Study Protocol

Official Title: Reducing OUD treatment dropout: Development and pilot test of a peer recovery support intervention in primary care

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Social and Behavioral Sciences Human Research Protocol Template

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PROTOCOL TITLE: Reducing OUD treatment dropout in primary care

INTRODUCTION AND PURPOSE:

Retention remains challenging for primary care patients receiving medications for opioid use disorder (OUD). Earlier qualitative and observational research from Aim 1 of this K23-funded project and the parent Penn Whole Health Study identified several factors within Peer Recovery Specialist (PRS) programs that potentially influence retention. These factors include quality of peer-patient relationships, meaningful documentation by peers in electronic health record (EHR), peer specialists' training and professional development, and continuity of peer-patient interactions. In Aim 2, we integrate these findings with input from experts in OUD and PRS programs to develop an optimized PRS program. Aim 3, for which we currently seek IRB approval, will pilot test the feasibility and acceptability of this optimized PRS intervention, laying the groundwork for a future randomized clinical trial (RCT).

OBJECTIVES:

Research Questions:

- Is the enhanced PRS intervention feasible and acceptable to patients and primary care teams?
- Can proposed outcome measures (treatment retention, medication adherence, opioid abstention) be reliably collected in the primary care?
- What are patients' and providers' experiences, perceptions, and recommendations regarding the PRS intervention and its role in supporting patient retention?

Primary Objectives:

1. Evaluate the feasibility and acceptability of the PRS intervention aimed at improving retention in OUD treatment in primary care from the perspective of patients and primary care team members.
2. Pilot test the primary outcome measures of retention in treatment (time to dropout), appointment attendance, and medication adherence to evaluate their appropriateness, clarity, and feasibility of collection.

Secondary Objectives:

3. Explore the PRS intervention's influence on self-efficacy, resilience, and coping skills as intermediate patient outcomes related to opioid abstinence.
4. Collect qualitative feedback to refine the intervention's design, assess feasibility for a larger RCT, and identify facilitators and barriers to future implementation.

BACKGROUND:

Opioid-related mortality in the US remains alarmingly high, with over 80,000 fatal overdoses recorded in 2021 alone.[1] Medication-assisted treatment (MAT), which combines medications for OUD and behavioral therapy, is the approved standard for treating opioid use disorder (OUD). Among medication options, buprenorphine, which is nearly as effective as methadone,[2-4] is preferred for its lower toxicity;[5] it also has a more flexible dosing schedule than methadone and is more acceptable to patients,[5] especially when prescribed in primary care.[6] For more than a decade, the use of buprenorphine to treat OUD has grown significantly, with primary care responsible for much of this increase.[7,8] Yet, OUD treatment in primary care has the same high rates of patient dropout observed in other settings.[9-12]

Peer Recovery Specialist (PRS) programs, which employ trained individuals in recovery, show promise for improving patient engagement and retention. Peers provide a range of services, including health education, encouragement and empathy, coping skills, crisis management, and concrete assistance in overcoming barriers to adherence, making them a promising form of support to patients in their struggle to stay engaged in

treatment.[13-18] Despite their potential, PRS programs have not been rigorously evaluated for their ability to improve retention in OUD treatment. Existing programs vary widely regarding structure, peer qualifications, training practices, supervision, and the quality of peer-patient interactions.

This pilot study will assess the feasibility and acceptability of an enhanced PRS intervention developed from earlier findings of this K23-funded study, the Penn Whole Health Study, and existing literature. Preliminary findings from Aim 1 indicate several factors may improve the effectiveness of PRS services, including relational compatibility between peers and patients, improved peer documentation in the EHR, structured professional development for peers, and trauma-informed peer-patient interactions. Results from this pilot will provide the foundation for a future large-scale RCT.

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CHARACTERISTICS OF THE STUDY POPULATION:

1. Target Population and Accrual:

The target population for this pilot study is adults aged 18 years or older who are receiving buprenorphine treatment for opioid use disorder (OUD) at a Penn Medicine primary care clinic.

The study aims to enroll 20 patients over a one-year period. Given the pilot and feasibility focus of this research, formal power calculations were not conducted. The sample size was chosen based on established standards for pilot behavioral health intervention studies, sufficient to evaluate feasibility, logistics, and data-collection procedures.

Participants will be recruited exclusively from Penn Medicine primary care practices; no external recruitment or institutional permissions will be required. Recruitment methods are described further in the "Subject Recruitment and Screening" section of this application. We anticipate successful accrual given the volume of eligible patients within Penn Medicine primary care clinics.

2. Key Inclusion Criteria:

Participants must meet **all** the following eligibility criteria:

1. Age ≥18 years
2. Diagnosed with OUD
3. Able to communicate in English
4. Access to a phone
5. Currently receiving or initiating buprenorphine treatment from a Penn Medicine primary care physician
6. Able and willing to provide written informed consent

Rationale for Inclusion and Exclusion Criteria:
The selected criteria ensure participants can safely engage in the PRS intervention and clearly communicate their experiences. The study targets adults (≥18 years) because the clinical, ethical, and social considerations for treating adult OUD differ substantially from pediatric populations. Participants are required to be English-speaking, as this aligns with the primary language of the peers, facilitating clear communication, effective engagement in the PRS intervention, and thorough comprehension of study procedures.

Justification Regarding Gender, Ethnicity, and Race:
Recruitment will actively reflect the population OUD in the Philadelphia area. Patient participants will not be excluded based on race, ethnicity, sex, or socioeconomic status.

