Feasibility of Opioid Injection Trial (FOpIT): Recruitment

Implementation of time-limited parenteral hydromorphone in people with treatment-resistant injecting opioid use disorder: Safety, feasibility, acceptability and cost

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Acknowledgement of Country

We acknowledge and honour the aboriginal elders of the Gadigal people of the Eora Nation-those who once lived here and first walked this land where we stand today and to their descendants who maintain their spiritual connections and traditions.

We acknowledge that the Gadigal people occupied and cared for this country over countless generations, and we celebrate their continuing contribution to the life of this region.

Background

- Australia has a well-developed opioid agonist treatment (OAT) system but not all individuals respond to current treatment
- 5-15% people engaged in treatment continue injecting street opioids and experience severe harms (Lintzeris 2009)
- Approximately 10% clients who visited MSIC to use opioids in 2017 first registered with the service in 2001 – 2002, indicating prolonged injecting opioid use
- A MSIC client survey in 2017 found 43% respondents were currently on methadone and a further 35% had been on methadone previously

Lintzeris, N. (2009). Prescription of heroin for the management of heroin dependence. *CNS drugs, 23*(6), 463-476.

Injectable opioid treatment

- Supervised injectable Opioid Treatment (SIOT) is a second-line treatment option for those individuals who persist with injecting opioids despite access to OAT [1, 2]
- Involves prescribing pharmaceutical heroin or hydromorphone for people who persist with injecting despite access to treatment
- People may also receive supplementation with oral methadone to prevent withdrawal during inter-dosing intervals
- Injected opioids are more rewarding that oral OAT and can attract and hold people in structured treatment where methadone and buprenorphine have not been effective

Injectable opioid treatment is not a new idea!

1. Bell, J., Belackova, V., & Lintzeris, N. (2018). Supervised Injectable Opioid Treatment (SIOT) for the Management of Opioid Dependence. *CNS drugs, online 21st August, 2018*. doi:DOI 10.1007/s40265-018-0962-y
2. Bell, J., van der Waal, R., & Strang, J. (2016). Supervised Injectable Heroin: A Clinical Perspective. *The Canadian Journal of Psychiatry, 62*(7), 451-456.

The ACT heroin trial proposal: an overview

Gabriele Bammer and Robert M Douglas

Med J Aust 1996; 164 (11): 690-692.

Published online: 8 June 1999

ARTICLE

AUTHORS

REFERENC

BMJ. 1998 Jul 4; 317(7150): 13–18.

doi: 10.1136/bmj.317.7150.13

PMCID: PMC28595

PMID: 9651260

Randor

conven

Thomas V

Harm Reduct J. 2009; 6:2.

Published online 2009 Jan 21. doi: 10.1186/1477-7517-6-2

PMCID: PMC2639576

PMID: 19159475

NAOMI: The

Randomized Controlled Trial > Lancet. 2010 May 29;375(9729):1885-95.

doi: 10.1016/S0140-6736(10)60349-

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Hydromorphone Compared With Diacetylmorphine for Long-term Opioid Dependence

A Randomized Clinical Trial

Eugenia Oviedo-Joekes, PhD[1,2]; Daphne Guh, MSc[1]; Suzanne Brissette, MD[3]; et al

» Author Affiliations | Article Information

JAMA Psychiatry. 2016;73(5):447-455. doi:10.1001/jamapsychiatry.2016.0109

Why FOpIT?

