Current and prospective treatments for heroin dependence in the light of a recent national evaluation (the NEPOD Report)

In 1998, the Commonwealth Government commissioned the National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD), a 3 year nationwide project to trial and evaluate a number of pharmacotherapies with different properties and treatment suitabilities for the treatment of heroin dependence.

The treatments trialed included methadone, LAAM (levo-alpha-acetylmethadol), buprenorphine and naltrexone. NEPOD reported its results to the Ministerial Council on Drug Strategy on 31 July 2001.

The focus of this Research Brief is on the prevalence of heroin use and dependence in Australia and treatment options for heroin dependent persons. The Brief reviews recent statistical data about the extent of illicit drug use in Australia, and places the extent of heroin use and dependence in this broader context. The Brief also describes a number of the pharmacotherapies used in the treatment of heroin dependency and examines selected results of the NEPOD project.

Cathy Green
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1 INTRODUCTION

There is an apparent increase in the incidence of heroin use and dependence in Australia. In relative terms, however, the prevalence of heroin use in the Australian population is lower than that of a number of other illicit drugs such as marijuana, amphetamines, LSD and synthetic hallucinogens and cocaine. However, problems related to heroin dependence – such as the transmission of blood borne diseases, early death from overdose, drug-related crime, and disruptions in family, workplace, and educational environments – impact adversely on the community producing an effect that is perhaps disproportionate to the relatively small proportion of Australians who are dependent on heroin.

A heroin dependent person may be faced with a range of intercurrent difficulties while attempting to overcome his or her dependence. A diverse range of treatment options may be needed to assist heroin dependent persons to stabilize their lives, thereby reducing the individual and social harms associated with drug dependence. The importance of treatment as part of the overall management of the drug problem in Australia is acknowledged in the National Drug Strategic Framework 1998-2003.

In 1998, the Commonwealth Government commissioned the National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD), a 3 year nationwide project to trial and evaluate a number of pharmacotherapies with different properties and treatment suitabilities for the treatment of opioid dependence. The treatments trialed included methadone, LAAM (levo-alpha-acetylmethadol), buprenorphine and naltrexone. NEPOD reported its results to the Ministerial Council on Drug Strategy on 31 July 2001. The promise of new treatments as a result of such research may provide hope for individuals who suffer from heroin dependence, for those around them and for the community at large.

2 THE PREVALENCE OF HEROIN AND OTHER ILLICIT DRUG USE IN AUSTRALIA

Statistical data collected from a number of recent Australian studies suggest that there is an increased prevalence of illicit drug use amongst the Australian
population. Illicit drug use in this context refers to the use of illegal drugs, volatile substances used illicitly and pharmaceuticals used for non-medical purposes.

Heroin use is less prevalent in Australian society than other illicit drugs. There is, however, an apparent increase in the incidence of heroin use and dependence in Australia. It is possible that the estimates of the prevalence of heroin use in Australia may be conservative as a result of factors such as the illicit nature of heroin use, the stigma attached to admission of its use and population sample numbers used. The importance of obtaining credible estimates of heroin use and dependence lies in their usefulness in facilitating service planning and the development of drug policies and in countering inflated popular media estimates of heroin use and dependence in Australia.

2.1.1 National Drug Strategy Household Surveys

In 1998, more than 10000 Australians aged 14 and over participated in the National Drug Strategy Household Survey (NDSHS) covering tobacco, alcohol and illicit drugs. This was the sixth survey in a series that began in 1985.

Results from the NDSHS in 1998 suggest that 46.4% of the Australians aged 14 years and over have used an illicit drug at least once in their life, while 22.8% report having used an illicit drug in the preceding 12 months. The most widely used illicit substance in Australia in 1998 was marijuana, with lifetime use (used at any time in one’s life) of 39.1% and recent use (used in the last 12 months) of 17.9%. The prevalence of lifetime use of pain-killers/analgesics (for non-medical purposes) was 12%, followed by LSD/synthetic hallucinogens (9.9%), amphetamines (8.8%), ecstasy/designer drugs (4.8%) and cocaine (4.3%).

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Only 2.2% of the Australian population surveyed had ever used heroin, an amount similar to the previous 5 NDSHS surveys (1985, 1987, 1991, 1993, 1995) that found the lifetime population prevalence use of heroin to be in the range of 1-2%. 0.8% of the 1998 NDSHS respondents reported recent usage in the past 12 months. Interestingly, although heroin was used at lower levels than other illicit drugs, it was more widely perceived amongst 1998 NDSHS respondents as the drug primarily associated with a drug ‘problem’ than any other category of illicit drug.

The 1998 NDSHS results for Queensland showed that, when compared with the 1995 NDSHS results, there appeared to be an increase in use across all drug groups surveyed, both in terms of lifetime use and recent use. This trend was also mirrored in the results relating to heroin use among survey respondents.

- All age groups surveyed in Queensland experienced increases in the proportion of people reporting lifetime use of heroin.
- The proportion of people aged 14 years and over in Queensland who reported heroin use at least once in their lifetime increased from 1% in 1995 to 2.3% in 1998.
- The proportion of the Queensland population who were estimated to have recently used heroin in 1998 (0.6%) was higher than in 1995 (0.3%). Notably, for both first and recent injecting drug use, the proportions of persons surveyed injecting amphetamines (68.2%) and heroin (53.5%) were far greater than the proportions injecting other drugs.
- In 1998, approximately 10000 males and 8000 females used heroin in the past 12 months.
- The age group with the highest number of recent heroin users was the 40 years and over age group, with about 8000 recent users.
- About 3000 Queensland teenagers (aged 14–19) used heroin in the preceding 12 months. There was a higher likelihood that females (2000) had used heroin in the last 12 months than males (1000).

2.1.2 Statistics on Drug Use in Australia 2000 (Australian Institute of Health and Welfare)


6 In 1998, people living in Queensland nominated heroin as the primary drug associated with a drug problem (30.1%), overtaking marijuana/cannabis (23.7%) which was the primary drug in 1995.
NHDHS, the 1991 and 1993 National Campaign against Drug Abuse Surveys, the Australian Bureau of Statistics, the Commonwealth Department of Health and Aged Care, the Australian Institute of Health and Welfare, the Australian Transport Safety Bureau, the Australian Bureau of Criminal Intelligence and the National Drug and Alcohol Research Centre.

The data collated in Statistics on Drug Use in Australia 2000 affirmed the increased prevalence of illicit drugs use since 1991. In relation to heroin use, the percentage of people aged 14 years and over reporting lifetime use was 1.7% in 1991, 1.7% in 1993, 1.4% in 1995 and 2.2% in 1998. These rates of use remained at a lower level in comparison with other illicit drugs.

2.1.3 National Drug and Alcohol Research Centre

2.1.3.1 A study applying indirect methods of estimation to quantify the number of dependent heroin users in Australia

A number of Australian researchers believe that the illegal and covert nature of heroin use makes it difficult to quantify using standard approaches such as a general population or household survey where heroin use may not be readily revealed. It is thought that such studies probably under-estimate the prevalence of dependent heroin use in Australia.

In 2000, the National Drug and Alcohol Research Centre (NDARC) published the results of a study that applied a number of indirect methods to make a best estimate of the number of dependent heroin users in Australia. NDARC estimated in that in 1997 there were 74,000 dependent heroin users in Australia (range from 67,000 to 92,000), which equated to a population prevalence of 6.9 per 1,000 population aged

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10 Barbiturates were the exception to this general trend of increased use in the period 1991–1998 with lifetime use statistics of 5.2% in 1991, 1.4% in 1993, 1.2% in 1995 and 1.6% in 1998 recorded.

