CLINICAL TRIAL PROTOCOL

Randomized Control Trial of the Opioid Use Disorder (OUD) CareConnect Textline

NCT05897788

03/03/2025

Protocol

This trial protocol has been provided by the authors to give readers additional information about their work.

This supplement contains the following items:

1. Original protocol
2. Consent

CLINICAL TRIAL PROTOCOL

Randomized Control Trial of the Opioid Use Disorder (OUD) CareConnect Textline
Version 2.0.
03/03/2025

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Table of Contents

A. Original Protocol

Appendices

TRIAL OVERVIEW Title	Randomized Control Trial of the OUD CareConnect Textline
Clinical Trials Number	853153
Sources of monetary or material support	
Study Sites	University of Pennsylvania Hospital System, Cooper Heath System Alameda Health System
Conditions studied	Opioid Use Disorder, OUD treatment, OUD engagement, Texting interventions, Contingency Management
Interventions	Augmented Usual Care Augmented Usual Care + Text Message Check-ins Augmented Usual Care + Contingency Management (CM) incentives Augmented Usual Care +CM incentives + Text Message Check-ins
Comparator	
Inclusion criteria	1. 18 years of age or older 2. Screen positive for OUD 3. English reading ability 4. Have a mobile phone capable of receiving text messages 5. Bridge buprenorphine prescription (emergency department (ED) enrollment - Buprenorphine prescription at ED discharge; Bridge clinic enrollment – new buprenorphine prescription associated with on-demand or drop-in encounter
Exclusion criteria	
Study type	Interventional • 14-day bi-directional intervention • 30-day follow-up • 3-month follow-up • 6-month follow-up
Target sample size	1,808 Participants

Primary outcome	Engagement in any addiction treatment at 30 days of randomization
Secondary outcome	Filled buprenorphine prescription within 14 days; engagement in addiction treatment within 14 days; number of days buprenorphine filled at 30 days; self-reported current substance use, self-care, relationships, resources, and outlook on life based on Brief Addiction Monitor and Substance Use and Recovery Evaluator measured at 15 days, 30 days, 3 months, and 6 months; ED visits, hospitalizations and Hospital Free Days (HFD), and deaths at 15 days, 30 days, 3 months, and 6 months.

1. Background and Significance

1.1 Background

The U.S. faces a crisis of OUD and overdose driven by fentanyl and other synthetic opioids. Overdoses are now the #1 cause of death for people aged 18-44 years old. Drivers of this crisis have only accelerated during the COVID-19 pandemic, with overdoses claiming 93,000 lives in 2020 – a 30% increase from the year prior. There has been a parallel increase in OUD-related ED visits, with OUD-related ED encounters increasing 100% in the last decade and further increases in overdose-related ED encounters during the pandemic. Acute care visits for an OUD-related condition strongly predict mortality.

EDs are critical touchpoints for engaging patients in OUD treatment. Treatment with medications for OUD (MOUDs), particularly opioid agonists buprenorphine or methadone, is the standard of care, reducing overdose and all-cause mortality by more than half. MOUDs also improve other mental and physical health outcomes, reduce illicit drug use, and increase treatment retention and quality of life. With over 1.5 million encounters annually for opioid overdose, withdrawal, or complications of substance use, the ED is one of the most important places for health systems to engage patients in effective care. Randomized controlled trials (RCT) have demonstrated ED-initiated buprenorphine doubles treatment engagement at 30 days compared to referral alone[9] and is cost-effective.

Despite strong evidence supporting ED-initiated buprenorphine, there are substantial implementation gaps in linking patients with OUD from the ED to continued treatment, including persistent racial disparities. Because ED-initiated buprenorphine increases treatment engagement, it has become a standard practice in our health systems and many EDs in recent years. However, initiating treatment for OUD in EDs is insufficient if patients do not continue in care. We found that only 17% of US patients with ED visits for opioid overdose received buprenorphine or other addiction treatment in the 90 days following ED discharge and that Black patients were half as likely as White patients to receive treatment. Even in our health systems, which have well-developed ED OUD treatment pathways and standardized referral procedures, treatment engagement rates are 35%. The National Academy of Medicine has identified closing this implementation and equity gap as a national public health priority.

There is strong evidence supporting several OUD treatment engagement strategies in other settings, but these strategies have not been adapted for or tested in the ED. Text-messaging enhanced telehealth services have been shown to overcome barriers and increase patient engagement in outpatient OUD treatment settings. Text messages are also feasible and acceptable as part of SUD treatment in addressing multiple dimensions

of engagement, including motivation, self-efficacy, social support and appointment attendance.15 Recent federal policy changes have loosened regulations for telehealth-based treatment of OUD by allowing initiation of buprenorphine via telehealth.16 The result has been a significant increase in telehealth-based treatment models, with promising early outcomes in terms of feasibility, acceptability, quality of care, and treatment retention.17-24 Telehealth models have enormous potential to overcome barriers to care access – ranging from troubleshooting pharmacy barriers, transportation challenges, work or childcare responsibilities, and stigma – and to deliver timely, flexible patient-centered addiction care.

There is also considerable evidence demonstrating effectiveness of financial incentives – also known as contingency management – in increasing OUD treatment engagement. Patients with OUD and other SUDs tend to have present bias, a tendency to favor short-term, immediate rewards rather than larger, more distant rewards. This tendency may contribute to the SUDs by driving urges to use substances despite the risks. Because patients with OUD experience substantial present bias and steeper delay discounting rates than other people, they prefer short-term, immediate rewards rather larger rewards in the more distant future. Therefore, providing short-term tangible rewards to reinforce treatment engagement and promote decreased drug use has been found to be one of the most consistently effective and cost-effective treatments for SUDs, including OUD. A recent randomized control trial that enrolled a predominantly low-income, non-white sample demonstrated that compared to usual care, patients receiving remotely distributed digital financial incentives engaged in buprenorphine treatment at much high-er rates (71% vs. 40%) over 6 months. Our team is the first to demonstrate the feasibility of delivering financial incentives for post-ED OUD treatment engagement in a pilot RCT indicating that this effective intervention is ready to be applied to the ED setting.

Despite the strength of the evidence for both text-messaging-enhanced telehealth services in promoting OUD treatment engagement in other settings, to our knowledge, there are no studies comparing the effectiveness of these interventions either alone or in combination for facilitating treatment engagement from the ED. Our team has been a leader in initiating buprenorphine in the ED, text-messaging based data collection and telehealth services, and contingency management and mobile phone-based continuing care interventions for SUDs. We propose to adapt these evidence-based strategies to the ED context to improve linkage to post-ED care and compare the effectiveness of these strategies alone and in combination, filling a critical evidence gap.

Telehealth and in-person “bridge clinics” now provide rapid, low-barrier access to buprenorphine for patients who need follow-up care from the ED or as alternative site of care for patients with acute needs. These prescriptions “bridge” patients until they can establish a regular source of follow up addiction care. In the fall of 2022, our emergency departments and addiction medicine care teams launched the **Way to Health CareConnect text line** as a new standard of care for OUD patients with OUD discharged from ED. It provides patients with the ability to reach on call substance use navigators (SUNs) 7 days a week from 9a-9p by phone or text message for assistance with obtaining buprenorphine, follow up appointments, and addressing barriers to engagement in treatment such as transportation and meeting social needs. To date the CareConnect textline has already served over 100 patients with OUD discharged from the ED.

With funding obtained from the Patient Centered Outcomes Research Institute (PCORI) we are planning to run a pragmatic, multi health system randomized trial to test alternative strategies to enhance addiction treatment engagement among patients with OUD who receive bridge buprenorphine prescriptions from the ED or via low-barrier bridge clinic. The planned launch of the full pragmatic trial is January 2024.

1.2 Significance

There is growing recognition of the need for approaches to initiate treatment wherever patients touch the health care system, including the ED and low barrier bridge clinics. Most research has focused on initiation of

MOUDs in the ED rather than ensuring continued treatment post-discharge. We propose to adapt evidence-based interventions to support patients' complex needs and facilitate continued treatment, rather than discharging them and having them navigate outpatient treatment systems with limited support. We will randomize participants into 1 of 4 arms to receive varying degrees of augmented usual care, including daily check-ins and contingency management. We plan to examine the equity of treatment effects among racial and ethnic subgroups and assess important moderators of treatment effects.

