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Injectable pharmacotherapy for opioid use disorders (IPOD)

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ABSTRACT

Background: Despite the growing prevalence of opioid use among offenders, pharmacotherapy remains an underused treatment approach in correctional settings. The aim of this 4-year trial is to assess the clinical utility, effectiveness, and cost implications of extended-release naltrexone (XR-NTX, Vivitrol®; Alkermes Inc.) alone and in conjunction with patient navigation for jail inmates with opioid use disorder (OUD).
Methods: Opioid-dependent inmates will be randomly assigned to one of three treatment conditions before being released to the community to include: 1) XR-NTX only; 2) XR-NTX plus patient navigation (PN), and 3) enhanced treatment-as-usual (ETAU) with drug education and a community treatment referral. Before release from jail, participants in the XR-NTX and XR-NTX plus PN conditions will receive their first XR-NTX injection. Those in the XR-NTX plus PN condition also will meet with a patient navigator. Participants in both XR-NTX conditions will be scheduled for medical management sessions twice monthly for months 1–3, monthly medical management sessions for months 4–6, with monthly injections for 5 months post-release (which, given the pre-release injection, results in a 6-month medication phase). Follow-up data collection will occur at 1, 3, 6, and 12 months post release.
Results: We discuss the study's rationale, aims, methods, and anticipated findings. The primary outcome is the presence of a DSM 5 OUD diagnosis 1 year after randomization (6 months after the end of the active treatment phase).
Discussion: We hypothesize that providing XR-NTX prior to release from jail will be particularly beneficial for this extremely high-risk population by reducing opioid use, associated criminal behavior, and injection-related disease risk.
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1. Introduction and background

In a given year, a quarter of all people in the United States who have HIV, a third who have HCV infection, and more than 40% who have tuberculosis disease will pass through a correctional facility that same year [1,2]. Likewise, the risk of death among parolees during the first two weeks following release from prison is nearly 13 times greater than those of similar demographic background—with drug overdose being the leading cause [3,4]. As dire as this finding is, it may be an underestimate of the problem. A study of newly released prisoners in England and Wales found that mortality rates among males were 29 times higher than the general population during the first two weeks of release [5].

The efficacy of naltrexone in the treatment of opioid dependence has been well established. Naltrexone, an opioid receptor antagonist, blocks the euphoric effects of heroin and other opioids. This characteristic has fostered growing acceptance of naltrexone by correctional authorities who prefer not to provide opioid agonist treatment with medications such as methadone or buprenorphine [6]. However, it is typically taken orally on a daily basis, making adherence a problem among all but the most committed patients. Cornish et al. [7] randomly assigned federal probationers to a 6-month program of probation plus naltrexone and brief drug counseling or to probation plus counseling alone and found that opioid use was significantly lower in the naltrexone group, with the mean percent of opioid positive urine tests among the naltrexone subjects at 8%, versus 30% for control subjects ($p < 0.05$). Likewise, 56% of the controls and 26% of the naltrexone group ($p < 0.05$) had their probation status revoked within the 6-month study period and were returned to prison. But treatment compliance was a problem, with only 52% of subjects in the naltrexone group continuing on medication for the 6-months duration of the study.

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Still, the effectiveness of oral naltrexone is mitigated by poor compliance, hampering clinical utility in real-world settings. In one study of a prison-based naltrexone program, only 7% of the enrolled patients remained in treatment for six months [8]. To address the issue of poor adherence, extended-release naltrexone (XR-NTX, Vivitrol® with 380 mg naltrexone delivered intramuscularly every four weeks; Alkermes, Inc.) was developed to provide long-acting pharmacotherapy for one month per dose. The purpose of this proposed study is to assess the relative effects and economic impact of this pharmacotherapy with and without a patient navigator (XR-NTX, XR-NTX plus PN) and compared to an enhanced treatment-as-usual (ETAU) condition consisting of drug eduction, overdose prevention information, and referral to community-based treatment for sentenced jail inmates.

This study is part of the Studies of Medications for Addiction Treatment in Correctional Settings (SOMATICS) project, a National Institute on Drug Abuse cooperative study that examines approaches to delivering FDA-approved pharmacotherapies to recently arrested adults with opioid dependence. The other two studies, focusing on interim methadone (Friends Research, Inc.) and XR-NTX (New York University), are described elsewhere in this issue.

