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Research Paper

Learning from the past, looking to the future - Is there a place for injectable opioid treatment among Australia's responses to opioid misuse?

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ABSTRACT

In the 1990s, a trial of prescribing pharmaceutical heroin for people with opioid-dependence had support from Australian State Health Ministers. However, in 1997 the proposal was vetoed by the federal Prime Minister in face of a negative tabloid media campaign. The debate then shifted to abstinence-orientated treatments. Later on, reduced heroin availability took opioid-related harms away from public sight. In this commentary, we aimed to explore the current need and the options to implement such program, lately referred to as supervised injectable opioid treatment (SIOT), in Australia. We argue that with the aging populations of opioid-dependent people who have not benefited from existing treatment options, increased misuse of prescription opioids, rising overdose rates, and the risk of unfolding overdose crisis, it seems timely to pilot SIOT here. Since the 1990s, seven RCTs as summarised in two systematic literature reviews, demonstrated that SIOT is effective for treatment-resistant opioid dependence. A sustainable SIOT model should, however, respond to key concerns related to its delivery, such as the lack of a patient exit strategy and the high cost of indefinite treatment. Evidence from long-term studies seem to support the notion that SIOT could be provided as a medium duration treatment (as opposed to short-term or indefinite), with the clear aim to stabilise patients, gradually wean them off injectable medication and transfer to opioid assisted treatment (OAT). Also, SIOT could be integrated into the existing public OAT clinics in Australia. This would reduce costs, but also provide a more patient-centred response to opioid dependence and further improve the acceptability and efficiency of OAT. The controversy that developed in the past should be mitigated by advances in research since the first Australian enquiry, use of a registered medication (open-label hydromorphone) rather than pharmaceutical heroin, and setting up clear treatment aims.

Introduction

A large discrepancy between science and practice in drug and alcohol services has been described in the literature (Marinelli-Casey, Domier, & Rawson, 2002). Medical and psycho-social interventions remain in place that have never been evaluated or have been shown to be ineffective, while evidence-based approaches remain unused (Miller, Sorensen, Selzer, & Brigham, 2006). The complexity of translating evidence into practice can be seen as a stakeholder interaction process, an outcome of a socially constructed narrative, or as an authoritative choice of policy makers (Stevens & Ritter, 2013). One example of an evidence-based program that has not been broadly adopted across the world includes supervised injectable opioid treatment (SIOT) with pharmaceutical heroin (diacetylmorphine) or hydromorphone.

Currently, the mainstream treatment for opioid dependence is opioid agonist treatment (OAT) with oral methadone or buprenorphine which has been demonstrated to be effective in reducing illicit opioid use, retaining patients in treatment, and reducing all-cause mortality among those retained in the treatment (Mattick, Breen, Kimber, & Davoli, 2009; Mattick, Breen, Kimber, & Davoli, 2014; Sordo et al., 2017). However, about 5–10% of people who are opioid-dependent do not respond to these treatments and represent the target group for SIOT (Lintzeris, 2009; Van den Brink et al., 2003). As an injectable, short-acting (pharmaceutical) drug, SIOT medication is more rewarding to patients than the long-acting oral medications (methadone, buprenorphine), and it attracts and retains patients in structured treatment on this basis (Bell, van der Waal, & Strang, 2016).

Seven randomized controlled trials (RCTs) have been conducted

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internationally that compare the effectiveness of SIOT with diacetylmorphine (mostly co-prescribed with oral methadone) to oral methadone alone (Demaret et al., 2015; Haasen et al., 2007; March, Oviedo-Joekes, Perea-Milla, & Carrasco, 2006; Oviedo-Joekes et al., 2009; Perneger, Giner, del Rio, & Mino, 1998; Strang et al., 2010; Van den Brink et al., 2003). A systematic literature review (Strang et al., 2015) and a Cochrane Review (Ferri, Davoli, & Perucci, 2010) of these RCTs concluded that SIOT with diacetylmorphine is superior to oral methadone in reducing illicit opioid use, retaining participants in treatment, and improving their health and social outcomes. On the other hand, diacetylmorphine is associated with more adverse events related to study medication than oral methadone, suggesting that supervision of every dose in SIOT is essential to achieve safety. In 2014, a Canadian RCT compared SIOT with diacetylmorphine to SIOT with hydromorphone. It concluded that the two treatments yielded comparable results (Oviedo-Joekes et al., 2016). This trial also showed that hydromorphone yielded less adverse events than diacetylmorphine (Oviedo-Joekes et al., 2017).