2. TRIAL DESIGN

2.1 Overview

We are proposing to conduct a randomized controlled trial to determine the effectiveness of various text-based and contingency management interventions on Opioid Use Disorder patients. Our goals are to measure their engagement with recovery treatment. We plan to enroll 1,808 participants into one of the following 4 arms.

Patients enrolled into the Way to Health CareConnect text line as part of usual care and meeting eligibility criteria will be enrolled in this randomized control trial and randomized to:

1. **Augmented usual care** (*standard Way to Health CareConnect Textline)* Patients can call or text the on-call substance use navigators (SUN) from 9a-9p, 7 days a week.
2. **Augmented usual care + text-message check-ins (***standard Way to Health CareConnect Textline*) Patients can call or text the on-call substance use navigators (SUN) from 9a-9p, 7 days a week AND (*text-message check-ins*) patients will receive automated text-message check-ins up to once per day for 30 days to see if the patient needs help with anything.
3. **Augmented usual care + contingency management** (standard Way to Health CareConnect Textline) and, participants will be compensated for going to their follow-up appointments.
4. **Augmented usual care + CM + Text-message check-ins** (standard Way to Health CareConnect Textline) AND text-message check-ins—patients will receive automated text-message check-ins up to once per day for 30 days to see if the patient needs help with anything AND, participants will receive compensation for attending their follow-up appointments.

Patients enrolled in the trial will also be invited to complete the intake survey and follow-up surveys. Patients will receive financial compensation for completing these surveys. We plan to enroll 1,808 participants for this study. However, when participants are presented with information about the study, they will only be notified they will earn compensation for completing surveys and may qualify for additional payments and may receive check-in texts and encouragement. However, while we disclose participants may qualify for additional payments, further details on intervention will not be detailed in the opt-out consent-message explaining the study as we believe incomplete consent is required for this population and this study design. Reasons why this is necessary for the execution of this research are highlighted in section 2.5 and 2.17 below.

Definitions:

Standard of Care: Patient receive access through discharge documents to local substance use navigators and follow-up clinic information. When patient engage with Substance Use Navigators (SUNs), members of the clinical team, they assist patients with accessing recovery care, including access to buprenorphine, scheduling follow-up appointments, providing transportation to treatment visits, and more. Patients can access the SUNs by calling or texting the CareConnect Warmline. All of the clinical care SUNs provide is documented in EPIC and RedCap for analysis and ways to improve the program.

Augmented Usual Care: patients receive a text message with information about how to more easily access the local substance use navigators by phone call or by text message through the Way to Health texting platform.

Enhancements to Augmented Usual Care to be tested in the RCT:

Bi-directional texting check-ins: patients randomized to this intervention will receive daily check-ins for the first 14 days after enrollment, then tapering check-ins for the remainder of the 30-day intervention period.

Contingency Management: participants randomized to this intervention will receive financial rewards for filling their buprenorphine prescription and for being engaged in addiction treatment at 14 and 30 days.

Survey administration: intake survey and recurring follow-up surveys to assess outcomes.

2.2 Setting

The study will recruit patients seen in Emergency Departments and low barrier addiction medicine clinics in three health systems:

- Penn Medicine: Hospital of the University of Pennsylvania (HUP Main and HUP Cedar), Penn Presbyterian, Pennsylvania Hospital, and the CareConnect addiction medicine virtual bridge clinic in Philadelphia, Pennsylvania
- Cooper University Hospital in the Cooper Health system emergency department and bridge/walk-in clinic in Camden, New Jersey
- Highland Hospital, San Leandro Hospital, and Alameda Hospital emergency departments and the Highland Hospital bridge clinic in the Alameda Health System in California.

2.3 Inclusion Criteria

1. 18 years of age or older
2. Clinical impression or Diagnosis code for OUD or ED triage screen positive for OUD
3. English reading ability
4. Have a mobile phone capable of receiving text messages
5. Bridge buprenorphine prescription (emergency department (ED) enrollment - Buprenorphine prescription at ED discharge; Bridge clinic enrollment – new buprenorphine prescription associated with on-demand or drop-in encounter
6. Not a prisoner

2.4 Participant Identification

Clinician enrollment pathway. Patients with OUD will be approached to participate in the Way to Health CareConnect Textline as is the current standard of care. ED and bridge clinic staff will continue to determine eligibility of patients, based on clinical inclusion criteria (age of 18 or older, clinical impression of opioid use disorder, and having a mobile phone). As is done currently, ED and bridge clinic staff will discuss the CareConnect textline with patients in the ED. After clinicians confirm that a patient is willing to received text messages from this program, the clinician navigates to the Way to Health section in the Epic EHR and completes a checkbox enrollment screener confirming the patient's phone number, age older than 18, and whether or not the patient is being given a bridge buprenorphine prescription, and then clicks the "enroll"

button. Patients will then receive the Augmented Usual Care “Welcome Text” Message (see attached message logic and copy).

The Welcome Text gives an explanation of the Clinical Care Program *CareConnect* and what it provides, as well as a number they can call and text for resources to assist with their OUD, a link to the *CareConnect* Warmline website that is run by Penn Medicine and hosted by the Center for Medicine and Policy. At this point, patients can text “bye” and will not receive further messaging. Patients enrolled in the CareConnect textline ~~that~~ that have received buprenorphine script at discharge will be invited to participate in the trial (see Section 2.5).

Patients without phones may be provided with a phone and a 30-day data plan depending on availability of phones for distribution in the ED. Patients can opt-out of receiving further text messaged by texting back the word BYE.

For patients enrolled at Cooper and Alameda emergency departments, they will receive the same explanation of the study, the same messaging with different nomenclature to highlight the branding of their SUNs hotline and research staff, and the link to the website will be for their respective bridge clinics.

Academic associates (AAs) at Penn’s Hospital of the University of Pennsylvania and Presbyterian Medical Center will also be in the ED to help identify patients that may be eligible for the study. The AAs will approach the physician if they believe a patient is eligible and suggest if they meet the eligibility criteria, to enroll the patient. AA’s will also have the opportunity to enroll the participant if the Clinician is unable to.

Staff enrollment pathway. For patients that were not approached by a physician or ED staff about enrollment into a study, research coordinators will review an Epic EHR report of patients that meet inclusion criteria for the trial (See Section 2.3). They will then use the Way to Health platform to send eligible patients a text-message about a program that may help them at Penn, Cooper or Alameda. As is now standard practice with other text message engagement programs approved by Penn’s privacy office, the text-message will provide their first name and last initial of the patient, and ask the patient to confirm their identity before sending the same “Welcome Text” as detailed above in the clinician enrollment pathway. After participants confirm their identity, they will then be invited to enroll in the trial (See Section 2.5) below).

2.5. Consent Procedures

We will seek approval from the University of Pennsylvania (Penn) IRB, as the central IRB of record, to conduct the trial using an opt-out consent process. This approach is known as a waiver or alteration of the requirement for individual informed consent and is advocated for pragmatic trials testing methods for comparing and improving the delivery of established interventions within health care systems (References 1-4).

Recent NIH-funded research by our group in the Center for Health Incentives and Behavioral Economics (CHIBE) and others reveals that patients generally endorse opt-out consent or simple notification approaches in pragmatic trials when such mechanisms help achieve the goals of the study (References 5-7). Although large-scale, pragmatic trials have previously been undertaken without consent at all, including by PI Delgado (IRB 844043) and other CHIBE faculty such as Scott Halpern (IRB Protocols 822134, 826933, and 814063) (References 8-9) both our investigative team and our study Stakeholder Advisory Committee strongly advocated for an opt-out consent process. This is the same opt-out approach was adopted in three prior studies addressing tobacco use disorder (a substance use disorder) that were conducted using a waiver or alteration of consent using the Way to Health platform (IRB Protocols 833713, 820451, and 814761) (References 10-12). Directly following eligibility screening, eligible participants will receive messaging in W2H about this voluntary program, will be directed to further information providing details on the study, and given

the opportunity to easily opt-out via text message. Please see language in the Way to Health Messaging _PCORI_10.6.23 document attached to this submission.

