The Substance Use Treatment and Recovery Team (START) study: protocol for a multi-site randomized controlled trial evaluating an intervention to improve initiation of medication and linkage to post-discharge care for hospitalized patients with opioid use disorder

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Abstract

Background: People with opioid use disorder experience high burden of disease from medical comorbidities and are increasingly hospitalized with medical complications. Medications for opioid use disorder are an effective, life-saving treatment, but patients with an opioid use disorder admitted to the hospital seldom initiate medication for their disorder while in the hospital, nor are they linked with outpatient treatment after discharge. The inpatient stay, when patients may be more receptive to improving their health and reducing substance use, offers an opportunity to discuss opioid use disorder and facilitate medication initiation and linkage to treatment after discharge. An addiction-focus consultative team that uses evidence-based tools and resources could address barriers, such as the need for the primary medical team to focus on the primary health problem and lack of time and expertise, that prevent primary medical teams from addressing substance use.

Methods: This study is a pragmatic randomized controlled trial that will evaluate whether a consultative team, called the Substance Use Treatment and Recovery Team (START), increases initiation of any US Food and Drug Administration approved medication for opioid use disorder (buprenorphine, methadone, naltrexone) during the hospital stay and increases linkage to treatment after discharge compared to patients receiving usual care. The study is being conducted at three geographically distinct academic hospitals. Patients are randomly assigned within each hospital to receive the START intervention or usual care. Primary study outcomes are initiation of medication for opioid use disorder in the hospital and linkage to medication or other opioid use disorder treatment after discharge. Outcomes
are assessed through participant interviews at baseline and 1 month after discharge and data from hospital and outpatient medical records.

Discussion: The START intervention offers a compelling model to improve care for hospitalized patients with opioid use disorder. The study could also advance translational science by identifying an effective and generalizable approach to treating not only opioid use disorder, but also other substance use disorders and behavioral health conditions.

Trial registration: Clinicaltrials.gov: NCT05086796, Registered on 10/21/2021.

Keywords: Opioid use disorder (OUD), Medications for opioid use disorder (MOUD), Addiction consult team, Collaborative care, Linkage to follow-up, Inpatient

Background
The US opioid epidemic continues to be of urgent national concern. Between 1999 and 2019, nearly 500,000 people died from an overdose involving opioids [1]. In 2020 and 2021, coincident with the COVID-19 pandemic, fatal and non-fatal opioid-related overdoses increased even more rapidly than in previous years [2–4]. People with opioid use disorder (OUD) experience high burden of disease from medical comorbidities [5] and are increasingly hospitalized with medical complications related to OUD [6–8]. Between 2002 and 2012, annual hospitalizations for OUD in the US nearly doubled, from 301,707 to 520,275, with inpatient charges for these hospitalizations nearly quadrupling [8]; by 2018, the number of inpatient stays related to OUD reached an estimated 748,900 [9]. Medications for opioid use disorder (MOUD) are highly effective and help reduce overdose rates, criminal behavior, infectious disease, and mortality [10–12] and are the standard of care for people with OUD, but patients with an underlying OUD admitted to the hospital seldom initiate MOUD while in the hospital or are linked with outpatient treatment for their OUD after discharge [13–15]. High rates of patient-directed discharges among people with OUD (about 15%) suggest failure to address issues related to OUD such as opioid withdrawal and pain while in the hospital [16] and also lead to failed transitions to follow-up care after hospital discharge [17]. Between 2011 and 2015, about half a million hospitalization discharges per year included a diagnosis of OUD without provision of treatment or prevention services [18]. Failing to address OUD while patients are in the hospital either for a complication related to their OUD or for another illness or injury is a missed opportunity to initiate critical and life-saving treatment and leaves patients at high risk of continued use, delays in care, overdose, and costly readmission [6, 14, 17, 19–21].

Hospitalization is a critical time to identify patients with OUD and to initiate evidence-based treatments [16, 22]. Starting MOUD in the hospital and linking patients with post-discharge care addresses a common treatment gap and could improve patient outcomes and lower readmissions and costs. Some studies suggest that the inpatient hospitalization is a reachable moment when patients with OUD may be willing to engage with treatment, including initiating MOUD, if barriers can be reduced [23–33]. Although inpatient physicians frequently manage clinical conditions related to OUD, such as acute overdose, withdrawal, and infectious diseases, many report lacking knowledge and skills for addressing OUD [34, 35]. Given pressures to minimize length of stay in the hospital on the acute cause of admission, hospital teams may defer addressing chronic conditions like OUD. Moreover, few hospitals have established organizational infrastructure to support effective treatment of OUD, such as addiction focused consultative teams, evidence-based protocols, or the ability to coordinate care transitions needed to link patients to community resources [36]. Stringent federal privacy regulations, prescribing, dispensing and tracking regulations, insufficient training and reimbursement issues, create additional barriers [37–39]. Not least of all, patients with OUD often may not perceive the need to start treatment [40–42], and they may also experience stigma in health care settings [43, 44], leading to even greater ambivalence.

