# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

17 Oct 2026

## Comparing Efficacy of Extended-release Injectable Naltrexone (XR-NTX) with Oral Naltrexone on Opioid Abstinence among People with Opiate Use Disorder: A Triple-blind Randomized Controlled Trial

## Protocol summary

**Study aim**

Determining the efficacy of treatment with extended-release injectable naltrexone compared to oral naltrexone and placebo in the treatment of opiate use disorder

**Design**

A phase 3, parallel group, triple blind randomized controlled trial in which 150 participants are randomly assigned to one of three study arms using www.sealedenvelope.com website.

**Settings and conduct**

Randomized controlled clinical trial in Iranian National Center for Addiction Studies (INCAS)'s clinic.

**Participants/Inclusion and exclusion criteria**

Inclusion criteria: • Age 18 to 65 years • Diagnosis of moderate to severe opiate use disorder, tendency to antagonist maintenance treatment, and completion of medically-assisted opioid withdrawal • Good physical health and hematology testing, liver and kidney function in the normal range • To use contraception in women • Living in Tehran • To have a family member or companion for regular visits and medication monitoring • ECG without severe abnormalities • Ability to understand and give informed consent Exclusion criteria: • Positive antagonist challenge test or positive urine test for opioids • Receiving opioids medications • Alcohol, stimulants or sedatives and hypnotics use disorder • Pregnancy or lactation • Uncontrolled major psychiatric disorder • Severe uncontrolled physical condition • Probability of surgery during the study period • Obesity or low weight for muscle injection • Sensitivity to study medications • Being on probation or under judicial supervision

**Intervention groups**

1- Extended-release injectable naltrexone + oral placebo 2- Injectable placebo + oral naltrexone 3- Injectable placebo + oral placebo

**Main outcome variables**

Average number of abstinence weeks (weekly till 24 weeks); Percentage of patients who have completed treatment.

## General information

**Reason for update**

**Acronym**

**IRCT registration information**

IRCT registration number: **IRCT20170702034844N6**
Registration date: **2020-07-31, 1399/05/10**
Registration timing: **registered_while_recruiting**

Last update: **2020-07-31, 1399/05/10**
Update count: **0**

**Registration date**

2020-07-31, 1399/05/10

**Registrant information**

**Name**

Alireza Noroozi

**Name of organization / entity**

Iranian National Center for Addiction Studies (INCAS)

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Iran (Islamic Republic of)

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**Recruitment status**

**Recruitment complete**

**Funding source**

**Expected recruitment start date**

2020-07-22, 1399/05/01

**Expected recruitment end date**

2021-12-22, 1400/10/01

**Actual recruitment start date**
empty
**Actual recruitment end date**
empty
**Trial completion date**
empty

**Scientific title**
Comparing Efficacy of Extended-release Injectable Naltrexone (XR-NTX) with Oral Naltrexone on Opioid Abstinence among People with Opiate Use Disorder: A Triple-blind Randomized Controlled Trial