Studies have also demonstrated that both SIOTs are cost-effective due to lower rates of criminal offending among SIOT participants compared to those on oral methadone (Bansback et al., 2018; Dijkgraaf et al., 2005; Nosyk et al., 2012), although the difference was not always statistically significant (see Byford et al., 2013 for details). At the same time, concerns related to SIOT implementation have been expressed, such as the lack of exit strategy (i.e. when should patients leave the treatment and what the follow-up options are) and the related high cost of indefinite SIOT provision to the health care sector (Lintzeris, 2009).

SIOT with diacetylmorphine has been introduced into practice in some countries that have conducted SIOT trials. In Germany and Spain (as a post-RCT support with DAM), in the Netherlands, United Kingdom (UK) and Switzerland (as regular treatment for the target group, however ceased in the UK in 2014 due to budget cuts). In Canada, regular treatment for the target group with both diacetylmorphine and hydromorphone was introduced after a period of provisional measures with hydromorphone (BCCS, 2017). In contrast with countries that implemented treatment after local RCTs, Denmark introduced SIOT with diacetylmorphine solely based on international evidence (Strang, Groshkova, & Metrebian, 2012).

SIOT has never been implemented in Australia where a diacetylmorphine trial was first proposed in the 1990s (Bammer, 1993); at that time, there was little evidence to support the work which, in itself, was seen as controversial. In this commentary, our aim has been to summarise key developments since, explore the current need to implement SIOT in Australia, and propose a potentially feasible model for SIOT delivery.

Australian opioid use – past and present

The Australian “heroin trial” (as it was known then) was a feasibility study of SIOT using diacetylmorphine which took several stages to develop and gained initial endorsements from the State Health Ministers (Bammer & Douglas, 1996; NCEPH & AIC, 1991). However, the then federal prime minister finally prevented the trial from proceeding and refused to amend legislation allowing diacetylmorphine being imported (Hall, Kimber, & Mattick, 2002). This was largely in face of a negative tabloid campaign which claimed that the trial was “rewarding/funding drug addicts” (Christie, 1998, p. 42; Lawrence, Bammer, & Chapman, 2000, p. 254). Public discourse at that time involved distrust of experts who were seen as elite groups pushing their own agenda (Johnson, 2007). In line with that, clinicians advocating for oral methadone treatment were being dismissed for being a part of the methadone industry (Hall, 2004). As a result, abstinence-orientated treatments, for example naltrexone, were seen as preferable options (Bell, 2009), despite only later found to be less effective than OAT (Digiusto et al., 2004). Such discourse appeared to be a major shift from the approach first taken up in Australia in 1985 and subsequently continued, as governments made commitments to harm minimisation (Dillon, 1995). A later, state-based New South Wales (NSW) 1999 Drug Summit re-affirmed strong commitment to OAT, through support by evidence and personal testimonies (Bell, 2009). Re-affirming support for replacement therapy with oral methadone, however, wasn`t followed by trialling SIOT. Furthermore, a shortage of heroin in the illicit drug market in 2001 moved the negative consequences of opioid use away from public sight (Degenhardt et al., 2005; Topp, Day, & Degenhardt, 2003). As such, an emerging debate about trialling the then under-researched hydromorphone in treatment of opioid dependence did not gain traction among the Australian experts (Ba, mmer, Dance, & McDonald, 2004).

Heroin and other opioid use in Australia has not disappeared though, and many people have continued to inject heroin and/or other illicit opioids since the 1990s. Service records of the Uniting Medically Supervised Injecting Centre (MSIC) in Sydney show that among approximately 2000 clients who visited the MSIC in 2017, about 10% were using opioids at MSICs already when it first opened (2001–2002). Many MSIC clients report previous enrolments in drug treatments. A recent census of 182 current MSIC clients showed that 94% have accessed drug treatment and experienced a mean of 10 treatment episodes (median = 6), having been referred to treatment by MSIC three times on average (Salmon, Belackova, Silins, Jauncey, & Day, 2018). These findings suggest that there is an aging cohort of people dependent on heroin and/or other illicit opioids in Australia who clearly have not benefited from available treatment options. This observation is reinforced by population-level data: the median age of people who recently used opioids in Australia increased from 27 to 37 between the years 2001 and 2013 (AIHW, 2017b).