A hospital-based addiction consultation service has the potential to increase delivery of MOUD to patients with OUD (as well as other substance use disorders) during their hospitalization and link them to treatment after hospital discharge [45]. Prior studies suggest that an inpatient addiction consult team may have a positive effect on MOUD initiation and linkage to post-discharge care [34, 46] and result in lower readmission rates [47], and that this type of team is feasible, acceptable to patients and providers, and cost-effective to implement [34, 48–53]. Additionally, studies also show that patients who initiate MOUD in the hospital are more likely to continue MOUD for their OUD after discharge.
However, while these descriptive, observational, and quasi-experimental studies [29, 31, 47, 49, 53, 55–63] provide high-quality evidence, there have been no randomized controlled trials (RCTs) to test effectiveness of this model specifically for patients with OUD. RCTs can add definitive evidence to inform decisions on adoption of models of care, which is particularly valuable in a resource-constrained health care system [64].

This article describes the protocol for a multi-site, RCT being conducted in three diverse hospitals in the United States to test whether an inpatient addiction consult team informed by the collaborative care model [65, 66] and evidence-based tools and resources, including motivational interviewing [67] and focused discharge planning [68, 69], improves MOUD initiation and linkage to post-discharge care for people with OUD compared to usual care.

Study objectives and specific aims
This study will evaluate whether an addiction consult team called the Substance Use Treatment and Recovery Team (START) increases initiation of any US Food and Drug Administration (FDA)-approved MOUD (buprenorphine, methadone, naltrexone) during the inpatient stay, and increases linkage to treatment after discharge among hospitalized patients with OUD, compared to patients receiving usual care. Secondary outcomes include having an OUD-specific discharge plan, post-discharge MOUD and medical care utilization, and past 30-day opioid use. We hypothesize that compared to usual care, a higher proportion of patients in the START arm will initiate MOUD in the hospital; have linkage to post-discharge OUD treatment, including MOUD and psychotherapy; have an OUD-specific discharge plan; will receive any medical care; and will have fewer days of opioid use.

Methods
Study design and setting
This study is a three-site, pragmatic randomized controlled trial (RCT) testing the effects of START versus usual care (UC) on primary care (PC) or primary medical care (PMC) on behavioral and substance use disorder outcomes but has not been previously adapted for a hospital-based addiction consult team [65, 66, 71, 72]. Collaborative care principles that inform this model include a patient-centered care team, population-based care that tracks patients using a registry, and use of evidence-and measurement-based care [73]. The START consists of an addiction medicine specialist (AMS) and a care manager (CM) who use a tailored intervention consisting of evidence-based tools and resources to overcome barriers to MOUD initiation and linkage to follow-up care. Table 1 details evidence-based tools and resources the START uses to address barriers to MOUD and linkage.

Participants
The study will enroll 414 patients across all three hospitals over the course of approximately 10 months. (Our timeline may extend beyond 10 months due to delays associated with the COVID-19 pandemic). In order to be eligible for the study, individuals must be current inpatients at one of the three participating hospitals; be 18 or older; have a probable OUD diagnosis, defined by scores of > 3 on the heroin or prescription opioid section of the World Health Organization Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) [70]; speak English or Spanish as a primary language; have a life expectancy of greater than 6 months (i.e., they are not in hospice); and be able to provide informed consent. Participants already receiving MOUD during their hospitalization will not be eligible for the study.

Study conditions
Intervention condition: START
The START is an addiction consultation team comprised of an addiction medicine specialist (AMS) and care manager (CM) utilizing evidence-based interventions for OUD. The START provides diagnostic assessments, makes appropriate treatment recommendations, assists with implementation of treatment plans, establishes OUD-focused discharge plans, and facilitates linkage to treatment after discharge. The START is informed by the principles of the collaborative care model, a team-based treatment approach typically delivered by a physician-care manager team that has been found effective in health care settings for increasing use of evidence-based care and improving patient behavioral and substance use disorder outcomes but has not been previously adapted for a hospital-based addiction consult team [65, 66, 71, 72]. Collaborative care principles that inform this model include a patient-centered care team, population-based care that tracks patients using a registry, and use of evidence-and measurement-based care [73]. The START consists of an addiction medicine specialist (AMS) and a care manager (CM) who use a tailored intervention consisting of evidence-based tools and resources to overcome barriers to MOUD initiation and linkage to follow-up care. Table 1 details evidence-based tools and resources the START uses to address barriers to MOUD and linkage.