Inclusion of Vulnerable Populations:
Patients with substance use disorders experiencing socioeconomic hardships or unstable housing are explicitly included to accurately reflect the real-world patient population targeted by PRS interventions. Effective follow-up with transient populations will be supported through multiple verified contact methods, collection of alternative contacts (e.g., family or friends), and flexible scheduling to accommodate participant availability.

3. Key Exclusion Criteria:

Participants will be excluded if they meet **any** of the following criteria:

1. **Acute suicidality:** Patients experiencing acute suicidal ideation or intent require immediate specialized mental health interventions beyond the scope and capacity of this study.
2. **Mania or psychosis:** Patients experiencing active manic or psychotic episodes may have impaired capacity to provide informed consent and effectively participate in the PRS intervention.

3. **Significant cognitive impairment:** Patients with severe cognitive impairment may not fully understand study procedures or reliably provide informed consent, potentially placing them at undue burden or risk.

Justification for Exclusions:
Patients experiencing acute suicidality, mania or psychosis, or significant cognitive impairment are excluded due to ethical considerations regarding patient safety, capacity to provide informed consent, and their ability to meaningfully engage with the intervention.

Exclusion of Transient Populations:
Transient populations or groups that may be difficult to locate are not explicitly excluded. To minimize participant loss and address potential follow-up challenges common in these groups, the study will proactively obtain alternative contacts (with participant consent) and employ flexible scheduling and follow-up methods, such as phone calls or text messages.

Other Populations Not Appropriate:
No additional populations are explicitly excluded.

4. Subject Recruitment and Screening:

Patient Identification and Recruitment Methods:
Patients will be recruited exclusively via clinician referrals and EHR screening at Penn Medicine primary care clinics. Informational flyers will be provided directly to interested patients during clinic visits but will not be publicly posted. Eligibility screening will be conducted by the Principal Investigator (PI) or research coordinator during chart reviews and regular primary care visits, privately and confidentially prior to enrollment.

1. **Clinician Referrals:** Primary care providers and care team members at Penn Medicine clinics will identify eligible patients using their clinical knowledge and electronic health records (EHR) screening, which is a common practice at Penn Medicine.
2. **In-Person Recruitment:** The Principal Investigator (PI) or a trained research coordinator will directly approach potential participants during previously scheduled primary care appointments. They will briefly describe the study's purpose, procedures, risks, and benefits, and invite patients to participate.

Patient Eligibility Screening Process:
Patients will be screened for study eligibility using information from the electronic health record (EHR) and standard clinical assessments to confirm:

- Age ≥18 years
- Diagnosis of OUD
- Current buprenorphine treatment at Penn Medicine primary care
- English-speaking
- Access to a phone

No additional eligibility screening instruments will be used.

Care Provider Recruitment:
The PI, as an addiction medicine attending physician, will identify and approach care providers. All providers directly involved in participants' care (approximately 3-4 providers and one case manager) will be invited to participate. Participation is voluntary and will not affect their employment or professional standing.

Recruitment Materials:
All potential participants will receive clear, IRB-approved recruitment materials, including a concise, plain-language informational handout summarizing the study purpose, procedures, eligibility criteria, risks and benefits, and contact information. These materials will be provided in English, written at an accessible (4th-grade) reading level to enhance participant comprehension.

Recruitment will not involve social media or external advertisements; therefore, Penn media services (e.g., social media, texting, blogging) will not be utilized.

IRB Approval of Recruitment Materials:
All recruitment materials (informational handouts, consent forms) are included with this submission for IRB review and approval prior to their use.

5. Early Withdrawal of Subjects:

Participants may be withdrawn early from the study under the following circumstances:

1. **Safety Concerns:** Participants will be immediately withdrawn and referred for appropriate clinical care if they exhibit acute suicidality, severe psychological distress, psychosis, mania, or any other medical or psychiatric condition that, in the judgment of the PI or clinical team, makes continued participation unsafe.
2. **Participant-Initiated Withdrawal:** Participants may voluntarily withdraw at any time, for any reason, without explanation. Withdrawal requests may be made verbally (in-person or by phone), by email, or through written communication, according to participant preference.
3. **Lost to Follow-up or Non-attendance:** Participants who repeatedly miss scheduled study visits or who cannot be reached despite multiple documented contact attempts (at least three attempts via phone, text, or alternative contacts) may be withdrawn by the PI due to inability to complete study procedures.

Withdrawal Procedures:
Participants may withdraw at any time using any convenient method, including verbal notification (in person, by phone, or by text), email, or other accessible forms of communication based on their circumstances. For vulnerable or transient populations, such as individuals experiencing housing instability or literacy challenges, verbal or phone-based withdrawal requests will be explicitly accommodated to ensure minimal barriers to exiting the study.

Post-Withdrawal Support and Services:
Participants who withdraw early, whether voluntarily or due to safety concerns, will receive appropriate recommendations for follow-up care. This may include referrals to mental health services, substance use treatment resources, counseling, or other clinical support as needed, ensuring continued patient safety and well-being.

6. Vulnerable Populations:

Vulnerable Populations:
Children, pregnant women, fetuses, neonates, or prisoners are not included in this research study.

7. Populations vulnerable to undue influence or coercion:

Participants in this study may include individuals who are economically disadvantaged, educationally disadvantaged, or affected by substance use disorders, which can make them potentially vulnerable to undue influence or coercion.

