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ANCD research paper

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a review of the evidence

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Australian National Council on Drugs, 2015

National Library of Australia Cataloguing-in-Publication entry

Dolan, Kate A., author

Medication-assisted treatment of opioid dependence: a review of the evidence / Kate Dolan and Zahra Alam Mehrjerdi.

ISBN: 9781877018350 (ebook)

ANCD research paper; 32

Includes bibliographical references.

Opioid abuse — Treatment — Australia
Buprenorphine — Therapeutic use — Australia
Methadone maintenance — Australia
Naltrexone — Therapeutic use — Australia

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616.8632061

Editor: Julie Stokes
Design: Inkwire, Canberra

The Australian National Council on Drugs funded the development of this information kit.

Contents

Opioids such as heroin are the third most commonly used illegal drugs in the world, after cannabis and amphetamine-type stimulants. Heroin dependence can lead to serious health, social and economic consequences for users, their families and society. However, heroin or opioid dependence can be treated with medication and psychosocial support. This form of treatment is called medication-assisted treatment of opioid dependence (MATOD). The most common medicines used in Australia are methadone, buprenorphine and naltrexone. There is a strong body of research that underpins the use of these and other medicines; however, some people are uncertain about the role of MATOD in treating heroin or opioid use and dependence.

This information kit includes two booklets. This booklet provides a review of evidence of MATOD, while the second booklet answers some of the most frequently asked questions about MATOD and addresses common misunderstandings.

A note on terminology

The term 'medication-assisted treatment of opioid dependence' is increasingly being used to refer to the different treatment approaches that combine medication and psychosocial support for people who are opioid-dependent. The term 'opioids' includes opiates, the natural alkaloids from the opium plant, as well as synthetic drugs like heroin, fentanyl and oxycodone.

How many people inject drugs or use heroin?

Injecting drug use has been identified in 148 countries and there are an estimated 16 million people who inject drugs in the world (Mathers et al., 2008). In Australia in 2008, there were an estimated 150 000 people who injected drugs (Mathers et al., 2008).

According to the 2013 National Drug Strategy Household Survey, about 15 per cent of Australians aged 14 years or older had used an illicit drug in the previous year (Australian Institute of Health and Welfare, 2014a). Approximately 57 000 (0.3%) of Australian adults had injected a drug and about 19 000 (0.1%) had used heroin in the previous year. These figures were similar to the 2010 Household Survey where 14.7 per cent had used an illicit drug, 0.4 per cent had injected a drug, and 0.2 per cent had used heroin (Australian Institute of Health and Welfare, 2014a).

The nature of drug dependence

The reasons why people start using drugs are varied. A range of factors influences initial and ongoing drug use. These risk factors or protective factors can be biological, sociological and psychological in nature (see Table 1).

Table 1: Factors that influence drug initiation and ongoing use

Risk factors	Protective factors
Individual characteristics (genetics)	Self-control
Parental attitudes	Parental monitoring and support
Chaotic home environment	Positive social environment
Drug availability and effects	Positive relationships
Social environment	Academic competence

Not everyone who uses a drug becomes dependent. About 23 per cent of people who use heroin will become dependent and develop a drug problem (Anthony & Helzer, 1995). It is estimated that genetic factors account for between 40 and 60 per cent of a person's vulnerability to addiction (National Institute on Drug Abuse, 2014). The age at first use, route of drug administration and individual responses to drug use can influence the progression onto regular use and dependence. Continued use leads to physiological and neurobiological changes that in turn lead to physical dependence, resulting in withdrawal on cessation of use, and ongoing craving leading to the resumption of drug use (Koob & Volkow, 2010).

Dependent drug users tend to be impulsive. They make choices based on immediate benefit, with little regard to long-term negative consequences and show poor impulse control, arising from a lack of activity in the area of the brain responsible for 'executive function'. Factors that affect the 'executive' area of brain function (responsible for planning, problem-solving and interpreting risk) include:

- characteristics of the person (genetics, early experiences)
- stage of brain maturation (this area is developed near 25 years of age, making adolescents more vulnerable to the development of problematic drug use), and
- brain damage, due to injury or neurotoxicity of drug use (Koob & Volkow, 2010).