Concurrently, the number of opioid-related deaths has been on the increase in Australia (from 3.8 to 6.6 per 100 000 between 2007 and 2017) and the majority of these deaths (70%) are now related to prescription opioids (Roxburgh & Burns, 2017). Prescription opioid misuse has been on the rise (AIHW, 2017b). Between 2013 and 2016, lifetime misuse of prescription pain killers almost tripled (from 3.3% to 9.7%) and recent misuse (in last 12 months) increased from 2.3% in 2013 to 3.6% in 2016 (AIHW, 2017b). These trends seem to parallel the development of the opioid overdose crisis in North America (Kolodny et al., 2015). Exacerbated by an influx of high-potency opioids onto illicit drug markets, places like British Columbia, Canada, are now facing a public health emergency with over twenty drug overdose deaths per 100,000 population (CSDRP, 2018). Yet, a high-potency opioid (carfentanil) was seized by Australian border control in 2017 (McVeigh, 2017), suggestive of the potential for Australia to experience a similar crisis in mortality from opioids.

Australian system of treatment for opioid dependence

There are systemic issues related to the accessibility, affordability and availability of OAT provision in Australia (Bui, Day, Hanrahan, Winstock, & Chaar, 2015; Rossmanith, 2011). Consequently, a large unmet demand for opioid treatment has been documented in the past (Ritter & Chalmers, 2009). A 2014 estimate suggests this persists; approximately 90,000 individuals inject opioids in Australia (Larney et al., 2017), while only about 48,000 receive OAT (AIHW, 2014). Some consumers perceive the Australian OAT as rather punitive, manifesting as “liquid hand-cuffs” (referring to limited take-aways requiring patients to attend the clinic every day over extended periods of time) and an impersonal approach (Crawford, 2013). This evidence suggests a need to improve OAT services for patients. Advances in OAT like the new transdermal buprenorphine depot offer the opportunity to reduce daily attendance in clinics (Ling et al., 2010; Rosenthal & Goradia, 2017; Rosenthal et al., 2013), but as individual treatment needs differ (Neale, Tompkins, McDonald, & Strang, 2018), it is yet to be determined which patients will most benefit from it (Sigmon & Bigelow, 2017).

The other major concern around OAT in Australia pertains to resources. Due to federal scheduling of medications, both oral methadone and buprenorphine carry dispensing fees (AUD 120–150 monthly), unless provided in public OAT clinics. As of 2016, there were only 36 public OAT clinics in NSW, with an additional eighteen in the remaining five Australian states, and none in Victoria (AIHW, 2017a). Most patients get their medication in over 2300 dosing pharmacies and from about 2150 private prescribers (AIHW, 2016). Public OATs have filled-up their capacity, as waiting lists document (Wodak, 2012). There are no official statistics on the wait times, but in the extremity, in 2012, in a part of NSW where general practitioners have been reluctant to take on methadone prescribing, up to two year wait lists have been in place (McNamara, 2012). The situation is probably even more difficult in rural and remote areas. Part of the capacity issues at public OATs might be that they aim to stabilise patients who continue with substance use and experience health and social issues whilst in treatment (NSW Health, 2018). These patients, in fact, could be the target group for SIOT.

Implementing SIOT in Australia – a way forward

Considering the continued illicit opioid use in the (mainly) aging cohort (AIHW, 2017b) and the increasing harms in Australia (Roxburgh & Burns, 2017), it seems timely to examine if and how a sustainable SIOT model could be implemented in Australian settings. Designing feasible SIOT needs to take into account that funding limitations in the drug and alcohol sector exist, and would equally apply to this treatment. Studies assessed SIOT as cost-effective on the basis of decreased cost of crime (Dijkgraaf et al., 2005; Nosyk et al., 2012). However, the extended operating hours and nurse-led supervision of several doses per day, as well as the injectable medication itself, make SIOT clinics a significant investment. This might be difficult at a time when drug and alcohol budgets are constrained.

To save resources, SIOT could be co-located within existing OAT clinics in Australia as has been the case in Switzerland and the Netherlands, as opposed to the Canadian or UK approach where SIOT clinics have been purpose-built (Strang et al., 2012). Such co-location could bring several advantages. The group of patients that do not stabilise on oral treatments likely make up a significant proportion of the OAT clinic`s current resources. It appears that OAT operation could efficiently streamline these patients into a co-located SIOT program to better fit their needs. Also, SIOT has been practiced as highly patient-centred care that regards patient`s own aims and agency (McCall, Phillips, Estafan, & Caine, 2018; Oviedo-Joekes et al., 2014). As such, it can stimulate the existing OAT programs to provide more patient-centred care overall and attract into treatment those who might have had negative experiences there in the past. Attracting more people into SIOT/OAT is increasingly important as the rates of accidental overdose continue to rise and even more so if a public health crisis similar to North America unfolds in Australia. Patients could also transfer from SIOT to standard OAT within the clinic, once stabilised.