**Public title**
Comparing Efficacy of Extended-release Injectable Naltrexone (XR-NTX) with Oral Naltrexone
**Purpose**
Treatment
**Inclusion/Exclusion criteria**
**Inclusion criteria:**
Diagnosis of moderate to severe opiate use disorder including only opium, Shireh (opium concentrate), heroin, and/or heroin crack based on DSM 5 Voluntarily seeking treatment and willingness to receive antagonist maintenance treatment Successful completion of medically-assisted opioid withdrawal (including a personal report of at least 7 days of abstinence from opioids, negative urinalysis test for morphine, methadone, buprenorphine and tramadol, and negative antagonist challenge test) Good physical health based on medical records, physical examination and measurement of vital signs Hematology tests, liver and kidney function tests in the normal range In women of childbearing age agree to receive a safe method of contraception Living in Tehran Having a family member or companion who can monitor regular visits and daily use of the study medication No severe abnormalities in the ECG Ability to understand and give written informed consent to enter the study
**Exclusion criteria:**
Positive antagonist challenge test Positive urinalysis test for opioids (morphine) or opioid drugs (methadone, buprenorphine, tramadol) Patients undergoing maintenance treatment with opioid drugs (methadone, buprenorphine, or opium tincture) Request treatment and desire to receive opioids maintenance treatments with medication like methadone and buprenorphine People treated with opioid antagonists or a history of continuous naltrexone injections in the past 6 months Need to receive opioid medications for medical purposes such as chronic pain disorder Concurrent diagnosis of other substance use disorders such as stimulants and sedatives (except nicotine and caffeine) Concurrent alcohol use disorder and people who are currently need medical management for alcohol withdrawal Pregnancy, lactation or women of childbearing age who are planning to become pregnant or do not use a contraceptive method Having uncontrolled, major psychiatric disorders at the time of referral (e.g. mood disorders with impaired function, schizophrenia, etc.) that can interfere with participation in the study Severe and uncontrolled physical conditions based on physical examination by study's physician and laboratory evaluations (e.g. uncontrolled hypertension or diabetes mellitus) Having uncontrolled medical illness that can interfere with study or significantly increase medical risk. (Such as high blood pressure and uncontrolled diabetes) Severe physical illness (including acute renal failure, endocarditis and tuberculosis) Liver failure, acute hepatitis or more than threefold increase in liver enzymes Thrombocytopenia and a history of coagulation disorders Planning for surgery during the study period Inadequate physical condition for safe intramuscular injection of extended-release naltrexone, body mass index above 40 (excessive adipose tissue in the buttocks) or severe weight loss The presence of AIDS-indicator disease Known sensitivity to naltrexone, polylactide-co-glycolide, arboxymethylcellulose, or other components of the effective and soluble extended-release injectable naltrexone Serious suicidality or a history of suicide last year Last year history of drug overdose that led to hospitalization Being on probation or under judicial supervision with the possibility of re-arrest and re-imprisonment Inability to understand the study protocol or respond to evaluations as well as lack of proper communication with therapists
**Age**
From **18 years** old to **65 years** old
**Gender**
Both

**Phase**
3
**Groups that have been masked**

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

**Sample size**
Target sample size: **150**
**Randomization (investigator's opinion)**
Randomized
**Randomization description**
Random codes are created by the person responsible for data randomization using the website www.sealedenvelope.com. Patients are randomly allocated to one of three study arms including injectable naltrexone + oral placebo, injectable placebo + oranl naltrexone and injectable placebo + oral placebo based on random sequence blocks with block size of 6. The codes created by the person responsible for the randomization, are attached to the medications of all three study groups, and each patient's code is given to the treatment provider in a sealed envelope, consecutively.
**Blinding (investigator's opinion)**
Triple blinded
**Blinding description**
Patients in all three groups receive either oral naltrexone or oral placebo as same size, color and shape gel capsules. Patients in all three groups also receive either injectable naltrexone or injectable placebo. The

injectable medications are prepared by a nurse and covered with an opaque tape, in order to make injectable naltrexone and injectable placebo indistinguishable.

**Placebo**
Used

**Assignment**
Parallel

**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**

**Name of ethics committee**
Vice- chancellor in research affairs, Tehran University of Medical Sciences

**Street address**
Keshavarz Blvd

**City**
Tehran

**Province**
Tehran

**Postal code**
1467664961

**Approval date**
2020-05-05, 1399/02/16

**Ethics committee reference number**
IR.TUMS.VCR.REC.1399.343

## Health conditions studied

### 1

**Description of health condition studied**
Moderate and severe opiates use disorder

**ICD-10 code**
F11.2

**ICD-10 code description**
Opioid dependence

## Primary outcomes

### 1

**Description**
Proportion of weeks of opioids use abstinence measured by self-report and negative urine test for morphine

**Timepoint**
Weekly till 24 weeks

**Method of measurement**
Self report and morphine urine test

### 2

**Description**
Treatment completion

**Timepoint**
Termination of the study

**Method of measurement**
Checklist for weekly visits

## Secondary outcomes

### 1

**Description**
Retention in treatment

**Timepoint**
Weekly till week 24

**Method of measurement**
Weekly visits check list

### 2

**Description**
Craving (severity)

**Timepoint**
Weekly till 24 week

**Method of measurement**
Visual analogue scale (VAS)

### 3

**Description**
Number of days using opioids during last week

**Timepoint**
Weekly (week 5 to 24)

**Method of measurement**
Clinical interview (week 5 to 24)

### 4

**Description**
Abstinence from opioids use measured by urine test

**Timepoint**
Weekly (week 5 to 24)

**Method of measurement**
Urine tests

### 5

**Description**
Adherence to treatment

**Timepoint**
Weekly

**Method of measurement**
Weekly physician's visit and patient's self-report on medication use adherence

### 6

**Description**
Time to dropping out of study due to positive naltrexone challenge test

**Timepoint**
Weekly till week 24

**Method of measurement**
Physician's visit

**7**

**Description**
Time to dropping out of study for any reason
**Timepoint**
Weekly till week 24
**Method of measurement**
Physician's visit