What is the definition of opioid dependence?

According to the World Health Organization's International Classification of Diseases (World Health Organization, 2011), an indication of opioid dependence is when three or more of the following features present simultaneously at any time in the preceding year:

- a strong desire or sense of compulsion to take opioids
- difficulties in controlling opioid use
- a physiological withdrawal state
- tolerance
- progressive neglect of alternative pleasures or interests because of opioid use, and
- persisting with opioid use despite clear evidence of overtly harmful consequences.

The cost of heroin use

The health, social and economic costs associated with heroin use are substantial. Three main areas of cost from heroin use are mortality, infectious diseases and drug-related crime.

In a cohort of Australian heroin users, the annual mortality rates ranged from 1 to 3 per cent (Darke et al., 2011). The major causes of death were overdose, suicide and trauma while the average age at death was 34.5 years. Their mortality rate was four and a half times the expected population rate, with overdose the leading cause of death.

While HIV prevalence among people who inject drugs in Australia remains below 2 per cent (National Centre in HIV Epidemiology and Clinical Research, 2009), the prevalence of hepatitis C infection is high. Unsafe injection practices are the main route of transmission for hepatitis C infection, accounting for an estimated 90 per cent of new cases (Australian Government Department of Health, 2014). In 2012, an estimated 230 000 Australians had chronic hepatitis C infection, including 58 000 with moderate to severe liver disease (Australian Government Department of Health, 2014).

There is a strong association between illicit drug use and property crime. One study estimated that the extent of involvement in property crime among people who are drug-dependent is about 10 times higher than among non-users (Egli et al., 2009).

Prescription opioid dependence

Opioids act on the central nervous system (CNS) to relieve pain. To misuse prescription opioids is to use opioids in a way other than intended, including taking an opioid at a higher dose, consuming it in a different way than it was intended, or taking opioids in conjunction with heroin or alcohol. The increase in prescription opioid medication in Australia over the past 20 years has led to increasing numbers of individuals who have developed pharmaceutical opioid dependence and require assistance in managing dependence in addition to any associated medical conditions (Gowing et al., 2014).

The main class of prescription opioids misused is opioid analgesics, which are pain relievers. Drugs in this category are oxycodone, fentanyl, codeine and morphine. A recent Australian study examined over 900 people living with chronic non-cancer pain who were prescribed opioids for pain. Participants had been living with pain for a mean of 14.2 years. Almost half (43%) were currently prescribed one opioid and 55 per cent had been prescribed two to five different opioids; the most common drug was oxycodone (Belcher et al., 2014). There were 465 oxycodone-related deaths recorded from 2001 to 2009 (Roxburgh et al., 2011).

Many people who develop an addiction as a complication of opioid treatment of chronic, non-malignant pain may have a lesser degree of social exclusion than heroin users, but the combination of pain and addiction can also result in complex treatment needs (Gowing et al., 2014).

Treatment for opioid dependence

To become drug-free, dependent users have to overcome the compulsion of drug use, ongoing cravings and the physical adaptation to chronic drug use. They also have to address psychological and social issues that may be underlying reasons for using drugs or the consequences of a drug-using lifestyle. Recovery from severe and long-standing dependence is likely to require substantial physical, psychological and lifestyle readjustments, which can take years.

Patients may require several different types of treatments in order to overcome their dependency. While detoxification is not considered a treatment, it is often the first step in overcoming drug dependence.

Detoxification

Detoxification refers to the elimination of heroin or other drugs from the body and takes about one week. People may detoxify in hospital, specialist drug and alcohol units, outpatient clinics or at home. Two distinct medication approaches to manage heroin withdrawal are (i) the abrupt cessation of heroin use and symptom relief using non-opioid drugs like benzodiazepines, anti-emetics, non-steroidal anti-inflammatory drugs and clonidine; and (ii) a short course of reducing doses of buprenorphine to manage withdrawal. This approach enables the transfer to naltrexone for relapse prevention treatment or to substitution treatment (Gowing et al., 2014).

