Study Protocol

A Bundled Intervention to End Opioid Overdoses by Increasing Treatment Uptake Post Emergency Department Discharge

National Clinical Trial (NCT) Identified Number: 06593093

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University of Alabama at Birmingham
Birmingham, AL 35294

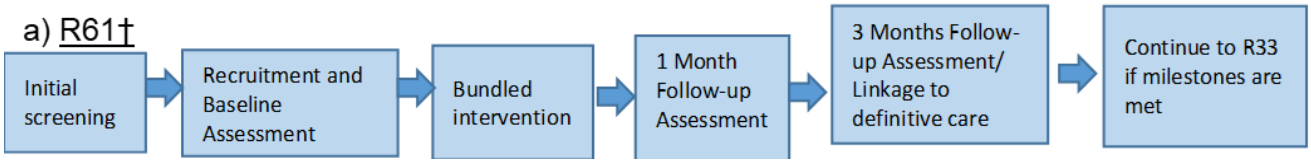
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Objectives: Treatment uptake (i.e., buprenorphine adherence and engagement in treatment programs) after emergency department (ED) discharge is critical in reducing the risk of repeat overdose and mortality. Increasing treatment uptake is the single best approach in reducing the risk of repeat overdoses and mortality. The main purpose of the study is to test if a bundled treatment, that includes a peer support specialist, buprenorphine prescription, and linkage to a community treatment program will be possible/feasible to be implemented and accepted by patients. Feasibility will be measured by rates of participant enrollment (i.e., able to enroll 18 participants in the first year and 12 participants in the second year with last enrollment in the 6th month of second year). Patient's acceptability will be measured using 2 surveys, including 1) patient satisfaction survey; and 2) Credibility and Expectancy Questionnaire (takes about 8-10 minutes to complete both surveys).

Design: Participants with opioid use disorder (OUD) and experiencing opioid overdose in the last 12 months are enrolled into a 3-month intervention for the R61 (see figure below). In the R61 phase, feasibility will be measured by rates of participant enrollment and study retention. Measure of acceptability will include participants' satisfaction, credibility, and expectancy. Participants will be asked to rate their satisfaction with intervention using the Patient Satisfaction Survey. Credibility and expectancy will be measured using the Credibility and Expectancy Questionnaire.



Methods

A. Recruitment site

Potential participants will be recruited from the inpatient and emergency department (ED) settings at University of Alabama at Birmingham (UAB) Hospital. Flyers should be posted at UAB hospitals, promoted via emails/departmental emails and meetings.

B. Screening and Consent

Inclusion Criteria

1. All participants

- Willing to give written informed consent before any assessment is performed.
- 19 years or older (the age of majority in Alabama).
- diagnosis of opioid use disorder (OUD) and experiencing opioid overdose in the last 12 months
- prescribed buprenorphine in the ED/inpatient and willing to continue buprenorphine post discharge
- English speaking
- not actively psychotic and suicidal, or cognitively impaired

2. OUD diagnosis confirmation and overdose

- One of the study physicians will interview each participant to confirm their diagnosis of OUD using the DSM-5 diagnostic criteria.
- History of nonfatal opioid overdose is determined by 1) self-report; 2) EMR review; and/or naloxone administration.

Exclusion Criteria

All participants

- living in a restricted environment (e.g., prison or jail facility, etc.)
- currently enrolled in other clinical studies that include buprenorphine treatment
- anticipated to take other prescribed opioids except buprenorphine for a medical condition longer than three months
- known allergic reaction to buprenorphine
- critically ill or injured
- Pregnant, trying to get pregnant within next 3-months (they are anticipated to request a higher level of care)

Consent

After the potential subjects have met the inclusion and exclusion criteria as above and have indicated a desire to participate, written informed consent will be completed. The subject will sign the informed consent form on paper or e-sign on iPad and will be provided with a copy prior to any study procedures. The original signed ICF will be placed in the subject's folder behind two locked barriers. Following written consent, as part of the identification process, participants will provide their phone numbers and email addresses that will be tested in the presence of the research assistant to make sure they are accurate. Several protocols will be used to maximize retention rates and follow-up assessment rates. During enrollment, all participants will complete a detailed locator form that includes contact information for the participant and at least two contacts of family and/or friends whom the study team, including research assistant, physicians, and peers could contact should the participant cease to respond to phone, text message, and email notifications about services and follow-up assessments. If participants' phones are disconnected and no replies are received via email and text message, participants' family and friends will be contacted.