2. Research design and study population

2.1. Overview of study design

The proposed four-year study is a randomized, open-label trial that will examine feasibility, efficacy, and economic impact of a depot, extended-release medication for opioid use disorders, alone or in conjunction with PN, and an ETAU condition with drug and overdose prevention information and referral to community treatment receiving no medication. Participants in the XR-NTX and XR-NTX plus PN groups will receive standard medical management. Before discharge from jail, participants randomized to one of two medication conditions receive XR-NTX and then receive subsequent injections every four weeks for 5 additional months. Those in the XR-NTX plus PN condition will meet with a PN before discharge and regularly (weekly in the first month; biweekly in months 2–3) after release to discuss barriers to treatment, possible treatment program participation following release, and will address social support and other participant needs. Before discharge, the ETAU condition group will participate in one session designed to provide a presentation and discussion of drug-related issues and receive a referral to treatment in the community. Following release from jail, all participants in the medication conditions will receive phone calls from the study team to schedule medical management appointments to occur twice monthly for the first 3 months after release then monthly for the last 3 months of the intervention phase for medical management and to complete assessments (see Fig. 1).

2.2. Duration of study and clinic visit schedule

The duration of this study will include a projected 2–4 weeks for screening/baseline assessments and medication induction before release from jail, and a 24-week intervention phase to include, specific to assigned condition, XR-NTX, PN, drug and overdose education and referral, assessments, and medical management (for participants in the XR-NTX conditions). The screening phase will differ in the length of time needed to complete eligibility assessments, random assignment, and to complete medication induction in the XR-NTX conditions. Induction will be scheduled to occur within the 4 weeks prior to discharge. Screening assessments will include the collection of laboratory samples and medical assessments to ensure participant safety, including confirmation of opioid-free status (urine drug screen [UDS] and naloxone challenge). Assessment visits at 1, 3, 6, and 12-months will take about 30–60 min, depending on the scheduled assessments. Medical management visits will last from 20–60 min and will include collection of urine specimens and other short measures of status and well-being. PN sessions are expected to take about 60 min. Drug education (DE) sessions will take about 20 min.

2.3. Study population

Participants will be 150 males and females sentenced jail inmates meeting DSM-5 criteria for opioid use disorders who are 18 years and older, have been detoxified from opioids in the Bernalillo County Metropolitan Detention Center and meet eligibility criteria.

2.3.1. Inclusion criteria

Study participants *must*:

1. Be at least 18 years of age or older,
2. Meet criteria for DSM-5 opioid use disorders,
3. Be detained for at least 48 h,
4. Have an expected release date within one year,
5. Plan to reside in area after release,
6. Have at least one instance of relapse to opioid use after a period of abstinence.

2.3.2. Exclusion criteria

Study participants *must not*:

1. Have a medical (e.g., liver failure, congestive heart failure) or psychiatric condition (e.g., suicidal ideation, psychosis) that would make participation unsafe in the judgment of the medical staff or the PI,
2. Have chronic pain and are currently or have plans to undergo pain treatment/therapy,
3. Have known sensitivity to naltrexone or naloxone,
4. Have participated in an investigational drug study within the past 30 days prior to screening,
5. Be a nursing or pregnant female, or not agree to use a medically acceptable form of birth control such as oral contraceptives, barrier (diaphragm or condom), levonorgestrel implant, intra-uterine progesterone contraceptives system, medroxyprogesterone acetate contraceptive injection, or complete abstinence. Females who become pregnant during the course of the study will be withdrawn from the study and, if requested, will be provided with referrals for drug treatment and/or medical care,
6. Have any pending legal action that could prohibit continued participation for the 24-week intervention period of the study, such as legal proceedings that could possibly result in incarceration,
7. Have a current pattern of alcohol, benzodiazepine, or other depressant or sedative hypnotic use, as determined by the study physician, which would preclude safe participation in the study.

2.3.3. Participant recruitment

Recruitment will occur through a close collaboration with jail staff, combined with IRB-approved presentations and posted announcements in the jail facilities and will proceed until 150 participants are recruited, consented, and randomized. Given the potential recruitment pool of more than 80 individuals per month, it is expected that an average of 6–8 individuals will be randomized per month across the 20-month enrollment period. Based on prior evidence in similar trials, refusals and early (pre-randomization) dropouts will account for approximately 20% of individuals presenting for screening. We expected that a baseline sample of 150 participants with 50 participants per condition would yield a final aggregate sample of approximately 120 participants, assuming 10–20% dropout. (Our similar studies have had 85–90% follow-up rates.) Thus, a final evaluable sample size of 120 participants would permit detection of a medium-large effect size (~0.60) between conditions for some of the outcome variables (at ~0.70 power) and 0.5 effect size (at 0.80 power) for others.

Recruitment plans include careful attention to the issue of voluntariness. All jail and study staff will be extensively trained on this issue to ensure that their actions and words do not convey any level of coercion.