The provision of detoxification services entails:

- assessment
- treatment matching
- planning for withdrawal
- supportive care, and
- linkages with services for further treatment and support.

Detoxification in opioid dependence should always be considered as part of a structured treatment approach.

Self-help groups

Narcotics Anonymous (NA) is a self-help group for individuals who work through 12 steps in order to maintain a drug-free lifestyle (Groh et al., 2008). One study of NA attenders in London found that, after six months, 50 per cent were still attending on average 2.2 meetings per week and 46 per cent were abstinent (Christo & Franey, 1995).

SMART Recovery (Self-Management and Recovery Training) is a cognitive group approach that promotes, but does not require, abstinence. This approach is particularly useful for patients in substitution treatment programs who might benefit from mutual support and networking with other recovering drug users but who may feel excluded by the drug-free emphasis of NA.

It is recommended that patients participate in self-help groups, as participation opposed to just attendance is related to effectiveness. However, attendance should not be mandatory, as this can be counterproductive (Gowing et al., 2014).

Therapeutic communities

Therapeutic communities (TCs) are residential programs where drug users live and usually work in a community of ex-users and professional staff. Programs can last between one and 18 months. TCs aim to build the skills and attitudes required to make positive, long-term changes towards a drug-free lifestyle. Program activities include relapse prevention training, group work, employment training, education, life skills training and counselling. A final component assists individuals to return to their community.

The We Help Ourselves (WHOS) program runs for three to six months, after which clients can move into supported accommodation. A study of 191 admissions to WHOS found that 17 per cent of entrants left in the first week, while 34 per cent successfully completed the program (Darke et al., 2012).

Medication-assisted treatment of opioid dependence (MATOD)

Medication-assisted treatment of opioid dependence is a combination of medication (methadone or buprenorphine for substitution treatment, or naltrexone for relapse prevention treatment) and psychosocial support. The medications eliminate withdrawal symptoms and cravings or block the euphoric effect of opioid use. Psychosocial support can range from the provision of food and shelter to psychotherapy (Gowing et al., 2014).

Methadone was introduced in Australia in 1969 (Gowing et al., 2014), buprenorphine (Subutex) in 2000, and buprenorphine–naloxone (Suboxone) in 2005 (New South Wales Department of Health, 2006). The film preparation of buprenorphine–naloxone combination became available in Australia in 2012 (Gowing et al., 2014).

In most Australian states it is necessary to visit a general practitioner and be assessed for MATOD. In 2013, there were 2025 prescribers of opioid pharmacotherapy drugs, an increase of 15 per cent from 2012 (Australian Institute of Health and Welfare, 2014b). In 2013, just over 47 000 people received pharmacotherapy at 2355 dosing points around Australia. Methadone was the most common pharmacotherapy drug, with around two-thirds (68%) of patients treated with this drug.

Methadone is a synthetic opioid used to treat heroin and other opioid dependence. It reduces opioid withdrawal symptoms, the desire to take opioids and the euphoric effect when opioids are used. It is taken orally on a daily basis.

Buprenorphine acts in a similar way to methadone, but is longer-lasting and may be taken daily or every second or third day. Two buprenorphine preparations are registered in Australia for the treatment of opioid dependence: a product containing buprenorphine only (Subutex) and a combined product containing buprenorphine and naloxone (Suboxone). The buprenorphine-only product is available as a tablet containing buprenorphine hydrochloride which is administered sublingually (by dissolving under the tongue) (Australian Government Department of Health and Ageing, 2007).