The START CM and AMS have interrelated roles providing patient care, at times providing recommendations to the primary medical team, at other times delivering services; responding to specific challenges related to addiction and its bio-psycho-social implications; and overseeing clinical team-based care regarding the patient’s OUD. Each AMS is a physician who holds a DEA X-waiver and/or board certification in addiction
medicine or psychiatry. The AMS conducts a medical assessment, including withdrawal potential, relapse risk, and relevant comorbidities that influence medical management of OUD, and evaluates whether the patient is a candidate for MOUD. FDA-approved MOUDs include methadone, buprenorphine/naloxone, and naltrexone. If appropriate for MOUD, the AMS discusses the treatment with the patient and the patient’s medical team and either will provide consultative guidance (if requested by the medical team) or prescribe the medication. The AMS provides ongoing clinical supervision to the CM and is available to communicate with aftercare providers to support continuous MOUD. The CM and AMS discuss patient care in terms of diagnosis, motivation for change, treatment and aftercare planning, barriers, and potential solutions. For patients in the one-month follow-up period, the CM provides updates to the AMS on measurement-based care elements including withdrawal symptoms, substance use, MOUD adherence, and side effects.

The CM (START CMs have an MSW, LCSW, and/or more than 5 years of experience working with people with substance use disorders) delivers an adapted Brief Negotiated Interview (BNI); a structured, evidence-based approach designed to improve readiness for substance use disorder treatment based on motivational...
interviewing (MI)] [74–76] to engage, assess, and help motivate the patient to initiate treatment and/or post-discharge care for their OUD; provides educational information to the patient about MOUD, psychosocial interventions, and overdose prevention; conducts psychosocial assessments and assesses for risk factors; and guides the patient through safety planning and crisis management as needed. Working with the AMS and the primary medical team the CM also works with the patient to develop an OUD-focused discharge plan using techniques and materials adapted from Project Reengineered Discharge (RED), an evidence-based discharge planning protocol [68], that include active planning and teach-back techniques, facilitated linkage to follow-up care, and post-discharge follow-up. For patients who do not initiate MOUD and do not wish to obtain follow-up care, the CM addresses harm reduction needs and helps facilitate linkage if the patient’s readiness changes. The CM uses a registry to track treatment and follow-up and to prioritize care based on the patient’s level of need.

The START “starts” where the patient is; that is, the START respects patients’ thoughts and feelings about their opioid use, does not confront them about their use, and does not try to persuade them to initiate MOUD or other treatment. Consistent with the BNI, the AMS and CM use a MI style in their approach to talking with patients [76]. MI is a client-centered, directive but non-confrontational counseling style for eliciting behavior change. The examination of ambivalence around behavior change is a central tenet of MI. The AMS and CM use MI in their encounters with the patient to help them resolve ambivalence about starting treatment for an opioid use disorder. The START also recognizes that personal and cultural backgrounds inform patients’ experiences with opioid use and treatment. The START practices trauma-informed care and cultural humility. Trauma-informed care involves engaging in shared decision-making, building trust, empowering patients, and creating a safe environment to respond to trauma in ways that are culturally and linguistically appropriate [77]. Nearly half of people with OUD have a lifetime history of post-traumatic stress disorder [78, 79], which makes addressing trauma an especially important part of care for this population. Cultural humility is a part of trauma-informed care, and it is crucial for providing equitable, effective care to diverse populations [80].
The components of the START workflow are as follows (see Fig. 2):

1. **Triage** The CM or AMS assesses the patient’s acute biopsychosocial stability and prioritizes interventions in accordance with clinical status and hospital course. Some patients may need an urgent intervention to address active withdrawal, or counsel to prevent a patient directed discharge. For other patients, intervention is deferred while acute medical conditions are stabilized.

