‘Naltrexone or methadone’? Debates about drug treatments for heroin dependence in the context of drugs policy

Matthew Thomas and Luke Buckmaster
Social Policy Section

Executive summary

There has been significant debate in the Australian Parliament and the wider community in recent years in relation to alternative drug treatments for opioid (mainly heroin) dependence. Within this debate, zero-tolerance-style arguments have been raised by many in favour of abstinence-based treatments using medications such as naltrexone. Alternatively, harm minimisation arguments have been used to support methadone and similar treatments.

This Research Paper examines the latest research on the treatments, identifies gaps in this research and distinguishes the various treatments’ respective costs and benefits.

The main conclusions of the paper are:

• uniform and detailed statistics on use of the various drug treatments for opioid dependence are not readily available, making it difficult to develop a clear picture of rates of use, safety and efficacy

• naltrexone has shown some promise in the treatment of some opioid dependent people under certain circumstances (e.g. those capable of remaining compliant with the treatment)

• for the majority of opioid-dependent individuals, naltrexone has been consistently linked with high rates of non-compliance, a greater risk of mortality and reduced likelihood of long-term success—this indicates the need for further research into its efficacy and safety

• methadone and other opioid substitution treatments (OST) continue to be widely acknowledged as effective in reducing opioid dependence and associated health and social problems

• the above findings highlight the need for a range of treatment options (including naltrexone) to meet individual needs, but also for the continued availability of OST for a majority of opioid-dependent people

• the paper concludes that the treatments should be considered on their individual merits, rather than on the basis of characterisations of their relevance to particular policy approaches such as ‘zero tolerance’ or ‘harm minimisation’.
Introduction

The Australian Government’s illicit drugs policy has been in the media spotlight recently. This is due, in no small part, to the Government’s very public recommendation that the Australian Football League (AFL) should adopt a zero-tolerance approach to players who test positive to illicit drugs. To do otherwise, the Australian Government argued, would be to undermine its own zero-tolerance stance and send the wrong message to young Australians who look up to footballers as role models. In response to the Government’s call, the Australian Drug Foundation’s Bill Stronach indicated that he felt the AFL’s current three-strike policy, showing concern as it does for player welfare, is a responsible one. He went on to describe the Government’s zero-tolerance approach as being not beneficial to players with illicit drug problems and as being driven by politics.1 This example illustrates the polarisation between harm minimisation and zero-tolerance approaches that typically arises when illicit drugs policy is considered in a public setting.

A similar form of polarisation is becoming evident in public debates played out over alternative drug treatments (or pharmacotherapies) for opioid dependence. Increasingly, zero-tolerance-style arguments are being mounted in favour of abstinence-based treatments using opioid-antagonist medications such as naltrexone, with harm minimisation arguments mobilised to support methadone and other forms of Opioid Substitution Treatment (OST) such as buprenorphine.

In the course of a recent parliamentary committee inquiry into the impact of illicit drug use on families, the chair expressed a clear preference for ends-oriented treatment – that is, for treatment that gets people off opioids altogether as soon as possible – over treatments that have as their objective stabilising the lives of heroin users with the assistance of opioid substitutes like methadone. Such ends-oriented treatment was described as being compatible with the Government’s zero-tolerance policy, which the chair described as having as its aim getting everyone off drugs.2 The chair’s stance closely parallels the position outlined in the 2003 report of the inquiry into substance abuse in Australian communities.3 In its recommendations, this report specified that, in providing pharmacotherapy treatment services to opioid-dependent people, governments should give priority to treatments such as

1. See also C. Scanlon, ‘Zero-tolerance drug policies too easily abandon the user’, The Age, 23 May 2007. Scanlon argues that the Australian Government’s strategy should be brought into line with the AFL’s harm-minimisation approach, with all of Australia’s illicit drug users having access to the same high levels of treatment and care currently afforded to AFL players.


naltrexone which ‘focus on abstinence as the ultimate outcome’. However, some members of the committee, critical of the report’s recommendation, and of the zero-tolerance approach more generally, point out that only a minority of heroin addicts actually achieve and maintain abstinence. For the remainder, they argue, heroin-dependence is ‘a chronic, relapsing disease’ for which the treatment focus should be management using treatments such as methadone or buprenorphine rather than cure. This dispute reflects a broader public debate about the virtues of naltrexone compared with OST that has been conducted along similar lines.

What is not clear in debates such as those described above is the question of whether or not health experts agree with such characterisations of the treatment types and of the connections drawn between them and the two illicit drugs policy approaches. Also obscured is the philosophy and rationale underpinning the two types of treatment and the relationships between them, including how and where, according to the research, they might be complementary.

This Research Paper draws together the latest research on the treatments, identifies gaps in this research and distinguishes the various treatments’ respective costs and benefits. In doing so, it sheds some light on the general position of health experts where it comes to the appropriate understanding and use of the different pharmacotherapy treatments for opioid dependence.

