainings, CoMPASS opened for enrollment on October 4, 2021. Recruitment and study implementation has been hindered by the COVID-19 pandemic with decreased client volume at the sites, study staff illness and turnover, but is ongoing. To enhance safety of all individuals involved, we have ensured study procedures focus on minimizing risk of COVID-19 transmission, optimize social distancing, and maintain flexibility given uncertainty with the circumstances and variable access to technology among potential participants.

The web-based survey of site clinicians, staff, and leadership was launched on April 7, 2022, and data collection is complete and analyses underway.

3. Discussion

CoMPASS will evaluate the impact of a novel, multi-targeted CM intervention with stepped care to structured PrEP navigation to promote HIV risk reduction and engagement in

OUD care among PWID accessing community-based services. Several aspects make our study innovative. First, it uses CM to promote PrEP with point-of-care testing to assess past-48-hour PrEP adherence to temporally link behaviors and rewards.[60] Second, it will be the first time a stepped care design is used to sequentially add PrEP navigation to adaptively promote sustained PrEP adherence among PWID and to incorporate multi-target CM design in a package of HIV prevention services for PWID.[61] Third, inclusion of diverse sites will allow for exploratory examination of whether site characteristics impact outcomes. Fourth, by triangulating participant-reported data with pharmacy fill/refill data and health department surveillance data, we will have robust measures of key outcomes. Fifth, consistent with a hybrid type 1 effectiveness-implementation design,[16] we will collect data from key stakeholders pre- and post-trial to inform future implementation efforts of CoMPASS. Lastly, the FRAME will guide systematic tracking of any modifications needed to enhance the intervention evaluation given the unpredictable circumstances and its consequences created by the COVID-19 pandemic. Studies focused on promoting PrEP among pregnant women with OUD should be conducted in the future given growing safety data.

3.1 Limitations

First, while the COVID-19 pandemic has improved and the participating study sites are functioning at full capacity, the unpredictable nature of the pandemic may impact future participant recruitment and protocol adherence. Second, this is a non-blinded study, research coordinators and PrEP navigators participating in data collection and CM and PASS delivery will not be blinded to treatment assignment of participants. However, our primary outcome is an objective biomarker-based testing of PrEP adherence. Third, all sites are located in the northeast US potentially limiting generalizability to other settings where resources may be different.

3.2. Conclusion

CoMPASS will generate data on the impact of a novel adaptive intervention employing CM and structured PrEP navigation components to promote linkage to PrEP and OUD-related care to reduce HIV transmission among PWID. Findings generated from this study will be directly relevant for informing delivery of these HIV prevention interventions in a variety of organizational settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Few persons who inject drugs (PWID) are taking HIV pre-exposure prophylaxis (PrEP).
- Contingency management with stepped care may promote sustained PrEP adherence.
- Point-of-care testing may be useful for verifying self-reported PrEP adherence among PWID.
- PWID may be reachable for HIV prevention in opioid treatment and harm reduction programs.