11 The view that the number of heroin users in Australia is probably under-estimated in household surveys is based on three assumptions. First, household surveys underestimate the number of dependent heroin users in the population because these users are concentrated in a small number of geographic areas where heroin is most readily available. Second, dependent heroin users’ lifestyles also make them less likely to live in conventional households and less likely to participate in household surveys either because of their unavailability at the time the interviewer calls or because of their reluctance to be interviewed. Third, when heroin users are selected in a household sample, their use is likely to be under-reported because it is an illegal and stigmatised behaviour: Hall, Ross, Lynskey, Law & Degenhardt, ‘How many dependent opioid users are there in Australia?’.
15-54 years. This figure represented a doubling of the 34,000 estimated in 1984-1987 and a 25% increase on the estimate of 59,000 in 1988-1993.  

NSW and Victoria accounted for about 75% of all the estimated heroin-dependent persons in Australia and the smaller States (such as Queensland) accounted for the remaining 25%. With an estimated 36% of dependent heroin users in Australia in methadone maintenance treatment, the authors of the study concluded that the results obtained for the smaller States appeared to be under-estimates in that they implied an implausibly high proportion of dependent heroin users are receiving treatment.  The study estimated there were 4,400 (range from 3,700 to 5,000) dependent heroin users in Queensland, compared with an estimated 3341 persons enrolled in methadone maintenance treatment. These estimates, by comparison, are close to the recorded number of participants in the Opioid Treatment Program in Queensland in 2000-2001.

The estimated incidence of heroin dependence in Australia equated to that in European Union countries.

2.1.3.2 Australian Drug Trends 2000. Findings from the Illicit Drug Reporting System (IDRS)

NDARC also published its findings about drug trends in Australia in 2000 through its Illicit Drug Reporting System (IDRS) that monitors the price, purity, availability and patterns of use of heroin, amphetamine, cocaine and cannabis. The IDRS study found that there was a progressive increase in heroin use and fatal opioid overdoses in most Australian jurisdictions. The findings reported for Queensland

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12 Hall, Ross, Lynskey, Law & Degenhardt, ‘How many dependent opioid users are there in Australia?’, p 51.
13 Hall, Ross, Lynskey, Law & Degenhardt, ‘How many dependent opioid users are there in Australia?’, pp 52, 53.
14 Hall, Ross, Lynskey, Law & Degenhardt, ‘How many dependent opioid users are there in Australia?’, pp 53, 54.
15 Queensland, State Budget 2001-2002, Ministerial Portfolio Statement: Minister for Health and Minister Assisting the Premier on Women’s Policy, p 29.
16 Hall, Ross, Lynskey, Law & Degenhardt, ‘How many dependent opioid users are there in Australia?’, pp 51, 52.
suggested that heroin is easily obtainable in Brisbane, but not in regional Queensland.

2.1.3.3 Illicit Drug Use in Australia: Epidemiology, Use Patterns and Associated Harm

A further study of illicit drug use in Australia by NDARC, published in 2000, reported that:

- Among new heroin users, the age of first heroin use is falling with initiation among younger cohorts occurring in the mid-teens.
- The injection of amphetamines prior to the commencement of heroin use is common amongst heroin users in Australia.

2.1.4 Australian Institute of Criminology

In February 2001, the Australian Institute of Criminology published a research paper, *Illicit Drug Use in Regional Australia, 1988 – 1998*, that analysed data gathered about illicit drug use in metropolitan and regional Australia between 1988 – 1998. The paper reported that, over the 10 year period, the use of illicit drugs increased in regional Australia by 77% for heroin, 131% for amphetamines, 37% for cocaine and 47% for cannabis. The 1998 levels remained lower than those found in metropolitan Australia and approximated rates observed in the cities just a few years ago. The paper, however, predicted that due to differential features between metropolitan and regional areas, it is unlikely that the rates of drug use in regional Australia will contemporaneously match those found in metropolitan areas of the country in the near future.

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19 S Darke, J Ross, J Hando, W Hall & L Degenhardt, ‘Illicit Drug Use in Australia: Australia. Epidemiology, Use Patterns and Associated Harm’, p 43.

3 THE CONSEQUENCES OF HEROIN USE AND DEPENDENCE

Heroin is a highly addictive drug. Heroin use does not always result in heroin dependence - about 1 in 4 people who use heroin will become dependent.21

Heroin dependence encompasses the use of an opioid accompanied by signs and symptoms of compulsive prolonged self-administration without legitimate medical purpose. The signs of dependence include tolerance (the use of more heroin to achieve the same intensity or effect), withdrawal, taking larger amounts or for a longer time than intended, desire or unsuccessful efforts to control use, spending a great deal of time obtaining, using or recovering from opiates, forgoing important social, occupational or recreational activities to use opiates and continued use despite recognition of adverse activities.22 The severity of dependence can range from mild to moderate or severe. Most heroin users report 1 to 2 years between their first use of heroin and their first period of dependent use.23

The repercussions of heroin use and dependence can extend beyond the individual user to their families, friends and the wider community, with health and social costs such as the risk of overdose, spread of blood borne viruses, and family breakdown; health costs (to both the individual and the community) associated with illicit drug consumption and morbidity; economic costs associated with morbidity, mortality and absenteeism related to illicit drug use; and the cost of law enforcement for drug related crime. Problems like this can impact adversely on the community producing an effect that is perhaps disproportionate to the relatively small proportion of Australian adults who are dependent on heroin.24


22 The diagnostic definition of opiate dependence is noted in Diagnostic and Statistical Manual of Mental Disorders (DSM- IV 1994).


24 National Buprenorphine Policy, p 1.
One of the greatest risks associated with heroin use is the risk to the user of fatal or non-fatal overdose. Recent studies of opioid overdose rates in Australia suggest that:

- Opioid overdose was responsible for 737 deaths in Australia in 1998. The death rate from opioid overdose doubled from 38.3 to 87.1 per 1 million adults from 1989 to 1998. It is also estimated that there are between 12,000 and 21,000 non-fatal overdoses in Australia annually.
- The number of opioid overdose deaths in Queensland in 1999 (70) was nearly double the number reported in 1998 (38).
- Polydrug, or concomitant drug use, is strongly associated with both fatal and non-fatal drug heroin overdose.

In 2001, the Australian National Council on Drugs released a research report, *Heroin overdose: prevalence, correlates, consequences and interventions*, about the emergence of fatal heroin overdose as a public health issue in Australia. The report provided an overview of the epidemiology and circumstances of heroin overdose and of strategies that could reduce the prevalence of heroin overdose. The report noted evidence that suggested treatment for heroin dependence substantially reduced the risk of overdose and that long-term untreated users are at the greatest risk of overdose. One of the key findings of the report was that:

> Opioid overdose fatalities are preventable. Treatment services, such as methadone, protect against fatality from overdose and should be expanded where possible. The range and availability of treatment services should be expanded where possible. Alternative pharmacotherapies should be trialed to attract high-risk untreated heroin users into treatment.