**Australian Government approaches to illicit drugs policy**

Until the 1980s, Australia’s illicit drug policies were primarily oriented towards prohibition and drug law enforcement. It was partly in response to the public health threat posed by HIV/AIDS and the recognition that strict prohibition measures were not working, that the Australian Government ameliorated the former hard-line stance, introducing ‘harm minimisation’ as the guiding principle of the 1986 National Campaign Against Drug Abuse (now the National Drug Strategy). There continues to be some conjecture as to precisely what harm minimisation means and how it should best be achieved. However, it is generally

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agreed that harm minimisation refers to the notion that drug policies should aim to minimise the harmful effects of drugs in Australian society, rather than simply attempting to eliminate drug use.\(^8\) The introduction of this pragmatic approach by the then Federal Health Minister, Neal Blewett, was aided by bipartisan political support and cooperation at both federal and state levels. It was also assisted by conservative politicians rejecting the opportunity to make political capital out of drug policy through reference to a US-style ‘War on Drugs’, with its associated emphasis on prohibition and abstinence.\(^9\)

The harm minimisation consensus continued more-or-less unchallenged until the Prime Minister, John Howard’s launch of the National Illicit Drug Strategy, ‘Tough on Drugs’, in 1997.\(^10\) While this strategy retained an explicit commitment to harm minimisation measures through community-based treatment and rehabilitation, its emphasis was predominantly on prohibition and law enforcement, with substantially increased funding for the Australian Federal Police and Australian Customs Service. The ‘Tough on Drugs’ strategy was expanded to include a range of new measures and given further financial support in the context of the 2001 election and the 2003-04 Budget.

The catalyst for the new, tougher policy approach was the Prime Minister’s (and the Cabinet’s) refusal to support, through the amendment of relevant legislation and allocation of funding, a scientific trial of prescription heroin in the Australian Capital Territory (ACT) in 1997.\(^11\) In personally intervening to block the proposed trial, the Prime Minister stood firmly against the stand taken by the Ministerial Council on Drug Strategy and a majority of state, territory and federal health and law enforcement ministers. He did so on the grounds that the importation of heroin for a trial would both contravene Australia’s international treaty obligations and send the message that heroin use was condoned (thereby undermining education and treatment efforts). Opposition to heroin trials (and later medically supervised injecting rooms) has remained a consistent theme in the Howard Government's approach to illicit drugs policy over the last decade.\(^12\)

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Again in keeping with his Government’s tougher approach, in 1998, the Prime Minister appointed Salvation Army Major Brian Watters (a vocal advocate of prohibition and abstinence strategies and critic of harm minimisation programs) to chair the newly established Australian National Council on Drugs, the peak body for providing drug policy advice to the Government.13

Opinion is divided regarding the success or otherwise of the ‘Tough on Drugs’ strategy. This is partly because of the polarisation that invariably occurs between committed zero-tolerance and harm minimisation stances, and related disagreement regarding what are appropriate measures of success or failure for illicit drugs policies. The ‘Tough on Drugs’ approach is generally agreed to have reduced the availability and use of heroin in Australia since this strategy’s introduction, and to have contributed to a reduction in the number of deaths from heroin overdose.14 However, some argue that the reduction in heroin supply has simply shifted the illicit drugs problem elsewhere. This, they argue, has created both new opportunities for manufacturing and trafficking in amphetamines: drugs for which (unlike heroin) there is no effective treatment for dependence or abuse, and resultant increases in the harms suffered by drug users.15

There is also some debate as to just how tough on drugs the Australian Government’s strategy really is. While the Howard Government has consistently emphasised publicly its hardline approach to illicit drugs and provided substantial funding increases for drug law enforcement in recent years, it also continues to support a number of significant harm


14. G. Bammer, W. Hall, M. Hamilton and R. Ali, ‘Harm minimisation in a prohibition context—Australia’, AAPS, 582, July 2002, p.85; J. Stewart, ‘War on drugs is an endless battle that can’t be won’ Canberra Times, 1 December 2006; M. Devine, ‘It pays to be tough on drugs’, The Sun-Herald, 9 March 2003. That said, some commentators have questioned whether it was the Government’s law enforcement measures that were the primary cause of the reduction in heroin availability in Australia from 2000, or some other factor. Andrew Macintosh has suggested that Australia’s ‘heroin drought’ is more likely to have been the result of a decision by heroin producers and traffickers to switch from heroin to metamphetamine production and supply. A. Macintosh, ‘Drug law reform. Beyond prohibition’, The Australia Institute, Discussion Paper No. 83, February 2006. Alex Wodak appears to agree with this assessment. He proposes as ‘a more credible explanation’ than the Government’s ‘Tough on Drugs’ policy a substantial fall in heroin production in Burma (a major source of the heroin reaching Australia) since 1996. This fall in production was attributed by the Commissioner of the Australian Federal Police, Mick Keelty to ‘a business decision by Asian organised crime gangs to switch from heroin production as their major source of income to the making of metamphetamine, or speed, tablets’. A. Wodak, ‘The heroin trial 10 years on: how politics killed hope’, Crikey, 22 August 2007.

minimisation initiatives. This has led one observer to conclude that the Howard Government supports zero-tolerance as a political strategy, but harm reduction as public policy. A number of commentators concur with such an assessment of the situation, and agree that the contradictions inherent in the government’s approach result in ‘a sensible stance in practice’. Nevertheless, some advocates of harm minimisation remain concerned that the tough on drugs rhetoric negatively impacts on harm reduction services, and that the Howard Government may increasingly be retreating from harm minimisation in favour of a more strict prohibition approach and focusing on strategies directed solely at enforced abstinence.

