

Statement from the FOpIT Investigators

September 2024

The Investigators from the Feasibility of Opioid Injectable Treatment (FOpIT) trial confirm and note:

1. There is consistent evidence from randomised controlled trials in Europe and North America that supervised short-acting injectable opioid treatment (diacetylmorphine, hydromorphone) is a safe, effective and cost-effective treatment option for people with treatment refractory opioid use disorder.¹
2. An open-label feasibility trial² of supervised short-acting injectable opioid treatment (using hydromorphone) funded by the NH&MRC and Uniting NSW.ACT and conducted at St Vincents Hospital Sydney has recruited 22 people with long-term refractory heroin use disorder. They agreed to attend the St Vincent's clinic up to twice a day for injectable hydromorphone along with standard opioid agonist treatment, predominantly oral methadone. This has given them the opportunity to reduce or stop street drug use, to stabilise into a daily routine, and to seek support in health and social areas. The treatment was time-limited, and all participants had to stop the injectable component of the treatment within the two-year maximum period, as intended. Publication of trial results is underway.
3. The key findings to date from this Australian trial include:
 - High acceptance by the participants;
 - High feasibility of implementation in the context of an existing Opioid Treatment Program (OTP) clinic;
 - Opioid safety was confirmed, with only two incidents where either oxygen or naloxone was required – both in the same participant and treated onsite with no complications;
 - Successful planned treatment discontinuation from hydromorphone with continuation of other forms of opioid agonist treatment as required.
4. The first-line treatments for opioid dependence remain methadone and buprenorphine maintenance treatment both of which are safe, effective and cost-effective. These treatments should be available and freely accessible to people with opioid use disorders.
5. Supervised injectable hydromorphone is a second-line treatment for people with an opioid use disorder if initial (first-line) treatments have failed, stopped working for the patient, or if side effects occurred that were not tolerated.³
6. As with most second-line medical treatments, supervised short-acting injectable opioid treatment is only indicated for and accepted by a relatively small proportion of all patients with an opioid use disorder. Internationally, it has been shown that this form of treatment (with diacetylmorphine or hydromorphone) is considered appropriate for around 5% of treatment-seeking people with an opioid use disorder.⁴
7. The recent detection of high potency synthetic opioids in the Australian illicit drug market (nitazenes and the threat of fentanyl and its analogues)⁵ is of extreme concern in relation to a potential escalation of opioid overdoses. Opioid agonist treatments are protective against

overdose⁶, and scale-up of all evidence-based programs is urgent, to meet individual needs and engage people at risk into care.

8. Second-line medical treatments are often more expensive than first-line treatments.⁷ However short-acting injectable opioid treatment can attract and retain patients with complex needs, severe physical health and psychiatric comorbidities, and those at risk of overdose, for whom first-line treatments have failed. Engaging patients in this form of treatment in a timely manner, even if a small group, will considerably reduce the high cost associated with untreated opioid use disorder.
9. The cost ranges (per annum per person) of providing various responses to opioid use disorder can be compared:

\$120,000 to \$260,000	= cost per person/per year in prison ⁸
\$82,000 to \$145,000	= cost per person/per year in AOD residential rehabilitation ⁹
\$22,000 to \$35,000	= cost per person/per year of supervised short-acting injectable treatment ¹⁰
\$5,000 to \$10,000	= cost per person/per year of opioid agonist treatment (methadone, buprenorphine) ¹¹

Supervised short-acting injectable treatment is significantly less costly than residential rehabilitation or prison, but also more costly than first-line opioid agonist treatment.

10. In general our public health system is geared towards first line treatments, as it should be. But second line options are not ignored in other areas of medicine - from management of hypertension, or diabetes to breast cancer. Unfortunately in opioid dependence, the small proportion of people who do not benefit from existing treatments have no access to second line alternatives. Progressive change is needed to ensure access to the best new technologies and therapies to treat opioid dependence.
11. The FOpIT Investigators are committed to ensuring a best-practice opioid dependence treatment system in NSW and nationally, allowing timely access to the best and most advanced therapies to provide the support and care patients need, including supervised injectable hydromorphone as a second line treatment.