A question has been raised as to whether SIOT could be aimed at stabilising patients, and over the time, gradually weaning-off injectable medication and transferring them to standard OAT (Bell, Belackova, & Lintzeris, 2018), as concerns around indefinite provision of SIOT both in terms of cost and clinical outcomes exist (Lintzeris, 2008). Previous studies concluded that patient outcomes deteriorate after short-term SIOT is terminated (Demaret et al., 2016; Oviedo-Joekes et al., 2014). Bell et al. (2018), however, argue that these study participants experienced benefits compared to baseline and that outcomes in long-term SIOT plateau around two years when many participants leave treatment (see Blanken, Hendriks, Van Ree, & Van Den Brink, 2010; Oviedo-Joekes, March, Romero, & Perea-Millia, 2010 for details). These findings suggest that SIOT could be piloted as a medium duration treatment (approximately two years, as opposed to short-term or indefinite) after which patients could be transferred to less intensive oral OAT. Co-prescription of small oral methadone doses that are gradually increased as injectable medication is decreased can facilitate this transfer. Such treatment modality might require further evaluation of whether there is a sustained SIOT effect after patients transfer to oral methadone. The key difference in comparison to previous studies would be the treatment duration and its main objective (stabilisation and transfer to OAT), and this being a part of the treatment contract between patients and the clinic staff from the onset.

Given the controversy of SIOT trial in Australia in the past, using an already registered medication such as injectable hydromorphone around which initial evidence has now been developed would alleviate the need for federal authorisation. Also, an already registered medication will likely not attract the kinds of negative publicity that prescription of (pharmaceutical) heroin did. Yet, while studies have demonstrated that participants were unable to distinguish between injectable diacetylmorphine and hydromorphone (Oviedo-Joekes, Guh et al., 2010), and hydromorphone has yielded comparable results to injectable diacetylmorphine (Oviedo-Joekes et al., 2016), no study has examined provision of open-label hydromorphone so far. It would be interesting to assess whether participants are equally attracted to hydromorphone and retained in treatment as they were in the Canadian RCT (Oviedo-Joekes et al., 2016) when there was a 50% probability of receiving diacetylmorphine.

Several issues are not entirely answerable by research and will likely become the subject of discussion among professional societies, consumers and policy makers. For instance, all trials of SIOT required that participants had a previous history of (unsuccessful) drug treatments, and oral methadone in particular. The UK RIOTT study required that participants had been in continuous oral methadone treatment for the past six months preceding the trial and that they had gained little benefit from it (Strang et al., 2010). However, it has been estimated in the UK that about 90 out of 100 people who inject opioids are in oral methadone treatment (Mathers et al., 2010). By contrast, Australia remains with a large unmet demand for treatment. Other areas of discussion could include whether SIOT is a viable demand reduction or rather a harm reduction intervention (McGowan, Viens, Harris, & Rhodes, 2017; Metrebian, Shanahan, Wells, & Stimson, 1998), notably in situations where the illicit market gets flooded by high-potency opioids like in North America. Also, learning from these experiences abroad, there might be conflicting opinions on whether access to opioids for people with dependence should remain a targeted medical intervention or if access to it is an overarching human right (Boyd, 2013; Boyd, Murray, & MacPherson, 2017). Consumers should be involved in these and other drug policy debates (Greer & Ritter, 2019).

Conclusions

A high level of evidence on SIOT has emerged since the first discussions in Australia took place in the mid 1990s. It shows that SIOT is an effective second line treatment for opioid dependence. Long-term studies seem to support potential clinical benefits of a medium duration SIOT (about two years) with the aim to gradually wean-off injectable medication and transfer to standard (oral) OAT. There have been recent advances in using hydromorphone in SIOT research and clinical practice.

We conclude that these findings seem to offer an opportunity for Australia to improve responses to its treatment-resistant opioid dependence, low OAT coverage, and increasing opioid overdose rates. SIOT in Australia could encourage treatment participation, increase operational efficiency of public OATs, and enhance patient-centred approaches. Such improvement of the OAT system and attracting will be essential especially if an opioid overdose crisis unfolds. Co-location with public OAT clinics as well as clear aim to stabilise patients on SIOT and then transfer to oral treatments can also help alleviate any policy-makers` concerns about aims and costs of SIOT.