In summary, the fundamental point of difference between the harm minimisation and zero-tolerance approaches is the question of whether or not it is possible, or morally right, to attempt to eradicate illicit drugs (or an individual drug) from any given society. Those who argue for a zero-tolerance approach typically maintain that a drug-free society is realistic, and should be pursued as an ideal, especially given the damage caused by drugs to individuals and society. From the harm minimisation perspective, the eradication of a drug or drugs from society is an unrealistic aim that typically causes more harm than good. As a result, according to this perspective, we would do better to restrict the damage caused by them.

The international perspective

The illicit drugs policy debates that are currently being conducted in Australia are characteristic of those played out in the wider, international setting. Many other countries are negotiating similar tensions between zero-tolerance and harm minimisation approaches in developing their policies. Like Australia, in terms of their overall policy stance, these countries can be mapped on a spectrum between the two approaches in their extreme forms.


17. A. Wodak, ibid.; P. Mendes, ‘Social Conservatism vs harm minimisation: John Howard on illicit drugs’, *Journal of Economic and Social Policy*, 6:1, Summer 2001. Mendes attributes Howard’s stance to his being a ‘cautious political pragmatist’. In Mendes’ view, while Howard personally favours a prohibitionist approach, he recognises the popularity of harm minimisation programs and has, as a result, chosen not to alter the Government’s formal commitment to harm minimisation goals and objectives. See also D. Weatherburn, ‘Has the war on drugs failed?’, *Australian Journal of Forensic Sciences*, 33:1, Jan/June 2001, pp. 15-21. Weatherburn notes that prohibition and harm reduction are not incompatible and that drug use can profitably be treated as both a legal and a public health problem. The key, for Weatherburn, would appear to lie in getting the balance right and being aware of the failings of the ‘Tough on Drugs’ approach.


19. A. Macintosh, op. cit.; C. Treloar, S. Loveday and N. Booker, op. cit.
Perhaps the two countries most frequently cited as evidence in support of arguments for either strong harm minimisation or zero-tolerance approaches to illicit drugs policies are the Netherlands and Sweden.\(^\text{20}\) Whereas in recent years Sweden has developed a zero-tolerance approach to illicit drugs, similar to the ‘War on Drugs’ mounted by the US, the Netherlands has fashioned a national drug policy that is liberal and primarily focused on harm minimisation. The coexistence of these diametrically opposed approaches within the European Union (EU), and their influence on other member states, poses significant barriers to the adoption of a unified EU approach to tackling large scale drug trafficking. The EU has settled on a pragmatic solution to the problem of divergent drug policies among member states by focusing on countries working together rather than attempting to develop identical policies. However, it still needs to carefully negotiate the divide between Swedish and Dutch policies, if it is to gain the cooperation of all member states in pursuit of collective goals. While the ongoing tension in the EU resulting from the influence of Dutch and Swedish policy renders a harmonisation of member states’ approaches unattainable, this tension has led to the development of a wide range of policy approaches and possible solutions. In the view of one commentator, this leaves the EU ‘in a stronger position to manage drug use’\(^\text{21}\).

Australia’s pragmatic approach to illicit drugs policy is generally agreed in the international community to have been reasonably successful, especially in the area of harm reduction. Indeed, some international commentators view Australia as an exemplar in progressive approaches to reducing harm risk to drug users and others through its introduction of measures such as medically supervised injecting facilities and needle exchange programs.\(^\text{22}\) To the extent that Australia has steered a course between the poles of strong harm minimisation and zero-tolerance approaches, it would appear to have successfully avoided some of the problems experienced by the US and some individual EU member states.

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Opioid use in Australia

According to the 2004 National Drug Strategy Household Survey, 384,800 Australians aged 14 years and older had used heroin, methadone and/or other opioids in their lifetime. While almost twice the number of males as females had used opioids in their lifetime (248,100 versus 137,200), this disparity is reduced where it comes to recent use of opioids (32,800 versus 23,600). Four in nine recent users of heroin and/or methadone (45 per cent) used these drugs weekly or more frequently, with three in ten (29.3 per cent) having used them only once or twice a year. The average age at which Australians first used heroin was 21.2 years, with methadone first used at an average age of 24.8 years. While the overall numbers of opioid users in the 2004 survey have increased slightly from the equivalent 2001 survey, the patterns of use are broadly similar.

According to the National Drug and Alcohol Research Centre (NDARC), there were 357 deaths attributed to opioids in 2004 (among those aged 15 to 54 years). The rate of accidental deaths due to opioids in Australia was 31.3 per million persons aged 15 to 54 years (effectively unchanged from 31.5 per million in 2003).