C. Procedures

1) Demographics

The following information will be collected from the participant: date of birth, gender, race, ethnicity, years of formal education, employment status, income, marital status, and living situation.

2) Clinical Interview for Substance Use History, psychiatric and medical history

During the interview, participants will be asked about substance use, including opioid use history, drug of choice, age of initiation, age of regular use, number of years of use, average amount per day, number of previous overdoses, previous quit attempts, previous substance treatment (e.g., use of MOUDs), and personal medical problems related to opioid misuse. Complete medical history and surgical history. A list of all current medication or medication

taken within the last 30 days, including drug name, indication, dose with units, frequency and start date.

All participants must have a psychiatric evaluation by a study physician that demonstrates they are appropriate subjects for the study. If a psychiatric evaluation has been completed by another clinician, study physicians will decide if another evaluation is necessary. If a participant has not previously had a psychiatric evaluation, they should be evaluated by a study physician.

3) Validates Scales

a. Patient Satisfaction Survey (PSS).

All participants will complete the PSS. This survey was developed by the Cole group to assess patient satisfaction with care and is a 16-item survey with questions to assess 5 domains, including communication, privacy, patient perception, technology utilization, and treatment access. We will adapt it to assess patient satisfaction with our intervention, including peer support specialists, telehealth, physician service, and the usual care model. It will be administered at baseline and subsequent two follow-up measurements.

b. Credibility and Expectancy Questionnaire (CEQ).

This 6-item scale asks participating patients about how they think and feel about the treatment. It is broken down into two main scales: credibility and expectancy for treatment. It has demonstrated good internal consistency and good test-retest reliability.

c. Pittsburgh Sleep Quality Index (PSQI).

This 24-item scale measures participants' sleep quality and factors that may interfere with their ability to sleep well. It is divided into seven subscales: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. It is measured at every time point (baseline, 1-month, and 3-month) of the study duration.

d. Childhood Trauma Questionnaire (CTQ) (at Baseline and 3-month follow up only)

All participants will complete the CTQ, which measures indicators of early life stress. If the CTQ was recently completed by the participant in a previous study, request a copy of the assessment and the score sheet. The participant will not need to retake it unless there was a significant lapse of time between the two studies. The CTQ has a total score (CTQ Total) and 5 component scores: physical neglect (CTQ PN), physical abuse (CTQ PA), emotional neglect (CTQ EN), emotional abuse (CTQ EA), and sexual abuse (CTQ SA). Scores can be calculated by using the CTQ Scoring Sheet located in the OUD folder under Folder Documents. A participant is considered to have undergone ELS if: PN score >8, PA score >8, EN score >15, EA score >10, SA score >8, or total score >35. If a participant does not meet these criteria, they are considered non-ELS.

e. Opioid Overdose Risk Behavior Scale, version 2 (ORBS-2)

A 39-item instrument that provides an index of proximal opioid-related overdose risks with six subscales, including prescription opioid misuse, risky non-injection use, injection drug use, concurrent opioid and benzodiazepine use, concurrent opioid and alcohol use, and multiple-

drug polysubstance use. Five out of six subscales are positively associated with self-report of nonfatal opioid overdose experiences.

f. GAD-7

A common self-report questionnaire designed to screen symptoms of generalized anxiety disorder. It consists of seven questions each asking how the participant has been bothered by certain anxiety-related symptoms. The symptoms covered include feelings of nervousness, worry, restlessness, difficulty relaxing, and physical symptoms like trouble sleeping or becoming easily annoyed.

g. PHQ-9

A 9 question assessment to measure the severity of depressive symptoms; this survey focuses on major depressive disorder asking specific question about symptoms during the previous 2 weeks. Symptoms covered include: lack of interest, hopelessness, troubles with sleep, appetite, slow movements, thoughts of self-harm, and lack of energy.

h. Opioid Craving Scale

All OUD participants will complete the craving scale, a brief 3-item assessment used to measure opioid craving. Craving scores can be calculated by taking the average of the 3 responses, which range from 0-10.

i. Barratt Impulsiveness Scale

A 30 item self-report measure of trait impulsivity. Scores are calculated by rating each item from 1–4, reverse scoring designated items, and summing responses to yield a total score from 30–120 (higher scores indicate greater impulsivity)