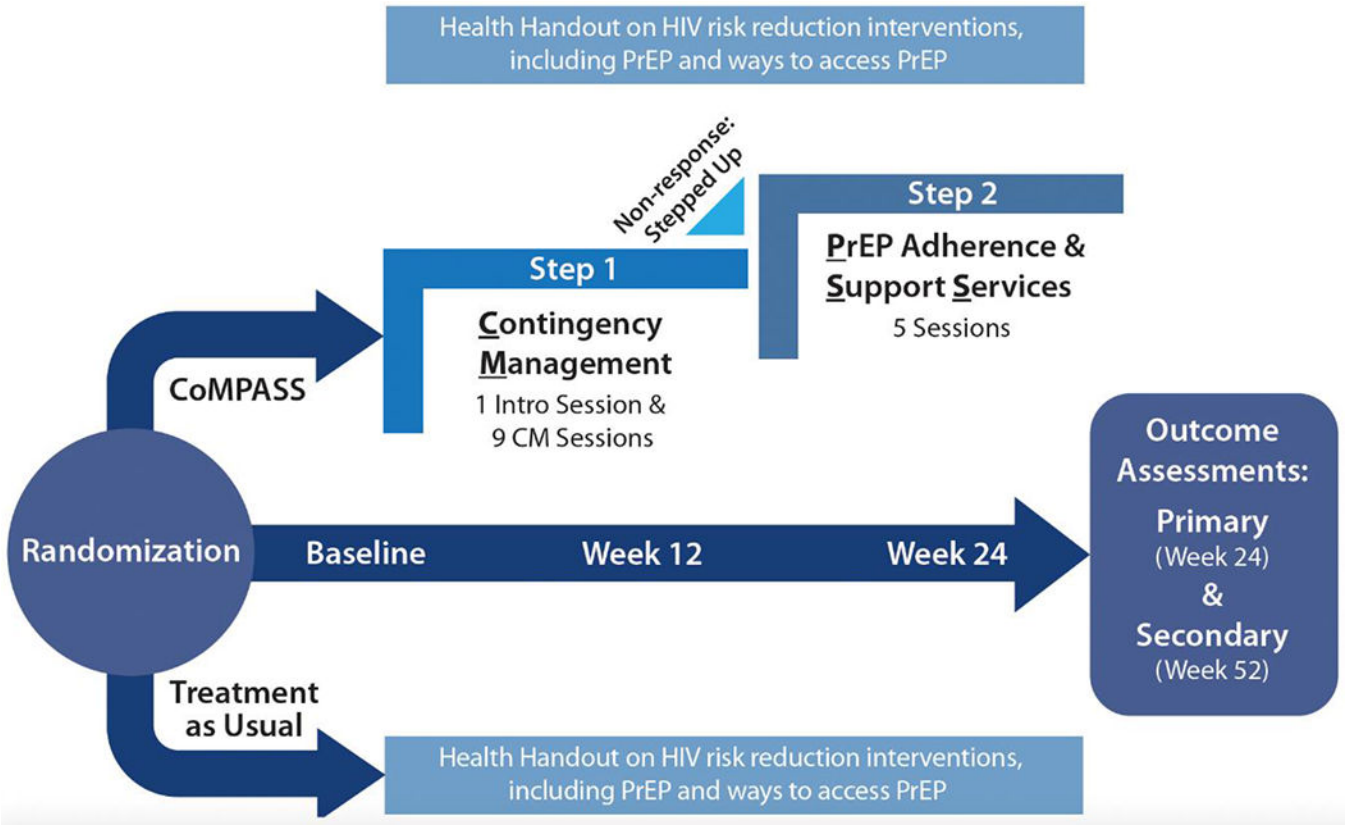

Figure 1.

Contingency Management and stepped-up (when indicated) to Pre-Exposure Prophylaxis (PrEP) Adherence and Support Services (CoMPASS) Trial Protocol Overview