To minimize these risks and protect participant rights and welfare, the following safeguards will be in place:

1. **Voluntary Participation:** Participation is entirely voluntary. This will be explicitly communicated both verbally and in consent documents, emphasizing that choosing not to participate will not impact clinical care.
2. **Clear and Accessible Consent:** The informed consent process will use simple language at or below a 4th-grade reading level, supplemented by clear verbal explanations, ample opportunities to ask questions, and adequate time to consider participation.
3. **Modest Financial Incentive:** Participants will receive modest compensation ($50 ClinCard) to acknowledge their time, designed to avoid undue financial influence.
4. **Flexible Communication Methods:** Recognizing potential resource limitations, multiple communication channels (phone, text messaging, and flexible scheduling) will be used to ensure ongoing engagement without undue burden.

5. **Support and Clinical Referrals:** Participants experiencing emotional distress or adverse events will be promptly referred to appropriate clinical resources, prioritizing participant safety and well-being over research objectives.

These safeguards ensure respectful, protective, and ethical treatment of all study participants, particularly vulnerable groups.

STUDY DESIGN:

Research Design and Justification: This pilot study employs a mixed-methods approach to evaluate the feasibility, acceptability, and preliminary effectiveness of an enhanced Peer Recovery Specialist (PRS) intervention designed to improve retention in opioid use disorder (OUD) treatment within primary care settings. This pilot is designed to inform the development of a larger randomized controlled trial (RCT).

Peer Recovery Specialist (PRS) Role:
The PRS, already employed by Penn Medicine and experienced through prior work with the Whole Health Study (parent study), will deliver the intervention and provide qualitative feedback as a research participant. The PRS holds state-approved PRS certification and extensive clinical training.

Protocol-specific PRS training, conducted by the PI, includes relationship-building skills, structured professional development, and tailored crisis management. Supervision and fidelity checks by the PI and research coordinator will occur bi-weekly.

Implementation Steps:
1. Eligible patients will be identified through clinician referrals and electronic health record (EHR) screening.
2. The Principal Investigator (PI) or research coordinator will approach eligible patients during primary care visits, explain the study, and obtain informed consent.
3. Baseline information, including sociodemographics and substance use history will be collected through the EHR.
4. Participants will engage in the enhanced PRS intervention, structured into weekly visits initially, biweekly thereafter, and monthly once treatment stabilizes.
5. Brief regular questionnaire data collection will be conducted with patients at the initial visit, ~month 3, and ~month 6.
6. Brief qualitative interviews with patients (at the initial visit, ~month 1, ~month 3, and ~month 6) and care team members (at the initial visit, ~month 3, and ~month 6) will assess feasibility, acceptability, implementation fidelity, and sustainability.

Research Methods:
- **Quantitative methods:** Standardized assessments including retention measures (appointment attendance, medication adherence, opioid abstention via urine drug screening and self-report will be captured through the EHR) and brief validated questionnaires for patient self-efficacy, resilience, and coping.
- **Qualitative methods:** Semi-structured interviews conducted with patients and care team members to explore perceptions, experiences, implementation fidelity, barriers, and facilitators.

Significance of Methods:
- Quantitative methods will provide objective data on retention measures (time to dropout, appointment attendance, medication adherence, and opioid abstinence). These data will allow the research team to assess the appropriateness, clarity, and feasibility of collecting these measures in a future RCT.
- Qualitative methods will deliver in-depth insight into participant experiences, acceptability, and intervention implementation processes, which are critical for refining the intervention for future RCTs.

Duration and Timeline:
- The pilot study will run for a total duration of 180 days (6 months).
- Individual participant involvement includes: a baseline visit with the peer (~30 minutes); weekly visits during the first two weeks (~30 minutes each); biweekly visits for the next 6–8 weeks (~30 minutes each); and monthly visits thereafter (~30 minutes each).

Research and Data Analysis Locations:

- Research activities, including recruitment, consent, assessments, and interventions, will be conducted at Penn Medicine primary care clinics.
- Data storage and analysis will occur at secure research facilities at the University of Pennsylvania, using secure electronic and physical data storage systems.

Participant Duration and Sequence:

- Baseline Assessment (Week 0): ~1-hour visit.
- Initial Engagement Phase (Weeks 1-2): weekly visits (~30 minutes each).
- Early Treatment Phase (Weeks 3-10): biweekly visits (~30 minutes each).
- Stable Treatment Phase (Weeks 11-26): monthly visits (~30 minutes each).

This structured design ensures comprehensive feasibility assessment and participant engagement, allowing aims and objectives to be met within the specified study duration.

METHODS:

This study uses a mixed-methods approach, combining quantitative assessments and qualitative interviews, to assess the feasibility and acceptability of an enhanced PRS intervention. The peers participating in this study are current Penn employees who previously received training and experience in their roles during the parent Whole Health Study.

Quantitative Methods:

1. **Patient Participant Assessments:**
    - Baseline assessment: At enrollment, we will gather data on demographics, substance use history, comorbidities, perceived barriers to retention and recovery, and social determinants of health (housing, food security, employment, transportation, legal issues, childcare). Patient baseline interviews will be conducted by the research coordinator, not by the PRS. The PRS role begins post-enrollment.
    - Follow-up assessments: Scheduled follow-up visits will measure treatment retention (appointment adherence, medication refill consistency), opioid abstinence (via self-report and urine drug screening), and medication adherence (through urine drug screening and Prescription Drug Monitoring Program data).
2. **Intermediate Outcome Assessments:**
    - Intermediate outcomes (self-efficacy, resilience, and coping skills) will be assessed using an adapted 30-item brief questionnaire developed from the Brief-COPE, Connor-Davidson Resilience Scale, and Alcohol Abstinence Self-Efficacy Scale.

