# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

10 Jul 2026

# Survey on Effect of Methadone to Buprenorphine Shift in the Maintenance Treatment on Profile of Gonadal Hormones and Semen Analysis of Infertile Men

## Protocol summary


**Summary**

Methadone and Buprenorphine have been used as opioid Substitution Treatment (OST) in the world since 40 & 18 years ago in order. Regardless of short period experience in the past, these treatments have 14 & 10 years history in Iran respectively. There is a lot of questions about unwanted side effects of these medications on structure & function of different organs of body which concerns clients & worries therapists. One of organs with most sensitivity about that, is Genital system and common questions of mostly young clients on maintenance treatments, especially those who tend to have child in the future, is about probable effects of methadone & buprenorphine on sperm & fertility. Accurate & scientific answer to this question and select of appropriate medication for each client, diminishes their concerns and increases therapeutic alliance. According to high prevalence & morbidity of opioid use disorder especially in young & middle-aged men, and widespread providing of OST with methadone & buprenorphine, we decided to substitute methadone by buprenorphine in men who receive OST and survey the effect of this shift on sexual hormones & sperm analysis. The study will be done on 40 participants from Rouyan institute who their infertility has been established and in the routine diagnostic procedures, there was not any finding except methadone consumption as an opioid substitution treatment. Primary routine laboratory tests (including TT, FT, LH, FSH, SHBG, PL, Semen Analysis) will done in the Rouyan Institute and after filling of inclusion criteria, clients will be refer to an experienced clinic in prescription of buprenorphine with appropriate access for continuing of study. Inclusion criteria: 1) men between 18 to 50 y/o; 2) at least 6 months on Opioid Substitution Treatment & 3 months from last illegal opioid use; 3) daily Methadone dose less than 60 mg/d; 4) certification of therapist physician on stability & readiness of client for shifting from methadone to buprenorphine; 5) diagnosis of methadone as the most important factor for undesirable hormonal & seminal analysis; 6) written & signed informed consent form. The participants will stay on 2 groups randomly. In the study group methadone will be substituted with buprenorphine and in the control group methadone will be continued. In both groups laboratory test including sex hormones (TT, FT, LH, FSH, SHBG, PL) and semen analysis will be done 3 times: before intervention,3 months & 6 months after beginning of intervention. Exclusion criteria: 1) evidence or signs of laps & relapse in buprenorphine treatment even with appropriate dose; 2) absence from treatment more than 2 consecutive or 3 undulant weeks; 3) absence from screening opioid urine test more than 2 consecutive or 3 undulant sessions; 4) absence from hormonal & seminal analysis more than 2 weeks after appointed time; 5) intolerance of methadone dose reduction for shifting to buprenorphine; 6) intolerance of buprenorphine side effects.


## General information

**Acronym**

**IRCT registration information**

IRCT registration number: **IRCT2016011626040N1**
Registration date: **2016-04-26, 1395/02/07**
Registration timing: **registered_while_recruiting**

Last update:
Update count: **0**

**Registration date**

2016-04-26, 1395/02/07

**Registrant information**

**Name**

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**Name of organization / entity**

Tehran University of Medical Sciences

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**Recruitment status**
**Recruitment complete**
**Funding source**
Tehran University of Medical Sciences

**Expected recruitment start date**
2016-04-03, 1395/01/15
**Expected recruitment end date**
2017-04-04, 1396/01/15
**Actual recruitment start date**
empty
**Actual recruitment end date**
empty
**Trial completion date**
empty

**Scientific title**
Survey on Effect of Methadone to Buprenorphine Shift in the Maintenance Treatment on Profile of Gonadal Hormones and Semen Analysis of Infertile Men

**Public title**
Effect of Substitution of Methadone by Buprenorphine on Gonadal Hormones and Semen
**Purpose**
Treatment
**Inclusion/Exclusion criteria**
Inclusion criteria: men between 18 to 50 y/o; at least 6 months on Opioid Substitution Treatment & 3 months from last illegal opioid use; daily Methadone dose less than 60 mg/d; certification of therapist physician on stability & readiness of client for shifting from methadone to buprenorphine; diagnosis of methadone as the most important factor for undesirable hormonal & seminal analysis; written & signed informed consent form. Exclusion criteria: evidence or signs of laps & relapse in buprenorphine treatment even with appropriate dose; absence from treatment more than 2 consecutive or 3 undulant weeks; absence from screening opioid urine test more than 2 consecutive or 3 undulant sessions; absence from hormonal & seminal analysis more than 2 weeks after appointed time; intolerance of methadone dose reduction for shifting to buprenorphine; intolerance of buprenorphine side effects.
**Age**
From **18 years** old to **50 years** old
**Gender**
Male