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This trial will be conducted with a waiver or alteration of informed consent, using an Opt-Out Consent procedure:

The research involves no more than minimal risk to subjects. The risks to subjects of participating in this comparative effectiveness study are minimal. Indeed, the only foreseeable study-related risk is a breach of confidentially. We outline below the safeguards we have in place to prevent any such breach. Furthermore, the risks are no more than minimal because both interventions exceed the standard of care routinely provided to patients with OUD discharged from the ED. The current standard of care for patients with OUD is to offer a discharge prescription for buprenorphine and provide discharge papers with a phone number to call to arrange a follow up appointment. To augment usual care, our clinical operations team has created the Way to Health

program CareConnect Textline to connect patients with phones directly to a team of substance use navigators (SUNs) available from 9a-9p by phone or text message. The SUNs assist with troubleshooting issues with obtaining buprenorphine, helping to arrange follow up appointments, and helping to address social needs such as transportation. To date the CareConnect Textline has already served over 70 patients with OUD discharged from the ED. Patients enrolled in this trial will continue to receive the same exact care as provided by the CareConnect Textline and can also reach the SUNs by the phone number provided on the discharge papers from the ED. The interventions tested here could be rolled out as part of normal operations and quality improvement Those enrolled in the trial will have the option to complete a baseline survey and two follow up surveys or opt-out. Completion of the surveys is voluntary. Survey data will be collected through HIPPA secure Way to Health mobile surveys and identifiers will be stored separately and securely from the survey data (see section 6 below).

Impact on Subject Rights and Welfare. The waiver will not adversely affect the rights and welfare of patients because they will receive information both prior to, and directly after, randomization about what is involved in the program. Patients will be informed that the care that they receive will not be affected if they decline the program. All materials on the Way to Health platform will use plain language and adopt messaging strategies developed with our patient stakeholder committee that are culturally competent and use supportive person first language.

The research aims cannot be practicably conducted without an opt-out consent process. This trial seeks to evaluate the effectiveness of adding automated text message check ins to the existing, standard of care of the existing OUD CareConnect program in an overall population of patients with OUD discharged from the ED. Requiring individual informed consent would introduce important selection biases. Specifically, socioeconomically disadvantaged populations who have experienced the greatest burden from OUD have historically participated in research at lower levels than the general population and would be less likely to enroll in this study. A major goal of this study is to understand and create knowledge that is generalizable to these marginalized populations. Furthermore, unlike a pharmaceutical trial where outcomes are primarily determined by physiologic effects of a medication, in this study of behavioral interventions, those who consent are likely to have behavioral characteristics that are not representative of those who would not consent and therefore potentially biasing the outcomes of a behavioral study. Therefore, requiring consent would render the study invalid since it would not have generalizability in applying to the desired population, particularly those experiencing the greatest disparities in outcomes due to OUD.

This population of patients with OUD discharged from the ED with a buprenorphine prescription is precisely the population of interest for health systems. There is no real-world setting in which the interventions would only be made available to those patients who were discharged from the ED with a buprenorphine prescription and would opt in to participate in a research study. Yet that is the sample that would be obtained if we did not use an opt-out consent model, whereby patients are engaged with the program unless they actively choose otherwise. As programs similar to the current trial are being developed and disseminated across the country, it is imperative that we examine how these interventions perform across diverse health systems using their full eligible patient populations, lest these systems will make care decisions based on flawed information from highly selected patient samples. Furthermore, employing a waiver of consent for this trial will help to connect high-risk patients with OUD to potentially helpful treatments that they may not otherwise seek out.

Although the foregoing discussion of how opt-out consent is the only way in which we can answer the research question is the most important reason by that approach is essential, there are also logistical considerations. Due to the large sample size needed for this study it would be impractical to employ study staff to manually recruit and consent 1,808 participants across more than 7 EDs and clinics in multiple health systems. Traditional recruitment, outreach, and consent by study staff for this trial would exhaust all of our financial and labor resources, as well as significantly lengthen the time needed to conduct this trial. It would be

impractical to conduct this study in the traditional manner. Using an opt-out approach will allow this research to be conducted in a more time- and cost-efficient manner.

The text opt-out messaging will be comprised of a link to the study landing page/informed consent form/study information. This page will outline the study in detail. The landing page will provide information on what potential participants can expect if they participate, including who is eligible, surveys they will be asked to complete, length of time the survey is available, and that a study team member can help the participant complete the survey over the phone if they'd prefer. The opt-out landing page will also detail compensation amounts and distribution type (a physical Clincard). If participants are uninterested, they will have to opt-out of the research team collecting their protected health information. The landing page will also highlight the HIPPA agreement and detail what study information will be collected, including name, telephone number, birth date, email, demographics, health conditions, ED/Hospital/CareConnect use, and opioid/other substance use. The HIPPA language will also detail who their data may be shared with. A majority of the data shared will be de-identified, if shared with study partners at research sites, our funders at PCORI and in agreement with their data sharing practices, and the data safety monitoring board. However, to confirm care engagement with care clinics outside of the Penn Health system, the research team may need to share the first and last name of patients, and potentially the DOB to confirm they've engaged with care at treatment centers or Primary care locations (outlined in image three). The portion of the landing page is the Release Agreement. This form is required for the research team to confirm patients have attended their follow-up care appointments outside of the Penn Health System, an outcome measure, and compensation requirement for some interventions arms. The Release Agreement information on the landing page will state that participants allow any treatment facility they receive care to release information from their Health record to the CareConnect study team, specifically information on their attendance at specialty clinics and treatment centers for Opioid Use Disorder. This information will cover a period from the day of enrollment until 180 days later. Patients will also be asked to sign a physical copy of a medical release form that may be shared with clinics to confirm engagement in care.

Based on feedback from peers in recovery, patients, and family, we've designed the opt-out consent to be easily understandable by participants. Usual HIPPA, Release agreements and Consent documents are written at reading levels that are not easy to understand by patients with low health literacy. We designed these forms to be written at a 6th grade reading level, which has been demonstrated to increase comprehension among patients with low health literacy. And furthermore, we designed these forms to be as succinct as possible to minimize cognitive load and increase patient autonomy and informed consent.

The final text participant will receive will ask patients to text "BYE" if they wish to be un-enrolled from the program.

Once a participant has received the opt-out consent message, they will then be enrolled into the trial and randomized to one of the four trial arms. If participants do not complete the intake survey, we have a reminder text notifying participants if they are interested and have read the consent, they are still enrolled and can participate. During this second text-message, the study team will send the reminder consent text as an image of the consent language.

To ensure we provide ample opt-out opportunities, during each of the initial survey messages sent, we will remind participants to text BYE if they would prefer to leave the study. The Medical release form and other patient facing materials will not detail the various intervention arms. We are seeking to apply for incomplete disclosure for the enrollment process as it is necessary to carry out this research, as fully disclosing the study purpose may affect the participant's responses, retention, and outcomes. This is standard practice in prior trials of contingency management interventions (Ghani et al, 2022; Hofmeyer, 2013). The following incomplete disclosure requirements are met:

1) The research is no more than minimal risk to participants. All participants will receive augmented usual care, will complete study questionnaires, and have their data collected from the electronic health record. The interventions do not introduce any significant risks to their typical standard or care.
2) The incomplete disclosure will not adversely affect the rights and welfare of participants for either the groups that do receive the contingency management intervention and those that do not.
3) The research cannot practicably be carried out without the alternation. Fully informing the participants that there may be financial rewards for engaging in treatment may have a subsequent effect on participation in the trial or their engagement in treatment if they are assigned to group without contingency management. Differential retention by randomization arm would bias outcomes and therefore prevent us from comparing the effectiveness of adding contingency management to usual care and text messaging facilitated telehealth for treatment engagement.
   Participants will be provided with additional pertinent information after participation. Once participants have been enrolled and randomized, they will receive a message explaining the study further, the details of the arm they have been randomized to, and for those enrolled in arms with contingency management, they will be informed of incentive amounts they will receive for engaging in care. We are requesting not to debrief the groups that are not receiving contingency management while they are actively participating in the trial because if they know that others in the study were receiving financial incentives that they are not receiving, they make think it is unfair and decide not to participate in the research and possibly their addiction treatment, which would have an impact on their health. However, participants will be debriefed once they have completed the study via end of study text message with a link to a debriefing statement (see attached).