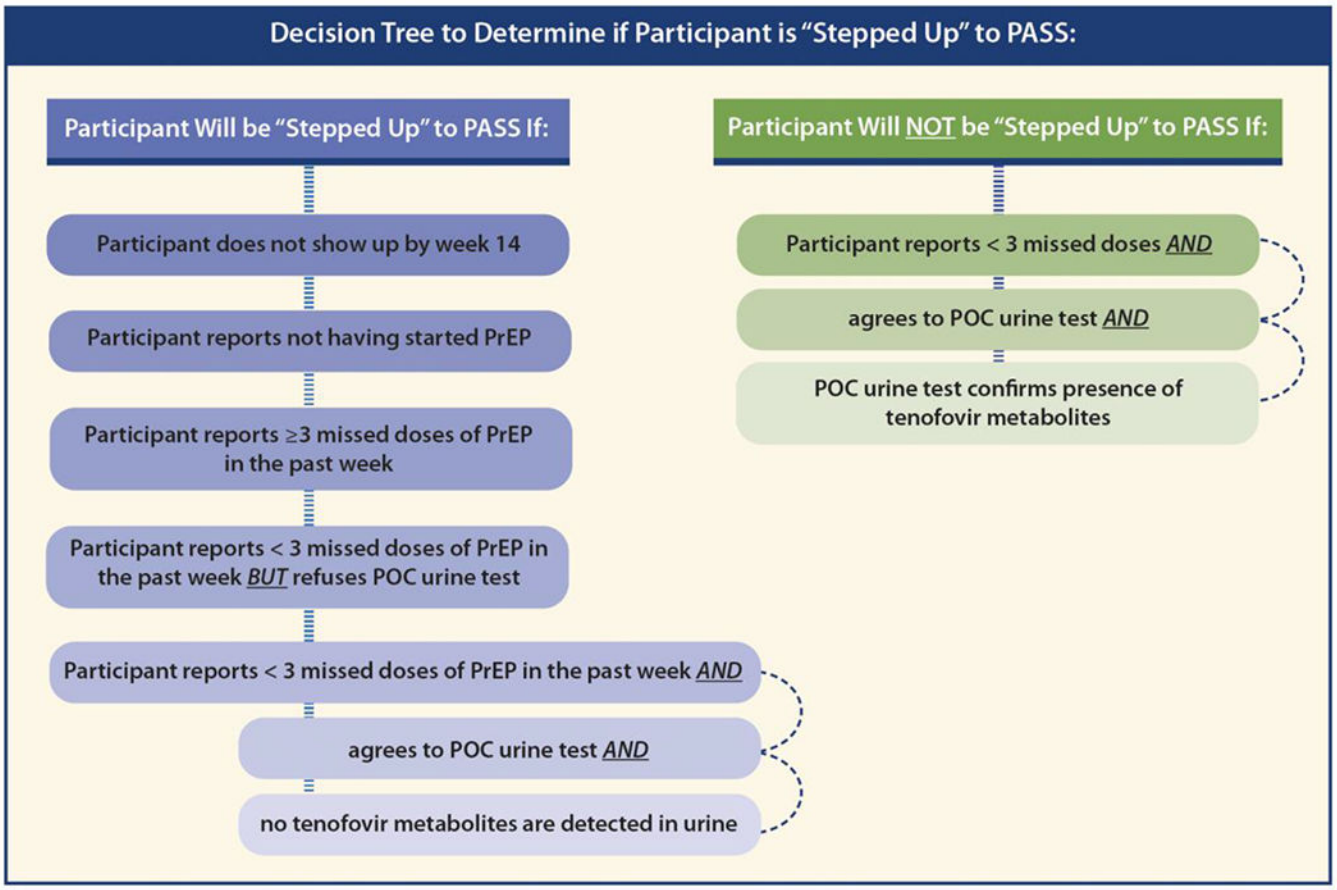

Figure 2.

Decision tree to determine if participant is stepped up to Pre-Exposure Prophylaxis (PrEP) Adherence and Support Services (PASS)

POC: Point of Care

Table 1.

Study site characteristics

Site characteristics	Study Site			
	Site A	Site B	Site C	Site D
Client gender identity (%)				
Female	31.5	27.7	32.6	47.9
Male	67.4	70.1	67.4	51.7
Transgender	0.2	0.2	--	0.2
Nonbinary	0.4	--	--	0
Other[a]	0.4	2.2	--	0.2
Client racial identity (%)				
American Indian/Native American	1.8	0.1	0.2	0.6
Asian/Pacific Islander	1.1	1.0	0.4	2.5
Black/African-American	10.3	24.9	32.9	6.9
White/Caucasian	76.6	43.2	41.6	66.9
Other[b]	10.0	--	21.5	23.0
Client ethnic identity (%)				
Hispanic/Latino/Latinx/Latine	27.4	29.1[c]	21.5[c]	14.7
Number of new clients in 2021	--	952	392	6081
Number of HIV tests performed	350	20	360	890
Number of clients with opioid use disorder	117	--	1133	3159
Presence of the following services (yes/no):				
On site HIV testing	Yes	Yes	Yes	Yes
On site PrEP[d]	Yes	No	No	Yes
On site medications to treat opioid use disorder (e.g.e.g., methadone, buprenorphine, naltrexone)	Yes	No	Yes	Yes
On site syringe exchange	Yes	Yes	No	Yes
On site naloxone provision and overdose education	Yes	Yes	Yes	Yes
Outreach services	Yes	Yes	Yes	Yes
Number of clinicians on site	7	1	4	23
Number of counselors/staff	10	5	25	327

[a] Other category includes: not asked, prefer not to disclose, questioning/unsure

[b] Other category includes: do not know, more than one race, declined to answer, not asked, Middle Eastern or North African

[c] Ethnic identity question was combined with racial identity question for this site

[d] PrEP: Pre-exposure Prophylaxis

[*] -- indicates that the data was not available

Table 2.