2. **Engage, assess, plan** If there is not an urgent need for medical intervention or after the urgent medical need is addressed, the CM and/or AMS:
   - Engages with the patient (CM and AMS)
   - Conducts a diagnostic and biopsychosocial assessment (CM)
   - Conducts a biomedical assessment and addresses comorbidities (AMS)
   - Delivers the adapted BNI to assess and increase readiness for treatment and develops a plan for initiating evidence-based treatment (MOUD, psychotherapy) during and after the hospital stay (CM)
   - Ensures the patient understands the follow-up plan and addresses barriers (CM)

3. **Treat** Treatment includes:
   - Facilitating appropriate management of intoxication, withdrawal symptoms, comorbidities, and MOUD (AMS)
   - Facilitating psychosocial treatment for OUD, if indicated and available (CM)
   - Educating patients about harm reduction strategies (CM), including use of overdose reversal kits (CM/AMS)

4. **Communicate and Coordinate**
   - The CM and AMS communicate with each other to continue care throughout 1 month after the patient is discharged
   - The CM and AMS communicate with the patient and medical team, and, when appropriate, the patient’s family and outpatient providers

5. **Follow up** The CM calls the patient once a week for 1 month after the patient is discharged from the hospital to assess whether the patient is following through with the discharge plan. The CM may also call outpatient providers to facilitate linkage to care.

**UC study condition**

UC consists of each hospital’s current practices for managing patients identified with OUD along with each patient enrolled in the study receiving MOUD education.
and referral information. We use UC as the comparator because there are no other evidence-based interventions for achieving our proposed outcomes. None of the hospitals currently employs an addiction consult team that consists of an AMS and CM that systematically uses a set of principles based on collaborative care along with evidence-based tools and resources (e.g., motivational interviewing, adapted BNI and Project RED resources) to support patients with OUD. A CM and AMS at each hospital serve as CM and AMS for the START study and will not see UC patients during the study period. At CSMC, patients randomized to the UC study condition may receive a referral to the existing consultation liaison (CL) psychiatry service if the patient’s medical team determines the need for a consult, or they will be treated and provided discharge planning directly by the medical team. The CSMC CL service has clinicians who can discuss opioid use with the patient and help the patient initiate medication, if indicated. These usual CL service providers also can provide consultation to the medical team on whether medication initiation in the hospital and treatment after discharge are indicated. At UNM and BMC hospitals, patients randomized to the UC study condition can be treated directly with MOUD and provided discharge planning by the medical team. At BMC Hospital, the referring physician will have the option of contacting the standard psychiatric CL or addiction consult service for patients in the UC study condition, which will not include an AMS or CM. If the START AMS or CM at any hospital is approached by a member of the medical team for consultation on an OUD patient, they will refer them to the California Bridge Program Tools and Resources website [81].

Study procedures

**Inclusion and exclusion criteria**

Inclusion criteria are as follows: (1) admitted to an inpatient bed at CSMC, UNM Hospital, or BMC; (2) age 18 and older; (3) have a probable OUD diagnosis, defined by scores of > 3 on the opioid section of the Alcohol, Smoking, and Substance Involvement Screening test (ASSIST) [70]; (4) speaks English or Spanish as primary language; (5) able to provide informed consent. An individual who meets any of the following criteria is excluded from participation in this study: (1) already receiving FDA-approved medication treatment for an opioid use disorder in the hospital, defined as not being on MOUD at the time the patient is approached by the study team; (2) < 6 months life expectancy.

**Patient identification and recruitment**

Approved study staff prescreen patients for screening and potential enrollment through a daily electronic medical record (EMR) report of risk factors for opioid use disorder that lists potentially eligible subjects (variables include demographics, opioid history, diagnoses, and screenings) and through clinician referral to the study. Upon consent from the requesting medical team (required at two of the three hospitals), study staff conduct eligibility screening. Screening is conducted in person or remotely using an approved and secure web-based data capture system (REDCap) [82] housed at the study statistics and data coordinating center (SDCC) at UNM.

**Consent, baseline and follow-up interviews, randomization**

Study staff conduct the informed consent process including reviewing the full consent form and/or the consent summary with the patient. Consent is obtained via electronic signature. All patients are given patient education materials on OUD and harm reduction. Approved study staff conduct an in-person or remote 30–40 min baseline interview. Interview data are recorded on a tablet or computer into REDCap. Each site is responsible for remunerating their participants $50 per their institutional practice. Following the baseline interview, approved study staff randomize the patient to the START or UC arm by accessing a site-specific randomization module in REDCap. Study staff randomize participants into START or UC using stratified, block randomization, stratified by site and prior MOUD exposure, and using randomly permuted block sizes of 2, 4, and 8 (all programmed into REDCap). All patients enrolled in the study receive information on OUD and MOUD, and on how and where to receive services. Enrollment is continuous with the goal of reaching the desired sample size (N = 414); some sites may enroll more or less than others. Interviewers from the RAND Corporation Survey Research Group (SRG) conduct a follow-up interview by telephone 1 month after the patient is discharged from the hospital, within a 2 month follow-up window. The UNM SDCC provides contact information to RAND SRG through secure REDCap access. The follow-up interview is 30–40 min, and RAND SRG remunerates participants $50 per each hospital’s practices. See Table 2 for SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) schedule of enrollment, interventions, and assessments.