Chief Investigators:

Dr James Bell
Prof Alison Ritter AO
Prof Carla Treloar AM
Prof Nadine Ezard
A/Prof Darren Roberts
Dr Krista Siefried

Trial coordinator:

Dr Craig Rodgers

Associate Investigators:

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

-
- ¹ 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* 247: 109869.
Ferri, M., Davoli, M. & Perucci, C.A. (2006). Heroin maintenance treatment for chronic heroin-dependent individuals: a Cochrane systematic review of effectiveness. *Journal of Substance Abuse Treatment* 30.1: 63-72.
Strang, J. et al. (2015) Heroin on trial: systematic review and meta-analysis of randomised trials of diamorphine-prescribing as treatment for refractory heroin addiction. *The British Journal of Psychiatry* 207.1, 5-14.
- ² Rodgers, C., Siefried, K. J., Ritter, A., Belackova, V., Treloar, C., Jauncey, M., . . . Bell, J. (2024). 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. *BMJ Open*, 14(8), e082553. 10.1136/bmjopen-2023-082553
- ³ By law, medicines can be prescribed for a second indication by a doctor, once a drug has been approved for a first indication (off-label use), but this requires that the associated clinical care costs are supported, beyond access to the drug.
- ⁴ Van den Brink, W., Hendriks, V.M., Blanken, P., Koeter, M.W., van Zwieten, B.J., Van Ree, J.M., (2003). Medical prescription of heroin to treatment resistant heroin addicts: two randomised controlled trials. *BMJ* 327 (7410), 310.
Lintzeris, N., (2009). Prescription of heroin for the management of heroin dependence. *CNS Drugs* 23 (6), 463–476.
Australian research found that 26% of those interested were likely to meet common eligibility criteria (Nielsen, S., Sanfilippo, P., Belackova, V., Day, C., Silins, E., Lintzeris, N., . . . Ali, R. (2021). Perceptions of injectable opioid agonist treatment (iOAT) among people who regularly use opioids in Australia: findings from a cross-sectional study in three Australian cities. *Addiction*, 116(6), 1482-1494).
- ⁵ Australian Federal Police (2024) 'Rising imports of potent drug nitazene raises concern,' media release.
National Centre for Clinical Research on Emerging Drugs (2024) *Emerging drug briefing: Increasing reports of nitazene toxicity in Australia*. Holland, A. et al, (2024), 'Nitazenes—heralding a second wave for the UK drug-related death crisis?' *The Lancet Public Health*, 9:2.
- ⁶ Degenhardt L, Bucello C, Mathers B et al.. (2011) Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies. *Addiction* 106:32–51.
Amato L., Davoli M., Perucci C. A., Ferri M., Faggiano F., Mattick R. P. (2005) An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. *J Subst Abuse Treatment*; 28: 321–329.
- ⁷ For HIV treatment, moving from first-line to second-line treatment may mean a nearly threefold increase in cost, and moving from second-line to third-line treatment may mean a nearly seven-fold increase in cost (eighteen-fold increase from first-line), depending on the country. (Wikipedia)
- ⁸ Prison costs vary widely depending on level of security. Sources: <https://ipa.org.au/research/rights-and-freedoms/the-cost-of-prisons-in-australia-2023#:~:text=The%20construction%20and%20maintenance%20of,day%2C%20or%20%24147%2C900%20per%20year.>
[IPA-Research-Note-June-2024-Cost-of-Prisons-2024.pdf](https://ipa.org.au/research/rights-and-freedoms/the-cost-of-prisons-in-australia-2023#:~:text=The%20construction%20and%20maintenance%20of,day%2C%20or%20%24147%2C900%20per%20year.)
In NSW it is an average of \$437.83/prisoner/day with annual cost of \$159,808 per person.
- ⁹ The cost of one year of residential rehabilitation per person varies by the type of residential program provided (and these figures assume 365 days of treatment). Australian sources were used to derive this range: <https://www.odysseyhouse.com.au/rehab-builds-lives-delivers-600-return-investment/#:~:text=Our%20residential%20rehabilitation%20program%20costs,the%20federal%20and%20NSW%20governments>. Pitts & Yates (2010), <https://atca.com.au/wp-content/uploads/2021/12/International-Journal-Therapeutic-Communities-2010-312.pdf#page=39> ; Moore, T., Ritter, A., & Caulkins, J. (2007). The costs and consequences of three policy options for reducing heroin dependency. *Drug and Alcohol Review*, 26(4), 369-378. Shanahan M, Havard A, Mills K, et al. Health services use and treatment costs over 12 months among heroin users: findings from the Australian Treatment Outcome Study (ATOS), Sydney: National Drug and Alcohol Research Centre, University of New South Wales, 2003. BAFM study, NSW Centre for International Economics (2021). We Help Ourselves, 2019
- ¹⁰ The range of costs varies depending on the type of clinic, economies of scale. No Australian data to date. Sources for the range provided: GBP: £8995 injectable heroin per person for 26 weeks: <https://www.cambridge.org/core/journals/the-british-journal-of-psychiatry/article/costeffectiveness-of-injectable-opioid-treatment-v-oral-methadone-for-chronic-heroin-addiction/34754ADCA3714FC662AB0D10D9D56E19>;