Fishbowl Rewards for Contingency Management[a]

Reward	Number of Slips	Value
Non-monetary affirmation (“good job!”)	250	$0
Small prize	109	$1
Medium prize	80	$5
Large prize	60	$20
Jumbo prize	1	$100
Total	**500**	---

[a]Slips are replaced between patients so that fishbowl probabilities stay constant over time.

Table 3.

Contingency Management and stepped-up to Pre-exposure Prophylaxis (PrEP) Adherence and Support Services (CoMPASS) Trial: Summary of Assessments and Schedule

Assessment	Screening	Baseline	Week 12	Week 24
Demographics	X	X		
HIV Status	X		X	X
HIV Symptom Index	X		X	X
PrEP Eligibility[4]	X			
Mini-SCID for Opioid Use Disorder[62]	X			
Medical/Psychiatric Comorbidities[63] *		X	X	X
Housing Status		X	X	X
Criminal Justice Involvement		X	X	X
PrEP Adherence[17]			X	X
PrEP for Health Measures		X	X	X
CTN HIV Risk Behavior Scale[64]		X	X	X
Substance Use[65,66]		X	X	X
ASSIST-Lite[67]		X	X	X
Overdose History and Risk[68,69]		X	X	X
Treatment Services Review and Health Services Utilization[51] *		X	X	X
Treatment Effectiveness Assessment[70,71]		X	X	X
Marijuana Assessment		X	X	X
Medical Mistrust and Discrimination[72–74] *		X	X	X
Transportation Insecurity Index[75]		X	X	X
Household Food Insecurity Access Scale[76]		X	X	X
PROMIS PROPr[52,53]		X	X	X

PrEP: Pre-exposure Prophylaxis; CTN: Clinical Trials Network; ASSIST: Alcohol, Smoking and Substance Involvement Screening Test; NIDA: National Institute on Drug Abuse; PROMIS: Patient-Report Outcomes Measurement Information System; PROPr: Preference; SCID: Structured Clinical Interview for DSM (Diagnostic and Statistical Manual of Mental Disorders)-5

* Modified

Table 4.

Contingency Management Reinforcement Schedule Overview[a]

	Metric		
	PrEP[b,c]	**MOUD and Other OUD-related Care**[b,d]	**Bonus**
Purpose	PrEP initiation and consistent PrEP adherence	Engagement in MOUD and OUD-related care	Reward achievement of both targets given independent health benefits
Visits potentially rewarded	Follow-up visits 1-9	Follow-up visits 1-9	Follow-up visits 1-9
Examples of potentially rewarded activities	Picked up a PrEP prescription at the pharmacy	Attended narcotics anonymous group meeting	
Initial reward	3 draws	3 draws	6 draws
Potential increase between visits	1 draw	1 draw	N/A
Maximum reward (cap)	8 draws	8 draws	N/A
Total potential rewards if consistently meet target	57	57	54

[a] PrEP and MOUD activities are reinforced on independent schedules, such that failure to complete the planned MOUD activity does not impact draws for the PrEP planned activity, and vice versa. The bonus is only earned if the participant provides verified evidence of completing both activities in a given week (i.e., completed both the PrEP activity and the MOUD activity as listed on the contract).

[b] PrEP: Pre-exposure Prophylaxis; MOUD: Medications for Opioid Use Disorder; OUD: Opioid Use Disorder; N/A: Not applicable

[c] If a participant reports no progress towards PrEP initiation or has initiated PrEP, but is non-adherent, no draws will be awarded for that session and the number of draws will reset to the initial value of 3 for the next demonstration of verified activity completion.

[d] If a participant reports no progress towards MOUD or other OUD-related care, no draws will be awarded for that session and the number of draws will reset to the initial value of 3 for the next demonstration of verified activity completion.