However, once a participant is randomized, we will then inform them of the arm they have been assigned to and what they can expect to occur. This language is in the Way to Health Messageing_PCORI_10.6.23 document attached to this submission.

Participants can unenroll from the study at any point by texting “stop” or “Bye”.

Participants that are enrolled in the ED will receive a ClinCard and will sign the Medical Release form. At Penn facilities, the ClinCard and medical release form will be distributed by Academic associates at HUP and Presby, a Clinical research coordinator that will rotate between all Penn sites, and Social Workers and Nurses at each site. The AAs, and other clinical staff distributing study materials, will also distribute a brochure with payment details for the surveys and length of the study to participants.

After the AAs, and other clinical staff, have provided the Clincard for the participant, they will complete a Qualtrics survey with information needed for the study team to register the ClinCard (First name, last name, DOB, ClinCard token number, Clincard number, and upload a copy of the Medical Release form signed and dated). The Medical Release forms will be stored in a locked drawer in an office that requires badge and security clearance to enter.

Addition of Consent for Qualitative Study. In addition to participation in the randomized controlled trial, we are also seeking consent to invite participants to a separate qualitative study designed to understand participants' experiences with the CareConnect program. Those who agree to participate in the RCT will also be informed that they may be contacted for an optional survey and interview to discuss their experiences.

Participants will receive a separate opt-in consent process for the qualitative study, where they can voluntarily agree to participate. Those who opt in will be provided with additional details regarding the qualitative study, including the nature of the interviews, the estimated time commitment, and confidentiality measures. Participation in the qualitative study is entirely voluntary and will not impact their participation in the main RCT.

2.6. Contact Information

When enrolling in the ED, participants will confirm their name, phone number, and DOB. If the patient does not have a cell phone, one may be provided to them depending on the availability of phones for distribution in the ED. The number will be entered by clinician enrolling the patients via the Way to Health CareConnect Textline enrollment screen in PennChart, and Cooper and Alameda's instance of EPIC.

After patients are enrolled into the CareConnect program in the ED, patients will be asked to sign a medical record release form at the time so that research staff can confirm engagement with OUD treatment during the study period. If patient is discharged from the ED and leaves before the research coordinator can provide them with a Clincard and medical release forms, the research coordinator will organize a time and place to meet the patients to distribute the Clincard and sign medical records release.

2.7 Intake Survey

After participants are enrolled into the program, they will receive a text-message containing a link to the intake survey. The survey will take 10 minutes or less to complete and will include demographic information, which includes sex, race, and ethnicity data. A shortened version of the Brief Addiction Monitor (BAM), which measures self-reported prior 7 or 14-day opioid, alcohol, cocaine, methamphetamine, and benzodiazepine use, prior addiction treatment history including MOUDs, and a baseline Substance Use Recovery Evaluator (SURE) assessment, a brief but comprehensive assessment of substance use, self-care, relationships, material resources, and outlook on life, and a Commitment to Sobriety scale Survey (CSS). Lastly, participants will complete the 5-trial adjusting delay discounting task, which takes 1 minute to complete and measures delay discounting function, a measure present bias. Participants will have 7 days to complete the intake survey before the survey is closed. Participants will be sent two survey reminders via text. Participants will have the option to have the survey administered over the phone by texting back SURVEY to the study message prompt or calling the study team. Participants will be compensated $20 for the intake survey which will be loaded onto their Clincard.

2.8. Follow-up Surveys

On Day 15 and 30, month 3 and 6, participants will receive a text-message to complete the follow-up surveys. Participants will have 7 days to complete the day 15 survey and 14 days to complete the day 30, 90, and 180 surveys and receive reminder messages on day 16, 17, day 31, 32, day 91, 92, and day 181, 182. Participants will have the option to have the survey administered over phone by texting back SURVEY to the message prompt or calling the study team. Participants that complete the survey will have $25 and $30 loaded onto their Clincards for the day 15, 30 survey and day 90 and 180 surveys, respectively.

The interventions for this survey will end at day 30. As part of the follow-up period, participants will receive a text-message to complete the follow-up surveys at day 90, and day 180. Participants will receive reminders to complete the surveys on day 91 and 92, and day 182 and 183. Participants will have the option to have the survey administered over the phone by texting back SURVEY to the message prompt or calling the study team. Participants that complete the survey will have $30 each loaded onto their Clincards for the day 90 and day 180 surveys.

2.9. Allocation to Treatment

Patients enrolled into the Way to Health CareConnect text line as part of usual care and meeting eligibility criteria will be enrolled in this randomized control trial and automatically randomized by Way to Health to 1 of 4 arms outlined in section 2.10. Randomization will be stratified by health system and by enrollment type (ED vs. bridge/walk-in clinic in-person, and bridge clinic telehealth). Within enrollment type, randomizations will be balanced in blocks of size 12.

2.10. Behavioral Interventions

Intervention Arm	Description	Incentive/Notification	
		Timing	**Size**
1. Augmented Usual Care (AUC)	AUC: Patients can call or text the on-call substance use navigators (SUN) from 9a-9p, 7 days a week	Intake Survey + survey at day 15, day 30, month 3 and month 6th.	$20 for Intake survey, $25 for completing day 15 survey, $25 for day 30 survey, $30 for month 3 survey, and $30 for month 6 survey.
2. AUC + text-messaging enhanced telehealth service	AUC: **(**Patients can call or text the on-call substance use navigators (SUN) from 9a-9p, 7 days a week Txt message check-in: Patients will receive daily SMS check-ins for the first 14 days, then staggered check-ins until day 30.	Intake survey + Daily SMS Check-in + survey at day 15, day 30, month 3 and month 6th.	$20 for Intake survey, $25 for completing day 15 survey, $25 for day 30 survey, $30 for month 3 survey, and $30 for month 6 survey.
3. AUC + financial incentives (for treatment initiation and early engagement)	AUC: Participant will receive a text message with the CareConnect number they can utilize if they are ever need of services. CM: Patients will also receive incentives for engagement with treatment	Intake survey + survey at day 15, day 30, month 3 and month 6th.	Same survey incentive structure + $25 for attending 1st treatment appointment, $25 for 2nd treatment appointment.
4. AUC + text messaging enhanced telehealth services + financial incentives	AUC: Patients can call or text the on-call substance use navigators (SUN) from 9a-9p, 7 days a week Txt message check-in: Patients will receive daily SMS check-ins for the first 14 days, then staggered check-ins until day 30. CM: Patients will also receive incentives for engagement with treatment	Daily SMS Check-in + Intake survey + survey at day 15, day 30, month 3 and month 6th.	Same survey incentive structure + $25 for attending 1st treatment appointment, $25 for 2nd treatment appointment

2.11 Observation Arm

Augmented usual care: Patients can call or text the on-call substance use navigators (SUN) from 9a-9p, 7 days a week

2.12: **Study Procedures**: by schedule

	Augmented Usual Care (standard clinical program)	Arm 1: Augmented Usual Care	Arm 2: Bi-Directional Text Messaging	Arm 3: Contingency Management	Arm 4: Bi-Directional Text Messaging + Contingency Management
Day 0 (pre-randomization):	Welcome text (1A)	Welcome text (1)	Welcome text (1)	Welcome text (1)	Welcome text (1)
Day 0 to 30. Appt information (sent if appt scheduled)	Text Appt Details for follow-up (1B)	Text Appt Details for follow-up (1B)	Text Appt Details for follow-up (1B)	Text Appt Details for follow-up (1B)	Text Appt Details for follow-up (1B)
Day 0 (pre-randomization)		Study Information/Opt-out Consent/Intake survey 1 (2)	Study Information/Opt-out Consent/Intake survey 1 (2)	Study Information/Opt-out Consent/Intake survey 1 (2)	Study Information/Opt-out Consent/Intake survey 1 (2)
Randomized					
Arm Assignment Message (post-randomization) Day 0 [1 hour after welcome messages)		Arm assignment message (1C.a)	Arm assignment message (1C.2)	Arm assignment message (1C.3)	Arm assignment message (1C.4)
Day 0 (post-randomization)			Bupe fill reminder (8)		Bupe fill reminder (14)
Day 0			Initial treatment engagement nudge (9)		Initial treatment engagement nudge (15)
Day 0				Contingency management reminders (11, 12)	Contingency management reminders (14, 15)

