Australia's first trial of supervised injectable opioid treatment (SIOT) with hydromorphone for people with opioid use disorder: initial outcomes

APSAD 11th November 2025

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Clinical Lead: FOpIT Trial (**F**easibility of **Op**ioid **I**njection **T**rial)

Acknowledgements

Acknowledgement of Country

This study was conducted on Gadigal land and I would like to pay my respects to elders past present and extend that to any Aboriginal and Torres Strait Islander peoples here today.

Acknowledgement of Community

This presentation would not be possibly without the contributions of people with lived and living experience – I extend my thanks to the participants of this study and our Consumer representative on the study, Maureen Steele

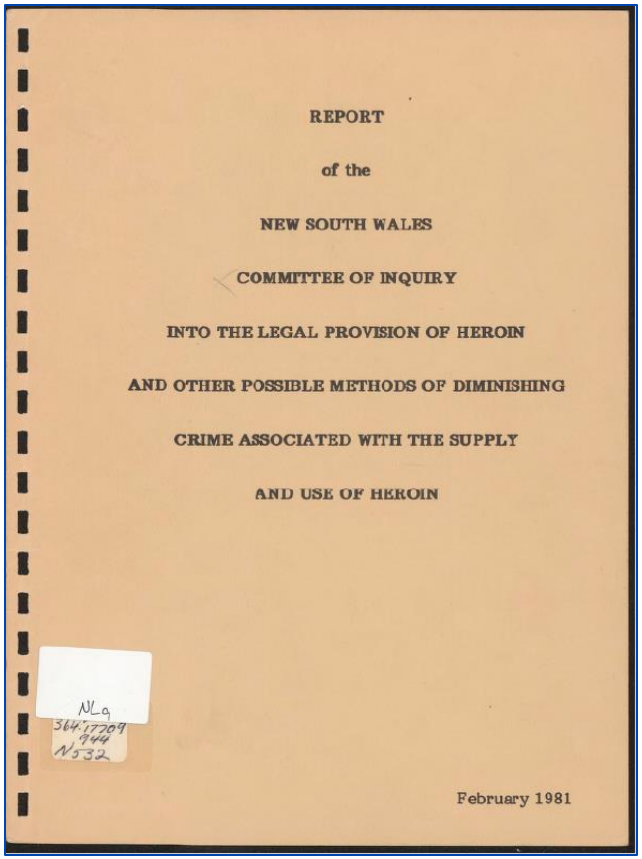
Conflicts of interest

- **Craig Rodgers: Nil to declare**

- **John Strang** through his university, has worked with several pharmaceutical companies to identify new or improved treatments and his employer (King's College London) has received grants, travel costs and/or consultancy payments. None of these has related to the FOpIT study which this paper describes.
- **Nicholas Lintzeris** has received funding for independent research from Indivior and Camurus for work unrelated to this project.
- **Krista Siefried and Nadine Ezard** have received funding from the Australian Department of Health and Aged Care, and is employed by the University of New South Wales and St Vincent's Hospital, Sydney.
- **Willem van den Brink,** has worked with several pharmaceutical companies to identify new or improved treatments and received speaker fees, travel costs and/or consultancy payments. None of these has related to the FOpIT study which this paper describes.

Background

- Use of heroin for OAT initially proposed in 1981(James Rankin et al)


REPORT

of the

NEW SOUTH WALES

COMMITTEE OF INQUIRY

INTO THE LEGAL PROVISION OF HEROIN

AND OTHER POSSIBLE METHODS OF DIMINISHING

CRIME ASSOCIATED WITH THE SUPPLY

AND USE OF HEROIN

February 1981

Background

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- Heroin trial proposed in the ACT 1996

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- A 2017 MSIC client survey found 43% respondents were currently on methadone and a further 35% had been on methadone previously

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Commentary

Bridging the evidence and the politics: Implementation trial of supervised injectable opioid treatment (SIOT) in Australia

Alison Ritter [a], James Bell [a b c], John Strang [c], Nadine Ezard [d e f g], Craig Rodgers [d e g], Vendula Belackova [b], Marianne Jauncey [b], Krista J. Siefried [d e f], Darren M. Roberts [h i], Wim van den Brink [j], Nicholas Lintzeris [e k], Adrian Dunlop [l], Eugenia Oviedo-Joekes [m], Carla Treloar [n]

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

Background

- Use of heroin for OAT initially proposed in 1981
- Heroin trial proposed in the ACT 1996
- 5-15% people engaged in treatment continue injecting street opioids and experience severe harms[1]
- A 2017 MSIC client survey found 43% respondents were currently on methadone and a further 35% had been on methadone previously
- 8 RCTs comparing methadone to SIOT[2]
- SIOT is a second-line treatment option for those individuals who persist with injecting opioids despite access to OAT[3,4]