**Measures**

**Outcome variables**

We provide our primary and secondary outcome variables and endpoints in Table 3.
MOUD, experience of chronic illness care, and opinions about the START intervention. Table 4 shows all measures and data sources for outcomes and potential covariates, mediators, and moderators.

**Intervention fidelity measures**
Fidelity to the START intervention key components (collaborative care, the brief negotiated interview, and addiction-focused discharged planning) as well as competency in using MI will be measured. Table 5 shows our fidelity and MI competency measures.

**Data safety and monitoring board (DSMB)**
The University of California Los Angeles (UCLA) Data and Safety Monitoring Board for Addiction Medicine (DSMBAM) serves as the DSMB for this study. DSMBAM members are multidisciplinary and include expertise in addiction medicine, biostatistics, basic science, epidemiology, clinical trial methodology, and biomedical ethics.

**Data management and quality control**
Data will be collected from multiple sources throughout the course of the study. All prospectively collected data will be directly entered into the UNM REDCap electronic data capture system which is administered by the UNM Clinical and Translational Science Center (CTSC). The UNM Statistics and Data Coordinating Center (SDCC) will develop electronic data collection forms of the patient interviews in REDCap. All data will be stored on UNM’s secured servers and behind their firewall. Other data sent to UNM will be transferred via SFTP following all institutional policies and executed data use agreements. The SDCC team at UNM will be responsible for data quality control, including evaluating data for adherence with the protocol and for accuracy. Site queries will occur every 2–4 weeks. Study status reports generated from the database will provide a basis for ongoing monitoring of subject accrual and retention, as well as completeness of data.

**Statistical analysis**
Baseline characteristics will be summarized with descriptive statistics including means and standard deviations or medians and interquartile ranges for continuous variables, and frequencies and percentages for categorical variables. Summaries will be presented overall, by intervention arm, and stratified by previous MOUD exposure. Continuous baseline demographics and characteristics will be compared with t tests or Wilcoxon rank sum tests, as appropriate. Categorical variables will be compared with chi-square or Fisher exact tests, as appropriate. Corresponding confidence intervals will be reported in addition to p-values. The primary and secondary analyses will be performed for the intention-to-treat population, which consists of all randomized subjects. Every effort will be made to obtain all necessary outcome and covariate data. We will use inverse probability weighting and multiple imputation to adjust for missing covariate data [83]. Specifically, we will examine whether observable baseline characteristics differ by attrition status, and if so, we will adjust our comparisons using weights. Multiple imputation will be used to impute intermittently missing data for study completers. We will not impute data for outcomes, only for covariates.

**Primary and secondary endpoint analysis**
Unadjusted point estimates and confidence intervals for proportions and means will be reported by arm and by prior MOUD use for endpoints. Primary endpoints will be compared between arms by fitting a multivariable logistic regression model to each that includes as independent variables: intervention arm, prior MOUD exposure and site, as well as relevant baseline characteristics as covariates, including age, insurance status (as a marker for income), race, and ethnicity. Additional covariates that may be included are substance use severity, homelessness, length of index hospitalization, comorbid medical and psychiatric conditions, as well as any other variables also thought to be associated with outcomes that demonstrated imbalance between treatment arms [84]. Site will be included as a fixed effect to reflect the study design and to control for potential variability in START implementation. Odds ratios and their Bonferroni-adjusted 97.5% Wald confidence intervals will be reported for the two primary endpoints. Should the prevalence of outcomes be relatively high in both arms, log-binomial or Poisson regression models will be considered with risk ratios and their 97.5% confidence intervals reported, instead [85]. Similar analyses as described for the primary endpoints will be performed for these secondary proportions outcomes, but instead reporting 95% confidence intervals. A general linearized model to number of days of opioid use will be fitted along with the covariates described for the logistic regression models. An appropriate link function will be identified and used based on the distribution of the outcome data.