Day 0		10 am: intake survey (3)	10 am: intake survey (3)	10 am: intake survey (3)	10 am: intake survey (3)
Day 1		Consent reminder message (for those that didn't complete survey) (2)	Consent reminder message (for those that didn't complete survey) (2)	Consent reminder message (for those that didn't complete survey) (2)	Consent reminder message (for those that didn't complete survey) (2)
Day 1		(10 am: intake survey reminder prn), (3)	(10 am: intake survey reminder prn), (3)	(10 am: intake survey reminder prn), (3)	(10 am: intake survey reminder prn), (3)
Day 1-14			11am: daily check-in (10a)		11 am: daily check-in (10b)
Day 15		10 am: Day 15 survey (4)	10 am: Day 15 survey (4)	10 am: Day 15 survey (4)	10 am: Day 15 survey (4)
Day 16-17		(10 am: Day 15 survey reminder prn), (4)	(10 am: Day 15 survey reminder prn), (4)	(10 am: Day 15 survey reminder prn), (4)	(10 am: Day 15 survey reminder prn), (4)
Day 18			Treatment engagement nudge (16a)		Treatment engagement nudge (16b)
Day 18				Contingency management reminder (17)	Contingency management reminder (16b)
Day 15-30			11am: daily check-in, tapered schedule (10)		11am: daily check-in, tapered schedule (10)
Day 30		10 am: Day 30 survey (5)	10 am: Day 30 survey (5)	10 am: Day 30 survey (5)	10 am: Day 30 survey (5)
Day 31-32		(10 am: Day 30 survey reminder prn) (5)	(10 am: Day 30 survey reminder prn) (5)	(10 am: Day 30 survey reminder prn) (5)	(10 am: Day 30 survey reminder prn) (5)
Day 90		Day 90 follow-up survey	Day 90 follow-up survey	Day 90 follow-up survey	Day 90 follow-up survey
Day 92-93		Day 90 follow-up survey reminder	Day 90 follow-up survey reminder	Day 90 follow-up survey reminder	Day 90 follow-up survey reminder
Day 180		Day 180 follow-up survey	Day 180 follow-up survey	Day 180 follow-up survey	Day 180 follow-up survey
Day 181-182		Day 180 follow-up survey reminder	Day 180 follow-up survey reminder	Day 180 follow-up survey reminder	Day 180 follow-up survey reminder
Active Program End (Day 30)	NPS survey (6)	NPS survey (6)	NPS survey (6)	NPS survey (6)	NPS survey (6)

Arm assignment message: After participants have been randomized to a study intervention arm. They will receive a message detailing the arm they have been randomized, what they can expect of the study, and how much they may receive in incentives depending on the arm they've been randomized to. This will include the frequency of text-message check ins, schedule and compensation for completing study assessments, and schedule and compensation for contingency management incentives [if patient was randomized to arms 3 or 4]).

CM management arm:

For participants enrolled in the Contingency management arms, a Clinical Research Coordinator will confirm patients have filled their buprenorphine script by checking the patients EMR before loading the compensation onto the patients Clincard.

The same process will be used to confirm patients attended their follow-up appointments. The CRC will review the EMR and compensate patients that complete their follow-up treatment within 14 days. The CRC will repeat this procedure for patients that engaged in follow-up care within days 15-30. If the EMR does not show a follow-up appointment at day 14, the CRC will call the patient to confirm they haven't attended a follow-up appointment. If the patient states they have attended an appointment and it is outside of the Penn Health system, the CRC will contact the clinic site the participant was treated at to confirm their attendance with the assistant of the Medical Release Form patients consented to prior to enrolling into the research study.

Surveys:

For all participants the surveys will be hosted on Way to Health. When a participant completes a survey, an alert will be sent to the research team, the patient will check Way to Health and confirm the survey was completed and then proceed to load the patients Clincard with the respective renumeration.

If a patient requests the CRC call the participant to administer the survey, the CRC will reach out to the participant to complete the survey over the phone and renumerate the participant via Clincard. If the participant has not completed the survey, the CRC will call the participant on day 3 of the survey and ask if the participant would like the survey administered over the phone. If the participant wants to complete the survey over the phone, the CRC will proceed to administer the survey over the phone and then upload the respective incentive for the completed survey.

2.13. Assessment Controls

Augmented usual care (standard Way to Health Care textline. Patients can call or text the on-call substance use navigators (SUN) from 9a-9p, 7 days a week).

2.14. Compensation

Participants have the potential to earn up to $70 in the form of a Clincard reloadable debit card for completing surveys during the intervention period.

Compensation structure for surveys:

- $20 for completing the intake survey
- $25 for completing the follow-up survey at day 15
- $25 for completing the follow-up survey at day 30.

Participants in the contingency management arms will have the ability to earn up to $75 additional dollars for attending their follow-up care appointments.

Compensation structure for Contingency Management:

- $25 for filling buprenorphine Rx
- $25 for attending follow-up appointment 1
- $25 for attending follow-up appointment 2

After the intervention period ends at day 30, participants will be asked to complete follow-up surveys at month 3 and 6. Participants can earn up to $60 added to their Clincard reloadable debit card.

Compensation structure for follow-up surveys:

- $30 for completing follow-up survey at month 3.
- $30 for completing follow-up survey at month 6.

Patients will be compensated via Clincard. Research staff will be available in EDs to distribute Clincard at time of enrollment. Patients will be asked to consent to a medical record release form at the time of enrollment so that research staff can confirm engagement with OUD treatment. If patient is discharged from the ED and leaves before the research coordinator can provide them with a Clincard, the research coordinator will organize a time and place to meet the patients to distribute the Clincard and sign medical records release. If the patient is unable to return to the ED, ClinCard will be mailed to the patient. Mailing address only will be collected if patient requests their materials be sent by mail. If patient cannot return to the ED, and the patient prefers a virtual card, a virtual card will be sent to patient by email and an electronic medical release consent will be sent to the patient using Qualtrics or RedCap. Email address will only be collected if patient requests a virtual card.

To confirm Contingency Management payments, clinical research coordinators will review the electronic medical record of participants enrolled to confirm buprenorphine prescriptions have been filled. As standard of care for OUD patients enrolled into clinical programs at Penn, their PDMP information is logged and entered into EPIC, and other treatment encounters. Clinical research coordinators will also confirm with clinic sites and or pharmacists that patient attended appointments or pharmacist received a prescription and pay the respective amount for filling their buprenorphine script and attending their follow-up appointments. Telehealth appointments will also be considered as attending follow-up appointments. The lead physician of this study may reach out to care clinics to confirm this information as well.

2.15. Regulatory

This study will be approved and monitored by the Institutional Review Board at the University of Pennsylvania.

2.16. Contingencies and Participant Withdrawal

If a participant withdraws from the study, further communication will be stopped. Data collected prior to withdrawal will be maintained in deidentified files and may still be used for research purposes. However, additional data will not be collected after the point of withdrawal.

Participants will be told that they can withdraw from the study at any time by texting “Bye”.