NDARC notes that both number and rate of opioid induced deaths in Australia in 2004 remain lower than figures recorded in the mid 1990s, when heroin use and harm were increasing. These figures peaked at 1,116 deaths (or 101.9 per million) in 1999.

However, as illicit drugs researcher, Professor Shane Darke notes, the number of opioid induced deaths are around the same as in the early 1990s, ‘when it was rightly regarded as a national tragedy’. Further, while there is now significant public emphasis on the harms associated with increased methamphetamine (or ‘Ice’) use in Australia, it is important to note that the rate of methamphetamine related deaths (6.6 per million persons aged 15 to 54 years) in 2004 is still substantially lower than the rate of opioid induced deaths in that year.

25. ibid.
Opioid use and dependence—the physiology

A range of factors, including individual and environmental characteristics, can influence whether an individual who begins to use opioid drugs such as heroin will continue to take them long enough to become dependent. The impact of opioid use on the brain is a key influence on dependence. When opioids travel through the bloodstream to the brain, the chemicals attach to receptors that trigger feelings of pleasure (the mu opioid receptors). While opioids are routinely prescribed for pain relief, the activation of these reward processes in the absence of significant pain can motivate repeated use of opioids simply for pleasure.

Compulsion to use opioids can then extend over time beyond a simple drive for pleasure as a result of tolerance and dependence. Opioid tolerance is the process through which opioid receptors in the brain gradually become less responsive to opioid stimulation. This means that over time more and more opioid is needed to produce pleasure comparable to that provided by previous use.

On the other hand, opioid dependence can be defined in terms of susceptibility to withdrawal symptoms triggered by changes elsewhere in the brain. For example, use of opioids suppresses the brain’s release of a chemical, noradrenaline (NA) that normally stimulates wakefulness, breathing, blood pressure, general alertness and other functions. Repeated exposure to opioids leads the brain to attempt to overcome this suppressive impact by increased release of NA. The presence of opioids is generally sufficient to offset this heightened activity and allow the person using them to feel more or less normal. However, when opioids are not present to suppress this activity, the brain releases excessive amounts of NA, leading to jitters, anxiety, muscle cramps and diarrhoea. This leads to daily drug use in order to avert these symptoms of withdrawal.

29. These reward processes include the release of the chemical dopamine and also the creation of a lasting record of memory that associates good feelings with the circumstances and environment in which they occur. These memories lead to craving for drugs when a person encounters persons, places or things associated with their drug use.
31. ibid., p. 15.
32. ibid.
33. While not discussed here, there is increasing evidence that prolonged use of opioids also produces more long-lasting changes in the brain that may entrench dependence and addiction.
Pharmacotherapy approaches to treating opioid dependence—an overview

It is important to note that there are a number of non-pharmacotherapy treatments for opioid addiction, including counselling, psychotherapy, detoxification using various methods and long-term rehabilitation through the activities of therapeutic communities. Each of these forms of therapy can play an important role in the overall treatment of opioid dependency. However, this paper focuses specifically on pharmacotherapy treatments.

Pharmacotherapy approaches to treating opioid dependence consist of two separate methods. The first of these is Opioid Substitution Treatment (OST), which involves the substitution of an illegal, short-acting, expensive opioid (heroin), which is usually injected, with a legal, longer lasting, inexpensive opioid (methadone or buprenorphine), which is taken orally. The second approach, abstinence-based or relapse prevention treatment, involves the use of opioid-antagonist medication (such as naltrexone) to bring about an opioid-free state in opioid users, while minimising withdrawal-related problems. Opioid-antagonist medication acts by inhibiting the mu opioid receptors in the brain, thereby blocking the pleasurable effects of opioids. Whereas detoxification using naltrexone is typically a rapid-withdrawal technique for which the goal is early abstinence, OST seeks to control a person’s drug use on a long-term basis while minimising the harms experienced.

Opioid Substitution Treatment

The basic idea behind OST is that it enables people to gain better control of their lives (for example, improve their health and, if need be, find accommodation) and reduce the risks associated with their heroin use without having to deal with the various problems associated with withdrawal. OST is provided by specialist clinics, medical practitioners and community pharmacies. In some states, treatment is provided free through publicly funded clinics, though increasingly treatment is provided through community pharmacies with a charge attached. Around one-third of dependent heroin users are in opioid substitution treatment. There is strong evidence that OST plays an important role in reducing overdose deaths, preventing HIV and reducing criminal behaviour.

Methadone

Methadone was officially introduced to Australia in 1970. It has been consistently used in OST since the mid-1970s and is currently the most widely used pharmacotherapy in Australia.\(^3^6\) It is listed as a Schedule 8 (Controlled) drug in Australia, meaning there are strict regulatory controls associated with its use. The Australian Government funds the cost of methadone for treatment of opioid dependence supplied under the Pharmaceutical Benefits Scheme (PBS) through clinics and pharmacies approved by state and territory governments. Methadone typically comes as a liquid that is swallowed.