We suggest that such SIOT implementation trial with a registered

drug (open-label hydromorphone) can help reframe this treatment modality and diffuse the past controversy of diacetylmorphine prescription which led to adverse media responses in the past. Drug and alcohol sector, policy makers responsible for OAT funding, and consumers should be involved in further discussions regarding the acceptability and feasibility of this treatment modality.

Author contributions

VB conducted consultations and literature review for a feasibility assessment presented in this paper and drafted the manuscript. AS and MJ have designed and led feasibility assessment that underlined this commentary. JB has consulted with Australian and international experts to design a SIOT implementation protocol upon which the principles outlined in this commentary. All authors have contributed to the manuscript and reviewed the final version.

Declaration of interest

The authors declare no conflict of interest.

Dr Bell is employed by Uniting MSIC to develop a clinical trial of Supervised Inejctable Opioid Treatment (SIOT). In the last 5 years he has received research support from Reckittbenckiser, served on an Advisory Board for Indivior, has received speaker fees and support to attend conferences from Indivior.

Dr Belackova is employed by Uniting MSIC in developing a trial of SIOT.

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References

AIHW (2014). *National opioid pharmacotherapy statistics*Retrieved fromhttps://www.aihw.gov.au/reports/alcohol-other-drug-treatment-services/national-opioid-pharmacotherapy-statistics-nopsad-2016/contents/introduction.

AIHW (2016). *National opioid pharmacotherapy statistics 2015*Retrieved fromhttps://www.aihw.gov.au/reports/alcohol-other-drug-treatment-services/nopsad-2015/contents/opioid-pharmacotherapy-dosing-points-nopsad-2015.

AIHW (2017a). *Alcohol and other drug treatment services in Australia 2015–16.* Retrieved fromhttps://www.aihw.gov.au/getmedia/bf851ed5-673c-4f5a-8ff6-49f3a85bd95a/20799.pdf.aspx?inline=true.

AIHW (2017b). *National drug strategy household survey 2016: Detailed findings (9781760541941)*Retrieved fromhttps://www.aihw.gov.au/reports/illicit-use-of-drugs/2016-ndshs-detailed/contents/table-of-contents.

Bammer, G. (1993). Should the controlled provision of heroin be a treatment option? Australia feasibility consideration. *Addiction, 88*, 467–475.

Bammer, G., & Douglas, R. M. (1996). The ACT heroin trial proposal: An overview. *Medical Journal of Australia, 164*(11), 690–691.

Bammer, G., Dance, P., & McDonald, A. M. (2004). *Report into the feasibility of trialling hydromorphone as a treatment for heroin dependence in the australian capital territory*Canberra: National Centre for Epidemiology & Population Health, The Australia National University.

Bansback, N., Guh, D., Oviedo-Joekes, E., Brissette, S., Harrison, S., Janmohamed, A., ... Schechter, M. T. (2018). Cost-effectiveness of hydromorphone for severe opioid use disorder: Findings from the SALOME randomized clinical trial. *Addiction, 113*(7), 1264–1273.

BCCS (2017). *Guidance for injectable opioid agonist treatment for opioid use disorder.* Vancouver: British Columbia Centre on Substance Use, Ministry of Health.

Bell, J. (2009). Politics, practice, and research into treatment of heroin addiction. In R. P. Mattick, R. Ali, & N. Lintzeris (Vol. Eds.), *Pharmacotherapies for the treatment of opioid dependence: Efficacy, cost-effectiveness and implementation guidelines: Vol. 1*, (pp. 520–). London: CRC Press.

Bell, J., van der Waal, R., & Strang, J. (2016). Supervised injectable heroin: A clinical perspective. *The Canadian Journal of Psychiatry, 62*(7), 451–456.

Bell, J., Belackova, V., & Lintzeris, N. (2018). Supervised injectable opioid treatment (SIOT) for the management of opioid dependence. *CNS Drugs, 78*(13), 1339–1352. https://doi.org/10.1007/s40265-018-0962-y.

Blanken, P., Hendriks, V. M., Van Ree, J. M., & Van Den Brink, W. (2010). Outcome of long-term heroin-assisted treatment offered to chronic, treatment-resistant heroin addicts in the Netherlands. *Addiction, 105*(2), 300–308.

Boyd, S. (2013). Yet they failed to do so: Recommendations based on the experiences of NAOMI research survivors and a call for action. *Harm Reduction Journal, 10*(1), 6.

Boyd, S., Murray, D., & MacPherson, D. (2017). Telling our stories: Heroin-assisted treatment and SNAP activism in the Downtown Eastside of Vancouver. *Harm Reduction Journal, 14*(1), 27.