The combination buprenorphine–naloxone product is a sublingual tablet or film containing buprenorphine hydrochloride and naloxone hydrochloride (Australian Government Department of Health and Ageing, 2012). It is recommended that buprenorphine–naloxone should be prescribed in preference to buprenorphine for most patients receiving takeaway doses (Australian Government Department of Health and Ageing, 2007). This is because, when taken as intended by dissolving the tablet or film under the tongue, the combined product acts as if it was buprenorphine alone. However, if the combined product is injected, naloxone can block the effects of buprenorphine and increases opioid withdrawal symptoms. This reduces the risk that those receiving buprenorphine–naloxone as a takeaway dose will inject it or sell it to others to inject (Australian Government Department of Health and Ageing, 2007).

Medications used in MATOD are of two broad types: opioid agonists and antagonists. Methadone, morphine, heroin, oxycodone and hydromorphone are full opioid agonists. These drugs bind to and activate *mu* opioid receptors in the brain. Increasing doses of full agonists produce increasing effects.

Buprenorphine is a partial opioid agonist. It binds to the *mu* opioid receptors in the brain and activates them, but not to the same degree as full agonists. This creates a ceiling effect, with the effect of buprenorphine reaching a maximum level that is not increased even with increasing doses of buprenorphine. Like antagonists, partial agonists occupy receptors and prevent further activation by a full agonist.

Naltrexone and naloxone are examples of opioid antagonists. These drugs also bind to *mu* opioid receptors in the brain, but do not activate them. In binding to the receptors, antagonists prevent the receptors from being activated by agonists. Hence antagonists are blocking agents.

The pharmacological properties of methadone and buprenorphine mean they can be substituted for other opioid drugs, and are referred to as opioid substitution treatment (OST). Naltrexone is a blocking agent used in abstinence-oriented programs to support relapse prevention.

Aims of medication-assisted treatment of opioid dependence

The aims of MATOD are to reduce or eliminate heroin or unsanctioned opioid use to improve the health and wellbeing of patients. Substitution treatment reduces the harms from using heroin, such as HIV and hepatitis C infections, involvement in drug-related crime, or death associated with opioid use.

Side effects of methadone

The long-term side effects of being on a stable oral dose of methadone are relatively minor for most patients. Methadone does not cause damage to any of the major organs or systems of the body. Methadone may lead to the following side effects:

- constipation
- increased sweating
- nausea and vomiting
- fluid retention and weight gain
- sleep disturbances
- dry mouth
- vasodilation and itching
- menstrual irregularities in women
- sexual dysfunction including impotence in males, and
- gynaecomastia in males (Gowing et al., 2014).

The major risk associated with methadone is the possibility of overdose especially when a patient commences treatment (Cornish et al., 2010), when other sedative drugs are also used or when their dose increases. When the patient reaches a stable dose, in about two weeks, the risk of overdose subsides (Cornish et al., 2010). When a patient leaves treatment, either by being discharged or by dropping out, their risk of overdose increases substantially (Cousins et al., 2011).

Effectiveness of substitution treatment

The duration in treatment and the dose of methadone are important factors in the treatment being effective. The most effective methadone maintenance treatment programs dispense doses of 60mg/day or more in the community (Faggiano et al., 2003) and have a philosophy of maintenance rather than abstinence (Gowing, et al., 2011). In New South Wales, the average duration of methadone treatment was six months for over 40 000 patients (Burns et al., 2009).

There is a very large body of evidence which shows methadone treatment is associated with reductions in opioid use (Henry-Edwards et al., 2003; Gossop et al., 2001), criminal activity (Oliver et al., 2010), deaths due to overdose (Degenhardt et al., 2009) and the risk of HIV transmission (Bukten et al., 2012; Cousins et al., 2011).

Not all patients on methadone treatment will stop heroin use. The Australian Treatment Outcomes Study (ATOS) followed four cohorts of heroin users. Three cohorts were recruited at entry to MATOD, detoxification or residential rehabilitation, while one cohort was not in treatment at the time of recruitment. At one-year follow-up, 57 per cent of all subjects were abstinent from heroin use: 65 per cent in the MATOD group; 52 per cent in the detoxification group; 63 per cent in the residential rehabilitation group; and 25 per cent of persons in the non-treatment group (Teesson et al., 2006).