**Exploratory analysis**
Mixed findings in past research of consult services suggest that sex possibly could moderate START effectiveness [86–88]. We will conduct exploratory analyses to see if patient sex or gender, as well as race/ethnicity, has an effect on primary outcomes or retention. Adjusted odds ratios and their 95% confidence intervals will be calculated from interaction effects between treatment group and sex or gender from the specified linear models for the
Table 2  SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) schedule of enrollment, interventions, and assessments

| Timepoint | Study period |
|-----------|--------------|
|           | Enrollment   | Post-enrollment |
|           | −T1          | T1             | T2             |
|           | Screening, consent | Baseline | Intervention (during hospital stay) | Intervention follow-up (post-discharge) | Follow-up interview (30–60 days post-discharge) |

| Eligibility screen | X |  |  |  |
| Informed consent | X |  |  |  |
| Randomization |  | X |  |  |

Interventions

| Intervention 1 | X | X | X | X | X |
| Control | X | X | X | X |

Assessments

| ASSIST | X |  |  |  |
| Demographics | X |  |  |  |
| MOUD utilization | X |  |  |  |
| Employment | X |  |  |  |
| Depression (PHQ-9) | X | X |  |  |
| Anxiety (GAD-7) | X |  | X |  |
| Social support (MSPSS) | X |  |  |  |
| Overdoses | X | X |  |  |
| Pain intensity and frequency (PEG) | X | X |  |  |
| 30-day opioid (and other substance) use (adapted from NSDUH) | X | X |  |  |
| SUD treatment utilization (adapted from NSDUH) | X |  |  |  |
| SUD healthcare and mental health utilization (adapted from GAIN) | X |  |  |  |
| Opinions about MOUD | X |  |  |  |
| Severity of substance use (PROMIS) | X | X |  |  |
| Patient experience of stigma | X |  |  |  |
| Significant other with OUD | X |  |  |  |
| Criminal justice involvement | X |  |  |  |
| Patient experience of chronic illness care (PACIC) |  |  | X |  |
| Therapeutic alliance (CAHPS) |  |  |  | X |
| Satisfaction with START |  |  |  | X |

* Intervention group only
primary and secondary outcome measures. To explore possible mechanisms of how START works, we will conduct the following exploratory analyses: (1) assess the mediating effect of inpatient MOUD initiation on use of MOUD and linkage with OUD treatment post-discharge; (2) assess the mediating effect of completion of an OUD-specific discharge plan on linkage with OUD treatment 30 days post-discharge; (3) assess the moderating effects of patient characteristics (e.g., gender, race, ethnicity, insurance status, comorbid conditions, prior MOUD use) on medication initiation and post-discharge linkage. We will summarize bivariate relationships between site and patient characteristics. To evaluate how these relationships may affect endpoints, we will assess the interaction effects between site and these covariates from the regression models described for the primary and secondary analyses. Additionally, of interest is time to linkage to care following discharge. A Cox proportional hazards model will be fitted to the time to linkage with intervention arm and other relevant baseline characteristics as covariates, including age, insurance status (as a marker for income), race, and ethnicity. Additional covariates identified for the primary and secondary analyses may also be included. The proportional hazards assumption will be assessed. The relative risk and 95% CI for the two arms will be reported.

**Sample size and power**

A sample size of \( n = 414 \) (allowing for 20% attrition) and adjusted type I error rate of 2.5% provides 84% power to detect an odds ratio of 2.3 comparing the inpatient MOUD initiation rates in the START and UC arms, stratified on prior MOUD use. Based on literature, 14% of UC patients who are MOUD-naïve initiate MOUD in hospital [19]. Assuming the average of MOUD-naïve and MOUD-experienced inpatient MOUD initiation rates is 20%, we have an adequate sample size and power to detect this increase in inpatient MOUD initiation in the START arm (37%) compared to UC [19, 54, 89]. We base the sample size estimate on the linkage to care measure (Primary Endpoint 2) since the probabilities of successful linkage are lower than for inpatient MOUD initiation. Linkage to care rates reported in the literature range between 10 and 17% in usual care settings. To err on the side of caution, we estimate linkage to care in UC for MOUD-naïve and MOUD-experienced to be 5% and 10% [19, 54, 89, 90], respectively, yielding an average of 7.5%. We hypothesize that at least 20% of patients randomized to the START arm will link to OUD care (attend at least one OUD-related visit) within 30 days following discharge. Assuming a Bonferroni-corrected, two-sided type I error rate of 2.5% to adjust for two primary endpoints, we will enroll a minimum of 414 patients (207 in each intervention arm) to have 80% power to detect this difference. This estimate includes an adjustment for up to 20% attrition. This effect size corresponds to a clinically meaningful odds ratio of 3.0. Prior studies in different settings have found larger effects [54, 84, 90], supporting our ability to conduct this test. Sample size calculations for the primary endpoints were performed in PASS 14 using stratified Mantel–Haenszel tests for two proportions between two groups [91], with strata defined as 50% MOUD-naïve and 50% MOUD-experienced [54, 84, 90, 92, 93]. Due to the short 1 month duration of participation, subject withdrawal from the study is not anticipated to be significant.