Bui, J., Day, C., Hanrahan, J., Winstock, A., & Chaar, B. (2015). Senior nurses' perspectives on the transfer of opioid substitution treatment clients from clinics to community pharmacy. *Drug and Alcohol Review, 34*(5), 495–498.

Byford, S., Barrett, B., Metrebian, N., Groshkova, T., Cary, M., Charles, V., ... Strang, J. (2013). Cost-effectiveness of injectable opioid treatment v. oral methadone for chronic heroin addiction. *The British Journal of Psychiatry, 203*(5), 341–349.

Christie, S. (1998). Trial by media: Politics, policy and public opinion, the case of the ACT heroin trial. *Current Issues in Criminal Justice, 10*(1), 38–51.

Crawford, S. (2013). Shouting through bullet-proof glass: Some reflections on pharmacotherapy provision in one Australian clinic. *The International Journal of Drug Policy, 24*(6), e14–e17.

CSDRP (2018). *BC coroners service death review panel: A review of ilicit drug overdose*Retrieved from. Report to the Chief Coroner of British Columbiahttps://www2.gov.bc.ca/assets/gov/public-safety-and-emergency-services/death-investigation/death-review-panel/bccs_illicit_drug_overdose_drp_report.pdf.

Degenhardt, L., Day, C., Dietze, P., Pointer, S., Conroy, E., Collins, L., ... Hall, W. (2005). Effects of a sustained heroin shortage in three Australian States. *Addiction, 100*(7), 908–920.

Demaret, I., Quertemont, E., Litran, G., Magoga, C., Deblire, C., Dubois, N., ... Ansseau, M. (2015). Efficacy of heroin-assisted treatment in Belgium: A randomised controlled trial. *European Addiction Research, 21*(4), 179–187.

Demaret, I., Quertemont, E., Litran, G., Magoga, C., Deblire, C., Dubois, N., ... Ansseau, M. (2016). Loss of treatment benefit when heroin-assisted treatment is stopped after 12 months. *Journal of Substance Abuse Treatment, 69*, 72–75.

Digiusto, E., Shakeshaft, A., Ritter, A., O'brien, S., Mattick, R. P., & Group, N. R. (2004). Serious adverse events in the Australian national evaluation of pharmacotherapies for opioid dependence (NEPOD). *Addiction, 99*(4), 450–460.

Dijkgraaf, M. G., van der Zanden, B. P., de Borgie, C. A., Blanken, P., van Ree, J. M., & van den Brink, W. (2005). Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials. *Bmj, 330*(7503), 1297.

Dillon, P. (1995). *Tha national drug strategy: The first 10 years and beyond. NDARC monograph, 27*. Retrieved from https://ndarc.med.unsw.edu.au/sites/default/files/ndarc/resources/Mono.27.pdf.

Ferri, M., Davoli, M., & Perucci, C. A. (2010). Heroin maintenance for chronic heroin-dependent individuals. *The Cochrane Database of Systematic Reviews*(8), https://doi.org/10.1002/14651858.CD003410.pub3.

Greer, A. M., & Ritter, A. (2019). “It's about bloody time”: Perceptions of people who use drugs regarding drug law reform. *The International Journal of Drug Policy, 64*, 40–46.

Haasen, C., Verthein, U., Degkwitz, P., Berger, J., Krausz, M., & Naber, D. (2007). Heroin-assisted treatment for opioid dependence. *The British Journal of Psychiatry, 191*(1), 55–62.

Hall, W. (2004). The contribution of research to Australian policy responses to heroin dependence 1990–2001: A personal retrospection. *Addiction, 99*(5), 560–569.

Hall, W., Kimber, J., & Mattick, R. P. (2002). Breaking the deadlock over an Australian trial of injectable opioid maintenance. *The Medical Journal of Australia, 176*(2), 72–73.

Johnson, C. (2007). John Howard's ‘values’ and Australian identity. *Australian Journal of Political Science, 42*(2), 195–209.

Kolodny, A., Courtwright, D. T., Hwang, C. S., Kreiner, P., Eadie, J. L., Clark, T. W., ... Alexander, G. C. (2015). The prescription opioid and heroin crisis: A public health approach to an epidemic of addiction. *Annual Review of Public Health, 36*(1), 559–574. https://doi.org/10.1146/annurev-publhealth-031914-122957.

Larney, S., Hickman, M., Guy, R., Grebely, J., Dore, G. J., Gray, R. T., ... Degenhardt, L. (2017). Estimating the number of people who inject drugs in Australia. *BMC Public Health, 17*(1), 757.