- Most studies have investigated the effectiveness of SIOT vs methadone and have not tested the effectiveness of 'time limited' SIOT
- Studies have shown that most benefit from SIOT occurs in the first 6 months of treatment [1,2]
- Data suggests that moderate-term SIOT and transfer to methadone may be a more effective use of resources than indefinite maintenance
- Participants in FOpIT will be offered parenteral hydromorphone as an adjunct to methadone (or other agonist treatment) for up to 24 months followed by transfer to oral methadone or other agonist treatment

1.Verthein, U., Bonorden-Kleij, K., Degkwitz, P., Dilg, C., Köhler, W. K., Passie, T., . . . Haasen, C. (2008). Long-term effects of heroin-assisted treatment in Germany. *Addiction, 103*(6), 960-966.
2. Oviedo-Joekes, E., Guh, D., Marchand, K., Marsh, D. C., Lock, K., Brissette, S., . . . Schechter, M. T. (2014). Differential long-term outcomes for voluntary and involuntary transition from injection to oral opioid maintenance treatment. *Substance Abuse Treatment, Prevention, and Policy, 9*(1), 23.

Partners

The project is a partnership between:

- Uniting NSW/ACT (MSIC)
- St Vincent's Hospital, Sydney
- University of NSW (UNSW)

Investigators

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Study design

- Single-site, uncontrolled, open-label implementation study recruiting 20-30 treatment resistant, injecting, opioid-dependent people
- Participants will be offered parenteral hydromorphone as an adjunct to oral methadone for up to 24 months
- Following transfer to oral methadone (or other agonist treatment), participants will be followed up for a further 3 months
- Participants will be people who inject opioids not previously responding to conventional opioid agonist treatment
- The study will investigate the feasibility, safety, and cost of time-limited injectable hydromorphone treatment

Objectives

Primary

- Feasibility (acceptability to participants and staff, assessed in qualitative interviews and by participation in treatment)

Secondary

- Safety (monitored by adverse events)
- Cost
- Changes in non-prescribed opioid use
- Changes in other non-prescribed drug use
- Changes in quality of life
- Change in mental and physical health
- Changes in social connectedness and wellbeing
- Changes in crime

Novel aspects of this trial - 1

ST VINCENT'S HEALTH AUSTRALIA

- It introduces an injectables treatment program in Australia
- SIOT provokes anxiety in staff, administrators, politicians, and many other stakeholders.
- Demonstrating that it can be done, and that many participants experience positive changes, is important in the local context

Novel aspects of this trial - 2

- Treatment takes place in an existing OAT clinic
- Participants share the waiting room with people waiting for methadone or buprenorphine treatment.
- Nursing staff cover both traditional dispensing and injectable treatment
- Rationale and importance of this:
- SIOT is intensive, involving twice daily attendance. People need to live in proximity to SIOT services
- There is a network of public clinics, potentially offering an accessible treatment and a meaningful public health intervention.

Novel aspects of this trial - 3

ST VINCENT'S HEALTH AUSTRALIA

- Treatment is time-limited – 2 years - with the objective of transfer to conventional OAT
- The aim is a period of intensive treatment to interrupt a long-term pattern of injecting, allowing people to experience the possibility of positive change
- Positive change in SIOT occurs within the first 2 years
- Studies indicate some prospective participants are deterred by the possibility they may never stop injecting if given access to endless prescribed injectables

Recruitment

- 6 month recruitment phase from early April 2022 until end of September 2022
- Recruited participants from nearby Medically Supervised Injecting Centre (MSIC), Rankin Court Treatment Centre (RCTC) and other services
- Aimed for minimum of 20 and maximum of 30 participants at 6 months
- Participants who drop out in the first year of treatment will have their place kept open for 3 months

Inclusion Criteria

- Aged 21- 60 years
- Minimum 5 years opioid dependence, and current physical opioid dependence as assessed using ICD-10 criteria
- Previous access to treatment
- Currently injecting opioids > 3 times weekly
- Evidence of harm from opioid use (self-reported crime, or comorbid health or mental health conditions, impaired social functioning)
- Ability to provide written, informed consent to participate as assessed by trial medical staff