ISAJE
INTERNATIONAL SOCIETY OF ADDICTION JOURNAL EDITORS

Drug and Alcohol Dependence
Volume 247, 1 June 2023, 109869

Review

Heroin assisted treatment for key health outcomes in people with chronic heroin addictions: A context-focused systematic review

Riley McNair [1], Mark Monaghan [2], Paul Montgomery

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1. Lintzeris, N. (2009). Prescription of heroin for the management of heroin dependence. *CNS drugs, 23*(6), 463-476.
2. McNair, R. Monaghan, M. & Montgomery, P. (2023). Heroin assisted treatment for key health outcomes in people with chronic heroin addictions: A context-focused systematic review. Drug and Alcohol Dependence Vol 247,
3. 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
3. Bell, J., van der Waal, R., & Strang, J. (2016). Supervised Injectable Heroin: A Clinical Perspective. *The Canadian Journal of Psychiatry, 62*(7), 451-456.

Partners

The project is a partnership between:

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

Investigators

Prof Nadine Ezard
Dr James Bell
Dr Darren Roberts
Prof Alison Ritter
Prof Carla Treloar
Dr Krista Siefried

Associate Investigators

Dr Marianne Jauncey
Dr Vendula Belackova
Dr Marian Shanahan
Prof Nick Lintzeris
Prof Adrian Dunlop
Prof John Strang
Prof Wim van den Brink
Prof Eugenia Oviedo-Joekes

Study design[1]

- Single-site, uncontrolled, open-label implementation study recruiting 20-30 people with opioid dependence (via injection) for whom current OAT was not effective
- Participants were offered parenteral hydromorphone as an adjunct to oral methadone (or other agonist treatment) for up to 24 months
- Following transfer to oral methadone (or other agonist treatment), participants were followed up for a further 3 months
- The study aimed to investigate the feasibility, safety, and cost of time-limited injectable hydromorphone treatment
- This presentation will focus on: feasibility (recruitment, retention and continuation on OAT at 3 months follow up) and safety

1. Implementation of time-limited parenteral hydromorphone in people with treatment-resistant injecting opioid use disorder: a protocol for a single-site, uncontrolled, open-label study to assess feasibility, safety and cost. Rodgers C, Siefried KJ, Ritter A, *et al* *BMJ Open* 2024;**14:**e082553. doi: 10.1136/bmjopen-2023-082553

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

Inclusion/Exclusion Criteria

Inclusion Criteria

- Aged 21- 60 years
- Minimum 5 years opioid dependence, current physical opioid dependence (ICD-10 criteria)
- Previous access to treatment
- Currently injecting opioids > 3 times week
- 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

Exclusion Criteria

- Pregnant, breastfeeding, or planning to become Advanced liver disease (Childs-Pugh B)
- Chronic airflow limitation or other respiratory compromise
- Other severe and active medical condition as assessed by study medical officer
- Severe psychiatric disorder at the time of assessment
- Severe cognitive impairment
- Requires prescribed medication which interacts with trial medication in ways which make treatment unsafe (MAOIs)
- Previous adverse reaction to hydromorphone
- Inability to provide informed consent, even with a registered medical interpreter

Data collection

Clinical data collection

- Number of days of injectable treatment
- Number of days receiving oral medication only
- Number of missed days
- Derived from dosing records to provide a picture of retention in treatment

Quantitative research interviews

- 3 confidential interviews with a researcher not involved in delivering treatment (reimbursed with $50 voucher)
- These interviews monitored changes in mental health (K10, SCL-90), quality of life (AQoL8), physical health and social functioning (ATOP) and non-prescribed drug use (TLFB), and occurred at baseline, 12 months and 27 months or 3 months plus 1 day after last hydromorphone injection