Qualitative Methods:

1. **Patient Interviews:**
    - Brief, semi-structured, open-ended interviews will assess patient experiences, satisfaction, and perspectives regarding the PRS intervention.
2. **Care Team Interviews:**
    - Interviews with primary care team members will explore intervention acceptability, feasibility, fidelity of implementation, and sustainability. These interviews will be guided by the Theory of Planned Behavior, a well-established implementation science framework.

Implementation Fidelity and Sustainability:

1. **Adherence Checklists:**
    - Bi-weekly adherence checklists will monitor fidelity to the intervention protocol and identify facilitators and barriers, such as resource constraints or administrative complexity.
2. **Sustainability Assessments:**
    - Periodic sustainability assessments will be guided by the Practical, Robust Implementation and Sustainability Model (PRISM). These assessments will examine sustainability dimensions, including patient choice, barriers addressed, ease of transition, complexity and cost minimization, patient satisfaction, and feedback on performance.

Data Management and Analysis:

All collected data will be securely stored in encrypted electronic databases and locked physical storage at a University of Pennsylvania facility.

Quantitative data will be analyzed using descriptive statistics, including means, medians, ranges, and percentages.

Qualitative interview data will undergo thematic analysis using NVivo software, employing a structured coding approach. Transcripts will first be reviewed independently by two researchers to identify initial codes, then refined collaboratively to generate themes that reflect participants' experiences and perspectives regarding the intervention.

1. Study Instruments:

The pilot study uses several validated, widely accepted research instruments and structured qualitative interview guides to comprehensively evaluate the enhanced Peer Recovery Specialist (PRS) intervention.

Quantitative Instruments (Standardized, Validated Measures):

1. **Urine Drug Screens (UDS):**
    - Objective biochemical tests to verify opioid, buprenorphine, and other drug use.
2. **Prescription Drug Monitoring Program (PDMP):**
    - Pennsylvania's state registry, used to objectively track prescription-filling behaviors for buprenorphine and other controlled substances.
3. **Brief Resilience, Coping, and Self-Efficacy Scale (30 items scale, adapted):** A composite scale created from validated instruments to assess intermediate patient outcomes:
    - **Alcohol Abstinence Self-Efficacy Scale (adapted for opioid abstinence):**
        1. Measures patients' confidence in maintaining opioid abstinence; validated in multiple substance use populations (DiClemente et al., 1994).
    - **Connor-Davidson Resilience Scale (CD-RISC):**
        1. Assesses resilience and adaptability to stress; widely validated across diverse populations (Connor & Davidson, 2003).
    - **Brief COPE Scale:**
        1. Evaluates coping strategies and styles in managing stress and life challenges; extensively validated across diverse populations (Carver, 1997).

Qualitative Instruments (Semi-Structured Interview Guides):

- **Patient Interviews:**
    - Interview guide topics include:
        - Experiences and perceptions of peer support
        - Acceptability and satisfaction with the PRS intervention
        - Suggestions to improve intervention delivery
        - Perceived barriers to retention and adherence to treatment
- **Care Team Interviews:**
    - Interview guide topics include:
        - Perceptions of PRS intervention effectiveness
        - Facilitators and barriers to implementation
        - Views on peer specialist training and skill utilization
        - Recommendations for improving intervention implementation and sustainability

Interview Procedures:

- Before beginning the interview, participants will be informed clearly about the interview's purpose, content areas, expected duration, and their right to participate voluntarily or withdraw at any time.
- With explicit participant consent, interviews may be audio-recorded, conducted in a private space to ensure confidentiality, and transcribed verbatim for qualitative analysis.

2. Group Modifications:

No modifications to the content or structure will be made across different demographic groups.

3. Method for Assigning Subjects to Groups:

This pilot study uses a single-group design without randomization.

4. Administration of Surveys and/or Process:

Administration of Surveys and/or Process:

1. Qualitative Patient Interviews:
- Frequency: Initial visit, and approximately at months 1, 3, and 6.
- Procedures: Brief, semi-structured interviews to explore patient experiences, perceptions, suggestions, and satisfaction with the PRS intervention.

2. Brief Patient Resilience, Coping, and Self-Efficacy Questionnaire
- Frequency: Initial visit, midway through the intervention, and at study conclusion.
- Procedures: Administered individually to assess changes in patient self-efficacy, coping strategies, and resilience during the PRS intervention.

3. Care Team Interviews:
- Frequency: Study initiation, midpoint, and completion.
- Procedures: Semi-structured interviews with clinicians to evaluate intervention acceptability, feasibility, sustainability, and to identify facilitators and barriers to implementation.

Administration Procedures:
- Surveys and interviews will be individually and privately administered by the research coordinator or PI, either in-person or by phone.
- Interviews may be audio-recorded, with explicit participant consent, in private spaces.
- Audio recordings will be securely encrypted and stored on password-protected computers behind the University of Pennsylvania firewall. Access is restricted to authorized research staff only.

Review of Identifiable Information:
- Medical records will be reviewed to verify eligibility and collect relevant clinical information, including OUD diagnosis, treatment details, medication adherence, and retention.
- Participant identifiers (e.g., name, date of birth, medical record number) will initially be collected for linking and verification purposes only.
- Collected data will be promptly de-identified by assigning unique participant study IDs. Identifying information will be stored securely and separately from de-identified data.
- All identifiable information will be securely maintained only for the duration of the study and will be destroyed upon study completion to protect participant confidentiality and privacy.

