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The SOMATICS collaborative: Introduction to a National Institute on Drug Abuse cooperative study of pharmacotherapy for opioid treatment in criminal justice settings

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Abstract

Background—Among the nearly 750,000 inmates in U.S. jails, 12% report using opioids regularly, 8% report use in the month prior to their offense, and 4% report use at the time of their offense. Although ample evidence exists that medications effectively treat Opiate Use Disorder (OUD) in the community, strong evidence is lacking in jail settings. The general lack of medications for OUD in jail settings may place persons suffering from OUD at high risk for relapse to drug use and overdose following release from jail.

Methods—The three study sites in this collaborative are pooling data for secondary analyses from three open-label randomized effectiveness trials comparing: (1) the initiation of extended-release naltrexone [XR-NTX] in Sites 1 and 2 and interim methadone in Site 3 with enhanced treatment-as usual (ETAU); (2) the additional benefit of patient navigation plus medications at

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Sites 2 and 3 vs. medication alone vs. ETAU. Participants are adults with OUD incarcerated in jail and transitioning to the community.

Results—We describe the rationale, specific aims, and designs of three separate studies harmonized to enhance their scientific yield to investigate how to best prevent jail inmates from relapsing to opioid use and associated problems as they transition back to the community.

Conclusions—Conducting drug abuse research during incarceration is challenging and study designs with data harmonization across different sites can increase the potential value of research to develop effective treatments for individuals in jail with OUD.

Keywords

Interim methadone; Extended-release naltrexone; Opioid relapse prevention; Jail; Criminal justice

1. Introduction and background

While the issue of the United States' large long-term prison population is widely recognized, the short-term detention of individuals in jails across the United States and associated health implications is an oft-overlooked problem. Recent data shows approximately 744,600 persons were detained in U.S. city and county jails at mid-year of 2014 [1]. These individuals struggle with numerous medical and mental health conditions and addressing their healthcare needs is an urgent public health problem [2–8].

Substance use is a common problem among this population and approximately 20–23% of those in the U.S. jail and prison system report past use of opioids [9]. Among jail inmates, 12% report using opioids regularly, 8% report use in the month prior to their offense, and 4% report use at the time of their offense [3]. Treatment for Opiate Use Disorder (OUD) is lacking in prisons and jails [4] although evidence exists that medications are effective and can be delivered in these settings [3,10]. Lack of treatment places persons suffering from OUD at high risk for relapse to drug use, overdose, and mortality immediately following release from incarceration [5,11,12].

The Studies on Medications for Addiction Treatment in Correctional Settings (SOMATICS) Collaborative, funded by the National Institute on Drug Abuse (NIDA) at the National Institutes of Health (NIH), aims to address this common but neglected health problem. The three studies from the collaborative will harmonize data to enhance scientific yield and investigate how to best prevent jail inmates from relapsing and overdosing as they transition back to the community from jail (see Table 1). Specifically, this harmonized dataset will examine whether medication initiated prior to release from jail with or without an additional behavioral intervention will reduce the likelihood of an ongoing OUD. Finally, the SOMATICS cooperative will include an economic component examining the cost, cost-effectiveness, and cost-benefit of the interventions within the three studies.

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2. Research design and study population

2.1. Study design

The SOMATICS research collaborative includes 3 research centers (RCs) each conducting an individual randomized trial while sharing one study arm with another RC and collecting several core assessments across all sites. SOMATICS RCs are conducting open-label randomized effectiveness trials comparing 1) the initiation of medication—Extended-release naltrexone ((XR-NTX) (also known as Vivitrol)–)–in Sites 1 (located in New York City) and 2 (located in Albuquerque, NM) and methadone in Site 3 (located in Baltimore, MD) vs. enhanced treatment-as-usual (ETAU); 2) the additional benefit of a behavioral intervention (patient navigators) plus medication (XR-NTX) Site 2 and methadone Site 3 vs. medication alone vs. ETAU for adults incarcerated in jail and transitioning to the community with a history of OUD. Site 1 also has a quasi-experimental methadone arm (see Table 2). The combined data from these trials will allow us to estimate the benefit of different medications alone and medication with a behavioral intervention for individuals transitioning from jail to the community under real-world conditions.