2.17 Deception

Participants will be informed that they may qualify for additional payments in the in the informed consent document, but we will not share further details about the Contingency Management arms during the consent process as we believe this will lead to bias (Hofmeyer, 2013 and Ghani et al. 2022). Fully informing the

participants that there may be financial rewards for engaging in treatment may have a subsequent effect on participation in the trial or their engagement in treatment if they are assigned to group without contingency management. Differential retention by randomization arm would bias outcomes and therefore prevent us from comparing the effectiveness of adding contingency management to usual care and text messaging facilitated telehealth for treatment engagement. However, we will notify participants once they've been randomized of the details of the intervention, they have been randomized to

A. Deception/incomplete disclosure is typically only acceptable in studies with no more than minimal risk. Please detail why this study is minimal risk.

This study is minimal risk, there is no harm in not disclosing the amount of money or the intervention arms participants may be enrolled into. Participants will not be at risk of additional harm while participating in this study than they already would be exposed to in usual care.

B. The deception/incomplete disclosure should have no adverse effects on welfare. Please outline how all adverse effects are minimized.

Incomplete disclosure of the intervention arms and incentive amounts for the respective arms, will have no adverse effects on the welfare of participants. Participants will still have access to care regardless of the arm they have been randomized to. The total contingency management incentive amounts that participants are eligible to receive if randomized to arms 3 and 4 ($75) is less than the total amount participants in all study arms can receive from completing all study assessments ($130).

C. The IRB must determine that the value of the study is sufficient to warrant waiving some aspects of the requirement for full disclosure in the informed consent process. Please outline the scientific validity for using deception in this instance.

Some arms involve contingency management as an intervention, being compensated for attending addiction recovery appointments. We believe for this population; participants may become upset and unenroll with the intention of re-enrolling with the intention of being randomized into a more favorable arm (the arm with additional incentives) for attending the same appointments they otherwise would not have been paid for attending. To maintain the integrity of the study design, we believe that incomplete disclosure of financial incentives is necessary.

D. There is no alternative to address the scientific question in a valid manner but to use deception/ incomplete disclosure. Other effective, non-deceptive approaches are not feasible. Please detail why alternatives are not feasible.

There is no alternative to studying the effectiveness of contingency management vs non-contingency management arms without deception for this population for the reasons listed in section C.

E. Debriefing is done, when appropriate, and the deception/incomplete disclosure is explained to the participant before the end of participation in the research. Please detail if you are debriefing participants, and if not, why not.

Participants will be debriefed once they have completed the study with an end of study text message and link to a study debriefing statement (see attached. We will also notify participants the study was posted on PCORI and Clinical trials websites, provide the NCT number if they are interested in viewing the results, and further explain that no identifiable information was added onto this website. We are neglecting to notify participants of the PCORI and Clinical Trials websites at the onset of the study for the reasons listed in sections a-d above.

F. When appropriate, subjects could be informed prospectively of the use of deception/incomplete disclosure and consent to its use: see the suggested consent language: "In some research studies, the investigators cannot tell you exactly what the study is about before you participate in the study. We will describe the tasks in the study in a general way, but we can't explain the real purpose of the study until after you complete these tasks. When you are done, we will explain why we are doing this study, what we are looking at, and any other information you should know about this study. You will also be able to ask any questions you might have about the study's purpose and the tasks you did. Though we may not be able to explain the real purpose of the study until after you complete the tasks, there are no additional risks to those that have been described in this consent form."

We don't believe it's appropriate to inform participants prospectively of the use of deception or incomplete disclosure for this study in the consent form for reasons listed in section a-e above.

3. OUTCOMES

3.1. Primary outcome

The primary outcome will be engagement in any addiction treatment at 30 days from randomization (measured on Day 31). Participants will consent to allow research coordinators to confirm this outcome via agreements with referral clinics; our sites are experienced with collecting this standardized outcome as part of a National Institute on Drug Abuse multicenter study (CTN-0099RCT). Data collected during this assessment includes provider type, program and treatments received (buprenorphine, methadone, naltrexone) using a standardized reporting form. Engagement in treatment at 30 days will be defined as either: (1) filling a buprenorphine prescription that covers Day 30 or a buprenorphine prescription that covers at least 7 of the 14 days between Days 15 and 30 based on documentation of PDMP review; (2) EHR documentation of engagement in addiction treatment including a telehealth clinic encounter, office based treatment, inpatient addiction detox or rehabilitation, intensive outpatient treatment, or opioid treatment program (including documentation of methadone dose confirmations or 2 or more visits on consecutive days for methadone guest dosing in the ED); or (3) contacting the patient up to 3 times for site of addiction treatment and then confirming with the treatment facility whether the patient was engaged with one of the above forms of addiction treatment. Data is expected to be missing at low frequency based on prior ED-based trials in which only 1% of patients had missing data on this outcome.[9] The combined absence of buprenorphine fills, EHR documentation of addiction treatment, and the inability to reach the patient will be counted as lack of engagement in addiction treatment at 30 days. This will be reassessed at 30 days, 3 months, and 6 months.

3.2. Secondary outcome

We will measure two key secondary outcomes:

Filling a buprenorphine prescription within 7 days of randomization based on documentation of PDMP review.

Engagement in treatment with 14 days will be defined as either: (1) filling a second buprenorphine prescription within 14 days of enrollment based PDMP review; (2) EHR documentation of engagement in addiction treatment including a telehealth clinic encounter, office based treatment, inpatient addiction detox or rehabilitation, intensive outpatient treatment, or opioid treatment program (including documentation of methadone dose confirmations or 2 or more visits on consecutive days for methadone guest dosing in the ED); or (3) contacting the patient up to 3 times for site of addiction treatment and then confirming with the treatment facility whether the patient was engaged with one of the above forms of addiction treatment. Data is expected to be missing at low frequency based on prior ED-based trials in which only 1% of patients had missing data on this outcome.[9] The combined absence of buprenorphine fills, EHR documentation of addiction treatment, and the inability to reach the patient will be counted as lack of engagement in addiction treatment at 14 days.

We will measure the following exploratory outcomes:

Patient reported outcomes. We will measure questions adapted from the SURE and BAM at intake and all follow-up assessments providing data on substance use, self-care, relationships, material resources, and outlook on life. We will also measure treatment appropriateness and acceptability 15 days using validated measures.

Subsequent ED and hospital utilization and mortality. We have developed standardized data queries to capture all ED visits, hospitalizations, and mortality out to 6 months from enrollment. To capture encounters outside study health systems, as we have done previously, we will obtain linked records from the regional health information exchanges (HIEs) – HealthShare Exchange for Penn and Cooper, Care Everywhere for Alameda). Will subsequently link the patient data to the National Death Index to capture of out-of-hospital mortality not captured in EHRs or HIEs.

4. STATISTICAL ANALYSIS PLAN

4.1. Analytic Methods

We will produce data summaries using frequencies for categorical variables and means, medians, and ranges for continuous variables. To evaluate randomization balance, we will compare baseline values of all variables across groups using nonparametric tests. We will include variables with imbalances as covariates in sensitivity analyses. In the models described below, we will check the validity using standardized residuals, influence diagnostics, and graphical displays.

We will use intention-to-treat analyses, in which all participants are analyzed as randomized to measure effectiveness. We will test our primary hypothesis using a logistic regression model[108] with a binary indicator of attendance at outpatient addiction treatment clinic 30 days post-randomization as the response. To accommodate the stratified randomization, the model will include categorical variables for hospital system, enrollment site (ED vs. bridge clinic), and for ethnicity (white/non-white). The hypothesis will be addressed by including binary factors for incentives and for telehealth, and we will include their interaction to allow the effect of either the telehealth or incentive intervention to vary across the levels of the other. Our main comparisons, of each of the three interventions vs. enhanced usual care, will be based on this interaction model. We will report the rates of attendance for each of the four treatment groups, and the odds ratios and relative risks corresponding to the three primary comparisons, along with associated standard errors, confidence intervals and p-values. We will also report the effect sizes for the pairwise comparisons among the three active intervention strategies.