As a long-acting opioid, unlike heroin, the effects of methadone can last for days. While methadone does create dependence in the user, because it has a steadier impact on the mu opioid receptors, it produces minimal tolerance and alleviates craving and compulsive drug use.\(^3^7\)

Rates of usage

There is very little publicly available information on participation rates in methadone maintenance treatment of opioid addiction in Australia. The information that does exist contains varying estimates. For example, self-reported data collected through the Australian Bureau of Statistics National Health Survey suggests that there were around 16,000 people in methadone maintenance treatment in Australia in 2004.\(^3^8\) On the other hand, an Australian Government interdepartmental committee reported that at June 2001, there were approximately 32,000 clients in methadone treatment in Australia.\(^3^9\) According to another estimate, around 102,615 episodes of methadone treatment were reported in Australia between 2000 and 2003.\(^4^0\) Latest pharmacotherapy statistics collected by state and territory governments and provided to the Australian Institute of Health and Welfare indicate that, on measures, including change in heroin-free days, abstinence from heroin and crime reduction, it is cost effective to provide on-going management treatment for heroin users.

38. AIHW, op. cit., cat. no. HSE 43, p. 68.
40. A. E. Gibson, L. Degenhardt and W. Hall, ‘Opioid overdose deaths can occur in patients with naltrexone implants’, The Medical Journal of Australia, 186:3, 2007, p. 27. An episode treatment refers to a period of contact, with defined start and end dates, between a client and a treatment agency.
a snapshot/specified day in June 2006, of an estimated 38,659 clients receiving pharmacotherapy treatment, some 27,588 (or 71 per cent) were receiving methadone.41

There are no publicly available statistics from which to determine the number of doses of methadone supplied annually through the PBS. This is because methadone is supplied through the PBS under a particular program (the opiate dependence treatment program, provided for under section 100 of the National Health Act 1953) for which statistics are not made routinely available in the same way as other PBS pharmaceuticals.

However, statistics are available for the total cost to the Australian Government of methadone prescriptions provided for opioid dependence under the PBS. Figures for the years 2001 to 2006 are shown in the table below.

**Table 1: Cost to the Australian Government of methadone prescriptions provided under the PBS annually between 2001 and 2006**

<table>
<thead>
<tr>
<th>Financial Year</th>
<th>Cost ( AUD thousand )</th>
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<tbody>
<tr>
<td>2001-02</td>
<td>$4,394</td>
</tr>
<tr>
<td>2002-03</td>
<td>$4,364</td>
</tr>
<tr>
<td>2003-04</td>
<td>$4,336</td>
</tr>
<tr>
<td>2004-05</td>
<td>$4,549</td>
</tr>
<tr>
<td>2005-06</td>
<td>$4,760</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>$22,403</strong></td>
</tr>
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</table>

Source: Department of Health and Ageing

**Evidence of benefit**

Methadone is regarded in Australia and internationally as an effective method of treating opioid dependence. Indeed, according to one review in the *Journal of the American Medical Association*, research has ‘consistently demonstrated that methadone maintenance effectively reduces drug use, reduces medical comorbidity, decreases transmission of human immunodeficiency virus, reduces mortality, and improves social functioning’.43

A number of Australian and international studies have indicated that when a whole-of-society perspective is taken into account, methadone treatment results in net financial benefits. A recent study conducted in Victoria found that each person in methadone treatment costs

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42. Despite methadone being far more widely used than buprenorphine in Australia, the total costs to the Australian Government for buprenorphine are higher due to this treatment’s greater expense.

$5000 less per year in attributed health and crime costs than an illicit drug user not in treatment.\textsuperscript{44} An earlier Australian study found that for every $1 spent on methadone maintenance treatment, the community gained $4-5 in terms of reduced health care costs, reduced crime and other benefits.\textsuperscript{45}

### Buprenorphine

Buprenorphine is a long-acting opioid that has been used in Australia for detoxification and maintenance treatment purposes since 2001. Like methadone, buprenorphine is listed as a Schedule 8 drug. It is also listed on the PBS for treatment of opioid dependence for supply through clinics and pharmacies approved by state and territory governments. Buprenorphine comes in tablet form and is taken sublingually (dissolves under the tongue). It is easier to withdraw from and is longer lasting (lasting up to two or three days) than methadone. Buprenorphine is a partial opioid agonist. That is, while the drug blocks the effects of any other opiate used (such as heroin), it also has some opioid properties and effects. Buprenorphine is less likely than methadone to result in overdose because it blocks other opioids and even itself as the dosage increases.\textsuperscript{46} International studies have shown that like methadone, buprenorphine is far more effective when used in maintenance treatment than for detoxification purposes.\textsuperscript{47}

### Rates of usage

There is very little publicly available information on rates of usage of buprenorphine treatment for opioid addiction in Australia. However, latest pharmacotherapy statistics reveal that on a snapshot/specified day in June 2006, 8,950 clients were receiving buprenorphine. This accounts for 23 per cent of the total estimated number of clients receiving pharmacotherapy treatment on that day.\textsuperscript{48} This figure corresponds with other estimates that


\textsuperscript{46} T. Kosten and T. George, op. cit., p. 19.