2.2. Research questions and hypotheses

The SOMATICS collaborative primary research question addresses whether the use of medication for individuals with OUD (XR-NTX or methadone) initiated prior to the release from jail, alone or in combination with a behavioral intervention (patient navigation), reduces the likelihood of an ongoing DSM-5 diagnosis for OUD. Secondary research questions will address whether medication initiated prior to release from jail, alone or in combination with a behavioral intervention, reduces the likelihood of: 1) drug use (measured by percentage of positive urine drug tests and self-report); 2) number of arrests and number of days incarcerated; 3) HIV risk behavior; 4) days in drug treatment; 5) drug craving; and 6) rates of opioid overdose. In addition, the SOMATICS collaborative will examine the cost-effectiveness and net economic benefits of these interventions relative to each other.

We hypothesize medication initiated in jail both combined with and without a behavioral treatment will have superior outcomes compared to ETAU. In addition, we hypothesize that the groups assigned to the combination of medication and patient navigation will have superior outcomes compared to medication alone or ETAU groups.

2.3. Study organization and sites

Three independently funded RCs are implementing different protocols under an NIH collaborative agreement U01 mechanism. Site 1: New York School of Medicine and Bellevue Hospital Center working in New York City Department of Corrections facilities on Rikers Island (New York, NY); Site 2: University of California Los Angeles in collaboration with Bernalillo County Metropolitan Detention Center and the University of New Mexico (Los Angeles, CA; Albuquerque, NM); Site 3: Friends Research Institute in collaboration with Maryland Division of Pretrial and Detention Services (Baltimore, MD). For detailed descriptions of each site/study's methodology, see McDonald et al., *Extended-Release Naltrexone Opioid Treatment at Jail Reentry* (*X*:*OR*) [13]; Farabee et al., *Injectable Pharmacotherapy for Opioid Use Disorders* (*IPOD*) [14]; *and* Schwartz et al., *Interim*

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Methadone and Patient Navigation in Jail: *Rationale and Design of a Randomized Clinical Effectiveness Trial* [15].

2.4. Study population and inclusion/exclusion criteria

Eligible subjects are adults (18 and older) incarcerated in jail at the time of enrollment meeting the DSM-5 criteria for Opioid Use Disorder in the past 12 months prior to incarceration. In addition, participants in the methadone study at RC 3 are detainees held for at least 48 hours on charges that if found guilty would likely result in a sentence of less than one year, while participants in the two XR-NTX studies are jail sentenced individuals with a scheduled release date. For all three studies, eligible subjects must plan to reside in the area after release, and be able to provide informed consent in English. Sites 1 and 2 have additional inclusion criteria based on the nature of the study medication (XR-NTX) requiring participants to be opioid-free at the time of enrollment and not planning to pursue opioid agonist (methadone, buprenorphine) treatment upon release. Site 3 requires subjects to be receiving opioid-withdrawal treatment as usual by medical providers (see Table 3).

Exclusion criteria are limited to maximize the likelihood of enrolling a sample representative of adults with OUD detained in jail. Exclusion criteria across all sites include: pregnancy, lactation, or planning conception; medical (e.g. liver failure, congestive heart failure) or psychiatric condition (e.g. suicidal ideation, psychosis) that would make study participation unsafe in the judgment of medical staff or the principal investigator; history of allergy to study medication (XR-NTX or methadone); and need for treatment for alcohol or sedative hypnotic withdrawal. In addition, Sites 1 and 2 exclude individuals with chronic pain prescribed or seeking treatment with opioids and Site 3 excludes individuals enrolled in methadone or buprenorphine treatment in the community at the time of arrest.

2.5. Recruitment procedures by study sites

Recruitment procedures vary by site and are dependent on site-specific requirements established by the jail and RC (see Table 3). Site 1 collaborates with the jail opioid treatment program to generate a list of potentially eligible participants from an electronic health records system, as well as distribution of flyers and business cards. Site 2 utilizes informational flyers as the main method of recruitment. Flyers are provided to inmates who are within 4 weeks of release and have been detoxified from opioid use. At Site 3 detention center medical staff refer newly-detained adults receiving opioid detoxification to speak with a Research Assistant about the study. Nurses coordinate the Research Assistant's visit for informed consent, baseline assessments, and the pre-screening medical eligibility visits with the methadone program physician.