4) Peer Support Specialist

Encounter	Frequency	Services
Emergency Department (ED) or inpatient setting if they are admitted to the hospital, in person	Daily	• Introduce them to participants. • Engage patients with motivational interviewing skills. • Lived experience as a peer recovery specialist to connect with patients. • Assist participants to establish telehealth platform. • Exchange contact information with participants. • Provide the referrals for buprenorphine clinics including state-funded clinics and community-based substance treatment programs.
Telehealth, 1-12 weeks post-ED discharge	Week 1: daily Week 2: 2 times Weeks 3-12: weekly	• Support participants' self-efficacy and prevent relapse. • Navigate services and resources of addiction treatment programs to increase treatment uptake following ED discharge. • Identify barriers and provide strategies to overcome barriers. • Continue to use motivational interviewing skills to engage patients. • Provide ongoing peer support/mentoring/coaching. • Share knowledge and information.

		• Provide life or vocational skills training. • Facilitate and connect participants with community-based substance treatment programs and buprenorphine providers. • Remind participants to be adherent to buprenorphine. • Warm handoff (providing patient education materials, providing fentanyl test strip and naloxone nasal spray kit (participating patients can obtain them at Jefferson County Department of Health at no cost), and sharing contact information of study team, including the PI, with participants).
Post-Intervention, 13-16 weeks	As needed	• If a participant refuses to be connected with Beacon Recovery Program and is unable to link with another definitive program, he/she will be followed for one more month to avoid care interruption and ensure the participant is connected with a community program. • Peers will follow a weekly contact schedule with supplementary contacts as needed.
18 months post intervention	Optional	• If a participant desires to continue working with the peer support specialist, they may do so for up to 18 months post the intervention. • No concrete contact schedule for peers will be followed. It is up to the peer and participant to coordinate meetings.
Stay Connected,	Optional	• A monthly meeting will be held for participants. The meeting will cover themes of recovery and encouragement in sobriety. • A group chat will be utilized to organize event details/location. Meetings could be in person or over telecommunication such as zoom. •

5) Physician service

Study physicians will continue assessing participants every other week in the first month and then monthly as well as PRN

6) Visits 2 and 3 Follow-up Assessments

There are two required follow-up assessments for each participant at 1-month (Visit 2) and 3-months (Visit 3). All participants will complete surveys at each follow up assessment except CTQ (not required at visit 2).

a. Grant-sponsored buprenorphine products (Suboxone or Subutex, not Sublocade).

It is at the discretion of the study physicians to provide buprenorphine medications to participants at no cost. Prescription should be eRx to Harbin pharmacy in downtown (521 Richard Arrington Jr Blvd S, Birmingham, AL 35233. #: (205) 323-2474.). Study team should receive their invoices on a regular basis.

b. W-9 Form

Subjects must fill out a W-9 form for compensation. They must have all information (including Address, SSN, and name to get compensation.)

c. Submitting Payment Requests

Payment requests should be submitted after each visit. The compensation for the first visit is $30, $50 for the second, and $100 for the third visit. The optional 4th visit (6-month post intervention) will compensate $30. Total compensation for this study is $210.

Payments will be processed through ClinCard. The card and instructions will be provided to the participant after they complete each visit. Notify participant that it might take 10-14 business days to approve and transfer the money onto the card. The coordinator will use the W-9 form to register the subject on the ClinCard website. They will then request a payment and wait for approval.

8 IRB

a. Amendments

In the case you will have to do an amendment, you will need to fill out an amendment request form. If any changes to the consent are made, there needs to be a highlighted copy of new consent (with tracked changes) and a clean copy of new consent that they can stamp. Make sure you change the version date at the bottom corner. If any other changes are made in other documents (such as flyers, telephone screens, or other forms that the patient will see), you will need to indicate on the amendment form and include the documents when you submit. Adding questionnaires to the consent form also requires sending copies of the questionnaires themselves. Personnel changes also require an amendment before new staff can work on the project.