The transmission of blood borne viruses, such as HIV and hepatitis, with the injection of heroin and other drugs constitutes another avenue of possible harm. To date, Australia has averted an epidemic of HIV infection among intravenous drug users with the use of strategies such as needle and syringe exchange programs that

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26 R McAllister, ‘Queensland Drugs Trends 2000: Findings from the Illicit Drug Reporting System (IDRS) (2001)’, p 2: The author suggests that the increased numbers of opioid related deaths could, to some extent, be attributable to an increased prevalence of intravenous use among heroin users.

provide sterile needles and syringes free or at minimal cost for injecting drug users. In 2000, NDARC researchers noted that the 1997 Needle and Syringe Exchange Program (NSEP) survey, reported a seroprevalence of HIV of 1.6%, mostly confined to homosexual intravenous drug users. The prevalence of intravenous drug users surveyed with antibodies to Hepatitis C was 50% and Hepatitis B was 30% -60%. The sharing of injecting equipment apparently decreased over the past decade, with about 15% of users sharing per month.

Heroin is illegal throughout Australia. In Queensland, heroin is classified as a First Schedule drug under the *Drugs Misuse Act 1986* (Qld), with the result that heroin related offences are subject to the highest level of penalties available under the Act.

- Arrest patterns for drug offences between 1995-1996 and 1998-1999 in Australia suggest an upsurge in the arrest patterns for heroin related offences in Australia since the mid-1990’s, with the percentage of persons charged with user-type offences more than doubling (7% in 1995-1996 to 16.1% in 1998-1999) and the percentage of people charged with supply-type offences almost tripling (7.9% in 1995-1996 to 21.1% in 1998-1999) in the 3 year period. The Australian Bureau of Statistics reported that Australia-wide, there were 14341 offenders arrested or proceeded against for heroin related offences in the period 1 July 1998 to 30 June 1999, an increase of 38% from the previous financial year.
- The estimated cost of heroin–related crime to the community was recently reported as up to $1.6 billion per year.

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29 S Darke, J Ross, J Hando, W Hall & L Degenhardt, ‘Illicit Drug Use in Australia: Australia. Epidemiology, Use Patterns and Associated Harm’, p 45.
4 APPROACHES TO THE TREATMENT OF HEROIN DEPENDENCE

Research about the impact of heroin use on public health and public order in Australia suggests that effective treatments for heroin dependence can reduce the adverse impact that heroin use has on the health of heroin users while improving public health and public order. Treatment of heroin dependence can assist those who receive it and be cost effective in terms of reduced crime, health costs and mortality.33

Numerous treatments and treatment approaches are available in Australia for people who are heroin dependent or heroin users. Drug free treatment, detoxification and drug substitution and other maintenance pharmacotherapies constitute the principal treatment options.

Heroin dependent people differ in their treatment needs. Ideally, the type of treatment provided to a heroin dependent person should be based on a comprehensive assessment of the individual’s objectives in undertaking treatment, their history of drug use and social circumstances and any relevant medical or psychiatric condition.34

People dependent on heroin may be faced with a number of intercurrent difficulties while attempting to overcome their dependence. Characteristically, these difficulties may include factors relating to the attitude of the person to treatment (eg level of interest in withdrawal, willingness to participate in the routine of treatment, perceived stigma associated with treatment), psychological disorders such as depression, anxiety disorders and antisocial personality disorder, polydrug use, unemployment, and the costs of treatment.35 The capacity for the expansion of treatment places within the context of finite resources may be another obstacle. If

the capacity is limited, there may be reduced access to treatment and less intensive treatment services.

It is of interest to note that the Australian National Council on Drugs, in its 2001 report, *Heroin Overdose: prevalence, correlates, consequences and interventions* cautions against judging the success of heroin treatment on the basis of the commonly used criteria of abstinence from heroin as a result of treatment. The report noted:

> ... It is more realistic to judge the outcome of treatment of heroin dependence by comparing the effects of drug treatment on the frequency of heroin use and crime, and the health and well-being of heroin dependent persons. When judged by these more realistic criteria, treatment for heroin dependence is a good investment of community resources.

Similarly, two Queensland authorities on drug treatment, Dr John Saunders and Alun Richards, suggest that pharmacological treatments for heroin dependence should be assessed and compared on the basis of outcomes such as mortality, morbidity, criminal behaviour, quality of life, social integration, economic productivity and cost-effectiveness.

### 4.1 Drug-Free Treatment

Drug-free treatment utilises a number of approaches such as residential treatment in therapeutic communities, outpatient drug counselling and self-help groups, which share a commitment to achieving abstinence from heroin and other illicit drugs. These treatments use group and psychological interventions to assist dependent heroin users to achieve long lasting abstinence from all drugs and to address their problems in ways other than with drug use.

Australian experts in the field of heroin dependence suggest that:

> In general, TC [therapeutic communities] and DC [drug counselling] are more demanding of drug users, and hence are less successful than MMT [methadone maintenance therapy] in attracting dependent heroin users into treatment and retaining them. They do nonetheless substantially reduce heroin use and crime in

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36 M Lenne, N Lintzeris, C Breen, S Harris, L Hawken, R Mattick, A Ritter, p 122
the minority of entrants who remain in the treatment long enough to benefit (at least three months). [notes added]

4.2 DETOXIFICATION

Detoxification is the supervised withdrawal of a drug dependent person from their drug of dependence with the aim of minimising the severity of the withdrawal process experienced in the process. Depending on individual differences, detoxification may be achieved in as little as 1 to 2 days with a procedure of rapid opiate detoxification, or take about 5 days or a little longer using more conventional procedures.

Treatment of heroin dependency usually begins with detoxification, followed by maintenance treatment. While some patients become abstinent, the majority of opioid addicts relapse to heroin use shortly after detoxification. Controlled studies show that people who have undergone detoxification are no less likely to relapse to drug use than those who have not. As a result, authorities in the field of drug dependence suggest that detoxification programs ought not be thought of as a treatment for drug dependence per se, but rather as a way to achieve a safe and humane withdrawal from a drug of dependence and as a prelude to a treatment designed to achieve abstinence.

A number of detoxification treatments have been developed using different drugs as detoxification agents. Buprenorphine and methadone are registered as maintenance or detoxification agents in the Australian Register of Therapeutic Goods whereas naltrexone is registered as an adjunctive therapy in the maintenance of formerly opioid-dependent patients who have ceased the use of opioids (such as heroin and morphine) but not as a detoxification agent.

4.3  DRUG SUBSTITUTION TREATMENT AND ALTERNATIVE PHARMACOTHERAPIES

Drug substitution treatment substitutes a longer acting, usually orally administered opioid drug for the shorter acting heroin, which is typically used by injection. The object of drug substitution and other maintenance treatments is to stabilise dependent heroin users so that they become more accessible and amenable to rehabilitation, reduce some of the health, social and financial risks associated with illicit drug dependence.

Queensland operates an Opioid Treatment Program that catered to about 4000 people in 2000/2001. Formerly known as the Methadone Maintenance Program, the name of the program was changed to reflect the inclusion in the program of alternative pharmacotherapies to methadone such as buprenorphine and naltrexone for participants.

In Queensland, the management and supply of controlled or restricted drugs and poisons in Queensland is prescribed under the Health (Drugs and Poisons) Regulation 1996 (Qld). The Regulation classes methadone and buprenorphine as controlled drugs. Under the Regulation, a doctor must not prescribe or administer a controlled drug to a person the doctor reasonably believes to be drug dependent without the approval of the Chief Executive. There is provision in the Regulation for the Chief Executive to provide an approval for a doctor to treat a class of drug dependent persons.