\textsuperscript{48} AIHW, op. cit., cat. no. HSE 53, p. 43.
around one in four of those on OST are taking buprenorphine. Approximately 49,950 episodes of buprenorphine treatment were recorded in Australia between 2000 and 2003.

Like methadone, buprenorphine is supplied through the PBS under the opiate dependence treatment program. As noted above, statistics on this program are not made routinely available.

The table below shows the total costs to the Australian Government of buprenorphine prescriptions provided for opioid dependence under the PBS for the years 2001 to 2006.

Table 2: Cost to the Australian Government of buprenorphine prescriptions provided under the PBS annually between 2001 and 2006

<table>
<thead>
<tr>
<th>Financial Year</th>
<th>Cost (’000)</th>
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<td>2004-05</td>
<td>$16,369</td>
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<td>2005-06</td>
<td>$17,833</td>
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<tr>
<td>TOTAL</td>
<td>$65,871</td>
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</table>

Source: Department of Health and Ageing

Evidence of benefit

Pooled data from Australian clinical trials of buprenorphine maintenance prior to registration of the drug and a subsequent systematic review of the treatment found that buprenorphine was comparable to methadone in suppressing heroin use, but less effective at retaining people in treatment. International studies support the first of these findings, but show that buprenorphine is equally effective in supporting treatment retention.

51. Despite methadone being far more widely used than buprenorphine in Australia, the total costs to the Australian Government for buprenorphine are higher due to this treatment’s greater expense.
OST policy issues and controversies

Consumer costs

Some commentators have argued that dispensing fees and charges associated with OST have caused some people to drop out of maintenance programs. Muhleisen et al. have argued that ‘there are few medication regimes that cost the person being treated as much as OST’.54 They note that methadone and buprenorphine do not attract PBS concessional or safety net benefits and suggest that in Victoria, the annual cost of methadone treatment for an individual amounts to over $1,700. They argue that even a partial government subsidy would reduce the difficulties and stress associated with fee collection (for both those dispensing the drug and the client) and increase retention in treatment.

‘Parked’ on methadone

Some people (including former addicts) have argued that OST does not enable people to make a proper break from drug use and hence to move on with their lives.55 Ross Colquhoun, director of a detoxification clinic (that uses naltrexone) has described it as a ‘form of social control’ with ‘no exit strategy’.56 It is difficult to obtain data to substantiate claims about significant numbers of addicts remaining on methadone/OST treatment for substantial periods of time. Nevertheless, it is probably to be expected that a large percentage of people in methadone treatment receive that treatment over an extended period of time, given the underlying objective of reducing harm associated with drug use while people gain better control of their lives. It should be noted that buprenorphine can itself be used to assist people to withdraw from methadone as part of a broad OST treatment approach.

Take-away methadone

Methadone use in Australia is typically supervised by a designated authority at a scheduled location. However, most jurisdictions (Victoria, NSW, ACT, Queensland, WA, SA and Tasmania) have policies that allow people on OST to consume their dose of methadone away from the premises where it was dispensed, under certain circumstances.57 There is evidence that this methadone is sometimes supplied to people who are not on a methadone program. In

55. See, for example, ‘Christian’, quoted in J. Robotham, ‘The great divide over detox’.
2006, the ACT Deputy Coroner called for the practice of ‘take-away methadone’ to be abandoned following several methadone-related deaths in the Territory—deaths he believes could have been prevented if the Government had scrapped its ‘take-away’ option.  

58 There have been several cases in recent years in which ‘take-away methadone’ has been a factor in the death of children.  

Methadone in prisons

Some commentators have criticised the practice (in most states and territories) of offering OST in prisons. One argument advanced is that this misses the opportunity presented by incarceration to ‘get offenders off drugs’.  

60 However, there is evidence that prison methadone programs not only prevent deaths from overdose and cut transmission of the potentially deadly hepatitis C virus, but also significantly reduce the likelihood that people will return to prison.  

61 By contrast, despite the wide-spread use of drug-free units in Australian prisons, very few of these units have been evaluated and little is known about their long-term effectiveness. Larney, Matters and Dolan conclude on the basis of available evidence that while drug-free units ‘may assist inmates to reduce their drug use while in prison and to access drug treatment on release from prison’, further research is required to establish the impacts of drug-free units and their programs on long-term drug use and criminal recidivism.  

Naltrexone

As noted earlier, naltrexone is an opioid receptor antagonist that acts to inhibit the effect of opioids such as heroin in the body. Naltrexone has been used for treating opioid dependence in Australia since the late 1990s, as an alternative heroin withdrawal method to methadone. Naltrexone is used not only to assist with heroin withdrawal, but also for the purposes of relapse prevention. Naltrexone can be used for relapse prevention after any type of withdrawal and not simply withdrawal from heroin use.  