Across the three sites, individuals reporting interest in the study to jail personnel will be referred to research staff. Research staff will provide a description of the study and move forward with the consent process including a detailed explanation of the study, risks and benefits, and that study participation is voluntary and will have no effect on a participant's sentence, jail term, probation, parole, or release.

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2.6. Informed consent

Informed consent processes for the three studies in the SOMATICS collaborative are comprised of similar activities with some site-specific variation. All three sites have an inperson meeting with potential research participants and review the detailed IRB-approved informed consent regarding the study, which includes the study's potential risks and benefits, and strictly voluntary nature of participation. Because this study involves incarcerated individuals, additional efforts are made to ensure that research participants do not feel coerced and that their refusal to participate will not impact their legal status. They are able to ask questions about the research study and their participation. Potential study participants must pass a consent quiz prior to enrollment to ensure they have a complete understanding of the research. Upon passing the quiz, the informed consent form is signed and study participants are given a copy for their records.

2.7. Screening, randomization, and follow-up procedures

Screening, randomization, and follow-up procedures vary somewhat among the three sites participating in the SOMATICS research collaborative. Generally, individuals providing written informed consent are screened for eligibility by research assistants who administer baseline assessments. Medical eligibility is determined by the medical providers following a review of medical records, physical exam, any necessary laboratory tests (including pregnancy tests), and an opioid urine screen (for the XR-NTX studies). Eligible participants are randomly assigned to study arms by the research assistants using either an onsite urn randomization program or consecutive pre-numbered, opaque envelopes containing treatment assignments based on a random number generator. Sites 2 and 3 do not provide incentives for study participation during incarceration; Site 1 deposits $20 per visit for two jail visits in the inmates commissary account while incarcerated, or provided as cash upon arrival for the first post-release community follow-up assessment. As stated earlier, all sites provide all study participants with a drug-education handout with direct referrals to local reentry community drug treatment programs and information on overdose prevention. Research participants are randomized to intervention groups 1:1 for comparing XR-NTX and ETAU (Site 1).). In the studies testing XR–NTX, XR-NTX + IM, and ETAU (Site 2) and IM, IM + PN, and ETAU (Site 3) participants are randomized 1;1;1. All studies conduct follow-up assessments at 3, 6, 9, and 12 months post-release.

3. Data management

Data for the SOMATICS collaborative are collected by research assistants on standardized case report forms (CRF). Baseline data in the jails are collected on paper teleforms (with participant study ID number and no other identifier) due to lack of internet connection and are subsequently uploaded as PDFs to the Data Management Center at UCLA. Follow-up interviews are entered directly into a web-based data entry system supported through the Research Electronic Data Capture (RED-Cap) system [6]. Specific information on the collection of follow-up data can be found in McDonald, Farabee and Schwartz [13–15].

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4. Regulatory affairs and data and safety monitoring

4.1. Approvals and certifications

Each of the SOMATICS studies were approved by site specific Institutional Review Boards (IRB) located at NYU, UCLA, and the Friends' Research Institute. In addition, the US Office of Human Research Protections approved study protocols and agreed with IRB determinations that the research was being conducted with prisoners in accordance with 44 CFR 46.3069(a)(2)(iv). Each study has been registered with ClinicalTrials.gov and received individual clinical trials registration numbers (see Table 1). Finally, federal Certificates of Confidentiality were obtained for each study to ensure protection of research participant data.

4.2. Data and safety monitoring

A single Data and Safety Monitoring Board located at the University of California Los Angeles' Integrated Substance Abuse Programs monitors the studies involved in the SOMATICS research collaborative. The research team and IRB at each individual site monitor recruitment, retention, and safety outcomes for their specific protocol. The University of California Los Angeles' Integrated Substance Abuse Programs Data and Safety Monitoring Board monitors accrual and adverse events across all sites as part of the SOMATICS protocol. Adverse Events and Serious Adverse Events are logged sequentially by each research site including a determination of whether they are related to the medication or psychosocial intervention tested. Serious Adverse Events are reported by each site to their own Internal Review Board, the Data and Safety Monitoring Board, and the study sponsor (NIDA). Medication-related AEs for XR-NTX are reported to the drug manufacturer.