4.3.1  Methadone

Methadone, a synthetic opioid, was developed in Germany in 1941 as a pain reliever. It was introduced as a maintenance treatment for heroin dependence in the United States in 1964 and in Australia in 1969. By the early 1970’s, all Australian States used methadone as a treatment regime to some extent. The methadone

46 Queensland, State Budget 2001-2002, Ministerial Portfolio Statement: Minister for Health and Minister Assisting the Premier on Women’s Policy, p 29.
47 Health (Drugs and Poisons) Regulation 1996 (Qld), ss 3, 5, Appendix 9 (definitions of ‘controlled drug’ and ‘standard’); Standard for the Uniform Scheduling of Drugs and Poisons, Schedule 8.
48 Health (Drugs and Poisons) Regulation 1996 (Qld), s 122.
program was embraced in Queensland, possibly as a result of its conceptualisation as a vehicle to achieve improved health and decreased crime. Methadone as a treatment option was less popular in other parts of Australia until the mid-1980’s, when the program underwent a major expansion, partly due to the emergence of a national approach to drug policy and the recognition of the role of methadone maintenance treatment (MMT) in reducing the risk of HIV infection.50

MMT is acknowledged in Australia and other countries as an effective treatment for opioid dependence. MMT is the predominant pharmacological treatment for opioid addiction in Australia. MMT enrolment numbers in Australia climbed from 3000 in the mid-1980’s to more than 25000 a little more than a decade later.51

Dependent heroin users experience withdrawal symptoms and narcotic cravings if the concentration of opiates in the body falls below a certain level. Methadone, an opiate agonist,52 provides a substitute for illicit heroin and other opioids thus easing the experience of withdrawal. The optimal dose of methadone is just enough to allay acute withdrawal symptoms and to reduce chronic narcotic craving (by stabilising blood levels of the drug and its metabolites) thus allowing normal functioning. Although methadone has similar depressant and analgesic effects to other opioids, its effects last much longer. Methadone does not have the euphoric effect that heroin does, however, people on methadone are still physically dependant on opioids.

Methadone can be taken as a syrup, in powder or tablet form or injected. Taking methadone can produce side effects such as sweating, constipation, aches, rashes, fluid retention, loss of appetite and stomach cramps. There may also be side effects that are dosage related.53 The use of other drugs with methadone such as alcohol, opiates (for example, heroin) or benzodiazepines (for example, Valium or Serapax)

51 M Lenne, N Lintzeris, C Breen, S Harris, L Hawken, R Mattick, A Ritter, p 121.
52 An agonist is a type of drug that binds to the opioid receptors, mimicking the actions of the body’s natural chemicals.
increases the risk of overdose. In Australia, deaths involving those in methadone treatment have occurred as a result of accidental overdose, suicide and accidents.54 The perceived advantages of MMT include: its relative effectiveness in retaining clients in treatment; the accessibility and affordability of methadone as a treatment agent; the encouragement of a stable and balanced lifestyle as a result of the routine of treatment; and a collective reduction in heroin use, injecting risk practices and criminality.55 MMT is also associated with lower rates of fatal opioid-related overdose and a reduction in deaths from all causes.

While the benefits of MMT are most evident while clients remain in treatment, an ultimate goal is for clients to end their period of treatment without relapse into dependent heroin use. Available literature suggests that only a minority of methadone clients complete an attempt at withdrawal from methadone and an even smaller proportion remain abstinent from heroin use after the completion of methadone treatment.56 Currently, there are a number of strategies used to assist people to withdraw off methadone including gradual tapering of dose, information provision, counseling and support services and the use of alternative medication. The factors that impact on the success of the withdrawal include the method used, client characteristics and the length of treatment.

The documented negative characteristics of MMT include: dependence on methadone; the potential for overdose from methadone among tolerant and non-tolerant individuals; the inconvenience of daily dosing; the diversion of takeaway doses; the stigma associated with MMT which may act as a barrier to treatment entry; and the desire among some users to inject methadone rather than ingest it orally.57 The variables that have been associated with riskier behaviours and a

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54 Australian Drug Foundation, Facts and Figures: Methadone, downloaded on 30 May 2001 from http://www.adf.org.au/ and follow the links: facts and figures>methadone. The Australian Drug Foundation notes that research has shown that the abuse of alcohol and benzodiazepines is common amongst methadone clients. Any combination of sensitive drugs such as opiates, alcohol or may result in coma or death. Emotional disorders are common amongst methadone clients.


56 M Lenne, N Lintzeris, C Breen, S Harris, L Hawken, R Mattick, A Ritter, p 121. The authors suggest that, after withdrawal from MMT, only about one quarter of clients remain abstinent from heroin use for an extended period of time (eg 3 months or more).

poorer outcome in MMT encompass polydrug use, psychopathology (e.g., antisocial personality disorder) and methadone diversion.

National guidelines for MMT, designed as a framework for Australian jurisdictions to formulate policies and procedures for methadone treatment, were first endorsed by the Australian Health Minister’s Conference in 1985. In 1993, the Commonwealth, State and Territory Governments decided to reformulate the guidelines as a national policy to assist the establishment of a shared set of standards for providing methadone treatment in Australia.

Although direct service provision is a State/Territory responsibility, State, Territory and Commonwealth governments, as well as clients, each contribute to the funding of MMT services.

4.3.2 Naltrexone

Naltrexone, a long-acting (24 hours or longer) opioid antagonist, displaces heroin from opioid receptors in the brain thereby blocking the effect of any opioid agonists (like heroin). It does not produce an euphoric effect, like heroin and other opioids, and is non-addictive. Naltrexone is prescribed to help people maintain abstinence after they have detoxified (withdrawn) from heroin or other opioids. It is also used in an experimental treatment to bring about rapid withdrawal from opioids.

Naltrexone can have some side effects, although it is generally well tolerated. These side effects (some of which may also be related to heroin withdrawal) include depression, sleep disturbances, headaches, loss of energy, nausea, abdominal pain, constipation, lack of appetite and anxiety.

61 An antagonist binds to opioid receptors in the brain, acting to block the body's natural chemicals. In heroin dependent people an antagonist would induce withdrawal. In people who have completed withdrawal it may assist in preventing a return to heroin use as it blocks the effects of heroin.
62 Rapid Opiate Detoxification (ROD) usually takes place in a hospital or similar situation and takes 2–4 days (compared with normal heroin detoxification that takes 7 days). The patient is normally heavily sedated and given naltrexone tablets. Ultra Rapid Opiate Detoxification (UROD or the “Israeli treatment”), normally takes place in a hospital where the patient is placed under general anaesthetic and given naltrexone: ‘The facts: Naltrexone a treatment for heroin abuse’, Drugs in Society, September 1999, p 20.
The greatest risk associated with naltrexone is the risk of death by opioid overdose. When the user stops taking heroin and uses naltrexone, their tolerance to heroin decreases rapidly. An overdose may occur if a person relapses to heroin use as they cannot tolerate the same doses as they could have before using naltrexone. In addition, if a naltrexone patient uses heroin or other opioids such as codeine, morphine or methadone there is a risk that these drugs can build up in the body. As the naltrexone leaves the receptor sites in the brain, the site may be rushed with opioids in quantities far greater than that person’s current level of tolerance.

The safety and efficacy of naltrexone as a treatment for opioid dependence has formed the subject of debate amongst the Australian community. While advocates of naltrexone promote it as possibly life-saving, those less supportive refer to the reported more modest success of naltrexone maintenance in the treatment of heroin dependence.