59. See, for example, P. Duncan, ‘Baby death shame file’, Hobart Mercury, 9 November 2006.  
60. See, for example, A. Mitchell, ‘Prison drug policy ‘creating addicts’’, Sun Herald, 17 November 2002.  
Naltrexone is typically taken orally in tablet form and is licensed in this form as a Schedule 4 (prescription only) drug. A single 50mg dose of naltrexone will block a person’s opioid receptors for around 24 to 48 hours, ensuring that any opioids taken during this time will produce no opioid effects. Naltrexone itself has no euphoric effects and, as such, does not induce either dependence or tolerance in its users. Naltrexone may also be administered through the insertion of an implant (typically into the abdomen). It is listed on the PBS for ‘use within a comprehensive treatment program for alcohol dependence with the goal of maintaining abstinence’ (but not for treatment of opioid dependence).63

Because, unlike methadone, naltrexone has no opioid-like properties, it is only as good as the motivation of its users. Naltrexone users are required to be opioid free before commencing treatment as the drug induces strong withdrawal symptoms in people who are opioid-dependent.

Where naltrexone implants are used, this is typically to counter the high rate of non-compliance when taken in tablet form.64 Implanted forms of naltrexone are designed to release naltrexone into the bloodstream for varying periods up to 6 months (but usually around 2 months).

By 2006, the Australian Government had invested over $1 million on a trial into the effectiveness of naltrexone implants.65 Naltrexone implants are not currently registered in Australia, but can be accessed through the Therapeutic Goods Administration Special Access Scheme.66 Production of implants was temporarily stopped in Australia (in 2001) because of safety concerns associated with their use.

Naltrexone is sometimes used overseas for rapid detoxification regimens under general anaesthesia or sedation. The principle of rapid detoxification is to induce opioid-receptor blockade while the patient is in a state of impaired consciousness so as to attenuate the withdrawal symptoms experienced by the patient. Rapid detoxification is followed by daily

63. Alcohol use stimulates opioid receptors and releases endorphins in the brain. It is believed that naltrexone both reduces the incentive and desire to drink by blocking the euphoric effects of alcohol. N. C. Latt, S. Jurd, J. Houseman and S. E. Wutzke, ‘Naltrexone in alcohol dependence: a randomised controlled trial of effectiveness in a standard clinical setting’, Medical Journal of Australia, 176:11, pp. 530-534.
64. A. E. Gibson and L. Degenhardt, op. cit, p. 6.
65. Hon. T. Abbott, Minister for Health and Ageing, Government response to inquiry on substance abuse, 10 August 2006. On 24 June 2007, key drug advisory groups and specialists met in Canberra to discuss the possibility of conducting a naltrexone implant trial in the ACT.
oral administration of naltrexone for opioid relapse prevention. Naltrexone is not currently registered for use in rapid detoxification in Australia.

Rates of usage

As with other forms of pharmacotherapy for opioid addiction, there is very little publicly available information on rates of usage of naltrexone treatment in Australia. Between 2000 and 2003, 6,337 private naltrexone prescriptions were filled in Australia, each of which provided one month of medication at the recommended dose of 50mg per day.

Data on the number of persons receiving naltrexone implant treatment is difficult to obtain, but as at February 2007, it was estimated that around 1,000 Australians had an implant for the treatment of opioid dependence.

Evidence of benefit

Naltrexone’s usefulness in treatment of opioid dependence is limited by the high rate of non-compliance, low uptake and varying retention rates. While these could be improved through careful induction and initial support, this could, in turn, impact on uptake rates by creating additional barriers to program entry.

It is generally agreed that while sustained-release naltrexone treatment is able to reduce craving for opioids and heroin use during treatment, the treatment is only really useful for a small percentage of heroin dependent persons. Those people who are more psychologically stable and who have a strongly supportive network of family and friends are the most likely to benefit from the use of naltrexone.

Policy issues, controversies

Overdose

A major problem with naltrexone treatment is that patients’ frequent relapse to heroin use is accompanied by a substantially increased risk of fatal heroin overdose. Research conducted by the National Drug and Alcohol Research Centre in Sydney indicated that while naltrexone patients had similar risks of death or heroin overdose during treatment as patients on buprenorphine or methadone, these patients are eight times more likely to overdose after leaving naltrexone treatment and had a death rate 19 times higher than patients on buprenorphine or methadone. Because initiation on naltrexone demands a period of abstinence from opioids, tolerance to opioids is reduced in naltrexone-treated patients and these patients are more likely to overdose at lower doses, especially if they return to pre-abstinence levels of opioid use. It is important to note, however, that it is not the naltrexone itself, but the abstinence from, and reduced tolerance to opioids that causes the increased risk of heroin overdose.

Mortality

Naltrexone-related deaths are more difficult to monitor than deaths associated with either buprenorphine or methadone. Unlike buprenorphine or methadone related deaths, a naltrexone-related death is identified by lack of the drug rather than its presence, and reliant on information on a person’s prior treatment history. Gibson and Degenhardt’s (2005) study is the first attempt to quantify the mortality rate associated with naltrexone treatment in an Australian context. Based on searches of the National Coronial Information System (NCIS), Gibson and Degenhardt found 32 deaths related to the use of oral naltrexone in the period 2000-2003 in Australia. This number is an underestimate, as the NCIS searches did not include a number of known oral naltrexone-related deaths and the NCIS does not include deaths related to naltrexone implants.