**Table 3 Outcome variables and endpoints**

| Outcome | Endpoint |
|---------|----------|
| Primary | In-hospital initiation of MOUD | Proportion of patients in each arm who initiate MOUD prior to discharge, defined as use of any FDA-approved pharmacotherapy for OUD, including buprenorphine, naltrexone and methadone |
|         | Linkage to follow-up OUD care | Proportion of patients in each arm who attend at least one OUD-related care visit within 30 days of hospital discharge |
| Secondary | OUD-specific discharge plan | Proportion of patients in each arm with an after-hospital care plan that specifies a date and time for a post-discharge addiction care appointment |
|         | Any post-discharge MOUD utilization | Proportion of patients in each arm who initiate MOUD or continue MOUD treatment within 30 days following hospital discharge |
|         | Post-discharge outpatient medical care | Proportion of patients in each arm who complete at least one visit to an outpatient medical provider within 30 days of hospital discharge |
|         | Past 30-day number of days with any opioid use | Mean (or median, depending on distribution) days of use in the past 30 days after hospital discharge |
The START, a collaborative care-informed consultative team, is proposed to increase adoption of evidence-based care and improve outcomes for hospitalized patients with OUD. Hospitals have extensive experience using care managers to improve in-hospital and follow-up care for several patient populations at high risk of readmission [94, 95], including acute medical patients [96], and some have a consultation service to support the medical team with patients in need of behavioral health care. More recently, addiction-focused consult teams have begun to emerge in hospitals across the United States and elsewhere [29, 31, 47, 49, 55–63]. However, patient-level randomized controlled trials are necessary to evaluate how addiction consult teams affect outcomes for hospitalized patients with OUD. The addiction consult team, along

| Variable                                         | Measure                                      | Data source                                      |
|--------------------------------------------------|----------------------------------------------|-------------------------------------------------|
| Sociodemographics                                |                                              |                                                 |
| Age, sex (assigned at birth), gender identity,  | N/A                                          | Eligibility screener                             |
| hispanic ethnicity, race, housing status        | N/A                                          | Baseline interview                               |
| Marital status, income, education and insurance  | N/A                                          | Eligibility screener                             |
| type                                             | N/A                                          |                                                 |
| Mental health status and symptoms                | N/A                                          |                                                 |
| Prior psychiatric diagnosis (bipolar disorder or  | N/A                                          |                                                 |
| schizophrenia)                                  | N/A                                          |                                                 |
| Prior psychiatric hospitalization                | PHQ-9 [106, 107], GAD-7 [108–110]            |                                                 |
| Anxiety (7 items)                                |                                              |                                                 |
| Social support                                   |                                              |                                                 |
| Social support: family, friends, significant     | Modified multidimensional scale of perceived |                                                 |
| other (6 items; 2 each scale)                    | social support [111]                         |                                                 |
| Medical symptoms/treatment                       |                                              |                                                 |
| Overdoses (lifetime, past 3 mos)                 | N/A                                          |                                                 |
| Primary and secondary diagnosis (inpatient stay) | Medical or mental health conditions as       | EMR                                             |
|                                                  | determined by the inpatient physician        |                                                 |
| Pain intensity and duration                      | PEG [112]                                    |                                                 |
| Length of hospital stay                          | Days in hospital                             | EMR                                             |
| Substance use treatment history                  |                                              |                                                 |
| Ever used MOUD; times started an MOUD; type of   | N/A                                          | Eligibility screener                             |
| MOUD; other treatment                            |                                              |                                                 |
| Recent substance use treatment utilization       | Adapted from National Survey on Drug Use and | Baseline interview (validation through follow‑up |
|                                                  | Health (NSDUH) [113]                          | with service provider)                          |
| Healthcare utilization (ER, inpatient, outpatient)| Adapted from Global Appraisal of Individual | Baseline interview                               |
| related                                          | Needs (GAIN) [114]                           | 1-month follow‑up                               |
| to SUD (5 items)                                 |                                              |                                                 |
| Opinions about MOUD                              | Adapted opinions about MAT (OAMAT) [115]     |                                                 |
| Severity of substance use                        | PROMIS                                       |                                                 |
| Patient experience of stigma                     | Adapted from Grosso et al. [116]              |                                                 |
| Patient experience of chronic illness care (11  | Patient Assessment of Chronic Illness Care   | 1-month Follow‑up                               |
| items)                                           | (PACIC) [117]                                |                                                 |
| Criminal justice involvement                     | Locally developed                            |                                                 |
| Intervention—related                             |                                              |                                                 |
| Intervention “dose”; exposure                    | Amount time spent with patient number of      |                                                 |
|                                                  | encounters with patient                      | START registry (Deidentified)                   |
| Therapeutic alliance                             | Consumer Assessment of Healthcare Providers   | 1-month follow‑up (START only)                  |
|                                                  | and Systems [CAHPS®] [118]                   |                                                 |
| Satisfaction with START intervention             | Locally developed                            | 1-month follow‑up (START only)                  |
with the evidenced-based tools and resources adapted for the START intervention, offers a novel, comprehensive approach for facilitating MOUD initiation in the hospital and linking patients to follow-up care for OUD. While other consult services described in the literature have additional professionals such as peer navigators and nurses on the team, [97, 98] we chose to test a foundational low-resource model, as many hospitals do not have the volume of patients with OUD to justify larger, more complex multidisciplinary consultation services. In future research additional models can be tested to identify core team members and components.