A number of medical practitioners in some Australian States have treated heroin dependent patients with naltrexone implants in place of oral naltrexone. The implants, which release controlled amounts of naltrexone into the bloodstream, are designed to alleviate the need for an addict to remember to take a tablet. The implants are not registered in Australia for therapeutic use in humans. An exemption in the *Therapeutic Goods Act 1989* (Cth) allows medical practitioners to administer a non-registered drug if it is necessary to treat a patient with a life-threatening illness. On 29 May 2001, the Medical Board of Queensland placed a ban on a Queensland doctor’s use of naltrexone implants after the reported deaths of a number of patients (24 out of almost 850) he had treated with naltrexone since 1998. The issue prompted a mixed response from experts on naltrexone. One Queensland researcher called for the implants to be subjected to a proper research and development program and controlled trials, while a naltrexone specialist in NSW described naltrexone implants as “the way of the future”. The decision of the Board is currently under appeal to the Health Practitioners Tribunal of Queensland.

The authors of a 2 year study recently completed in Western Australia report that addicts coming off naltrexone treatment have a much higher risk of death (1 in 61) than untreated addicts (1 in 74) or addicts on methadone (1 in 458).

65 Eg. *Therapeutic Goods Act 1989* (Cth), s 18; *Therapeutic Goods Regulations 1990* (Cth), reg 12A.
A number of Australian authorities on heroin dependence caution that naltrexone treatment is suited to only a select number of heroin dependent persons, characteristically those who are committed to abstinence and have social and employment stability.\footnote{70}

Australian experts in the field of heroin dependence suggest that:

*One of the biggest determinants of the effectiveness of naltrexone’s efficacy is the client’s motivation to remain abstinent. … Such motivation may not characterise the majority of opiate-dependent persons, may of whom enter treatment through coercion (either legal or social). Research has shown that 90 per cent of individuals on naltrexone maintenance resume illicit opiate use within 12 months in the absence of outpatient treatment. Resumption of heroin use following naltrexone maintenance may constitute a high–risk period for overdose due to reduced tolerance. The success of naltrexone maintenance, as for any treatment, depends ultimately upon the outpatient treatment program, the nature of the client group and the appropriateness of the program to the client group. [notes omitted]*\footnote{71}

In 1999, the **National Expert Advisory Committee on Illicit Drugs**, an advisory body under the National Drug Strategic Framework, formulated national interim clinical guidelines relating to the use of naltrexone in relapse prevention of persons who are already detoxified from opioids (heroin or methadone) and seeking assistance to remain abstinent.\footnote{72}

### 4.3.3 Buprenorphine

Buprenorphine is both a partial opioid agonist and an opioid antagonist – it acts to produce opioid responses while blocking the effects of additional heroin use. The effect produced by buprenorphine is milder, less euphoric and less sedating than full opioid agonists such as heroin, morphine and methadone. It has few side effects, appears to induce a low level of physical dependence, is safe and has a long


\footnote{National Alcohol and Drug Research Centre, ‘Heroin overdose: prevalence, correlates, consequences and interventions’, Appendix A, pp 51, 52.}

duration of action. Withdrawal from buprenorphine is thought to be mild and the overdose risk is lower than with full opioid agonists like methadone. The duration and severity of withdrawal is related to the duration of treatment, the dosage withdrawn from and the reduction regime employed. Its limitations include the sublingual (under the tongue) route of administration, which may prove cumbersome and inconvenient; the ease with which it can be injected; and a ceiling effect that may limit its applicability to more severely dependent clients.

Buprenorphine has been used in France and England and evaluated in a number of countries, with results that are generally comparable with methadone maintenance.

Buprenorphine, in sublingual tablet form, is registered in Australia for the management of opioid dependence including maintenance and detoxification, within a framework of medical, social and psychological treatment. Buprenorphine as a detoxification or maintenance agent was recently trialled at a number of sites across Australia (see Section 4: National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD)) and received a positive evaluation as an effective treatment for both detoxification and maintenance of opioid dependent people.

The drug was listed as a treatment of opioid dependence under the Pharmaceutical Benefits Scheme from 1 August 2001 to facilitate the access to, and affordability of, the drug as a treatment option for opioid dependent people.

In March 2001, the Intergovernmental Committee on Drugs (IGCD) sub-committee, Methadone and Other Treatments published the National Buprenorphine Policy, to provide a broad policy context and a framework for State and Territory Policies and guidelines. In June 2001, the Commonwealth Department of Health and Aged Care also published national clinical guidelines for the use of buprenorphine in the treatment of heroin dependence to assist in the safe and effective implementation of buprenorphine treatment in Australia.

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74 NHMRC, p 49.


4.3.4 LAAM (leva-alpha-acetylmethadol or levomethodyl acetate)

LAAM (leva-alpha-acetylmethadol or levomethodyl acetate), like methadone, is a synthetic opioid agonist that can be used to treat heroin dependence. LAAM has a longer duration of action than that of methadone which allows dosing every 2-3 days; greater flexibility for the patient; and less opportunity for illicit diversion.\footnote{NHMRC, p 48.}

In 1993, the Food and Drug Administration approved the use of LAAM for treating heroin dependent people in the United States of America. LAAM is not registered for use as a treatment agent for opioid dependence in Australia.

5 NATIONAL EVALUATION OF PHARMOCOTHERAPIES FOR OPIOID DEPENDENCE (NEPOD)

There is a new pluralism of approaches to treating heroin dependence.

While it is desirable to provide a diversity of treatment options that are responsive to the needs of the individual illicit drug user and the community, service planners, treatment providers and drug researchers generally also acknowledge the desirability of subjecting such treatments to rigorous scientific and ethical evaluation.

In addition to the development of effective and cost-effective treatments, such an evaluation process may assist governments and other policy-makers with policy direction and assist governments to better allocate expenditure in the management of the drug problem.

The National Health and Medical Research Council, in its \textit{Information Paper on the Current State of Research on Illicit Drugs in Australia}, published in December 1998, discerned that structured scientific research was needed to establish the efficacy of opioid withdrawal agents other than methadone and the efficacy of non-pharmacological approaches for opioid withdrawal.\footnote{NHMRC, p 46.}

In 1999, Wayne Hall and Alex Wodak, two Australian authorities on drug dependence, observed with respect to the development and introduction of new approaches in the pharmacological treatment of opioid dependence:

\begin{quote}
\ldots decision-making about research and service provision for illicit drug dependence requires the same rigour and evidence demanded elsewhere in medicine. In the absence of this evidence, false expectations of cure will continue to be raised and
\end{quote}
dashed, scarce research and treatment funding will be wasted, and little progress will be made in improving treatment outcomes. Management of drug dependence has more in common with a marathon than a 100m sprint. ... [A]ll new treatment interventions in medicine should be assumed ineffective and possibly unsafe until proven otherwise.

In 1998, the Ministerial Council on Drug Strategy decided that a coordinated, national approach should be taken in investigating the nature and potential role of several “new” (in Australia) pharmacotherapies for opioid dependence. As a result, the Commonwealth Government commissioned a National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD), the goal of which was to contribute to a national effort to develop and implement a range of effective, evidence-based, best practice treatment options for people who are opioid dependent.