Buprenorphine treatment

The two buprenorphine products registered in Australia are Subutex and Suboxone. Subutex is a sublingual tablet containing buprenorphine hydrochloride and comes in 0.4mg, 2mg and 8mg strengths. Suboxone is a sublingual film and contains buprenorphine hydrochloride and naloxone hydrochloride in a ratio of 4:1. Suboxone is available in two dose strengths: 2mg buprenorphine and 0.5mg naloxone; and 8mg buprenorphine and 2mg naloxone. Supervising the administration of the film is easier compared to tablets (Lintzeris et al., 2013).

The properties of the buprenorphine and naloxone combination (Suboxone) are such that, when taken sublingually, buprenorphine will act alone. However, if the combination is injected, the naloxone will reduce the effects of the buprenorphine in the short term and induce withdrawal symptoms in opioid-dependent individuals using other opioid drugs. These properties of Suboxone minimise the potential misuse and diversion of buprenorphine, as buprenorphine–naloxone combination preparations are less likely to be injected than mono preparations containing only buprenorphine. This attribute makes Suboxone the preferred option for 'takeaway' doses (Yokell et al., 2011).

Side effects of buprenorphine

The side effects of buprenorphine are similar to those of other opioids (Lofwall et al., 2005), although many patients report less sedation on buprenorphine than on methadone (Fischer et al., 1999; Holt et al., 2007). The reported side effects of buprenorphine include:

- constipation
- disturbed sleep
- drowsiness
- sweating
- headaches
- nausea, and
- reduced libido (Gowing et al., 2014).

Effectiveness of buprenorphine

Patients in buprenorphine treatment report that it reduces cravings for heroin, reduces heroin use and alleviates opioid withdrawal symptoms (Gowing et al., 2014). A systematic review of 5400 patients in buprenorphine maintenance treatment or in a control group found that buprenorphine was superior to no treatment in reducing illicit opioid use when doses exceeded 16mg (Mattick et al., 2014). Buprenorphine is associated with low physical dependence and a relatively mild withdrawal syndrome, which makes detoxification from heroin easier than using methadone.

Both methadone and buprenorphine are effective therapies for heroin dependence. A systematic review found no difference between buprenorphine (7–15mg) and methadone (40–85mg) in treatment retention or in reducing heroin use.

Other benefits of opioid substitution treatment include reductions in the frequency of injecting, in the sharing of injection equipment (Gowing et al., 2011) and in the transmission of HIV and hepatitis C infection (Vickerman et al., 2012). MATOD improves adherence and response to antiretroviral treatment for HIV infection, which reduces the risk of HIV transmission (Roux et al., 2008; Palepu et al., 2006).

Studies show that MATOD reduces patients' involvement in crime. Court records of 11 126 people in a New South Wales methadone program in 1999 and 2000 were examined. Offending rates were significantly lower when people were in methadone treatment than when they were not in treatment. It was found that, for every 100 individuals in methadone each year, there were 12 fewer robberies, 57 fewer break and enters, and 56 fewer motor vehicle thefts (Lind et al., 2004).

MATOD improves physical and mental health and social functioning

Heroin use can lead to poor physical and mental health. However, MATOD can help patients reduce their frequency of heroin use, alleviate withdrawal symptoms and improve overall health (Joseph et al., 2000). The quality of life among heroin users is improved during treatment (Xiao et al., 2010). MATOD contributes to improved social functioning among heroin users. A return to employment, taking up study, improved parenting, relationships with others and residential stability are all important treatment outcomes. With improved social functioning, patients can become more financially independent. A study of 553 methadone patients in Taiwan showed significant improvements in the psychological and social domains after six and 12 months of treatment (Chou et al., 2013).