5. Study treatments

5.1. XR-NTX injection visits

Research participants enrolled and randomized in the two studies to receive XR-NTX receive the first injection within the week of their scheduled release to maximize the time the medication is active post-release. Prior to receiving XR-NTX participants must self-report no recent opioid use (last 7 days), provide an opioid (buprenorphine, oxycodone, methadone, opiates) negative urine sample, and only then undergo a challenge consisting of 0.8 mg or more of naloxone. If the participant is opioid-free and the confirmatory naloxone challenge is negative, a single 380 mg XR-NTX is administered intramuscularly by the study clinician. XR-NTX injections are continued every 3–4 weeks during the 6-month treatment phase for a total of 6 injections (every 3 weeks in the case of significant cravings or opioid use, per clinician's discretion). Research staff arrange transfer to community based treatment providers upon release at both sites providing XR-NTX. Research participants receive information about how and where they will receive community based treatment upon release. XR-NTX is administered pre and post jail by research study staff. At the conclusion of the active treatment phase, participants will be followed for an additional 4 weeks and 12 months to gather data on immediate post treatment outcomes including opioid relapse, AEs, and other treatment participation. Participants are provided with appropriate aftercare referrals prior to the discontinuation of study XR-NTX, which may include continued non-

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study naltrexone treatment in the community. All XR-NTX medication was donated by Alkermes, Inc.

Medical management counseling is provided to participants receiving XR-NTX, as is information on anticipated side effects, community-based resources for recovery support and treatment, and relapse and overdose risk-reduction counseling.

5.2. XR-NTX injection visits and patient navigation

In addition to receiving XR-NTX with medical management participants randomized to this treatment will also receive the patient navigation (PN) psychosocial intervention. PNs provide assistance on an individual basis to aid participants in dealing with barriers to engaging into and adhering to drug abuse treatment. This strengths-based case management model assists participants with a variety of activities including scheduling appointments, transportation, appointment reminders, assistance with insurance and other medical forms, and other social support needs [17]. The PN intervention is provided to research participants for three months on an as needed basis. Most participate in weekly sessions for the first month and less frequently thereafter. PNs are individuals recruited and hired by study staff to provide the intervention to participants. Selection is based on a number of factors including education and prior experience working with individuals struggling with addiction. Detailed information about the PN intervention can be found in Schwartz [15] and Farabee [14]. PN will be tested as an adjunct to XR-NTX at RC 2 [14] and an adjunct to interim methadone at RC 3 [15]. One SOMATICS site (RC 1) will not use PN [13].

5.3. Interim methadone

Interim methadone (IM) will be tested at one site. IM refers to providing methadone without routine counseling and has been shown to be an effective approach to assist opioid-dependent individuals reduce heroin use when counseling services are not routinely available [18–20]. Because the medication is effective and counseling is often not available in jails, IM is being studied as a potentially practical approach to engaging newly-arrested individuals who may experience withdrawal. Participants randomized to this condition will receive a gradual dose induction of methadone administered under direct observation through the jail-based methadone treatment program which, except for the present study, only provides continued methadone for individuals who are in treatment programs at the time of detention. Methadone will be provided until their release to the community, unless a request is made to discontinue treatment or the individual is transferred to another facility. If methadone is discontinued, participants will undergo a gradual dose reduction under medical supervision. Upon release, nurses at the jail-based methadone program arrange transfer for ongoing treatment to one of four community methadone programs of the research participant’s choice which have existing resources in the form of grants, Medicaid, or both. Research participants are encouraged to report for an appointment the next day to receive methadone and complete the process of formally enrolling into that program. More detailed information regarding IM can be found in Schwartz et al. [15].

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5.4. Interim methadone and patient navigation

IM participants randomly assigned to PN will receive the same PN psychosocial intervention described above in Section 5.2.