This three-year project, which commenced in July 1998, was coordinated by the National Drug and Alcohol Research Centre (NDARC). NEPOD included 13 treatment outcome studies and other studies that evaluated a range of opioid detoxification and maintenance treatments using methadone, naltrexone, buprenorphine, and LAAM, with associate psychosocial and medical interventions:

- methadone maintenance
- buprenorphine maintenance
- LAAM maintenance
- naltrexone treatment
- rapid opioid detoxification with anaesthesia or sedation
- outpatient detoxification using buprenorphine
- conventional inpatient detoxification
- conventional outpatient detoxification.

One thousand four hundred and twenty five patients participated in these studies which were conducted variously in New South Wales, Victoria, South Australia, Queensland, the Australian Capital Territory, and Western Australia.

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82 Of these 1,425 patients, 1,070 were current Heroin Users who had not received any treatment for a minimum of one month prior to entering a trial and 355 were Methadone Patients, currently participating in a methadone program.
Three of the trials evaluated as part of the NEPOD project were conducted in Queensland, or partly in Queensland:84

- Naltrexone induced rapid opioid detoxification under anaesthetic vs methadone maintenance treatment (vs naltrexone induced rapid opioid detoxification under sedation) - Brisbane
- Methadone detoxification using buprenorphine – Melbourne, Brisbane, Gold Coast and Sydney
- Buprenorphine assisted detoxification vs gradual methadone withdrawal (followed by option of naltrexone treatment) – Sydney, Brisbane, Gold Coast and Perth

The Queensland Government funded two of these trials: the trial of rapid opiate detoxification and the trial of detoxification using buprenorphine.85

A report of results and recommendations based on the findings from the NEPOD trials (the “NEPOD report”) was presented to the Ministerial Council on Drug Strategy on 31 July 2001.

An Executive Summary of those findings, with a series of Recommendations about clinical practice and further research related to pharmacotherapies for opioid dependence, from the NEPOD report are attached as Appendix A and Appendix B, respectively, to this Research Brief. Selected findings from the trials are extracted below:

- Methadone maintenance, buprenorphine maintenance, LAAM maintenance, and naltrexone treatment all produced substantial reductions in heroin use while patients remained in treatment.
- Rapid opioid detoxification under anaesthesia or sedation is the most effective method for inducting patients onto naltrexone and achieving short-term abstinence. Both procedures were more effective than conventional detoxification.
- The trials of methadone, buprenorphine and LAAM maintenance produced similar results, although LAAM was superior to methadone. Approximately 60% of Heroin Users (individuals not in pharmacological treatment for their opioid dependence when they entered the trial) were retained in treatment at 3 months, and 44% at 6 months. Heroin Users who remained in treatment substantially reduced their heroin use, with the number of heroin-free days increasing from 3 days in the month prior to

85 Hon WM Edmond MP, Minister for Health and Minister Assisting the Premier on Women’s Policy, ‘Drugs’, Ministerial Statement, Hansard, 8 August 2001, p 2315.
treatment to 22 - 24 heroin-free days in the third month of treatment. Complete abstinence from heroin use was achieved by over ¼ of Heroin Users who remained in treatment in the third and sixth month.

- There was a large reduction in heroin use for already abstinent heroin users treated with naltrexone who remained in treatment. Complete abstinence from heroin was achieved by 66% of heroin users who were still in treatment at 3 months and 27% for those still in treatment at 6 months. A reduced use of heroin was also noted for those users who entered naltrexone treatment after rapid detoxification and remained in treatment. Seventy-five percent of heroin users still in treatment at 3 months, and 19% of those in treatment in the sixth month, achieved complete abstinence. Naltrexone treatment after conventional inpatient detoxification had poor results, retaining only 2% of heroin users in treatment at 3 months and none at 6 months.

- Self-reported criminal behaviour among Heroin Users was halved at the 3 month follow-up. The average monthly expenditure of Heroin Users on heroin correspondingly decreased from $2611 to $572, consistent with the decreases in heroin use.

- While patients were in treatment, most serious adverse events (SAEs) occurred in naltrexone treatment (56 SAEs per 100 patient-years), and fewest occurred in methadone maintenance and LAAM maintenance (10 SAEs per 100 patient-years). Naltrexone treatment was associated with a significantly higher (non-fatal and fatal) heroin overdose rate (11 heroin overdoses per 100 patient-years in treatment; and 35 overdoses per 100 patient-years if patients ceased naltrexone) compared with methadone, buprenorphine and LAAM (which had in total 5 heroin overdoses per 100 patient-years in and out of treatment). Naltrexone treatment was also associated with a trend towards a higher death rate (4 deaths among 454 patients, a rate of 9 deaths per 1000 patients) with 2 deaths for the methadone, buprenorphine and LAAM maintenance therapies combined (2 deaths among 1067 patients, a rate of 2 per 1000). This difference was not statistically significant. SAE rates increased after patients left treatment.

- Rapid detoxification under sedation was the most cost-effective method of detoxification at a cost of $3317 per abstinent patient. Conventional outpatient detoxification was found to be the least cost-effective detoxification procedure at a cost of $16945 per abstinent patient (although a very low rate of initial abstinence made this finding unstable). Rapid detoxification under anaesthesia achieved high rates of abstinence in the first week but its expense reduces its cost-effectiveness.

- Overall, the daily costs of providing maintenance treatments were similar for methadone and LAAM, with naltrexone treatment being slightly more
expensive. With improved cost-efficiency, the cost of buprenorphine maintenance would be similar to the other treatments.

- Methadone maintenance is the most cost-effective treatment currently available in Australia for the management of opioid dependence. Methadone maintenance also achieved one of the highest rates of retention among the four pharmacotherapies examined.

- LAAM is not registered for use in Australia, but it was more cost-effective than methadone maintenance due to its better retention and slightly better ability to suppress heroin use. Given the small sample of patients in the LAAM trial, the report noted that result should be interpreted with caution.

- Buprenorphine ranked third overall in cost-effectiveness at both three and six months with retention rates of 50% and 38% respectively. The report noted that any reductions in the price of buprenorphine and increased efficiency in administering it could reduce its total cost and increase its cost-effectiveness. (Author’s Note: largely as a result of its positive evaluation in the NEPOD trials, buprenorphine was listed as a treatment of opioid dependence under the Pharmaceutical Benefits Scheme from 1 August 2001).

- Naltrexone treatment appeared to be the least cost-effective pharmacotherapy compared with methadone, LAAM and buprenorphine. The proportion of patients retained in treatment was much lower in naltrexone treatment than in the maintenance treatments. Only 1 in 7 of all naltrexone patients completed 3 months of treatment, and 5% completed six months treatment.

- On 8 August 2001, the Queensland Minister for Health, Hon WM Edmond MP, made a Ministerial Statement in the Queensland Parliament relating to the NEPOD report. The Minister stated that:

  Ministers have agreed that results [the NEPOD report] will be disseminated widely to provide accurate information to treatment providers, patients and the general community. The use of naltrexone to treat opioid dependence will be referred to the Pharmaceutical Benefits Advisory Committee. …[B]uprenorphine is now available from all existing Queensland Health opioid treatment programs and through authorised private prescribers throughout Queensland.[note added]

86 Hon WM Edmond MP, Minister for Health and Minister Assisting the Premier on Women’s Policy, ‘Drugs’, Ministerial Statement, Hansard, 8 August 2001, p 2315.
6 CONCLUSION

The number of Australians dependent on heroin is increasing. Heroin dependence can cause a range of problems for the individual user and the community at large. Evidence suggests that effective treatments for heroin dependence can reduce the health and social consequences of heroin use and dependence. The challenge for service planners and treatment providers is to provide a range of treatments for heroin dependence that is properly evaluated and responsive to the individual differences and treatment suitabilities of heroin dependent persons. Projects such as National Evaluation of Pharmacotherapies for Opioid Dependence play an important part in establishing the effectiveness of drug treatments for heroin dependence.