Factors related to selecting methadone or buprenorphine

A number of factors should be considered when choosing methadone or buprenorphine, such as the preference of the patient, their past experience of treatment and individual variations in absorption, metabolism and clearance of medications. Patients experiencing side effects from one opioid medication may benefit by switching to the other medication. It is relatively easy to transfer from buprenorphine to methadone (Sigmon et al., 2012). Some patients prefer buprenorphine, as methadone has a more sedating effect (Fischer et al., 1999).

Naltrexone treatment

Naltrexone is used in patients who have ceased the use of opioids, such as heroin or morphine, with the aim of preventing relapse to drug use. Psychosocial support is an integral component of naltrexone maintenance treatment.

A standard maintenance dose of naltrexone is 50mg/day, but this can result in side effects. To minimise side effects, patients can be maintained on 25mg/day. Naltrexone treatment for dependence is a long-term undertaking, as relapse to heroin dependence can occur even after two or three years of treatment.

Side effects of naltrexone treatment

Side effects of naltrexone treatment are common but mild and short-lived in most patients. About one in ten patients report the following side effects:

- difficulty in sleeping
- loss of energy
- anxiety
- abdominal pain
- nausea and vomiting
- joint and muscle pain, and
- headache (Gowing et al., 2014).

The major risk associated with naltrexone treatment is the increased probability of death from overdose when patients relapse to heroin use as their tolerance to opioids diminishes. Previous doses that could be tolerated can now be fatal for the heroin user (Gowing et al., 2014).

Effectiveness of naltrexone treatment

Naltrexone treatment is most effective in patients who are highly motivated with good social support. Parents or partners may be involved in supervising the patient taking their dose, which can improve treatment compliance. An Australian study found naltrexone had limited acceptability and a high rate of drop-out. In Melbourne, just 30 per cent of people screened actually commenced naltrexone treatment and only 30 per cent of those completed 12 weeks of treatment (Tucker et al., 2004).

Patient retention is higher in methadone and buprenorphine treatment than in naltrexone treatment. Among patients who have withdrawn from opioids and are motivated to cease opioid use completely, abstinence is higher in naltrexone treatment than with no treatment (World Health Organization, 2009).

Naltrexone implants

As some patients find it hard to comply with the daily regimen of naltrexone, there is considerable interest in the use of depot and implant preparations of naltrexone. These are designed to slowly release naltrexone into the body over a period of weeks to months. Implant preparations of naltrexone are not currently registered in Australia.

Psychosocial interventions

Psychosocial interventions are an integral component of MATOD (Gowing et al., 2014). Drug counselling on a regular basis can facilitate the engagement of the patient in a treatment program. Reducing or ceasing heroin use generally involves major social and lifestyle changes. Counselling can help individuals make these changes, as well as prevent relapse to heroin use. In counselling sessions, heroin users are encouraged to discuss their drug use and related problems, such as family or relationship issues. The client and counsellor work together to set goals and design an appropriate treatment plan. Sessions focus on developing problem-solving and drug-refusal skills, identifying risky situations where an individual may feel tempted to use heroin, and working out ways to deal with these situations. Psychosocial sessions can be delivered in one-on-one or group sessions and can include cognitive–behavioural therapy and contingency management. These approaches, which are one component of MATOD, increase patient compliance (Gowing et al., 2014).

Drug use and pregnancy

Substance use during pregnancy can have an adverse effect on the mother, on foetal development and infant outcomes (Bauer et al., 2002). Women who are opioid-dependent and pregnant need to be referred to specialist, multidisciplinary drug and alcohol antenatal clinics. Substitution treatment is the preferred approach for opioid-dependent pregnant women (Burns et al., 2007) as it will

- improve their access to antenatal care
- improve the health and social functioning of pregnant women
- reduce heroin or other drug use, and
- reduce maternal and infant deaths associated with heroin use.

Opioid substitution treatment, such as methadone and buprenorphine, has minimal long-term developmental impact on children when compared to the risk of ongoing heroin use during pregnancy (World Health Organization, 2009). Studies show positive results using buprenorphine in pregnancy involving nearly 900 buprenorphine-exposed infants (Jones et al., 2012).