**Phase**
N/A
**Groups that have been masked**
*No information*
**Sample size**
Target sample size: **40**

**Randomization (investigator's opinion)**
Randomized
**Randomization description**
**Blinding (investigator's opinion)**
Not blinded
**Blinding description**
**Placebo**
Not used
**Assignment**
Parallel
**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**
**Name of ethics committee**
Tehran University of Medical Sciences
**Street address**
Secretariat of Ethics Committee, Sixth Floor, Tehran University of Medical Sciences, Qhods St. Keshavarz Blvd.
**City**
Tehran
**Postal code**
**Approval date**
2015-11-16, 1394/08/25
**Ethics committee reference number**
IR.TUMS.REC.1394.1172

## Health conditions studied

### 1

**Description of health condition studied**
Male infertility in opioid substitution treatment
**ICD-10 code**
N46
**ICD-10 code description**
Male infertility

## Primary outcomes

### 1

**Description**
Follicle-stimulating hormone (FSH) blood level
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
mIU/ml (ELISA)

### 2

**Description**
Luteinizing hormone (LH) blood level

**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
IU/L (ELISA)

### 3

**Description**
Free Testosterone (FT) blood level
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
pg/ml (ELISA)

### 4

**Description**
Total Testosterone (TT) blood level
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
ng/ml (ELISA)

### 5

**Description**
Prolactin (PRL) blood level
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
ng/ml (ELISA)

### 6

**Description**
Sex Hormone Binding Globulin (SHBG) blood level
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
nmol/l (ELISA)

### 7

**Description**
Semen Volume
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
Ml

### 8

**Description**
Level of PH of semen
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
Ph Scale

### 9

**Description**
Number of spermatozoid in 1 Ml of semen
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
Million/ml

### 10

**Description**
Time for fluidity of semen
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
minute

### 11

**Description**
Shape of spermatozoides
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
Percentage of spermatozoides with normal shape

### 12

**Description**
Normal motility of spermatozoides
**Timepoint**
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
**Method of measurement**
Percentage of spermatozoides with normal forward motion

## Secondary outcomes

### 1

**Description**
Daily methadone dose
**Timepoint**
Before substitution by buprenorphine
**Method of measurement**
mg/d

### 2

**Description**
Daily buprenorphine dose
**Timepoint**
After substitution of methadone
**Method of measurement**
mg/d

## Intervention groups

### 1

**Description**
According to a randomized categorization, participants will be classified in 2 groups that will be informed. In the intervention group methadone will be substitute with buprenorphine, and maintenance treatment will continue for 6 months. Prescribed medication in the study group is buprenorphine hydrochloride (2 mg SL tablet) manufactured by Faranchimie, 8-16 mg/day, single dose for 6 months. Sampling for laboratory tests (5 cc blood for sex hormones and Seminal fluid volume in 1 ejaculation for semen analysis) will be taken 3 times: before intervention, 3 months, & 6 months after beginning of intervention. Opioid screening test will be done (by taking urine sample 10 cc) every month.

**Category**
Treatment - Drugs

### 2

**Description**
In the control group methadone will be continued as maintenance treatment for 6 months. prescribed medication in the control group is 5 mg methadone hydrochloride tablet, 40-60 mg/day, single dose, for 6 months. Sampling for laboratory tests (5 cc blood for sex hormones and Seminal fluid volume in 1 ejaculation for semen analysis) will be taken 3 times: before intervention, 3 months, & 6 months after beginning of intervention. Opioid screening test will be done (by taking urine sample 10 cc) every month.

**Category**
Treatment - Drugs

## Recruitment centers

### 1

**Recruitment center**

**Name of recruitment center**
Iranian National Center for Addiction Studies

**Full name of responsible person**
Mohammad Reza Haddadi

**Street address**
No. 669, Qazvin Square, Sout Kargar Avenue

**City**
Tehran

## Sponsors / Funding sources

### 1

**Sponsor**

**Name of organization / entity**
Tehran University of Medical Sciences

**Full name of responsible person**
Nasim Vosoughi, Ph.D

**Street address**
No. 88, School of Advanced Technologies in Medicine, Italia st. , Keshavarz Blvd.

**City**
Tehran

**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**
100

**Public or private sector**
*empty*

**Domestic or foreign origin**
*empty*

**Category of foreign source of funding**
*empty*

**Country of origin**

**Type of organization providing the funding**
*empty*

## Person responsible for general inquiries

**Contact**

**Name of organization / entity**
Iranian National Center for Addiction Studies

**Full name of responsible person**
Mohammad Reza Haddadi

**Position**
Medical Degree/ Director of Buprenorphine Clinic

**Other areas of specialty/work**

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## Person responsible for scientific inquiries

**Contact**

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Maryam Farahmandfar

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Ph.D in Physiology

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## Person responsible for updating data

**Contact**
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Iranian National Center for Addiction Studies
**Full name of responsible person**
Mohammd Reza Haddadi
**Position**
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**Other areas of specialty/work**
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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**
*empty*
**Study Protocol**
*empty*
**Statistical Analysis Plan**
*empty*
**Informed Consent Form**
*empty*
**Clinical Study Report**
*empty*
**Analytic Code**
*empty*
**Data Dictionary**
*empty*