Exclusion Criteria

- Pregnant, breastfeeding, or planning to become pregnant; participants who become pregnant will be transferred to oral OAT
- Advanced liver disease (Childs-Pugh B)
- Chronic airflow limitation or other respiratory compromise producing dyspnoea on mild exertion
- Other severe and active medical condition as assessed by study medical officer
- Requires prescribed medication which interacts with trial medication in ways which make treatment unsafe
- Concurrent monoamine oxidase inhibitors (MAOIs), or within 14 days of treatment with MAOIs
- Severe psychiatric disorder at the time of assessment (e.g. acute psychosis, severe anxiety and/or mood disorder, intent to harm self or others assessed by study medical officer and/or psychiatrist)
- Severe cognitive impairment making it difficult for person to complete study requirements
- Inability to provide informed consent, even with a registered medical interpreter
- Previous adverse reaction to hydromorphone

Study procedures

- Participants will self administer (intravenous or intramuscular) parenteral hydromorphone (listed on Australian Register of Therapeutic Goods) twice-daily for 24-months under direct observation by nursing staff.
- Participants will either **commence methadone in the week prior or have 3 observed doses** before commencement of hydromorphone
- Hydromorphone will commence at 10mg and increase incrementally each dose
- Medical officers will need to write regular prescriptions during the induction phase depending on the participants' response (RNs may make dose adjustments as per the medical officer's prescription)
- Dosage range **50-400 mg/day** (maximum 200 mg/dose)
- Co-administration of methadone (or other OAT) **prior to** any injection of hydromorphone
- Injection will need to be in **upper limbs only**
- Participants will only have **approximately 5 minutes to inject**
- At 24 months all participants will transfer to standard OAT

General care

Doctor's appointments & Care Co-ordination

- Participants need to see the study doctor approximately every 3 months.
  - Respond to any issues they are having
  - Identify an goals they might want to achieve
- Participants are expected to meet with a Care Co-ordinator regularly during the study with more formal review (ATOP and UDS) every 3 months as per standard of care in opioid treatment programs

Recruitment

- 69 people expressed interest in the trial during the 6 month time frame
- 53 people underwent pre-screening with a trial nurse
- 22 participants screened by Medical Officer and deemed eligible
  - unfortunately unable to screen further participants due to limitations of space, staff and dosing times

Characteristics

- Age range 28 – 59 yrs (average 46 yrs age)
- 59% male, 36% female, 5% transgender
- 9% Aboriginal
- 36% identify as LGBTI
- 68% on current regular OAT at enrolment
    - (90% methadone, 5% Suboxone, 5% Buvidal)

…it's so liberating. It makes us free. It changes us from being criminals to being, you know, productive members, you know.

I'm on the verge of homelessness almost, so I need this to work. I can't afford to be spending $700 a week on heroin. I can't afford that. … And this gives me the opportunity to at least take a step back, breathe and get financial counselling

Qualitative interviews

'A complete 180': how a trial treatment in Sydney for heroin addiction is changing lives | Health | The Guardian

Well, the thing that I've always wanted: just my injection. My shot, you know. I get two shots a day and they're really good quality. And I don't have to … I'm not going to be, you know, deported for doing it and … yeah. And it changes the whole dynamic. It's amazing.

It's comforting waking up and going to bed knowing that I've got a shot the next day…. So, it's quite a, a reassuring feeling for me.

Conclusion:

- Many trials have had difficulties recruiting participants [1,2]

- Possible factors:
  - Applicants ‘lost to follow up’
  - Entry criteria
  - Limited clinical capacity
  - Too ‘clinical’

- Recruitment was relatively easy for FOpIT trial

- Indicates that demand for supervised injectable opioid treatment (SiOT) as a second-line treatment exists for people who inject drugs

1. Supervised injectable heroin or injectable methadone versus optimised oral methadone as treatment for chronic heroin addicts in England after persistent failure in orthodox treatment (RIOTT): a randomised trial. Strang et al. *Lancet* 2010; 375:1885-95
2. The SALOME study: recruitment experiences in a clinical trial offering injectable diacetylmorphine and hydromorphone for opioid dependency. Oviedo-Joekes et al. *Substance Abuse Treatment, Prevention and Policy* 2015