5.5. Enhanced treatment as usual

The enhanced treatment-as-usual (ETAU) condition will be offered to participants randomized to this intervention across all studies of the SOMATICS collaborative. This condition consists of one brief in-person counseling session centered on overdose protection and post-release drug abuse treatment resources. This intervention does not utilize any medication assisted treatment. A handout will be reviewed and provided to participants in this condition prior to release, providing information on local community-based treatment and recovery support services, risk and symptoms of relapse to opioid use upon release from jail, and overdose prevention information. This brief interaction exceeds the standard jail release procedures across the three sites and provides a direct health benefit to individuals participating in the research regardless of assignment to treatment arm in accordance with Department of Health and Human Services prisoner research standards.

6. Assessments

6.1. Primary outcome

The primary outcome for the SOMATICS research collaborative is: active DSM-5 OUD Diagnosis during the past 30 days. This will be collected using a modified Composite International Diagnostic Interview (CIDI) 2 Substance Abuse Module [21] that will be administered at the 6-month post-release assessment.

6.2. Secondary outcomes

Secondary outcomes include (see Table 3):

1. *Illicit opioid use*: measured by urine drug testing results at 6 months post-release.
2. *Number of days incarcerated*: Measured by self-report during the 6 months post-release.
3. *HIV risk behavior*: Measured by self-report (*HIV Risk Assessment Battery* [*RAB*] *Needle Use score*) [22] at the 6-month post-release follow-up assessment.
4. *Number of days of Opioids*, *Cocaine*, *Alcohol*, *Benzodiazepines*, *and/or IV Drug Use*: Measured by Time Line Follow Back techniques at 6 months post-release follow-up [23].
5. *Non-opioid drug use* (Cocaine, Amphetamines, and Benzodiazepines): measured by urine drug testing at 6 months post-release.
6. *Number of days in any drug abuse treatment*: Measured by self-report at 6 months post-release.
7. *Number of arrests and type of offense*: Measured by self-report data collected at 6 months post-release.

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8. *Craving scores* (*for NYU and UCLA sites only*): Measured by self-report craving scale at 6 months post-release.
9. *Non-lethal overdose* (*Yes*/*No*): Measured by self-report during the 6 months post-release.
10. *Lethal overdose* (Yes/No): Measured by public records data reviewed at 6 months post release.
11. *WHO Quality of Life-BREF* (*WHOQOL-BREF*) *score* [24]: Measured by self-report at 6 months post-release.

7. Statistical analysis

7.1. Statistical analysis of the primary outcome measure

7.1.1. Primary outcome measure—The primary outcome measure is the DSM-5 diagnosis of OUD at 6 months post-treatment (see Section 6.1 Primary outcome), which is a binary indicator.

7.1.2. Statistical method for the primary outcome measure—A mixed effects logistic regression will be utilized to model the first primary outcome measure using a logit link function, with two levels in the model: within sites and between sites. SAS GLIMMIX will be used to conduct all inferential analyses.

7.1.3. Structure of the model—The model will include treatment, and the baseline covariates age, gender, stimulant (number of days of cocaine and/or methamphetamine use) as fixed effects and study site as a random effect. Four indicator variables will identify which or the five treatments that a participant has received.

7.1.4. Primary contrast—The primary contrast is a comparison of the probability of a DSM-5 OUD Diagnosis at 6-month assessment for those participants on medication versus those participants receiving ETAU: [1] Primary: (XR-NTX or IM) medication only versus ETAU.

This will be a single-degree-of-freedom contrast of the XR-NTX and ETAU conditions from Sites 1 and 2, pooled, versus the Interim Methadone and ETAU conditions from Site 3, pooled. The medication plus PN treatment arms will not be included in the contrast.

7.1.5. Missing data for the primary outcome measure—Missing scores on the primary outcome measure will be deemed to be positive.

7.2. Statistical analysis of secondary outcome measures

7.2.1. Secondary outcomes measures—Secondary outcomes are those variables that are measured on a single occasion at 6 months (e.g., illicit opioid use measured by urine drug testing results at 6 months post-release), (see Section 6.2 Secondary outcomes). All binary outcomes will be assumed to follow a binomial distribution, while discrete random variables will be assumed to follow a Poisson distribution. Continuous outcomes (e.g.,

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craving scores, HIV risk behavior) will be assumed to follow a normal distribution or will be transformed as appropriate. In choosing a transformation, preference will be given to those that permit clinical interpretation of the transformed measure. Binary and Poisson variables will be examined for under- or over-dispersion in the logistic and Poisson regression analyses using the usual regression diagnostics which may lead to the use of, zero-inflated Poisson or negative binomial models.