5. Data Management:

Data Collection:
Data will be collected by the PI and research coordinator at Penn Medicine primary care clinics. Survey responses and interview notes will be documented using RedCap. Audio recordings from qualitative interviews will be securely collected following participant consent.

Data Entry and Storage:
- Paper-based data collection forms will be promptly entered into a secure electronic database (REDCap), managed by the PI and research coordinator.
- Electronic data will be securely stored in encrypted, password-protected databases behind the University of Pennsylvania firewall, ensuring compliance with institutional standards.
- Audio recordings of interviews will be securely transferred, encrypted, and stored on password-protected devices accessible only to authorized research personnel.

Data Corrections:

Any corrections to data entries will be documented with a clear audit trail, including the date, reason for the correction, and identity of the individual making the correction. Original data entries will be retained to ensure data integrity and transparency.

Identifiers and Confidentiality:

- Each participant will be assigned a unique study identification (ID) number. All research data will reference this ID only and will not include personally identifiable information (e.g., names, birthdates, medical record numbers).
- A master linkage file connecting participant identifiers to study IDs will be securely maintained in an encrypted, password-protected file accessible only to the PI and authorized research team members. This file will be stored separately from the research data.
- After study completion and analysis, the master linkage file containing identifiers will be securely destroyed.

Access to Data:
Only authorized research team members listed on the IRB-approved study protocol will have access to identifiable or de-identified data. No identifiable or confidential data will be shared or disclosed to any individuals not listed on the approved protocol.

Data Analysis:
Data analysis will be conducted exclusively on de-identified datasets, using secure, password-protected computing resources, in accordance with University of Pennsylvania guidelines for data security, privacy, and confidentiality.

7. Subject Follow-up:

Participants will be enrolled in the study for a total duration of 180 days (6 months), involving multiple structured visits.

Follow-Up Procedures and Methods of Contact:

- Participants can provide primary and alternative contact information (e.g., friends, family members) at enrollment to facilitate consistent communication.
- Study personnel (PI or research coordinator) will schedule and remind participants of follow-up appointments via phone calls or text messages.
- Appointment scheduling will be flexible, accommodating alternate days/times and remote check-ins (phone or video calls) when necessary to enhance retention.

Lost to Follow-up or Non-Contactable Subjects:

- Participants missing scheduled visits will be proactively contacted using multiple methods (phone, text, alternate contacts) with up to three documented attempts.
- If a participant cannot be contacted after multiple documented attempts, they will be considered lost to follow-up, and their collected data will be analyzed per established protocols.
- Partial data from participants who withdraw or become unreachable will be included in analyses to the extent possible, minimizing data loss.

Management of Special Circumstances:

- Participation in the intervention will be discontinued if a participant becomes incarcerated, admitted to a mental health or residential treatment facility, or hospitalized long-term during the study. Previously collected data will be retained and included in analyses.

Tracking Subject Compliance:

- Adherence with study visits and intervention requirements will be systematically documented in secure, confidential records.
- Instances of non-compliance or significant deviations from expected participation will be documented, including reasons when available.

These follow-up procedures and contingencies ensure adherence to ethical standards, prioritize participant safety, and maximize data quality, particularly considering the potentially transient or vulnerable nature of the study population.

STUDY PROCEDURES:

1. Detailed Description:

Step-by-Step Procedures:

1. Initial Contact and Screening (Enrollment Visit):

- Participants will be identified through clinician referrals and EHR screening.
- The PI or research coordinator will approach eligible patients during a scheduled primary care visit to explain the study.
- Interested patients will undergo a brief eligibility assessment, and written informed consent will be obtained.

2. Initial Engagement Stage (Visits 2-3, Weeks 1-2):

- Frequency: weekly visits (in-person or by phone)
- Procedures: Initiate structured PRS intervention sessions focused on patient engagement, rapport building, and immediate support needs.

3. Early Treatment Stage (Visits 4-7, Weeks 3-10):

- Frequency: Biweekly visits
- Procedures: PRS sessions will focus on behavior change strategies, coping skills enhancement, resilience building, and continued engagement in treatment.

4. Stable Treatment Stage (Visits 8-11, Weeks 11-26):

- Frequency: Monthly visits
- Procedures: PRS sessions will emphasize treatment maintenance, reinforcing successful strategies, and facilitating connections with ongoing community-based support services.

5. Transition of Care (conclusion of study, Week 22-24)

- The peer will offer to help transition interested patients to community-based peer recovery support programs if they wish to continue receiving peer support after the study ends.

Safety and Monitoring Procedures:

- Participants will be regularly monitored at each visit for emotional distress, adverse events, or unexpected issues impacting their participation.
- Immediate referrals to clinical services or mental health resources will be provided if emotional distress or crisis situations arise.
- Bi-weekly fidelity assessments using adherence checklists will ensure accurate implementation of the intervention and ongoing participant safety.
- Patient progress will be assessed regularly through brief patient interviews and EHR review of retention outcomes (appointment attendance, medication adherence, routine urine drug screening), and structured supervision check-ins with the PRS.

Management of Sensitive Situations:

- The PI, a family medicine and addiction medicine physician, will provide supervision and support for both the peer specialist and research coordinator.
- The research coordinator and peer will be trained to recognize and respond promptly to signs of emotional or psychological distress.
- Established protocols will ensure rapid referral to appropriate clinical or counseling resources, prioritizing participant safety and well-being throughout the study.
- PRS-Patient Relationship: Patient preferences regarding PRS interactions will be respected. Patient feedback will be collected confidentially by research staff and securely stored separately from identifiable PRS employment records. Critical or negative feedback will generally be addressed sensitively, privately, and constructively with the PRS, emphasizing professional development, training, and support rather than disciplinary actions. However, if feedback raises serious ethical, safety, or legal concerns, the PI will follow institutional guidelines, including reporting to appropriate supervisors or authorities as required.