Women in opioid substitution treatment should be encouraged to continue in treatment for a substantial period after giving birth (Gowing et al., 2014). Newborn infants should be observed for withdrawal symptoms which generally start within two days of delivery but may be delayed for 7–14 days in some cases. Follow-up of one to two years is required to monitor any developmental abnormalities.

The safety and efficacy of naltrexone in pregnancy have not been established. If pregnancy is planned, the use of naltrexone should be ceased in advance and women taking Suboxone should be transferred to Subutex (Gowing et al., 2014).

MATOD in prison

In 2013, there were 30 775 prisoners in Australia (Australian Bureau of Statistics, 2013), of whom 3265 were in MATOD (Australian Institute of Health and Welfare, 2014b). Some inmates continue to inject in prison and, as a result, may acquire hepatitis C (Dolan et al., 2010) or HIV infection (Dolan & Wodak, 1999). MATOD reduces heroin use in prisons (Dolan et al., 2005) and fatal overdose after release (Christensen et al., 2006).

A systematic review found that inmates in MATOD had their risk of injecting reduced by 55–75 per cent and their risk of syringe sharing reduced by 47–73 per cent compared to those who went untreated (Larney, 2010).

A New South Wales study of inmates released between 2000 and 2012 found 1050 deaths had occurred during 100 978 person-years of follow-up. The lowest post-release mortality rate was among those continuously retained in MATOD and the highest rate was among those without MATOD. Being in MATOD in the four-week period post-release reduced the hazard of death by 75 per cent (Degenhardt et al., 2014).

Prison-based MATOD also reduces the re-incarceration of drug users (Larney et al., 2012; Dolan et al., 2005). Being in methadone treatment at release from prison and continuing in treatment in the community produced a significant reduction in the risk of re-incarceration by an average of 20 per cent among a group with a heightened rate of re-incarceration (Larney et al., 2012).

Involuntary withdrawal

A decision to discharge a patient involuntarily needs careful consideration given the increased risk of death that this involves. Patients can be discharged from treatment for their own safety or wellbeing, or that of other patients or staff. This may be the result of violence or threat of violence against staff or other patients, property damage or theft from the clinic or dosing pharmacy, drug dealing or the repeated diversion of medication. Occasionally problems may be resolved by transferring the patient to another program rather than discharging them from substitution treatment (Gowing et al., 2014).

Completing substitution treatment

The issue of completing MATOD needs to be discussed with the patient on a regular basis during treatment. Successful cessation involves the safe and comfortable withdrawal from opioid medication without relapse into opioid or other substance dependence. Leaving treatment too early can be associated with relapse to drug use. Often patients want to stop treatment prematurely. Most patients take one to two years of substitution treatment to stabilise.

It is important to discuss the predictors of successful cessation of opioid substitution treatment with the patient (Gowing et al., 2014). These include:

- gradual withdrawal over months rather than weeks, days or sudden cessation
- good patient understanding of the process and involvement in decision making
- use of psychosocial interventions to address coping strategies, risk behaviours and support systems
- regular review of progress and plans
- no unstable or problematic use of alcohol or other drugs, and
- a stable medical and psychiatric condition and social conditions.

A survey of 145 patients found that 71 per cent had previously attempted to leave treatment and 23 per cent had achieved abstinence for at least three months (Winstock et al., 2011). The withdrawal syndrome on cessation of buprenorphine is milder than withdrawal from heroin, morphine and methadone (Jasinski et al., 1982; Mudric et al., 1998). Self-help groups such as NA and SMART Recovery may be beneficial when leaving MATOD.

Cost-effectiveness of MATOD

The cost-effectiveness of MATOD, especially for methadone treatment, has been well documented for over 30 years. A failure to provide adequate MATOD for heroin users is costly for government and the community (World Health Organization, 2004).

Many studies have found that the benefits of MATOD far exceed the costs. Economic evaluations of MATOD programs have produced positive results in terms of cost-effectiveness in the United Kingdom (National Institute for Health and Care Excellence, 2007) and in the United States (Zaric et al., 2000).