Lawrence, G., Bammer, G., & Chapman, S. (2000). Senting the wrong signal": Analysis of print media reportage of the ACT heroin prescription trial proposal, August 1997. *Australian and New Zealand Journal of Public Health, 24*(30), 254–264.

Ling, W., Casadonte, P., Bigelow, G., Kampman, K. M., Patkar, A., Bailey, G. L., ... Beebe, K. L. (2010). Buprenorphine implants for treatment of opioid dependence: A randomized controlled trial. *JAMA, 304*(14), 1576–1583.

Lintzeris, N. (2008). Future challenges for heroin and other opioid substitution treatment. *Addiction, 103*(6), 967–968. https://doi.org/10.1111/j.1360-0443.2008.02260.x.

Lintzeris, N. (2009). Prescription of heroin for the management of heroin dependence.

CNS Drugs, 23(6), 463–476.
March, J. C., Oviedo-Joekes, E., Perea-Milla, E., & Carrasco, F. (2006). Controlled trial of prescribed heroin in the treatment of opioid addiction. *Journal of Substance Abuse Treatment, 31*. https://doi.org/10.1016/j.jsat.2006.04.007.
Marinelli-Casey, P., Domier, C. P., & Rawson, R. A. (2002). The gap between research and practice in substance abuse treatment. *Psychiatric Services, 53*(8), 984–987.
Mathers, B. M., Degenhardt, L., Ali, H., Wiessing, L., Hickman, M., Mattick, R. P., ... Strathdee, S. A. (2010). HIV prevention, treatment, and care services for people who inject drugs: A systematic review of global, regional, and national coverage. *Lancet (London, England), 375*(9719), 1014–1028.
Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2009). Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *The Cochrane Database of Systematic Reviews*(3), https://doi.org/10.1002/14651858.CD002209.pub2.
Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *The Cochrane Database of Systematic Reviews*(2), https://doi.org/10.1002/14651858.CD002207.pub4.
McCall, J., Phillips, J. C., Estafan, A., & Caine, V. (2018). Exploring the experiences of staff working at an opiate assisted treatment clinic: An interpretive descriptive study. *Applied Nursing Research, 45*, 45–51.
McGowan, C., Viens, A., Harris, M., & Rhodes, T. (2017). Risk environments and the ethics of reducing drug-related harms. *The American Journal of Bioethics, 17*(12), 46–48.
McNamara, S. (2012). *Serious shortage of methadone programs.* Retrieved fromInSight [serial on the Internet]https://insightplus.mja.com.au/2012/12/serious-shortage-methadone-programs/.
McVeigh, S. (2017). *A deadly drug being passed off as MDMA and heroin has hit Australian shores, authorities have warned.* Retrieved fromABC Newshttp://www.abc.net.au/triplej/programs/hack/carfentanil/8281370.
Metrebian, N., Shanahan, W., Wells, B., & Stimson, G. (1998). Feasibility of prescribing injectable heroin and methadone to opiate-dependent drug users: Associated health gains and harm reductions. *The Medical Journal of Australia, 168*(12), 596–600.
Miller, W. R., Sorensen, J. L., Selzer, J. A., & Brigham, G. S. (2006). Disseminating evidence-based practices in substance abuse treatment: A review with suggestions. *Journal of Substance Abuse Treatment, 31*(1), 25–39.
NCEPH, & AIC (1991). Heroin treatment—New alternatives. In G. Bammer, & G. Gerrard (Eds.). *Proceedings of a seminar held on 1 November 1991*. Ian Wark Theatre, Becker House, Canberra: National Centre for Epidemiology and Population Health, Australian Institute of Criminology, National Drug and Alcohol Research Centre.
Neale, J., Tompkins, C. N., McDonald, R., & Strang, J. (2018). Implants and depot injections for treating opioid dependence: Qualitative study of people who use or have used heroin. *Drug and Alcohol Dependence, 189*, 1–7.
Nosyk, B., Guh, D. P., Bansback, N. J., Oviedo-Joekes, E., Brissette, S., Marsh, D. C., ... Anis, A. H. (2012). Cost-effectiveness of diacetylmorphine versus methadone for chronic opioid dependence refractory to treatment. *Canadian Medical Association Journal, 184*(6), E317–E328.
NSW Health (2018). *NSW clinical guidelines: Treatment of opioid dependence.* North Sydney: NSW Ministry of Health.