This structured, systematic approach ensures clear communication, participant safety, and consistent adherence to study procedures, aligning with research objectives and ethical standards.

2. Data Collection:

This study involves prospective collection and analysis of new data obtained directly from participants enrolled during the research period. Additionally, existing clinical data from participants' EHR at Penn Medicine will be reviewed to confirm eligibility, verify diagnoses, and document medication treatment history, adherence, and clinical outcomes relevant to OUD treatment. The research team will not collect urine drug screens. Only the urine drug screens ordered by clinical providers will be reviewed.

No existing biological specimens (blood, tissue, or other biological samples) will be collected or analyzed.

3. Genetic Testing:

Not applicable. This study does not involve genetic testing.

4. Use of Deception:

Not applicable. This study does not involve any form of deception or incomplete disclosure. Participants will be fully informed about all aspects of the study, its objectives, procedures, and risks, prior to enrollment.

5. Statistical Analysis:

This pilot study is primarily designed to assess feasibility, acceptability, and implementation processes rather than formally testing intervention efficacy. Therefore, analyses will be predominantly descriptive, supplemented by qualitative thematic analysis.

1. **Quantitative Data Analysis:**
    - Descriptive statistics (means, medians, ranges, standard deviations, percentages) will be used to summarize demographic characteristics, treatment retention outcomes (appointment attendance, medication adherence, opioid abstinence), and intermediate patient outcomes (self-efficacy, resilience, coping skills).
    - Exploratory analyses will describe trends in outcome measures over time, offering preliminary insights into intervention feasibility and guiding preparations for a future RCT.
2. **Qualitative Data Analysis:**
    - Interviews will be transcribed verbatim and analyzed using NVivo software.
    - Transcripts will first be reviewed independently by two researchers to identify initial codes, then refined collaboratively to generate themes related to patient and care team experiences, intervention acceptability, barriers, facilitators, fidelity, and sustainability.

Justification for Sample Size:

A sample size of 20 participants was selected based on accepted guidelines for pilot and feasibility studies. Although this sample size is not intended or powered to formally test intervention effectiveness, it is sufficient to assess practical feasibility, logistical considerations, intervention acceptability, and to generate qualitative insights critical for refining study methods in preparation for a future large-scale randomized controlled trial. This aligns with established methodological standards for behavioral health pilot research.

RISK/BENEFIT ASSESSMENT:

1. Risks:

This pilot study presents minimal risks to participants; however, the following potential risks should be acknowledged:

1. **Psychological and Emotional Risks:**
    - Participants with OUD and potentially co-occurring mental health conditions may experience emotional discomfort, anxiety, sadness, or distress when discussing sensitive topics such as their substance use history, recovery barriers, or personal experiences.

- Participants with existing psychological conditions (e.g., anxiety, depression, post-traumatic stress disorder) may be particularly sensitive to emotional distress triggered by study assessments or interventions. This risk is expected to be minimal due to the supportive nature of peer interactions and established referral protocols.

2. **Risks Associated with Confidentiality:**
    - Although minimal, there is a foreseeable risk of confidentiality breaches. A breach could potentially result in social stigma, discrimination, or negative impacts on personal relationships, employment, or legal status within the community.

Safeguards to Minimize Risks:

- **Psychological and Emotional Risks:**
    - All research team members (peer and research coordinator) will receive training to recognize signs of emotional distress in participants. The PI, a family medicine and addiction medicine physician, will provide supervision and support.
    - Established protocols will enable immediate referral to clinical or psychological care if emotional distress or crisis situations occur.
    - Participants will be explicitly informed that their participation is voluntary and they may discontinue at any point without penalty or negative consequences.
- **Confidentiality Risks:**
    - Strict data management practices will be employed to ensure participant privacy and confidentiality; including secure storage using encryption and password protection.
    - Identifiable information will be stored separately from research data.
    - Access to identifiable data will be restricted solely to the PI and authorized research personnel.

Overall risks associated with this study are anticipated to be minimal and similar to those encountered in routine clinical practice. Comprehensive safeguards are in place to proactively minimize and promptly address any psychological, emotional, or confidentiality-related risks.

2. Benefits:

Potential Benefits to Participants:
Participants may directly benefit from enhanced, personalized support provided by the peer. This intervention may improve participants' retention in OUD treatment, leading to better medication adherence, increased abstinence, improved overall well-being, and enhanced quality of life.

Potential Benefits to Society and Research Community:
This study provides valuable information regarding the feasibility, acceptability, and preliminary effectiveness of PRS interventions within primary care settings. Insights gained may inform improved strategies for supporting individuals with OUD, potentially reducing treatment dropout rates, enhancing clinical outcomes, and contributing to decreased opioid-related mortality.

Findings from this pilot study will guide the design and execution of future large-RCTs, contributing to public health efforts to manage OUD effectively in primary care.

Participants will be clearly informed that these potential benefits cannot be guaranteed.

3. Subject Privacy:

To protect participant privacy throughout this research, the following safeguards will be implemented:

1. **Private Setting for Consent and Interviews:**
    - Informed consent, assessments, surveys, and interviews will take place in private rooms, ensuring participants feel comfortable discussing sensitive topics without concern of being overheard or interrupted.
2. **Sensitive Discussions:**
    - Research staff will be trained to discuss opioid use, treatment histories, mental health, and other sensitive topics respectfully and discreetly.