Our study is a multi-site, randomized pragmatic trial that will enroll patients at three diverse academic hospitals, allowing for a real-world implementation context, which will inform and potentially accelerate translation of the START into practice. Moreover, the START has potential for high impact because it can both improve public health and advance translational science. The undertreatment of OUD is an important public health and translational science problem. In 2015, 11.5 million individuals reported misusing opioids, and 1.9 million reported being addicted to opioids [99], yet fewer than 20% received any treatment [101]. By experimentally testing the effects of the START, this study could both improve public health by identifying an efficient and generalizable model to increase OUD treatment delivery and decrease the downstream effects of untreated OUD. This study can also advance translational science by identifying an effective and generalizable approach to address translational roadblocks that result in the undertreatment of substance use disorders and behavioral health conditions in hospital settings.

**Abbreviations**

AMS: Addiction medicine specialist; ASAM: American Society of Addiction Medicine; ASSIST: Alcohol, smoking, and substance involvement screening test; BMC: Baystate Medical Center; BNI: Brief Negotiated Interview; CAHPS: Consumer Assessment of Healthcare Providers and Systems; CL: Consultation liaison; CM: Care manager; CSMC: Cedars-Sinai Medical Center; DEA: Drug Enforcement Administration; FDA: Food and Drug Administration; EMR: Electronic medical record; GAD-7: General anxiety disorder-7; GAIN: Global Appraisal of Individual Needs; MAT: Medication assisted treatment; MI: Motivational interviewing; MITI: Motivational interviewing treatment integrity; MOUD: Medications for opioid use disorder; MSPSS: Multidimensional scale of perceived social support; NSDUH: National Survey on Drug Use and Health; OAMAT: Opinions about MAT; OUD: Opioid use disorder; PACIC: Patient experience of chronic illness care; PEG: Pain, enjoyment, general activity; PHQ-9: Patient health questionnaire-9; RCT: Randomized controlled trial; SDCC: Statistics and data coordinating center; SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials; SRG: Survey research group; START: Substance Use Treatment and Recovery Team; SUD: Substance use disorder; UC: Usual care; UNM: University of New Mexico.

**Acknowledgements**

We acknowledge Ninna Gudgell for her contributions to the study and manuscript. We acknowledge the START study team for their contributions to successfully executing the study.

**Author contributions**

AJO contributed to the study design and execution, intervention development, will contribute to the analysis, and drafted the manuscript. CMK contributed to the design, proposed analyses, manuscript review and revisions, and will contribute to the acquisition, analysis, and interpretation of the data. KP contributed to design, and manuscript review and revisions. PDF contributed to design, and manuscript review and revisions. SH contributed to intervention development and execution, and manuscript review and revisions. SR contributed to intervention development and execution, and manuscript review and revisions. MM contributed to study design and execution and manuscript review and revision. IL contributed to study...
design and execution and manuscript review and revision. GM contributed to intervention development and execution, and manuscript preparation, review and revision. KEW contributed to study design and manuscript review and revision. TN contributed to study design and manuscript review and revision. ID contributed to the study design and execution, intervention development, will contribute to the analysis, and drafted the manuscript with AJO. All authors read and approved the final manuscript.

Funding
Grant Number: 1U01TR002756-01A1: National Center for Advancing Translational Sciences, National Institute on Drug Abuse.

Availability of data and materials
The datasets generated and analyzed during this study are not publicly available due to the sensitive nature of the data. They can be made available from the corresponding author on reasonable request and with execution of appropriate Data Use Agreements.

Declarations

Ethics approval and consent to participate
The CSMC institutional review board (IRB) serves as the single-site IRB for the study. All patients must provide informed consent to participate.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Received: 8 April 2022   Accepted: 1 July 2022

Published online: 28 July 2022

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