7 DRUG-RELATED RESOURCES ON THE INTERNET


APPENDIX A – EXECUTIVE SUMMARY (NEPOD REPORT)


1 EXECUTIVE SUMMARY

This report provides the findings from trials of pharmacotherapies for opioid dependence. The treatment categories are methadone maintenance, buprenorphine maintenance, LAAM maintenance, naltrexone treatment, rapid opioid detoxification with anaesthesia or sedation, outpatient detoxification using buprenorphine, conventional inpatient detoxification and conventional outpatient detoxification. The data reported herein include short-term outcomes of detoxification. In addition, for naltrexone treatments and maintenance treatments, outcomes at three and six month follow-ups are reported relating to: retention of patients in treatment; heroin use; abstinence rates; criminal behaviour; incidence of serious adverse events. Costs and cost-effectiveness of detoxification and maintenance treatments are also reported.

1.1 Overall impact of maintenance treatments and naltrexone treatments

The treatments examined in the NEPOD project were methadone maintenance, buprenorphine maintenance, levo-alpha-acetylmethadol (LAAM) maintenance, and naltrexone treatment. These pharmacotherapies produced substantial reductions in heroin use while patients remained in treatment.

The 1070 Heroin Users [individuals not in pharmacological treatment for their opioid dependence when they entered the trial] in these trials reported substantial reductions in heroin use and criminal activity after entering treatment. [note added]

Very good outcomes were achieved for Heroin Users while they remained in treatment. A key challenge is to improve patient retention in all pharmacotherapies, because a substantial proportion of patients dropped-out of treatment.

There were 355 Methadone Patients (who were already in methadone maintenance) who either remained in methadone maintenance or switched to buprenorphine, LAAM, or naltrexone. These Methadone Patients had relatively low levels of heroin use when they entered the trials.

Methadone Patients who entered the alternative maintenance treatments showed no significant changes in their low levels of heroin use and criminal behaviour.

Methadone Patients who sought to withdraw from treatment using buprenorphine seem to have worsened slightly in terms of heroin use.

1.2 Short-term detoxification outcomes

Rapid opioid detoxification under anaesthesia or sedation is the most effective method for inducting patients onto naltrexone and achieving short-term abstinence.

Rapid detoxification under anaesthesia had no advantage over rapid detoxification with sedation. Both procedures were more effective than conventional detoxification.

Outpatient buprenorphine detoxification is less effective in achieving initial abstinence, but it links patients into ongoing treatment. Heroin Users who completed buprenorphine detoxification and entered post-detoxification treatment preferred buprenorphine maintenance or methadone maintenance, over naltrexone treatment.

Detoxification using buprenorphine was equally effective in specialist clinic and general practice (shared-care) settings.
1.3 **Methadone, buprenorphine and LAAM maintenance treatment**

The trials of methadone, buprenorphine and LAAM maintenance with 572 Heroin Users produced similar results, although LAAM was superior to methadone.

Approximately 60% of Heroin Users were retained in treatment at three months, and 44% at six months.

Heroin Users who remained in treatment substantially reduced their heroin use, with the number of heroin-free days increasing from 3 days in the month prior to treatment to 22 - 24 heroin-free days in the third month of treatment.

Complete abstinence from heroin use was achieved by over one quarter of Heroin Users who remained in treatment in the third and sixth month.

Taking account of all Heroin Users who entered maintenance treatment with methadone, buprenorphine or LAAM (and assuming that patients who dropped out of treatment resumed their pre-treatment levels of heroin use), a large overall decline in heroin use was still observed. There was an increase of 9 -15 extra heroin-free days at the three month follow-up, and 6 -15 extra heroin-free days at six months.

1.4 **Naltrexone treatment for already abstinent Heroin Users**

Naltrexone treatment was provided to a group of Heroin Users who were already detoxified and abstinent when they entered treatment (a self-selected patient group with relatively good prognosis).

Naltrexone treatment retained 33% of Heroin Users at the three month follow-up, and 5% at six months.

Naltrexone treatment produced a large reduction in heroin use for patients who remained in treatment, with 8 heroin-free days in the month prior to detoxifying increasing to 27 heroin-free days for the 38 patients still in treatment at three months.

Complete abstinence from heroin was achieved by 66% of Heroin Users who were still in treatment in the third month, and 27% of those still in treatment at six months.

Taking account of all previously detoxified Heroin Users who entered naltrexone treatment (and assuming that patients who dropped out of treatment resumed their pre-treatment levels of heroin use), a large decline in heroin use was still observed.

There was an increase of nine heroin-free days in the third month of treatment, and this was gain was maintained in the sixth month.

1.5 **Naltrexone treatment after rapid detoxification**

Naltrexone treatment after rapid detoxification from heroin was provided to Heroin Users and Methadone Patients.

This treatment retained 18% of Heroin Users in naltrexone treatment at the three month follow-up, and 9% at six months.

It produced a large reduction in heroin use for patients who remained in treatment, with only two heroin-free days in the month prior to commencing treatment, increasing to 26 heroin-free days in the third month of treatment, and 28 heroin-free days in the sixth month.

Complete abstinence from heroin use in the previous month was achieved by 75% of Heroin Users who were still in treatment in the third month, and 19% of those in treatment in the sixth month.

Taking account of all Heroin Users who entered rapid detoxification followed by naltrexone treatment (and assuming that patients who dropped out of treatment resumed their pre-treatment levels of heroin use), a large decline in heroin use was
still observed. There was an increase of 8 heroin-free days in the third month of treatment, and this was gain was maintained in the sixth month.

1.6 Naltrexone treatment after conventional inpatient detoxification

Naltrexone treatment after conventional inpatient detoxification (using clonidine and symptomatic medications) for Heroin Users had poor results.

This treatment retained only 2% of Heroin Users (1 of 50) in treatment at the three month follow-up, and none at six months.

Complete abstinence from heroin use was achieved by 4% of the Heroin Users in the third month of treatment, and 6% of Heroin Users in the sixth month.

Taking account of all Heroin Users who entered conventional inpatient detoxification followed by naltrexone treatment (including those who dropped out of treatment), there was an average increase of 3 heroin-free days in the third month of treatment, and 7 heroin-free days in the third month of treatment.

This was a relatively poor result, which may have been influenced by the fact that the Heroin Users in the relevant trial had been randomly allocated to conventional inpatient detoxification rather than (their preferred) rapid detoxification under anaesthesia.

1.7 Criminal behaviour

Self-reported criminal behaviour was more common among Heroin Users prior to entering trials than among Methadone Patients.

Property crime was reported at baseline by a significantly greater proportion of Heroin Users (20%) than Methadone Patients (5%), as was drug dealing (23% vs. 8% respectively); fraud (8% vs. 2% respectively); and violence (3% vs. 1% respectively. Criminal behaviour among Heroin Users was halved at the three month follow-up.

Heroin Users’ average monthly expenditure on heroin decreased from $2,611 at baseline to $572 at three-month follow-up, consistent with the decreases in heroin use.