## Intervention groups

**1**

**Description**
Intervention group: Injectable naltrexone + oral placebo: Participants in this group receive extended release naltrexone (Exopio, Nano daroo pazhouhan, 380 mg, IM) every 4 weeks and oral placebo. After preparation, extended-release naltrexone is covered by an opaque tape and is given to physician or another nurse within study site. Patients in this group is received daily placebo capsule.
**Category**
Treatment - Drugs

**2**

**Description**
Intervention group: Injectable placebo + oral naltrexone: Participants in this group receive injectable placebo (vial 2 of Exopio medication package) covered by an opaque tape every 4 weeks and oral naltresone capsule 50 mg per day
**Category**
Treatment - Drugs

**3**

**Description**
Control group: Injectable placebo + oral placebo: Participants receive injectable placebo (vial 2 of Exopio package) covered with opaque tape every 4 weeks and oral placebo capsule daily.
**Category**
Treatment - Drugs

## Recruitment centers

**1**

**Recruitment center**
**Name of recruitment center**
Iranian National Center for Addiction Studies' Clinic
**Full name of responsible person**
Behrang Shadloo
**Street address**
Kargar St
**City**
Tehran
**Province**
Tehran
**Postal code**
1336616357
**Phone**
+98 21 5542 1144
**Email**
behrang.shadloo@gmail.com

## Sponsors / Funding sources

**1**

**Sponsor**
**Name of organization / entity**
Nanodaroo Pazhouhan Pardis Company
**Full name of responsible person**
Navid Goodarzi
**Street address**
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**Province**
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**Postal code**
1417614411
**Phone**
+98 21 8864 9082
**Email**
goodarzi_n@razi.tums.ac.ir
**Grant name**
**Grant code / Reference number**
**Is the source of funding the same sponsor organization/entity?**
Yes
**Title of funding source**
Nanodaroo Pazhouhan Pardis Company
**Proportion provided by this source**
85
**Public or private sector**
Private
**Domestic or foreign origin**
Domestic
**Category of foreign source of funding**
*empty*
**Country of origin**
**Type of organization providing the funding**
Industry

**2**

**Sponsor**
**Name of organization / entity**
Tehran University of Medical Sciences
**Full name of responsible person**
Mohammad Ali Sahraian
**Street address**
Keshavarz Blvd
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**Province**
Tehran
**Postal code**
1467664961
**Phone**
+98 21 8163 3685

**Email**
vcr@tums.ac.ir
**Grant name**
**Grant code / Reference number**
**Is the source of funding the same sponsor organization/entity?**
Yes
**Title of funding source**
Tehran University of Medical Sciences
**Proportion provided by this source**
15
**Public or private sector**
Public
**Domestic or foreign origin**
Domestic
**Category of foreign source of funding**
*empty*
**Country of origin**
**Type of organization providing the funding**
Academic

## Person responsible for general inquiries

**Contact**
**Name of organization / entity**
Iranian National Center for Addiction Studies
**Full name of responsible person**
Alireza Noroozi
**Position**
Psychiatrist
**Latest degree**
Specialist
**Other areas of specialty/work**
Psychiatrics
**Street address**
Kargar St
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## Person responsible for scientific inquiries

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## Person responsible for updating data

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**Latest degree**
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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**
Yes - There is a plan to make this available
**Study Protocol**
Yes - There is a plan to make this available
**Statistical Analysis Plan**
Undecided - It is not yet known if there will be a plan to make this available
**Informed Consent Form**
Undecided - It is not yet known if there will be a plan to make this available
**Clinical Study Report**
Yes - There is a plan to make this available
**Analytic Code**
Undecided - It is not yet known if there will be a plan to make this available
**Data Dictionary**
Undecided - It is not yet known if there will be a plan to make this available
**Title and more details about the data/document**
It is planned to share IPD, study protocol and report of the clinical study.
**When the data will become available and for how**

**long**

IPD will be shared after completion of the data gathering phase. Study protocol will be available within 3 months after successful registration of the trial. Report of the clinical study will be finalized at the end of study .

**To whom data/document is available**

Clinical researchers

**Under which criteria data/document could be used**

IPD will be available for researchers who are conducting review studies. Study protocol and report will be published as English articles.

**From where data/document is obtainable**

Email to the individual who is responsible for scientific inquiries of this project

**What processes are involved for a request to access data/document**

It will be responded after processing within the project team.

**Comments**