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Design and methods of a double blind randomized placebo-controlled trial of extended-release naltrexone for HIV-infected, opioid dependent prisoners and jail detainees who are transitioning to the community

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ABSTRACT

Background: People with opioid dependence and HIV are concentrated within criminal justice settings (CJS). Upon release, however, drug relapse is common and contributes to poor HIV treatment outcomes, increased HIV transmission risk, reincarceration and mortality. Extended-release naltrexone (XR-NTX) is an evidence-based treatment for opioid dependence, yet is not routinely available for CJS populations.
Methods: A randomized, double-blind, placebo-controlled trial of XR-NTX for HIV-infected inmates transitioning from correctional to community settings is underway to assess its impact on HIV and opioid-relapse outcomes.
Results: We describe the methods and early acceptability of this trial. In addition we provide protocol details to safely administer XR-NTX near community release and describe logistical implementation issues identified. Study acceptability was modest, with 132 (66%) persons who consented to participate from 199 total referrals. Overall, 79% of the participants had previously received opioid agonist treatment before this incarceration. Thus far, 65 (49%) of those agreeing to participate in the trial have initiated XR-NTX or placebo. Of the 134 referred patients who ultimately did not receive a first injection, the main reasons included a preference for an alternative opioid agonist treatment (37%), being ineligible (32%), not yet released (10%), and lost upon release before receiving their injection (14%).
Conclusions: Study findings should provide high internal validity about HIV and opioid treatment outcomes for HIV-infected prisoners transitioning to the community. The large number of patients

Abbreviations: SUDs, substance use disorders; CJS, criminal justice system; cART, combination antiretroviral treatment; CD4, CD4+ T lymphocyte; VS, viral suppression; MMT, methadone; BMT, buprenorphine; NTX, naltrexone; XR-NTX, extended-release naltrexone; MAT, medication assisted therapy; NIDA, National Institute on Drug Abuse; NIH, National Institute of Health; STTR, seek, test, treat and retain; RCT, Randomized Control Trial; IRB, Internal Review Board; CTDOC, Connecticut Department of Correction; HCCC, Hampden County Correctional Center; OHRP, Office of Human Research Protections; CoC, Certificate of Confidentiality; ITT, intention-to-treat; IDN, Infectious Disease Nurse; ROI, release of information; RA, Research Assistant; MINI, Mini International Neuropsychiatric Interview; AUDIT, Alcohol Use Disorders Identification Test; SAFTEE, Systemic Assessment For Treatment Emergent Effects Intervention; CASI, computer-assisted survey; IDS, Investigational Drug Service; CR, Clinician Researcher; LFT, liver function test; COWS, clinical opioid withdrawal scale; MM, Medical Management.

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who ultimately did not receive the study medication may raise external validity concerns due to XR-NTX acceptability and interest in opioid agonist treatments.
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1. Introduction

The dramatic growth in the U.S. inmate population over the last three decades has resulted from the increased detention of individuals for drug-related offenses and recidivist offenders. As a result, those with substance use disorders (SUDs) with or at risk for HIV infection are concentrated within the criminal justice system (CJS). The prevalence of HIV and AIDS is 3- and 4-fold greater, respectively, among incarcerated persons compared to the general population [1,2]. In 2004, the U.S. Department of Justice reported that 53% of state prisoners met DSM-IV criteria for drug abuse or dependence, 56% reported regular use in the month prior to their offence, specifically, 13.1% reported using heroin and opiates [3,4]. In a study conducted in CT, among HIV-infected prisoners with SUDs, 61% met criteria for opioid dependence [5–8].

The revolving door of prisons and jails results in 12 million people being released annually to communities, oftentimes with undiagnosed or untreated medical conditions [9]; including one-sixth of the nearly 1.2 million people living with HIV/AIDS (PLWH) [2]. Though HIV-infected prisoners markedly reduce HIV-1 RNA levels and achieve markedly high levels viral suppression (VS) during incarceration due to the availability of combination antiretroviral therapy (cART) and the structure of the facilities [10–12], these benefits are lost soon after release [10,13,14], especially due to drug and alcohol relapse [15], especially heroin. The negative consequences of opioid relapse for HIV-infected patients include poor retention in care [14,16–18], cART adherence [5,6] and increased recidivism to prison/jail [19,20]. This is in addition to the increased early mortality risk upon release [21–27], mostly associated with opioid overdose [22,25–27], affirms the need for evidence-based transitional interventions.

According to the International Association of Physicians in AIDS Care (IAPAC) guidelines, only directly administered antiretroviral therapy (DAART) is effective for transitioning HIV-infected prisoners [28]. One randomized controlled trial (RCT) of DAART for released prisoners, however, showed that for the subset meeting criteria for opioid dependence, those retained on buprenorphine post-release markedly increased their likelihood of achieving VS [7,8], suggesting that medication-assisted therapies (MATs) might be a more effective and less costly strategy for released prisoners with HIV and opioid dependence. Despite there being three FDA-approved pharmacological treatments for opioid dependence, methadone (MMT), buprenorphine (BMT) and extended-release naltrexone (XR-NTX), with rare exception, have they not been empirically tested as transitional care for released prisoners [29–33]. Despite preliminary successes using MAT among HIV seronegative subjects [31,32,34,35], these treatments have not been deployed systematically within the CJS [36–39] nor deployed to optimize HIV treatment, as recommended by the IAPAC for PLWH and SUDs in the community[28].

As part on the National Institute of Drug Abuse's (NIDA) initiative to examine the impact of the seek, test, treat, and retain model of care (STTR) for criminal justice populations [40], this study directly examines the ability of XR-NTX to effectively "treat and retain" opioid dependent prisoners through the post-release transitional period. To test whether XR-NTX effectively stabilizes patients through this precarious post-release period, we have implemented a novel double-blind, placebo-controlled RCT of XR-NTX among opioid dependent HIV-infected prisoners and jail detainees transitioning to the community, with an examination of both HIV and substance abuse treatment outcomes.

2. Methods

2.1. Study design

Project NEW HOPE (Needing Extended-release Wellness Helping Opioid dependent People Excel) is a multi-site, double-blind, placebo-controlled RCT of XR-NTX among opioid dependent HIV-infected prisoners and jail detainees transitioning to the community. The study design is shown in Fig. 1.

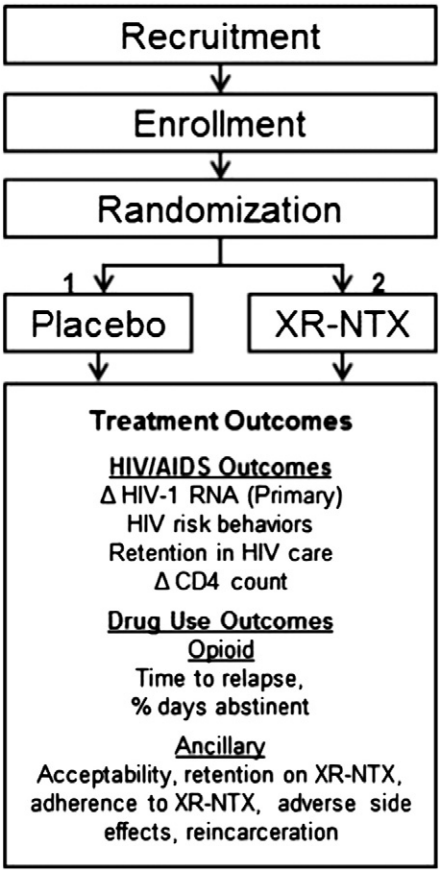

Fig. 1. Study design.