#		Approval Date	Summary of Changes	Effective Date
1		12/15/2024	Addition of hardcopy/paper consent to enrollment protocol (originally e-consent only); provision of encrypted phones to facilitate telehealth.	09/19/2025
2		03/16/2025	Compensation change ($50 to $100 for 3-month follow-up); addition of 4 surveys (CTQ, PHQ-9, GAD-7, Craving Scale); enrollment expanded to include inpatient settings; 30-40% of peer sessions audio-recorded for fidelity; telehealth/remote options for follow-up assessments.	09/19/2025

3		05/13/2025	Expanded contact methods to include social media and email; addition of PSQI at baseline, 1-month, and 3-month; addition of CTQ at 3-month follow-up.	09/19/2025
4		10/21/2025	Updated consent form to include permission for study team to contact participants for future studies if eligible.	09/09/2026
5		11/09/2025	Addition follow-up checkpoint using same surveys plus 5 additional questions on opioid use/relapse/abstinence/treatment. Participants compensated $30.	09/09/2026

b. Project Renewal (current IRB approval will be good until Sep 10, 2026)

Every year you will need to renew the study. The renewal process should start two months before the study is set to expire. To renew the study, you fill out the Investigator's Progress report (IPR), and include the HSP, the most recent consent form, all amendments submitted that year, and any problem summary reports to be submitted.

c. Problem Reports

If a problem happens, it is classified as a non-reportable or reportable event. Reportable events consist of severe adverse events and adverse events at the discretion of the study team, including repeat ED visits, repeat non-fatal overdose, and relapse. Due to the nature of the study, these events may not be reported. However, for the best practice, all events could be reported to the IRB which will make the final decision. Non-reportable events include anything else (something that does not constitute possible patient harm, but the IRB needs to know about). Always ask the IRB and the PI if you aren't sure whether you need to report an incident.

d. IRAP

All IRB correspondence is done through the IRAP online system at University of Alabama at Birmingham.

9 Data Safety and Monitoring Board Invitation (DSMB): meeting q6 months and PRN

Per protocol, DSMB occurs every 6 months and as needed (PRN). The study coordinator will schedule the meeting and the team will report on the progress, issues, and adverse events. After each meeting, the PI will provide a written report to the DSMB members for their feedback, comments, and signature which is anticipated to return to the PI within one month.

10 Stakeholder Meeting

Per protocol, stakeholder meeting occurs every 3 months and as needed (PRN). The study coordinator will schedule the meeting, and the team will report on the progress, issues, and adverse

events. The stakeholder meeting will evaluate the study protocol and provide their feedback and make sure the study still meets the needs in the community.

11. R61 Statistical Analyses. Our analysis will adhere to an intention-to-treat principle, including all participants irrespective of their intervention adherence level. This approach ensures the robustness and generalizability of our findings. Specific Aim 1 evaluates the feasibility and acceptability of recruiting patients with OUD and experiencing opioid overdose to participate in the bundled intervention. This will be defined in terms of accrual ("conversion") rates and study retention rates. Among the eligible patients, we will calculate the proportion of who after completing the screening procedure: (1) decline to participate, (2) sign the consent form but do not participate, (3) participate but drop out, and (4) complete the intervention. Study retention will be defined as the amount of time that elapses from the time of signing the consent to the patient's final contact with the study team. For enrolled participants, we will also gather information about the patient's satisfaction, credibility, and expectancy. Specific Aim 2 tests the effects of the intervention on OUD treatment uptake, frequency of repeat opioid overdose and opioid-related ED revisits among the participants. These will be evaluated at 1-month (25-35 days) and 3-month (85-95 days) intervals post-ED discharge. OUD treatment uptake includes buprenorphine adherence rates and linkage rates with definitive addiction programs. Buprenorphine adherence rate is determined by a composite measure of any or all of the following: participant self-report, PDMP, or EMR documentation of an active prescription. Linkage rate is also determined by a composite measure of any or all of the following: participant self-report, EMR documentation of attendance at an OUD treatment program, or reports from addiction programs. Additionally, we will monitor for repeat opioid overdoses and ED revisits through the participant, family, and friend reports, and EMR documentation at UAB Hospital. Given the potential for the 3-month intervention period to be insufficient for observing repeat overdose and ED revisits, we will extend the monitoring of repeat overdoses and ED revisits through EMR documentation quarterly throughout the R61 study period. This comprehensive approach allows us to not only assess the feasibility and initial effectiveness of the intervention but also to collect essential data for refining our intervention strategy and planning the more extensive R33 phase.