The most cost-effective public health strategy for managing heroin dependence is MATOD, primarily through the use of methadone or buprenorphine. Naltrexone treatment appears to be the least cost-effective treatment compared with methadone and buprenorphine. A randomised controlled trial for assessing the safety, efficacy and cost-effectiveness of buprenorphine versus methadone was conducted in two Australian cities with 405 subjects. Treatment with methadone was found to be both less expensive and more effective

than treatment with buprenorphine. However, no difference was found between the cost-effectiveness of methadone and buprenorphine treatments. The results of this study indicated that buprenorphine provided a viable alternative to methadone in the treatment of opioid dependence (Doran et al., 2003).

A New South Wales study analysed the cost of MATOD per heroin-free day compared to no MATOD for prisoners. The average cost of the treatment was AU$3234 per prisoner per year (Warren et al., 2006). The analysis showed that only 20 days of incarceration needed to be avoided to offset the annual cost of methadone treatment per patient in New South Wales prisons.

Support for MATOD

Methadone and buprenorphine are included on the Model List of Essential Medicines issued by the World Health Organization (World Health Organization, 2013). The World Health Organization recommends that all countries experiencing problems with heroin dependence and injection-related HIV infections should ensure methadone or buprenorphine is available for heroin users at an affordable price (Narayanan et al., 2008). In 2012, 77 countries provided MATOD in the community (Stoicescu, 2012) and 41 countries provided MATOD in prisons (Dolan et al., 2014).

The World Health Organization estimated that if MATOD was made readily available globally, it could prevent up to 130 000 new HIV infections annually, reduce the spread of hepatitis C infection, and decrease death from opioid overdose by 90 per cent (World Health Organization, 2009).

Australia's National Drug Strategy is based on the principles of harm minimisation. It emphasises the importance of assisting people to recover from drug use, including the provision of MATOD. The 2013 National Drug Strategy Household Survey found two-thirds of Australians support the use of MATOD for the treatment of opioid dependence (Australian Institute of Health and Welfare, 2014a).

Needle and syringe programs in Australia

As some drug users continue to inject, they need access to sterile injecting equipment. Needle and syringe programs (NSPs) provide sterile injecting equipment as well as referral to health, social and drug treatment agencies. From 2000 to 2009, the funding for NSPs in Australia was $243 million, which yielded healthcare cost savings of $1.28 billion. During this time, NSPs averted 32 061 HIV infections and 96 918 hepatitis C infections (National Centre in HIV Epidemiology and Clinical Research, 2009). Needle and syringe programs are endorsed in Australia's National HIV Strategy.

Useful internet sites

Australia's National Drug Strategy
http://www.nationaldrugstrategy.gov.au/

2013 National Drug Strategy Household Survey
http://www.aihw.gov.au/alcohol-and-other-drugs/ndshs

National clinical guidelines on the management of drug use in pregnancy
http://www.health.nsw.gov.au/pubs/2006/ncg_druguse.html

Australia's Seventh National HIV Strategy 2014–2017
http://www.health.gov.au/internet/main/publishing.nsf/Content/8E87E65EEF535B02CA257BF0001A4EB6/$File/HIV-Strategy2014-v3.pdf

Information kit on needle and syringe programs: your questions answered
http://www.hep.org.au/documents/nsp-questions-answered-160KB.pdf

Fourth National Hepatitis C Strategy 2014–2017
http://www.health.gov.au/internet/main/publishing.nsf/Content/A68444CDED77B3A9CA257BF0001CFD80/$File/Hep-C-Strategy2014-v3.pdf

World Health Organization's International Classification of Diseases, 10th edition (ICD–10)
http://www.who.int/classifications/icd/en/

SMART Recovery
http://smartrecoveryaustralia.com.au/

Narcotics Anonymous Australia
http://na.org.au/

National Institute on Drug Abuse
http://www.drugabuse.gov/

National Drug and Alcohol Research Centre
https://ndarc.med.unsw.edu.au/

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