Safety

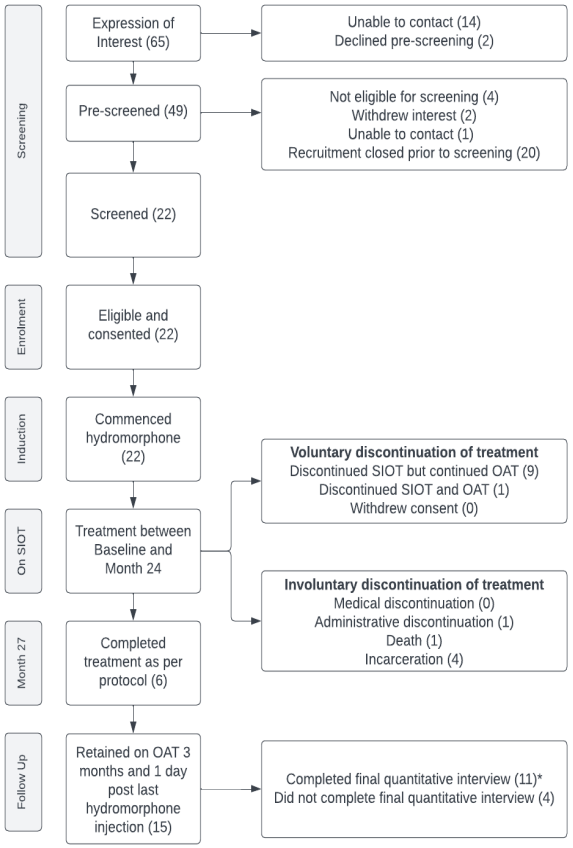
- Assessed by treatment emergent Adverse Events (AEs), using Therapeutic Goods Administration (TGA) criteria
- For the purposes of the study, a ‘Serious Adverse Event’ also included an event where airway management was required, and any event where naloxone was administered
- A Data Safety Monitoring Board was convened for the purposes of ensuring participant safety for the duration of the study

Results

Recruitment and retention

- Recruited between April and October 2022
- 65 people expressed interest in the trial
- 49 people pre-screened
- 22 people eligible and consented
- Recruitment closed to further screening due to clinic limitations

- 22 people commenced hydromorphone (HM)
- 7 people were not retained in treatment
- 15 people were continuing on OAT at 3 months post HM dosing
- 9 people completed HM prior to 24 months
- Only 6 people completed the whole 24 months of HM dosing



Participants

Characteristics

- 14 (64%) male, 7 female (32%), 1 non-binary (5%)
- 14 (64%) identified as straight or heterosexual
- 2 (9%) identified as Aboriginal
- Median age was 47 years (interquartile range [IQR] 42 – 52)
- Most participants were unemployed (n=20, 91%)
- Stable accommodation (n=14, 64%) or some form of temporary accommodation (n=8, 36%)
- Most participants (n=15, 68%) living within a 5km radius of the service.

Participants

Drug use history

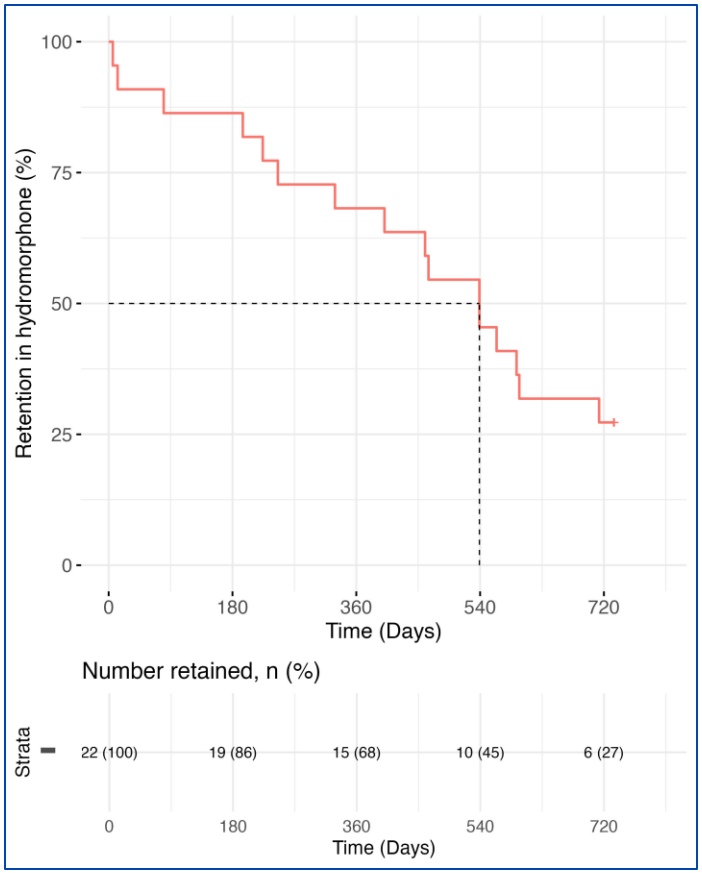
- Median age at first opioid use: 17 years (IQR 14 – 22),
- Median age at first opioid injection: 20 years (IQR 16 – 26)
- Median length of injection drug use: 21 years (IQR 18 – 30).

Treatment history

- Median number of treatment episodes of OAT: 3 (IQR 2.0 – 4.0).
- 18 participants (82%) on OAT at enrolment
  - 16 on methadone
  - 1 on sublingual buprenorphine
  - 1 participant on depot buprenorphine
- The median methadone dose for those on treatment at enrolment was 67.5 mg (IQR 46.3 – 87.5)
- Median duration on current regimen 5.5 years (IQR 1.0 – 12.8).