7.2.2. Structure of the model for the secondary outcome measures—The statistical model will be the same as that described for the primary outcome (see Section 7.1.3 Structure of the model).

7.2.3. Statistical methods—Estimation and tests of significance for binary outcomes will utilize the method described for the primary outcome measure (Section 7.1.2 Statistical method for the primary outcome measure). The Poisson regression models will use a natural log link function and maximum likelihood estimation. An overall asymptotic chi-square test of the model will be computed based on deviance, which is similar to the ANOVA F-test.

7.2.4. Missing data—Missing urine results will be deemed to be positive. Multiple imputation using a Markov chain Monte Carlo (MCMC) method will be used to estimate missing data for the outcomes assumed to follow the Poisson and normal distributions. Estimation of missing data will be conditional based on information from covariates, but not site or treatment condition.

7.3. Additional treatment contrasts conditional on the results of the analysis of the primary outcome measure

The primary contrast is described above (*see* Section 7.1.4 Primary contrast of interest). The following four single-degree-of-freedom contrasts are planned (see Section 7.4 Closed testing approach, below).

[2] (XR-NTX or IM) + PN versus (XR-NTX or IM).

[3] (XR-NTX minus ETAU) versus (IM minus ETAU).

[4] (XR-NTX + PN minus ETAU) versus (IM + PN minus ETAU).

[5] (XR-NTX + PN minus XR-NTX) versus (IM + PN minus IM).

7.4. Closed testing approach

We will use closed testing, also known as a fixed sequence testing procedure, to test serially the null hypotheses, in the order listed above. To protect the familywise error rate at 0.05, each test will be performed using a two-sided 0.05 alpha level test until the first failure to reject the null hypothesis. At this point the formal testing procedure will be terminated [25,26]. The remaining tests will be performed but the corresponding significance levels will not be interpreted as valid.

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7.5. Economic analysis

The aim of the economic component of the SOMATICS Cooperative is to conduct cost, cost-effectiveness, and cost-benefit analyses of the randomized clinical trials described above. The economic study will be conducted from the provider perspective. To estimate costs, we will use a modified Substance Abuse Services Cost Analysis Program [27] questionnaire to collect activity-level resource use and cost data. Using these data, we will derive provider cost estimates for each of the interventions following an activity-based approach that will allow us to de-rive estimates at the service-level for each participant. The total provider cost for each of the interventions will be the sum of [1] staff labor costs (e.g., time spent performing intervention activities) [2], costs of building space [3], costs of any equipment [4], costs of medication [5]; costs of any supplies or materials, and [6] costs of any other miscellaneous resources used in the intervention. Results of the cost analyses at each RC will be summarized as total intervention costs and mean cost per participant.

The cost effectiveness methodology to be used for this study follows the standard approach described in the literature [28–30]. Following the contrasts outlined in Section 7.2, we will compare differences in provider costs and client outcomes in each treatment condition relative to the alternatives and produce incremental cost effectiveness ratios. This method entails tabulating the costs and effectiveness measures for each intervention under study in increasing order of cost (or effectiveness). Starting with the intervention with the smallest cost (or effectiveness), incremental cost-effectiveness ratios are then computed for each intervention relative to the next most expensive option after eliminating intervention options that are dominated by other interventions [29]. An intervention may be either strictly dominated (higher cost and lower effectiveness than another option) or weakly dominated (higher cost-effectiveness ratio than a more effective option). Three outcomes will be the primary focus of the cost-effectiveness analysis [1]: the percentage of days abstinent from opioid use) [2]; the percentage of days not incarcerated; and [3] the proportion of participants not engaging in HIV-related risk behavior.

Finally, we also will estimate the economic benefits associated with each of the treatment conditions in terms of reductions in criminal activity and criminal justice system costs, improved employment, and reduced health care use (e.g., ER visits, hospitalizations). These outcomes are measured through patient self-reports of health care utilization, arrests, and employment status assessed at baseline and post-treatment. Dara are collected using a set of questions drawn from the Economic Form 90 and modified set of Form 90 instruments collecting self-reported alcohol use and economic outcome data for alcohol treatment studies [31–34]. The primary objectives of the benefit analysis are to convert these outcomes into dollar equivalents using monetary conversion factors, and estimate the interventions' economic benefits. The difference between economic benefits and intervention treatment cost for each treatment condition represents its net economic benefits (or cost savings). Net economic benefits can be compared across treatment conditions and with other treatment alternatives or social programs.