76. A. E. Gibson, L. J. Degenhardt and W. D. Hall, ibid., p. 36.
Nevertheless, according to all measures used by Gibson and Degenhardt, the mortality rate for oral naltrexone treatment was higher than that for either buprenorphine or methadone treatment during the same period.\textsuperscript{78}

A recent Australian study of opioid overdose deaths associated with naltrexone implants is the subject of some controversy in the medical community. In their paper, Gibson, Degenhardt and Hall identify, through the use of Australian coronial records, five deaths that they claim to be more-or-less directly related to the use of naltrexone implants. However, a number of critics agree that because three of the people included in the study no longer had active naltrexone implants at the time of their death, their deaths could not be linked to the implants, and should not have been included in the study.\textsuperscript{79} Given that one of the two remaining deaths involved the use of drugs other than opioids, these same critics also questioned the linking of this death to the presence of a naltrexone implant. Indeed, a majority of the study’s critics have questioned whether, on the basis of the data presented, a clear causal link could be drawn between the the sole remaining death and the relevant naltrexone implant.\textsuperscript{80}

The study was not only criticised for its lack of methodological rigour, but also for raising more questions than it answered. One commentator noted that the five deaths highlighted important clinical and forensic issues that the study failed to address. Among other things, the study did not comment on the lack of clinical care provided to the patients, evidenced by the combination of drugs found in their bloodstream at the time of death. Indeed, Batey viewed ‘the need for close supervision and appropriate clinical response to instability’ in naltrexone patients as being the most significant point raised by the study.\textsuperscript{81}

**Discussion**

As noted earlier, the pharmacotherapies considered above are only part of a broad range of treatments for opioid dependence. Many other non-pharmacotherapy treatments for opioid

\textsuperscript{78} A. E. Gibson and L. Degenhardt, ibid., p. xvi.


\textsuperscript{80} M. G-B. Sim, op. cit., p. 54; C. L. Brewer, op. cit., p. 55; E. Khong and W. Choy, op. cit. p. 56; N. Kunøe and H. Waal, op. cit., p. 56.

\textsuperscript{81} R. G. Batey, op. cit., p. 55.
addiction are also available. These different treatment types, along with OST and naltrexone, need to be understood as methods used in a process of treatment towards abstinence from opioids. This treatment process must be tailored according to the needs of the individual and their readiness for abstinence. Methadone, buprenorphine and naltrexone each have relative advantages and disadvantages in terms of treatment effects. However, these advantages and disadvantages need to be considered in the context of an overall treatment process and the individual situations and needs of patients, and not in isolation.

It is important to note that, from the perspective of a majority of health experts, the goal of all treatments for opioid addiction is the cessation of heroin use. Arguably, then, methadone and buprenorphine can be applied in a zero-tolerance policy context (where the intent is to get people off heroin), just as naltrexone can be used in a harm minimisation policy context (as part of an overall treatment process). The key issue for these health experts is that a wide range of treatment options should be available for patients at different stages in their drug-use terms, so as to best ensure the reduction of heroin use, while minimising opioid-related harm.  

**Conclusion**

OST is widely acknowledged to be effective for the treatment of opioid-dependent persons, with research consistently demonstrating the general effectiveness of methadone (and buprenorphine) maintenance in reducing opioid use. Indeed, based on the results of substantial research of detoxification and OST, O’Connor describes methadone maintenance as ‘the gold standard for the treatment of opioid dependence’.  

Relapse prevention treatment using naltrexone may have advantages for specific low-risk populations. Those people who are compliant with the treatment are usually successful in maintaining abstinence. However, for the majority of opioid-dependent individuals, the treatment has consistently been associated with high rates of non-compliance, a greater risk of mortality and reduced likelihood of long-term success. If the success of relapse prevention treatment using naltrexone is to be improved and the treatment made a viable option for a wider range of opioid-dependent people, this would appear to require a range of accompanying resources and support services. This may, in turn, require the reconceptualisation by some of naltrexone treatment as a ‘harm minimisation’, rather than an abstinence-based, ‘zero-tolerance’ measure.

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A recent review of pharmacotherapy approaches to treating opioid dependence highlighted the need for a range of treatment options (including naltrexone) to meet individual needs. At the same time, the review stressed the need for extensive OST treatment availability for a majority of opioid-dependent people. Thus, while naltrexone has shown some promise in the treatment of some opioid-dependent people under certain circumstances, the evidence suggests that OST will continue to play a significant role in the treatment of opioid dependency. This would be consistent with Australia’s traditionally evidence-based, pragmatic, outcomes-oriented approach to illicit drugs policy.

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85. ibid. See also M. Wenham, ‘No easy fix’, The Courier-Mail, 21 September 2002.