Retention in HM treatment

- Retention in HM decayed steadily over time
- 15 (68%) participants retained to day 360
- 10 (45%) retained to day 540
- 6 (27%) completed 24 months of HM dosing
- Note that KM curve does not show participants other OAT



Hydromorphone (HM) and OAT dosing

ST VINCENT'S HEALTH AUSTRALIA

- Total of 14,104 doses HM administered
- Median days attended for HM 96%
- Median doses delivered 64%
- Median dose of HM 90mg
- Mean daily dose of HM 160mg
- Median attendance for OAT 98%
- Median dose of methadone 3 months post completion of HM was 92.5mg (IQR 80 -111mg)

Characteristic	Median (Q1, Q3) of total sample (N=22)
Total days enrolled in trial[1]	597 (316, 826)
Hydromorphone, total days possible	539 (246, 734)
Hydromorphone, number of days attended	508 (212, 692)
Hydromorphone, % days attended of total	96 (77, 99)
Hydromorphone, total number of doses	687 (318, 1,055)
Hydromorphone, % doses administered of total	64 (49, 77)
Hydromorphone, median mg per dose administered	90 (25, 120)
Hydromorphone, median mg per day	160 (130, 240)
OAT, number of days attended[2]	622 (291, 800)
OAT, % days attended of total[2]	98 (88, 99)
Methadone, median mg per day[3]	70 (60, 85)

1. Includes hydromorphone dosing and 3 months post hydromorphone dosing
2. Does not include 1 participant on depot buprenorphine
3. Does not include 1 participant on sublingual buprenorphine and 1 participant on depot buprenorphine

Secondary outcomes: results

- Median days of heroin use decreased from 26 (IQR 7-28) in previous 28 days to 4 (IQR 0-28)
- No increases in other drug use
- Mild improvements in quality of life (AQoL) and mental health questionnaires (K10, SCL90)
- Physical health remained stable
- Decreased involvement in crime

Adverse events (AEs)

- 141 AEs related to hydromorphone
  - Largely gastrointestinal and 'histamine related'
- 2 serious adverse events (SAEs)related to hydromorphone
- Only 1 participant required naloxone in over 14,000 doses of HM
- 1 participant death – not in the immediate dosing period and concluded not related to HM dosing

Adverse events (AEs)	Total (n [%])
Total AEs	379
Participants with AEs	20 (90.9%)
AEs related to hydromorphone	141 (37.2%)
AEs related to hydromorphone	
Gastrointestinal issues (total)	67 (47.5%)
Nausea	- 33 (23.4%)
Vomiting	- 16 (11.3%)
Constipation	- 8 (5.6%)
Histamine reaction (total)	44 (31.2%)
Pruritis	- 10 (7.1%)
'Pins and needles'	- 10 (7.1%)
Rash following injection	- 7 (5.0%)
Hot flushes	- 6 (4.3%)
Welts/hives	- 5 (3.5%)
Injection site issues (total)	13 (9.2%)
Swelling	- 7 (3.5%)
Bruising	- 3 (2.1%)
Other	17 (12.1%)
Desaturation	- 3 (2.1%)
Hypotension	- 2 (1.3%)
Sedation/drowsy	- 3 (2.1%
Total SAEs	8 (2.1%)
Participants with SAEs	4 (18.1%)
SAEs related to hydromorphone	2 (25.0%)
SAEs requiring airway management only	1 (12.5%)
SAEs requiring airway management and naloxone	1 (12.5%)

Limitations

- Small sample size and lack of a control arm meant we were unable to determine baseline features that would result in retention or non-retention
- Only able to use hydromorphone: results possibly different if diacetyl morphine available
- Highly motived sample: nil other options for SIOT

Conclusion:

- Feasible to recruit to supervised opioid injection treatment in Australia within an existing opioid treatment service
- Majority of participants were retained in hydromorphone treatment for at least 12 months
- Serious adverse events were rare and well managed within an existing opioid treatment clinic
- Improvements were noted on illicit heroin use, quality of life and well being
- Demonstrated that SIOT could be conducted in an existing OTP and hence 'disrupting' the normal treatment regimens in Australia

Acknowledgements

- **Current and past researchers and staff:** Katerina Zavitsanou, Anna McVinish, Ruthy McIver, Brendan Clifford, Teodora Zanesheva-Karamanlieva, Arabella McMahon, Nader Malek, Gabrielle Kookarkin, Ellie Camov, Eleanor Kessler and all the nursing staff working in the clinic.
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- **Dr David Goodman-Meza**, who assisted with statistical analysis
- Members of the **Data Safety Monitoring Board**: Jonathan Brett, Merissa Cappetta and Anthony Shakeshaft.
- **Dr Krista Siefried and Prof Greg Dore** (PhD Supervisors)