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7.6. Exploratory analyses

Other measures involving time-to-event variables, such as time-to-relapse (as defined by 7 days of consecutive use OR 2 consecutive positive urines OR an opioid detox admission), may be examined for the studies involving XR-NTX. In this event the model will include the same factors as in the analysis of the primary outcome in a Cox proportional hazards regression model. The proportionality of the relative hazard assumption will be examined via the treatment-by-time interaction term. An asymptotic 95% Confidence Interval for the hazard ratio of the difference between the treatment arms in time-to-relapse will be constructed. A further analysis of between group differences in time-to-relapse will be based on a "cure model." This statistical strategy is designed to disentangle the issue of estimating the survival distribution of time-to-relapse when there are participants who do not relapse (at least during the study). A cure model takes the form $H(t) = (1 - p) + pS(t)$; where $H(t)$ is the survival distribution, p is the probability of relapse and $S(t)$ is the survival distribution of time-to-relapse, conditional on relapse occurring [29,35]. The parameters will be estimated based both on Kaplan Meier methods and parametrically. The equality of the values of p for the two treatment arms will be tested using a non-parametric likelihood ratio test. For the parametric test, a logistic regression analysis will be used to model p and a Weibull survival distribution will be used to model time-to-relapse, $S(t)$. Both analyses allow the use of covariates. In all analyses, the assumptions underlying the application of all the statistical methods that are used will be examined, principally through examination of standardized residuals, influence diagnostics, and graphical displays.

7.7. Sample size, power, and effect size

Each study in the SOMATICS research collaborative calculated the sample size needed to determine a statistical difference between randomized study arms. More information on sample size calculations and effect size can be found at McDonald, et al., *Extended-Release Naltrexone Opioid Treatment at Jail-Reentry* (*XOR*) [13]; Farabee, *Injectable Pharmacotherapy for Opioid Use Disorder* (*IPOD*) [14]; *and* Schwartz, *Interim Methadone and Patient Navigation in Jail*: *Rationale and Design of a Randomized Clinical Effectiveness Trial* [15].

We project 620 persons will be randomized in the five treatment conditions being tested: XR-NTX 170×; XR-NTXX plus PN 50; IM 100, IM plus PN 100, ETAU 235. An additional quasi-experimental non-randomized comparison cohort at the New York Site plans to enroll 85 participants newly enrolling in methadone maintenance, which is standard treatment available to detainees and sentenced inmates in NYC jails. As descried above, SOMATICS collaborative will be examining differences in outcomes among treatment conditions between medication alone (n = 235), medication plus a psychosocial intervention (n = 150) and ETAU (n = 235), with some exploratory analyses including the methadone group (n = 85).

8. Results

All three studies are actively recruiting participants. Recruitment began in June 2014 for Site 1, in August 2015 for Site 2, and in December 2014 for Site 3. Enrollment and follow-up is

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expected to continue until May 2018 for all sites. As of February 2016, 161 participants have been consented and 134 randomized to study conditions across the sites.

9. Discussion

Individuals suffering from OUD are at particularly high risk for relapse, re-incarceration, overdose, and death after release from jail [5]. Many individuals relapse to drug use within the first few days of release to the community [5,25]and the risk of death from overdose of opioids is 13 times greater than individuals of similar demographic background living in the community [5]. Despite the urgent need to address the use of opiates, city and county jails have no mandate to provide drug abuse services to individuals detained in their facilities. The lack of treatment services forces those using illicit opioids and often even patients participating in methadone or buprenorphine treatment at the time of arrest into uncomfortable opioid withdrawal. Lack of referral to community-based drug treatment leaves these individuals vulnerable to relapse and overdose upon release.