Sample size and power. Primary Outcome: Engagement in Treatment at 30 days. An important strength of this study, unlike prior RCTs of text-messaging, telehealth interventions, and incentives for OUD, is that we will be

powered to determine whether these interventions are effective among non-white patients. Specifically, we power the study to provide 80% power to detect differences of 17.5% or greater between the interventions and usual care, within the non-white subgroup. We use two-sided tests, with a Bonferonni-corrected alpha level of 0.05/3=0.017. We also assume a 10% dropout rate between randomization and the 30-day time point. Based on prior data from the study sites, we expect a 35% engagement rate at 30-days in the usual care group, and that approximately 48% of our sample will be non-white. With these assumptions, a full sample of 1628, equally distributed across the four groups, yields 80% power for a risk difference of 17.5% or more for comparisons with usual care within the non-white subsample. For the full sample, this sample size yields 80% power for a corresponding risk difference of 12% or more. However, while we anticipate that we will lose contact with some participants through the first 30 days, our engagement outcome will be available on all randomized participants, as "loss of contact" will be regarded as equivalent to "non-engaged". Under this assumption, we have 89% power to detect a difference of 17.5% at 30-days, and 82% power to detect a difference of 16% at 30 days. For the full sample (white and non-white) we have power for smaller effects: with the same alpha level of 0.017, we have 84% power to detect a risk difference of 11% (35% vs 46%) in the three comparisons with control.

Secondary Outcome: Engagement in Treatment Within 14 Days. Based on the nature of the interventions, we anticipate a potentially smaller effect than at 30-days. Therefore, to have 80% power for risk differences of 15% in the non-white population, we would need total sample size of 1808, which will be the target enrollment for trial.

Missing data. We anticipate that between 10% and 15% of the sample will drop out between randomization and 30-day assessment. When possible, we plan to record and report all reasons for patient drop-out, including non-response and patient choice to not participate assessments. We will characterize the subgroup of participants who drop out in terms of baseline demographic, socioeconomic, and behavioral characteristics. Next, we will use a logistic regression model, including most of the baseline variables, treatment group, and interactions, to develop a prediction model for dropout. From this model, we will obtain predicted probabilities of treatment retention through 30-days, and use these predicted probabilities as weights in an inverse-probability-weighted re-fitting of the models described for Aim 1 and 2.

Adherence to assigned intervention. We expect that some participants will not adhere to their assigned treatment. Non-adherence will be defined as not responding to intervention text-messages in the active treatment arms. To accommodate this in our analyses, we will use an instrumental variables approach, using the randomization variable as an instrument, to separately compare the usual care group to each of the other three groups, using a two-stage least squares approach. Next, we will use the multiple-group methods [110,111] to obtain adherence-adjusted estimates of effect for all groups simultaneously.

Secondary hypotheses. We will test the secondary hypotheses on filling the initial buprenorphine prescription within 7 day and engagement in treatment within 14 days using logistic regression models specified in the same way as those above. We will use similarly specified generalized linear models,[112] with link functions and mean-variance relationships chosen as appropriate for the various response distributions, to test the secondary hypotheses on the patient-reported measures.

Exploratory hypotheses. For the exploratory outcomes at 30-days post-randomization, we will use similar logistic regression models to compare the groups on enrollment and receipt of treatment, and on UDS for illicit opioids. For ED visits and hospitalizations, we will use zero-inflated negative binomial regression models[113] if there is sufficient variability in these responses, and logistic regression models (for dichotomized versions of these responses) otherwise. We will also conduct interaction analyses to determine if enrollment site (ED vs. bridge clinic) moderates the intervention effects on the primary and secondary outcomes.

5. DATA COLLECTION AND MANAGEMENT

5.1. Data Collection Process

The solicitation text message will include a link to Way to Health's study page. Contact information, and survey data will be collected by Way to Health. Outcome variables will be obtained prospectively from elective surveys, through EHR and/or health information exchange, local research coordinator chart review/phone calls, and Way to Health Data. Way to Health will access SMS messaging, mobile survey, or central research coordinator phone call, and include EPIC integration.

5.2. Variables

A detailed account of the data we will obtain, our Measures library, is included in the Appendix.

5.3 Transfer of Data

Once participants have enrolled and completed the intake process, the research team will export their participant information (EPIC data, comorbid conditions, ED encounter data, Prior ED/Hospital use) will be integrated into Way to Health. Way to Health's integration with EPIC will log each participant's phone number, Study ID, and study name, which will then trigger a message to each participant with a link to the study site. Health information exchange data from Cooper and Alameda will be collected by their respective sites, linked with the MRNs. Once the data has been linked, the MRNs will be removed and the data will be de-identified and shared to the Penn team via RedCap.

5.4. Data Storage and Security

Any datasets and computer files are referred to by study ID. The study ID is also used on all analytical files. Way to Health will store all data securely sent to the Penn research team. All data for this project will be stored on Way to Health, or Pennbox, in data files that will be protected by multiple password layers, requiring staff with access to the folders to sign-in to Pennbox with their Penn ID and duo dual authentication, Penn has executed HIPPA-compliant Business Associate Agreements with the Box services.

All personal information that the participant is asked to provide will be collected via Way to Health. Through Way to Health, we will collect participants' names, dates of birth, email addresses, and phone numbers. To assure that participant confidentiality is preserved, individual identifiers are stored in a single password protected system that is accessible only to study research, analysis, and IT staff. An investigator or statistician who logs in will be able to access only non-identifiable data. The Way to Health administrative group and research coordinators responsible for contacting participants for follow-up study visits or responding to questions about the study are able to view participant names and contact information. The Way to Health web development team and Project Director currently have administrative access to PHI. All of these personnel will have completed Human Subjects Protection and HIPAA privacy training. The system automatically generates logs of all data queries which can be reviewed by research staff to ensure that no unauthorized persons have gained access to identifiable information.

This system is hosted on site at The University of Pennsylvania and is protected by a secure firewall and several layers of operational security. Once a participant has been entered into this system, they are given a unique study identification number (ID). Any datasets and computer files that leave the firewall are stripped of all identifiers and individuals are referred to by their study ID. The study ID is also used on all analytical files. The Penn Medicine Academic Computing Services (PMACS) is the hub for the hardware and database infrastructure that supports the project and the Way To Health web portal is built on this infrastructure. The data collected for Way To Health based studies is stored in mySQL databases on a PMACS-operated blade server environment devoted specifically to Way To Health. The data center is housed in Information Systems

and Computing at 3401 Walnut Street. All data are stored in a single relational database, allowing researchers to correct mistakes. Every SQL transaction, including accessing and changing data, is logged for auditing purposes. Datasets are stripped of all personally identifiable information when exported for analysis. The web application automatically removes all identifiers when a researcher requests an analytic dataset. The only people with access to identifiable participant information are pre-specified Research Coordinators responsible for contacting participants for follow-up. Personal information and research data will be stored in separate SQL tables and will be linked by a computer-generated ID number. Additionally, any information that leaves this system to communicate with third party data sources (i.e. survey software) is stripped of any identifiers and transmitted in encrypted format.

6. HUMAN SUBJECTS

6.1. Risks to Human Subjects

This project poses minimal risk. There is a risk of breach of confidentiality for participants receiving study information on their phones. Any demographic, survey, and EPIC data will be stripped of identifiers before the datasets are combined and analyzed. Penn will collect contact information (cell phone for SMS communication, and DOB for ClinCard registration required for compensation).

6.2. Protection against Risk

In order to protect study participants from potential risks related to the loss of confidentiality and due to any discomfort that they may experience in answering any questions, the following steps will be taken: 1) Participants will be told that they can withdraw from the study at any time by contacting us. They will also be able to stop receiving text messages simply by replying, “STOP” to the study phone number at any point during the study; 2) All information provided by the participant will be referenced to a Study ID. The participant’s contact information will not be connected to any other study data. Their survey data can only be connected to their demographic and survey data through the Study ID, which will be created and stored on Way to Health. All data and files will be entered on computers protected by passwords and stored in a locked office. 3) All research staff will be trained in the importance of maintaining confidentiality and will meet all training requirements for human subjects’ research. 4) All participant data will be presented in aggregate and no individuals will be identified individually. Additionally, all datasets will be de-identified before analysis. Once all data has been linked for analysis, identifiers will be stripped and identifiable data will be destroyed a year after data analysis is complete. All data on Way to health will be destroyed 6 months after the study has closed.