1.8 Serious adverse events

Overall, serious adverse events (SAEs) were not common in the trials. However, several important observations were made.

While patients were in treatment, most SAEs occurred in naltrexone treatment (56 SAEs per 100 patient-years), and fewest occurred in methadone maintenance and LAAM maintenance (10 SAEs per 100 patient-years).

Naltrexone treatment was associated with a significantly higher (non-fatal and fatal) heroin overdose rate (11 heroin overdoses per 100 patient-years in treatment; and 35 overdoses per 100 patient-years if patients ceased naltrexone) compared with methadone, buprenorphine and LAAM (which had in total five heroin overdoses per 100 patient-years in and out of treatment).

Naltrexone treatment was also associated with a trend towards a higher death rate (four deaths among 454 patients, a rate of nine deaths per 1000 patients) with two deaths for the methadone, buprenorphine and LAAM maintenance therapies combined (two deaths among 1067 patients, a rate of two per 1000). This difference was not statistically significant.

SAE rates increased after patients left treatment.
1.9 Costs and cost-effectiveness

For detoxification short-outcome was defined as achieving abstinence for one week.

Rapid detoxification under sedation was the most cost-effective method of detoxification at a cost of $3,317 per patient who achieved one week of abstinence.

Conventional outpatient detoxification was found to be the least cost-effective detoxification procedure at a cost of $16,945 per abstinent patient. The very low rate of initial abstinence (2 of 50 patients) achieved for this procedure makes this finding unstable. A small increase in abstinence rates would significantly increase its cost-effectiveness.

It is, by far, the least cost-effective withdrawal treatment in this study.

Rapid detoxification under anaesthesia achieved high rates of abstinence in the first week. Its expense reduces its cost-effectiveness. Any efficiencies that could be achieved by streamlining this relatively new procedure would increase its cost-effectiveness.

For maintenance treatments:

Overall, the daily costs of providing maintenance treatments were similar for methadone and LAAM, with naltrexone treatment being slightly more expensive.

Buprenorphine maintenance was more expensive, but there may be potential for improving its cost-efficiency, that would make its cost similar to the other treatments.

Methadone maintenance is the most cost-effective treatment currently available in Australia for the management of opioid dependence. Methadone maintenance also achieved one of the highest rates of retention among the four pharmacotherapies examined.

LAAM is not registered for use in Australia, but it was more cost-effective than methadone maintenance due to its better retention and slightly better ability to suppress heroin use. Although this is a promising result, it is based on a small sample of patients, and the superiority of LAAM over methadone has not been observed in other studies. This result therefore needs to be interpreted cautiously.

Buprenorphine ranks third overall in cost-effectiveness at both three and six months with retention rates of 50% and 38% respectively. Any reductions in the price of buprenorphine and increased efficiency in administering it (such as reductions in dosing time) may reduce its total cost and increase its cost-effectiveness.

Naltrexone treatment appears to be the least cost-effective pharmacotherapy compared with methadone, LAAM and buprenorphine. The proportion of patients retained in treatment was much lower in naltrexone treatment than in the maintenance treatments. Only one in seven of all naltrexone patients completed three months of treatment, and 5% completed six months treatment.

Across treatment modalities, treatment in the G.P. setting appears to be more cost-effective than the clinic setting at both three and six months. While every effort has been made to include all costs in the G.P. setting, there may be other costs such as outside counselling, support costs by the clinic and the Divisions of G.P.s which have not been captured. Although inclusion of these cost components may not change the results, it is also important to note that these GP trials were conducted in the context of support from specialist clinics.
APPENDIX B – RECOMMENDATIONS (NEPOD REPORT)


2. RECOMMENDATIONS

2.1 Recommendations regarding clinical practice

1. Promote diversity of treatment options. Noting that the new treatments evaluated by NEPOD resulted in a substantial reduction in heroin use, and that patients will require different forms of treatment at different stages of their drug-use career, there should be emphasis on providing a range of treatment options that includes methadone, buprenorphine and naltrexone to reduce opioid-related harm.

2. Continue to support methadone maintenance treatment. As methadone maintenance is the most cost-effective treatment currently available in Australia, it should continue to be supported as a treatment for opioid dependence. LAAM (which is not currently available in Australia) should be examined further as it was more cost-effective than methadone, a result that requires replication before it is accepted. It may be possible to increase the cost-efficiency of buprenorphine treatment by altering dosing practices to reduce staff costs. The cost of buprenorphine would also be reduced if a Commonwealth Government purchase price was negotiated that is lower than the current listed price.

3. Improve retention in treatment. As better outcomes are achieved by patients who remain in treatment, there should be increased emphasis on improving treatment retention, especially in naltrexone treatment, but also in methadone, buprenorphine and LAAM. This may involve a review of current policies and treatment practices to ensure availability of a variety of treatment options, and flexibility, accessibility and attractiveness of treatment services. It may be possible to improve retention and treatment outcomes by effectively addressing psychological comorbidity.

4. Encourage general practitioner involvement in a shared-care model. Treatment can be provided effectively, safely and cost-effectively in primary care (general practitioner) settings. No significant differences in outcomes (heroin-free days) were found between specialist clinic settings and GP treatment settings (which involved experienced GPs engaging in shared-care with specialist clinics). As the GP setting provides improved treatment access, an optimal mix of primary care, specialist clinics, and shared-care arrangements should be developed.

5. Link detoxification to continuing treatment. Detoxification does not ensure long-term abstinence from opioids, and should be regarded as a starting point for ongoing treatment, rather than as a complete treatment in its own right. It may be appropriate to reflect this concept in performance measures for detoxification services.
6. Encourage the use of buprenorphine for outpatient detoxification. Outpatient detoxification using buprenorphine is more cost-effective than conventional detoxification (inpatient or outpatient), less expensive than rapid detoxification procedures, and allows flexibility in post-detoxification linkage to either maintenance treatment (with methadone or buprenorphine) or naltrexone treatment.

7. Make rapid detoxification under sedation available for Heroin Users seeking induction into naltrexone treatment. There was no evidence that rapid detoxification under anaesthesia provides better outcomes than rapid detoxification under sedation. As the sedation procedure is less expensive, it should be made available following development of approved clinical guidelines. It should be noted that naltrexone is not currently registered for use in rapid detoxification.

8. Disseminate the results of the NEPOD project. All jurisdictions should review their clinical guidelines, policy documents and systems of service delivery relating to opioid detoxification and maintenance treatment in the light of the NEPOD findings. An active, coordinated dissemination program should be implemented to maximise incorporation of the NEPOD findings into clinical practice throughout Australia, with the aim of increasing the effectiveness and cost-effectiveness of treatment services, and increasing the number of Heroin Users who participate in treatment. An outline of such a program is provided in Appendix 8.7.

2.2 Recommendations regarding further research

1. Investigate some current clinical issues.

- The role and use of buprenorphine in pregnancy should be addressed given its categorisation of risk in pregnancy.

- The use of buprenorphine in “medical maintenance” (dispensing to stable patients up to a week or more supply of buprenorphine to take-away) should be investigated to determine whether it can be effectively prescribed more liberally without increased rates of adverse events.

- The relative efficacy and acceptability to patients of the combined buprenorphine/naloxone (Suboxone ®) tablet warrants investigation.

- Optimal methods for transferring from buprenorphine to naltrexone treatment require further attention.

Research into methods of optimising retention in naltrexone treatment and achieving abstinence needs to be undertaken.
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