3. **Minimizing Identifiability:**
    - Participants will be assigned unique study identifiers. Identifiable information will be securely stored separately from research data to reduce the risk of unintended disclosure.
4. **Audio Recordings:**
    - Interviews will only be audio-recorded with explicit participant consent. Recordings will be securely stored on encrypted, password-protected devices, accessible solely by authorized research personnel.

These measures ensure participant dignity, comfort, and confidentiality throughout their involvement in the study.

4. Subject Confidentiality:

How will confidentiality of data be maintained? Check all that apply.

☒ Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.

☒ Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.

☒ Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.

☒ Whenever feasible, identifiers will be removed from study-related information.

☐ A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.

☐ A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)

☐ Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.

☒ Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.

☐ Other (specify):

Data Collection and De-identification:

- Participants will be assigned a unique study identification number (study ID).
- All research data (surveys, assessments, interview transcripts) will be labeled using only this study ID, without participants' names or personally identifiable information.
- Identifiable information (names, contact details, medical record numbers) will be securely stored separately from research data and linked solely through a protected master linkage file.

Data Storage and Protection During Research:

- Identifiable participant information will be stored securely and separately from research data. De-identified data may be shared in research presentations, publications, or future research studies.
- Identifiable information, including substance use data or urine test results, will not be entered into the EMR nor shared outside the approved research team.
- Paper-based records (e.g., signed consent forms) will be stored securely in locked cabinets within locked offices at Penn Medicine, accessible only to authorized research personnel.
- Electronic records (survey data, transcripts, audio recordings) will be stored securely in RedCAP, a database hosted on encrypted, password-protected servers behind the University of Pennsylvania firewall. Access will be strictly limited to the PI and research staff listed on the IRB-approved protocol.
- Interview audio recordings will be securely stored, transcribed verbatim, de-identified during transcription, and destroyed upon study completion to eliminate identifiable voice recordings.
- Identifiable data will be destroyed post-study.
- De-identified data will be retained securely and may be used for future research, following IRB approval.

Access to Data:

- Only the PI and trained research personnel listed on the IRB-approved protocol will have access to identifiable or de identified data.

Data at Study Completion:

- Identifiable information and audio recordings will be securely destroyed at the conclusion of the study.
- De-identified data (containing only study IDs) will be securely retained for at least five years, following University of Pennsylvania guidelines.
- De-identified data may be shared with other researchers only under explicitly defined and IRB-approved data-sharing agreements that exclude any personal identifiers.

Permanent Records:

- Research data will not become part of participants' permanent records, such as medical, employment, or academic files. Study participation is entirely separate from clinical or professional records.

Focus Groups and Interviews:

- No focus groups will be used; individual interviews only.
- Participants will not be identified by name in recordings or transcripts; only pseudonyms or study IDs will be used.
- Explicit participant consent will be obtained for interview recordings. Participants will be clearly informed about data usage, secure storage practices, protection measures, and the ultimate destruction of recordings post-analysis.

These robust confidentiality measures ensure secure handling and storage of data, significantly minimizing risk to participant privacy.

5. Protected Health Information

The study will collect the following protected health information (PHI):

- Name
- Telephone numbers
- Mail addresses
- Medical record numbers
- Dates directly related to an individual (e.g., date of birth, dates of clinical encounters)

These identifiers will be collected solely for participant recruitment, eligibility verification, and follow-up purposes. They will be securely stored separately from research data and linked only via a unique study identification number. No other protected health information will be collected.

6. Compensation:

Patient participants will receive a $50 Greenphire ClinCard at the conclusion of their participation in the study. This payment acknowledges the time and effort involved in completing study procedures, surveys, and interviews.

The $50 amount is modest and considered appropriate for the expected time commitment, which includes multiple visits and assessments over a six-month period. This level of compensation aligns with standard practices for similar studies conducted at the University of Pennsylvania, ensuring it adequately recognizes participant efforts without creating undue influence.

Participants will not receive additional reimbursement for expenses such as travel or meals, as study visits will coincide with their regular clinic appointments and involve minimal additional burden.

Participants will be explicitly informed that compensation is not a direct benefit of participation but rather serves as acknowledgment of their time and contribution to the research.

7. Data and Safety Monitoring:

Safety Monitoring and Oversight:

- Continuous monitoring of participant safety will be conducted by the PI, research coordinator, and peer through bi-weekly review meetings. The PI will also regularly meet with her primary mentor, with additional meetings scheduled as needed.
- Any adverse events, serious distress, or participant safety concerns will be immediately reported to the Penn IRB and addressed with clinical referrals as necessary.

Privacy and Confidentiality:

- All data will be securely collected, stored, and managed using encryption, password protection, and secure physical storage.
- Identifiable information will remain separate from the research data, linked only by unique study ID numbers, ensuring privacy and confidentiality throughout the study.

Data Integrity:

- Regular checks will be conducted to ensure the accuracy, completeness, and consistency of data entry and management.
- Fidelity and adherence to study protocols will be assessed bi-weekly using structured adherence checklists.

Interim Analyses and Stopping Rules:

- No formal interim analyses are planned due to the pilot study's small sample size and non-experimental design.
- The PI may stop the intervention for any individual participant at any time if significant psychological distress, medical or psychiatric emergencies, or substantial safety concerns arise.

