

A Literature Review of OAT and Implications of Depot Buprenorphine in Custodial Settings

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Introduction

This review summarises the effectiveness opioid agonist treatment (OAT: methadone and buprenorphine), the rationale for treatment in custodial settings and examines the emergence of novel methods for the delivery of OAT that may present safety and cost-effectiveness benefits over current treatment.

Methods

Medline, Psychinfo, Embase and Cochrane databases were searched from 2000-; keywords: methadone, buprenorphine, RBP6000, CAM2038, prison, treatment, focussing on original studies and review articles for methadone and buprenorphine and clinical trials for depot buprenorphine

Key Findings

393 articles were identified concerning opioid treatment in prisons, including 48 review articles. Two randomised controlled trials, one of each of CAM2038 and RBP600 for outpatient opioid treatment (in the community) were identified.

OAT (methadone and buprenorphine) are effective and currently the first-line treatment for opioid dependence but are not provided in many countries in custodial settingsⁱ. Opioid dependence among people in custody, and the incarceration of opioid dependent individuals, are substantial problems in Australia and internationally.

Opioid dependence among prison inmates results in harms that include overdose and violent death in jail^v and after release, with substantial increases in death post release^{iv}, predominantly due to drug related deaths. OAT in prison is associated with reduced drug use^{i, ii}, reduced mortality in prisonⁱⁱⁱ and post-release^{iv}, increased engagement post release if initiated in prison^{ii, viii} but not if delayed to post-release. OAT in prison is cost effective and associated with reduced crime post release^x.

Two formulation of long acting or extended release buprenorphine, CAM2038 (Bupival) and RBP6000 (Sublocade) have been demonstrated in randomised controlled trials to be non-inferior to sublingual buprenorphine^{xi} or superior to placebo for the treatment of opioid dependence in outpatient (community) settings^{xii}.

Results

Finding	NHMRC/NICE level of evidence	Author
People who use opioids have an increased mortality post release from custody	Level I	Merrall 2010
OAT associated with reduced drug use in prison	Level I	Moore 2019, Hedrich 2011, Stallwitz 2006 (<u>not</u> Perry 2015)
OAT associated with reduced mortality post release	Level III-2	Marsden 2017
OAT initiated in prison associated with increased engagement post release	Level I	Moore 2019, Heidrich 2011
OAT in prison is cost-effective	Level III-3	Gisev 2015
OAT initiated on release not associated with engagement in treatment or reduced mortality	Level III-2	Pierce 2018
OAT in prison associated with reduced crime post release	Level 1	Perry 2015
OAT in prison associated with reduced deaths in prison	Level III-2	Larney 2012

Discussion

Depot buprenorphine treatment has the potential advantages of:

- Greater convenience for patients in that they will not have to attend dosing sites (pharmacies, clinics) on a frequent basis for supervised dosing
- Reduced treatment costs for patients and service providers
- Less risk of diversion and non-medical use of the medication, enhancing safety
- Greater medication adherence and enhanced treatment outcomes for some patients who struggle to attend regularly for dosing with SL BPN^{xiv}.

There are three trials of depot buprenorphine in custodial settings:

- A trial of CAM2038 in 8 NSW jails compared to methadone assessing safety and cost-consequences (n=129, recruited) PI A Dunlop (ACTRN1261800942257)
- An RCT of RBP6000 compared to sublingual buprenorphine in jail and at community re-entry in New York. PI Joshua Lee (NCT03604159)
- A study of CAM2038 in jail in Baltimore under development. PIs Frank Vocci, Robert Schwartz

Depot buprenorphine has significant potential for enhancing OAT in prison due to anticipated reduced health and correctional staff time and costs.

Whilst OAT protects people in custody from harms associated with illicit opioid use during incarceration and in the high-risk period following release, current programs are resource-intensive. Safety concerns exist due to diversion of current treatments. Novel buprenorphine depot preparations have the potential to mitigate these challenges.