Byford S, Barrett B, Metrebian N, et al. Cost-effectiveness of injectable opioid treatment v. oral methadone for chronic heroin addiction. *British Journal of Psychiatry*. 2013;203(5):341-349. doi:10.1192/bjp.bp.112.111583

Banerjee S, Wright MD. Injectable Opioid Agonist Treatment for Patients with Opioid Dependence: A Review of Clinical and Cost-Effectiveness. Canadian Agency for Drugs and Technologies in Health, Ottawa (ON); 2020. PMID: 33231961.

<https://europepmc.org/article/nbk/nbk564232>.

Bansback, N., Guh, D., OviedoJoeques, E., Brissette, S., Harrison, S., Janmohamed, A., Krausz, M., MacDonald, S., Marsh, D. C., Schechter, M. T., and Anis, A. H. (2018) Cost-effectiveness of hydromorphone for severe opioid use disorder: findings from the SALOME randomized clinical trial. *Addiction*, 113: 1264–1273. doi: [10.1111/add.14171](https://doi.org/10.1111/add.14171). Strang J, Groshkova T, Metrebian N. Recent evidence and current practices of supervised injectable heroin treatment in Europe and beyond. Luxembourg: Publications Office of the European Union; 2012. Dijkgraaf MG, van der Zanden BP, de Borgie CA, Blanken P, van Ree JM, van den Brink W. Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials. *BMJ*. 2005;330(7503):1297.

¹¹ The cost estimates for methadone/buprenorphine vary depending on whether it is clinic-or GP- based care, and the differing medication and formulation costs. The range was derived from multiple Australian studies, including the CoLAB study (Settumba et al (in press) Provider costs of treating opioid dependence with extended release buprenorphine in Australia. *Drug and Alcohol Review*); Bell, et al., (2007), A randomized trial of effectiveness and cost-effectiveness of observed versus unobserved administration of buprenorphine–naloxone for heroin dependence. *Addiction*, 102: 1899-1907. <https://doi.org/10.1111/j.1360-0443.2007.01979.x>; Dunlop, et al (2017). Effectiveness and cost-effectiveness of unsupervised buprenorphine-naloxone for the treatment of heroin dependence in a randomized waitlist controlled trial. *Drug and Alcohol Dependence*, 174, 181-191. <https://doi.org/10.1016/j.drugalcdep.2017.01.016>; Doran et al (2003). Buprenorphine versus methadone maintenance: a cost-effectiveness analysis. *Drug and Alcohol Dependence*, 71(3), 295-302. [https://doi.org/10.1016/S0376-8716\(03\)00169-8](https://doi.org/10.1016/S0376-8716(03)00169-8)