Management of High-Risk Situations (Depression or Suicidal Ideation):

If a participant exhibits or reports severe depression, suicidal ideation, or intent during assessments or interactions, study staff will follow an established safety protocol:

- If a participant exhibits or reports severe depression, suicidal ideation, or intent during assessments or interactions, study staff will follow an established safety protocol:
- Immediately notify the participant's treating clinician.
- Arrange for immediate assessment by licensed clinical staff to determine risk level and the need for emergency intervention. The PI, a family medicine and addiction medicine physician, will also be available to evaluate the participant if necessary.
- Facilitate referral to crisis intervention services or emergency psychiatric care as appropriate.
- Conduct ongoing follow-up to ensure participant safety and confirm connection with suitable care services.

These measures ensure participant safety, maintain confidentiality and data integrity, and provide prompt, appropriate responses to urgent participant needs throughout the duration of the study.

8. Investigator's Risk/Benefit Assessment:

The risks associated with this study are minimal. Participants might experience mild emotional discomfort or distress when discussing sensitive topics related to their substance use history, mental health, or personal challenges. Additionally, there is a minimal risk of confidentiality breach, though robust data security and privacy measures significantly mitigate this concern.

These minimal risks are clearly outweighed by the potential benefits. Participants may directly benefit from enhanced peer support services, potentially improving their retention in OUD treatment and overall treatment outcomes. Moreover, the research community and society will benefit from gaining valuable insights into effective PRS interventions. Such insights could inform improved clinical practices and retention strategies, ultimately enhancing care for individuals with OUD.

Overall, the anticipated benefits to participants and society clearly justify the minimal risks of study participation.

INFORMED CONSENT:

1. Consent Process:

Care team member and PRS Consent Procedures:
Consent from PRS and care providers will be obtained by the PI under conditions of privacy, either in-person or remotely before study participation.

Patient Consent Procedures:

How, When, Where, and by Whom:
- Patient consent will typically be obtained shortly after eligibility confirmation. This may occur immediately following a clinic appointment or at a later time convenient for the patient, either in-person at the clinic or by telephone.
- Informed consent will be obtained individually by the PI or a trained research coordinator.
- The consent process will occur at the initial enrollment visit, prior to any study assessments or interventions.
- Prospective participants will receive a clear verbal explanation of the study purpose, procedures, risks, benefits, confidentiality measures, and their rights as research participants. The research staff member obtaining consent will read aloud and discuss the informed consent document with participants.

Ongoing Consent Process:
- Participants will be regularly reminded of their voluntary status in the study at each subsequent visit.
- Any significant new information that may influence a participant's willingness to continue participation will be communicated promptly and clearly.

Waiting Period:
- Participants will be given adequate time (at least 15-30 minutes, or more as needed) to carefully review the consent document, ask questions, and discuss participation with family or friends before providing consent.

Minimizing Coercion or Undue Influence:
- Participants will be explicitly informed that participation is entirely voluntary and not required to receive clinical care or treatment.
- Compensation is modest ($50 ClinCard), clearly described as reimbursement for time and effort rather than as an inducement to participate.
- Study staff obtaining consent will emphasize participants' right to withdraw at any time without penalty or negative impact on their clinical care.

Language Used in Consent:
- The informed consent document and discussions will be provided in clear, plain language at no greater than a 4th-grade reading level.
- Consent materials and discussions will be conducted in English.

Competency to Consent:
- All adult participants will be competent to provide informed consent.

- Competency will be informally assessed by the PI or research coordinator during the consent discussion by ensuring that participants understand key study details, can ask meaningful questions, and can clearly communicate their willingness to participate.

Children or Adolescents:
- Not applicable. No children or adolescents will be enrolled.

Through these careful consent procedures, participants will be fully informed, empowered, and supported throughout their participation.

2. Waiver of Informed Consent:

Not applicable. This study does **not** seek a waiver of informed consent or waiver of documentation of informed consent. All participants will provide written informed consent prior to participation.

RESOURCES NECESSARY FOR HUMAN RESEARCH PROTECTION:

Research Staff Adequacy and Qualifications:
- The PI, Dr. Rebecca Harris, MD, MSc, is a clinician-researcher experienced in addiction medicine, primary care, and clinical research protocols.
- A trained research coordinator will assist the PI in recruitment, consent, data collection, and follow-up procedures. The coordinator will have experience in clinical research, confidentiality protocols, and working sensitively with vulnerable populations.
- A peer, adequately trained through comprehensive, structured protocols, will implement the PRS intervention.

Staff Training and Protocol Knowledge:
- All staff will receive thorough training on the study protocol, ethical considerations, informed consent procedures, data management practices, and confidentiality measures.
- Staff will be required to complete IRB-required human subjects protection training and certification prior to study initiation. Regular meetings will ensure protocol adherence, ongoing education, and clear communication.

Population Access and Recruitment Feasibility:
- Recruitment from Penn Medicine primary care clinics ensures feasibility in enrolling the target number of 20 participants within the proposed study timeframe.

Medical and Psychological Services:
- If participants experience psychological distress, acute mental health crises, or any adverse reactions during participation, immediate referrals to clinical services within Penn Medicine or appropriate community resources will be made promptly and clearly documented.

Facilities Adequacy:
- All study procedures (recruitment, consent, interviews, and assessments) will occur in private settings. These include confidential clinical spaces within Penn Medicine primary care practices or the patient participant's home if they prefer phone-based communication. This ensures privacy, participant comfort, and appropriate environements for data collection.

Sufficient Time and Resources:
- The study timeline (180 days per participant, total enrollment of 20 participants) is realistic and achievable, given adequate staffing, institutional support, facilities access, and prior experience conducting similar research within the University of Pennsylvania Health System.

These comprehensive resources ensure ethical, safe, and effective implementation and completion of this research.