The SOMATICS research collaborative aims to address this problem by developing and testing approaches to provide effective treatment to individuals in jail for OUD, including on-going care following release to the community. Harmonizing three independent studies will maximize scientific yield providing a larger more diverse sample of research participants to determine the effectiveness of medication alone, medication with an additional psychosocial intervention, or enhanced treatment as usual in reducing drug use, overdose, and death.

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Table 1

SOMATICS collaborative sites and investigators.

Site number	ClinicalTrials.Gov number	NIH grant number	PI(s)	Institute(s)	Jail setting
1	NCT01999946	U01 DA033336	Joshua D. Lee, MD MSc	New York University	Riker's Island, New York City
2	NCT02110264	U01 DA034743	David Farabee, Ph.D. Timothy Condon, Ph.D.	University of California, Los Angeles University of New Mexico	Bernalillo County Metropolitan Detention Center, Albuquerque
3	NCT02334215	U01 DA013636	Robert P. Schwartz, M.D.	Friends Research Institute	Baltimore City Pretrial and Detention Services

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Table 2

SOMATICS collaborative treatment arms by site.

Site	Interventions			
	Medication	**Medication and PN**	**ETAU**	**Totals**
Site 1 New York City[a]	XR-NTX n = 85	–	85	170
Site 2 Albuquerque	XR-NTX n = 50	n = 50	50	150
Site 3 Baltimore	IM n = 100	n = 100	100	300
Totals	235	150	235	620

[a]New York site also includes a non-randomized quasi-experimental methadone treatment arm (n = 85); IM = Interim Methadone; PN = Patient Navigation; ETAU = Enhanced Treatment-as-usual.

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Table 3

SOMATICS collaborative outcomes and inclusion criteria.

	New York	Albuquerque	Baltimore
Primary outcome	Active DSM-5 OUD Diagnosis during the 30 days prior to the 6 months post jail release follow-up assessment measured by a modified Composite International Diagnostic Interview (CIDI) 2 Substance Abuse Module [21].		
Secondary outcomes (all sites)	1. Illicit opioid use: measured by urine drug testing results at 6 months post-release 2. Number of days incarcerated: Measured by self-report during the 6 months post-release 3. HIV risk behavior: Measured by self-report (HIV Risk Assessment Battery [RAB] Needle Use score) [22] at the 6-month post-release follow-up assessment. 4. Number of days of Opioids, Cocaine, Alcohol, Benzodiazepines, and/or IV Drug Use: Measured by Time Line Follow Back [23] techniques at 6 months post-release follow-up. 5. Non-opioid drug use (Cocaine, Amphetamines, and Benzodiazepines): measured by urine drug testing at 6 months post-release 6. Number of days in any drug abuse treatment: Measured by self-report at 6 months post-release 7. Number of arrests: Measured by self-report data collected at 6 months post-release 8. Non-lethal overdose (Yes/No): Measured by self-report during the 6 months post-release 9. Lethal overdose (Yes/No): Measured by public records data reviewed at 6 months post release 10. WHO Quality of Life-BREF (WHOQOL-BREF) [24] score: Measured by self-report at 6 months post-release 11. Analyses of above self-same outcomes at 12 months follow-up		
Secondary outcomes (site specific)	Craving scores (for NYU and UCLA sites only): Measured by self-report craving scale at 6 months post-release	Craving scores (for NYU and UCLA sites only) Measured by self-report craving scale at 6 months post-release	
Inclusion criteria (all sites)	• 18 years old • Incarcerated at enrollment • DSM-5 Opioid Use Disorder • Able to provide informed consent in English • Plan to reside in the area after release		
(Site specific)	• Have a scheduled release date • Opioid-free at the time of enrollment • Not planning to pursue opioid agonist treatment upon release	• Have a scheduled release date • Opioid-free at the time of enrollment Not planning to pursue opioid agonist treatment upon release	• Held for at least 48 h on charges that if found guilty would likely result in a sentence of less than one year • Receiving opioid-withdrawal treatment as usual by medical providers
Follow-up months from release (all sites)	1, 3, 6, 12		
HIV status at baseline (site specific)	• No testing at baseline • Site will download known HIV status of enrolled patients from the jail's records • For those without a recent test, self-report is collected • Status is not an exclusion criterion	• Site tests at baseline • Status is not an exclusion criterion	• No testing at baseline • Status is not an exclusion criterion