References

- i. Stallwitz A, Stöver H. The impact of substitution treatment in prisons – a literature review. *Int J Drug Policy*. 2007 Dec;18(6):464-74. DOI: 10.1016/j.drugpo.2006.11.015
- ii. Hedrich D, Alves P, Farrell M, Stöver H, Möller L, Mayet S. The effectiveness of opioid maintenance treatment in prison settings: a systematic review. *Addiction*. 2012 Mar;107:501-17. DOI: 10.1111/j.1360-0443.2011.03676
- iii. Larney S, Toson B, Burns L, Dolan K. Effect of prison-based opioid substitution treatment and post-release retention in treatment on risk of re-incarceration. *Addiction*. 2012 Feb; 107(2):372-80. DOI: 10.1111/j.1260-0443.2011.03618
- iv. Marsden J, Stillwell G, Jones H, Cooper A, Eastwood B, Farrell M, et al. Does exposure to opioid substitution treatment in prison reduce the risk of death after release? A national prospective observational study in England. *Addiction*. 2017 Aug;112(8):1408-1418. DOI: 10.1111/add.13779
- v. Larney S, Gisev N, Farrell M, Dobbins T, Burns L, Gibson A, et al. Opioid substitution therapy as a strategy to reduce deaths in prison: retrospective cohort study. *BMJ Open*. 2014 Apr 2;4:e004666. DOI: 10.1136/bmjopen-2013-004666
- vi. Merrall EL, Kariminia A, Binswanger IA, Hobbs MS, Farrell M, Marsden J, Hutchinson SJ, Bird SM. Meta-analysis of drug-related deaths soon after release from prison. *Addiction*. 2010 Sep;105(9):1545-54.
- vii. Stöver H, Michels I. Drug use and opioid substitution treatment for prisoners. *Harm Reduction Journal*. 2010;7:17. DOI: 10.1186/1477-7517-7-17
- viii. Moore KE, Roberts W, Reid HH, Smith KM, Oberleitner LM, McKee SA. Effectiveness of medication assisted treatment for opioid use in prison and jail settings: A meta-analysis and systematic review. *Journal of substance abuse treatment*. 2019 Apr 1;99:32-43.
- ix. Pierce M, Bird SM, Hickman M, Marsden J, Dunn G, Seddon T, Millar T. Effect of initiating drug treatment on the risk of drug-related poisoning death and acquisitive crime among offending heroin users. *International Journal of Drug Policy*. 2018 Jan 1;51:42-51.
- x. Gisev N, Shanahan M, Weatherburn DJ, Mattick RP, Larney S, Burns L, Degenhardt L. A cost-effectiveness analysis of opioid substitution therapy upon prison release in reducing mortality among people with a history of opioid dependence. *Addiction*. 2015 Dec;110(12):1975-84.
- xi. Perry AE, Neilson M, Martyn-St James M, Glanville JM, Woodhouse R, Godfrey C, Hewitt C. Pharmacological interventions for drug-using offenders. *Cochrane Database of Systematic Reviews*. 2015(6).
- xii. Lofwall MR, Walsh SL, Nunes EV, Bailey GL, Sigmon SC, Kampman KM, Frost M, Tiberg F, Linden M, Sheldon B, Oosman S. Weekly and monthly subcutaneous buprenorphine depot formulations vs daily sublingual buprenorphine with naloxone for treatment of opioid use disorder: A randomized clinical trial. *JAMA internal medicine*. 2018 Jun 1;178(6):764-73.
- xiii. Haight BR, Learned SM, Laffont CM, Fudala PJ, Zhao Y, Garofalo AS, Greenwald MK, Nadipelli VR, Ling W, Heidbreder C, Andersen JL. Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *The Lancet*. 2019 Feb 23;393(10173):778-90.
- xiv. Lintzeris N, Dunlop A, Masters D (2019) Clinical guidelines for use of depot buprenorphine (Bupival® and Sublocade®) in the treatment of opioid dependence. NSW Ministry of Health, Sydney Australia <https://www.health.nsw.gov.au/aod/Pages/depot-buprenorphine.aspx>

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