6.3. Adequacy of Protection Against Risk

Participants are Emergency Medicine patients that have screened positive for OUD. The study poses no more than minimal risk, as it’s testing various interventions that have been tested in the field previously and showed to be of minimal risk. We intend to apply these interventions on top of to the current standard of care. The current standard of care is discharging OUD patients with access to the CareConnect warmline. A Penn run program that staffs substance use navigators from 9 am – 9 pm, to assistant patients with opioid use disorder access care. Cooper and Alameda have similar clinical programs staffed by substance use navigators as the standard of care at their sites. We will be applying these interventions over their current standard of care.

Way to Health will assign a study ID to each Study Participant. Data will be transferred between EPIC with Way to Health, secure email, and SecureShare. Penn and the other sites will collect contact information (cell phone for SMS communication, DOB for ClinCard registration). When files are exported from Way to Health to Pennbox, this identifiable information will be stored in a file separate from survey data, demographic data, and EPIC data.

6.4 Potential Benefits to Individual Participants

This information could allow the research team to gain insight about effective program strategies for increasing engagement in OUD research. Participants may gain more access to the health system and open avenues for personal care and recovery treatment.

6.5 Clinical Trials

This study will be registered on clinical trials.gov once the study has received IRB approval. An NCT registration number will be added to the IRB once it has been created. Language regarding the study being on clinicaltrials.gov will not be added to any consent or patient facing document as it will allow participants to see the study intervention, which we are purposely blinding participants to. We will provide participants with the Clinical Trials NCT number once they have completed the study at 6 months.

7. Data and Safety Monitoring

All data received will be de-identified and will remain de-identified. All data obtained in the study will be used exclusively for the purposes of the proposed research. Users of this platform have been assigned a Study ID# and no identifiers will be contained in this file. This data will be linked by a programmer utilizing coded study IDs and operating behind a University firewall. Data from Way to health will be protected by a strong password to access the computer of the user who has access to the database and a strong password to access the database. No results will be reported in a personally identifiable manner. (Variables in Appendix)

8. FUNDING

Funding for this trial is provided by the Patient Centered Outcomes Research Institute (PCORI). Penn is responsible for the overall design, conduct, collection, management, analysis, and interpretation of the data; preparation, review, and approval of the manuscript; and the decision to submit the manuscript for publication.

9. PUBLICATIONS

We plan to publish the findings in conference proceedings and/or peer-reviewed journals.

10. DATA SHARING

Data for this study may be shared in aggregate with our collaborators at Highland Alameda Health System and Cooper Health and resolve any technical issues with Way to Health, where they will act as enrollment sites. No PHI will be shared in this process. However, we will receive PHI from these institutions, as their patients will be enrolled into Way to Health and this data will be de-identified for analysis purposes. We will also comply with the sponsor (PCORI) data sharing policy in which de-identified study data will be transferred to a repository managed by PCORI at the end of the study https://www.pcori.org/about/governance/policy-data-management-and-data-sharing).

We will enter into a Data Use Agreement with Alameda and Cooper regarding how the data will be transferred to Penn for analysis. Any data that is not collected in Way to Health from the Cooper and Alameda sites, will be extracted from EPIC and Health Exchange data. The sites will use the MRNs to link all of the data, once the data has been linked by the sites, the identifiers will be stripped, and the Way to Health identification number will be added. The EPIC and health exchange data will be entered into a RedCap data base with to

link the Way to Health ID. Penn will download the de-identified data for analysis purposes and use the W2H ID in the RedCap forms to link the patient data with the W2H data.

A main outcome of our study is confirming engagement with OUD care. At Alameda and Cooper, they have integrated systems that allow for this care to be done within the health system and stored in EPIC. However, at Penn, patients that engage with the emergency department for OUD often receive follow-up care from clinics outside of Penn's system. To account for this, we will have participants that enroll into the study complete a Medical Release form (detailed in sections 2.5 and 2.6), where patients have agreed to have the research team contact their clinical sights to confirm they've received care via text and further by filling out the medical release form.

We will have CRC's, PM's and or Clinicians on the team, call the clinics and share the participant's first and last name, and DOB with the clinic sites to confirm the patient attended care, and will receive the dates the patient attended care at the clinics. If the clinics request a medical release form, we will then fax or email a copy of the patient's signed medical release form to the clinic to receive this information. This information will be logged into Way to Health. Those in the contingency management arm will be compensated once we've confirmed engagement in care.

11. TASKS AND RESPONSIBILITIES

Principal investigator: Overall responsibility for protocol development, intervention development, budget overview, data dictionary development, ethical approval, trial registration, trial oversight, and the data and safety monitoring board, assessment of overall recruitments, potential, data analysis, and dissemination and presentation of results.

Co-Investigators: Protocol development, data dictionary development, trial oversight, dissemination of results.

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Appendix

Table of Measures

Data collected by or transferred to Penn		
Source	Variables	Time from ED Discharge
EHR		
	Demographics	Intake
	Comorbid conditions	Intake
	ED Encounter data	Intake
	Prior ED/Hospital Use	Intake
Way to Health		
	W2H ID	Intake
	Engagement with substance use navigators	Intake
Local Research Coordinator chart review/phone calls		
	Engaged in Addiction Treatment	Intake, day 15, day 30, month 3, month 6
Mobile Survey		
	Addiction treatment history	Intake,
	Brief Addiction Monitor -Revised (BAM-R)	Intake, day 15, day 30, month 3, month 6
	Substance Use Recovery Evaluator (SURE)	Intake, day 15, day 30, month 3, month 6
	Commitment to Sobriety Scale (CSS)	Intake, day 15, day 30, month 3, month 6
	Immediate barriers to addiction treatment and recovery	Intake, day 15, day 30, month 3, month 6

	Delay discounting function	Intake
	Appropriateness	Intake
	Acceptability	Intake

2. Study Consent

We want to improve CareConnect and are enrolling patients prescribed buprenorphine to be in a 6-month research study. Those who participate may benefit from improved treatment. Unless we hear from you, you will be enrolled in the study. If you do not want to be in the study, text BYE. You will still have access to CareConnect helpline.

In the study you'll be texted links to 5 optional surveys about opioid use. You'll receive a survey tomorrow and in 15, 30, 90, and 180 days, and have 3 days to take each. A CareConnect member can also call you to ask the survey questions. Each pays $20, $25 or $30 by ClinCard debit card. You may be eligible for additional payments. You may also get texts that check in or encourage you to attend treatment. After 30 days, you may be invited to an optional survey and interview about CareConnect ($50 payment).

By participating you agree to allow the research team to use your protected health information and access information about your addiction treatment. See HIPAA and release agreements. Data will be securely stored and shared for future research. Identifying info will be removed. We strive for confidentiality, but there's always a risk.

You can withdraw from the study at any time by texting BYE. We can also end the study anytime. Study questions? Call 609-248-0229. Questions about your rights? Call Penn IRB at 215-898-2614 and ask about study #853153.

HIPAA Agreement

Our study uses protected health information from your survey responses and medical records: name, telephone #, birth date, medical record #, demographics, health conditions, ED/hospital/CareConnect use, opioid/other substance use, addiction medication and treatment. This information is needed to do, evaluate, and oversee the study. It will be stored in electronic medical record and Way to Health, which meet HIPAA standards. ClinCard will use name, birth date; possibly email.

Besides the study team, other approved people at Penn may access your information. It may also be shared with addiction treatment centers, subcontractors, non-Penn study researchers, Patient-Centered Outcomes Research Institute, U.S. Office of Human Research Protections, the study's data and safety monitoring board. If your information is shared outside Penn, it may no longer be covered by federal privacy regulations. By participating you agree to allow this use of your protected health information with no end date. To end this agreement, text BYE.

Release Agreement

By participating, you agree to allow any treatment facility where you receive care to release information from your health record to the CareConnect study team. The study team will request information on your attendance at specialty clinics and treatment centers for opioid use disorder. This information will cover a period from today until 180 days later. The purpose of this information is to let the team know if you got treatment as a follow up to care in the emergency department or bridge clinic. You may end this agreement by texting BYE; ending the agreement means that new information cannot be shared with the study team.