Oviedo-Joekes, E., Brissette, S., Marsh, D. C., Lauzon, P., Guh, D., Anis, A., ... Schechter, M. T. (2009). Diacetylmorphine versus methadone for the treatment of opioid addiction. *The New England Journal of Medicine, 361*(8), 777–786.
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.
Oviedo-Joekes, E., Guh, D., Brissette, S., Marchand, K., MacDonald, S., Lock, K., ... Krausz, M. (2016). Hydromorphone compared with diacetylmorphine for long-term opioid dependence: A randomized clinical trial. *JAMA Psychiatry, 73*(5), 447–455.
Oviedo-Joekes, E., Brissette, S., MacDonald, S., Guh, D., Marchand, K., Jutha, S., ... Anis, A. H. (2017). Safety profile of injectable hydromorphone and diacetylmorphine for long-term severe opioid use disorder. *Drug and Alcohol Dependence, 176*, 55–62.
Oviedo-Joekes, E., Guh, D., Brissette, S., Marsh, D. C., Nosyk, B., Krausz, M., ... Schechter, M. T. (2010). Double-blind injectable hydromorphone versus diacetylmorphine for the treatment of opioid dependence: A pilot study. *Journal of Substance Abuse Treatment, 38*(4), 408–411.
Oviedo-Joekes, E., March, J. C., Romero, M., & Perea-Millia, E. (2010). The Andalusian trial on heroin-assisted treatment: A 2 year follow-up. *Drug and Alcohol Review, 29*(1), 75–80.
Perneger, T. V., Giner, F., del Rio, M., & Mino, A. (1998). Randomised trial of heroin maintenance programme for addicts who fail in conventional drug treatments. *British Medical Journal, 317*(7150), 13–18.
Ritter, A., & Chalmers, J. (2009). *Polygon: The many sides to the Australian opioid pharmacotherapy maintenance system.* Canberra: Australian National Council on Drugs.
Rosenthal, R. N., & Goradia, V. V. (2017). Advances in the delivery of buprenorphine for opioid dependence. *Drug Design, Development and Therapy, 11*, 2493.
Rosenthal, R. N., Ling, W., Casadonte, P., Vocci, F., Bailey, G. L., Kampman, K., ... Sigmon, S. (2013). Buprenorphine implants for treatment of opioid dependence: Randomized comparison to placebo and sublingual buprenorphine/naloxone. *Addiction, 108*(12), 2141–2149.
Rossmanith, A. (2011). *Fees for pharmacotherapy: An unfair burden. Of substance: The national magazine on alcohol, tobacco and other drugs, Vol. 9* (3).
Roxburgh, A., & Burns, L. (2017). *Accidental drug-induced deaths due to opioids in Australia, 2013.* Sydney: National Drug and Alcohol Research Centre.
Salmon, A. M., Belackova, V., Silins, E., Jauncey, M. E., & Day, C. (2018). Beyond a safe injection: What are the health and social needs of clients of a supervised injecting facility? *Paper presented at the APSAD*.
Sigmon, S. C., & Bigelow, G. E. (2017). Food and Drug Administration approval of sustained-release buprenorphine for treatment of opioid dependence: Realizing its potential. *Addiction, 112*(3), 386–387.
Sordo, L., Barrio, G., Bravo, M. J., Indave, B. I., Degenhardt, L., Wiessing, L., ... Pastor-Barriuso, R. (2017). Mortality risk during and after opioid substitution treatment: Systematic review and meta-analysis of cohort studies. *BMJ, 357*, j1550.
Stevens, A., & Ritter, A. (2013). How can and do empirical studies influence drug policies? Narratives and complexity in the use of evidence in policy making. *Drugs Education Prevention & Policy, 20*, 169–174.
Strang, J., Metrebian, N., Lintzeris, N., Potts, L., Carnwath, T., Mayet, S., ... Groshkova, T. (2010). 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. *The Lancet, 375*(9729), 1885–1895.
Strang, J., Groshkova, T., & Metrebian, N. (2012). *Recent evidence and current practices of supervised injectable heroin treatment in Europe and beyond.* Luxembourg: Publications Office of the European Union.
Strang, J., Groshkova, T., Uchtenhagen, A., van den Brink, W., Haasen, C., Schechter, M. T., ... Oviedo-Joekes, E. (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.
Topp, L., Day, C., & Degenhardt, L. (2003). Changes in patterns of drug injection concurrent with a sustained reduction in the availability of heroin in Australia. *Drug & Alcohol Dependence, 70*(3), 275–286.
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.
Wodak, A. (2012). Serious shortage of methadone programs. *Medical Journal of Australia (MJA Insight)*(12).