



Australian Government

Clinical guidelines and procedures
for the use of methadone
in the maintenance treatment
of opioid dependence



*National
Drug Strategy*

Clinical Guidelines and Procedures for the Use of Methadone in the Maintenance Treatment of Opioid Dependence

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Introduction

Methadone was first used as a treatment for heroin dependence in Vancouver in 1959 and was subsequently introduced into Australia for the same purpose in 1969. Methadone Maintenance Treatment (MMT) was endorsed by State, Territory and Commonwealth Governments as an appropriate and useful treatment for heroin dependence at the launch of the National Campaign Against Drug Abuse in 1985. Since that time there has been substantial growth in the number of individuals receiving methadone treatment in most jurisdictions of Australia.

The aims of Methadone Maintenance Treatment are to:

- Reduce or eliminate illicit heroin and other drug use by those in treatment.
- Improve the health and well-being of those in treatment.
- Facilitate the social rehabilitation of those in treatment.
- Reduce the spread of blood borne diseases associated with injecting opioid use.
- Reduce the risk of death associated with opioid use.
- Reduce level of involvement in crime associated with opioid use.

These clinical guidelines have been prepared to aid authorised medical practitioners in the selection and management of patients seeking methadone maintenance treatment for opioid dependence. The content has been designed to complement the National Policy on Methadone Treatment and local jurisdictional policies and requirements for methadone prescribing.

These guidelines were prepared under the auspices of the National Expert Advisory Committee on Illicit Drugs (NEACID) in collaboration with the National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD) project, the Royal Australian College of General Practitioners (RACGP) and the Australian Professional Society on Alcohol and Other Drugs (APSAD), and are funded by the Commonwealth Department of Health and Ageing.

The clinical guidelines are based on national and international research literature, previously published guidelines and clinical experience with the use of methadone in Australia. They have undergone a rigorous process of review and have been formally endorsed by the RACGP and APSAD.

The authors gratefully acknowledge the contribution of a number of individuals and organisations in the drafting and review of these guidelines. Mr Andrew Preston generously gave permission for material from his book *The New Zealand Methadone Briefing* to be included in the guidelines. Dr Tony Gill and the Drug Programs Bureau, NSW Health Department gave valuable feedback and allowed us to reproduce sections of the *NSW Methadone Maintenance Treatment Clinical Practice Guidelines* in the appendices. Dr Hendree Jones, Director of Research at the Centre for Addiction and Pregnancy in the USA, provided valuable comments on the sections on Pregnancy and Lactation. We are indebted to Dr Michael Farrell and the UK Department of Health for permission to use the table of drug interactions which appears at Appendix 1. To all those who patiently reviewed and commented on successive drafts of the document – our grateful thanks.



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1 Clinical pharmacology

1.1 General Information

What is Methadone?

Methadone is a potent synthetic opioid agonist which is well absorbed orally and has a long, although variable plasma half life. The effects of methadone are qualitatively similar to morphine and other opioids.

Effects of Methadone

Actions

- Analgesia
- Sedation
- Respiratory depression
- Euphoria (oral methadone causes less euphoria than intravenous heroin)

Other Actions

- **Decreased blood pressure**
- **Constriction of the pupils**
- **Gastrointestinal tract actions**
 - Reduced gastric emptying
 - Reduced motility
 - Elevated pyloric sphincter tone
 - Elevated tone of Sphincter of Oddi can result in biliary spasm
- **Skin actions**
 - Histamine release
- **Endocrine actions** including
 - Reduced Follicle Stimulating Hormone
 - Reduced Luteinising Hormone
 - Elevated Prolactin
 - Reduced Adreno-Cortico-Trophic Hormone
 - Reduced testosterone (Endocrine function may return to normal after 2-10 months on methadone)
 - Elevated Anti Diuretic Hormone
- **Antitussive**

Side Effects

- **Sleep disturbances**
- **Nausea and vomiting**
- **Constipation**
- **Dry mouth**
- **Increased sweating**
- **Vasodilation and itching**
- **Menstrual irregularities in women**
- **Gynaecomastia in males**
- **Sexual dysfunction including impotence in males**
- **Fluid retention and weight gain**

Most people who have used heroin will experience few side effects from methadone. Once on a stable dose, tolerance develops until cognitive skills and attention are not impaired. Symptoms of constipation, sexual dysfunction and occasionally increased sweating can continue to be troubling for the duration of MMT.

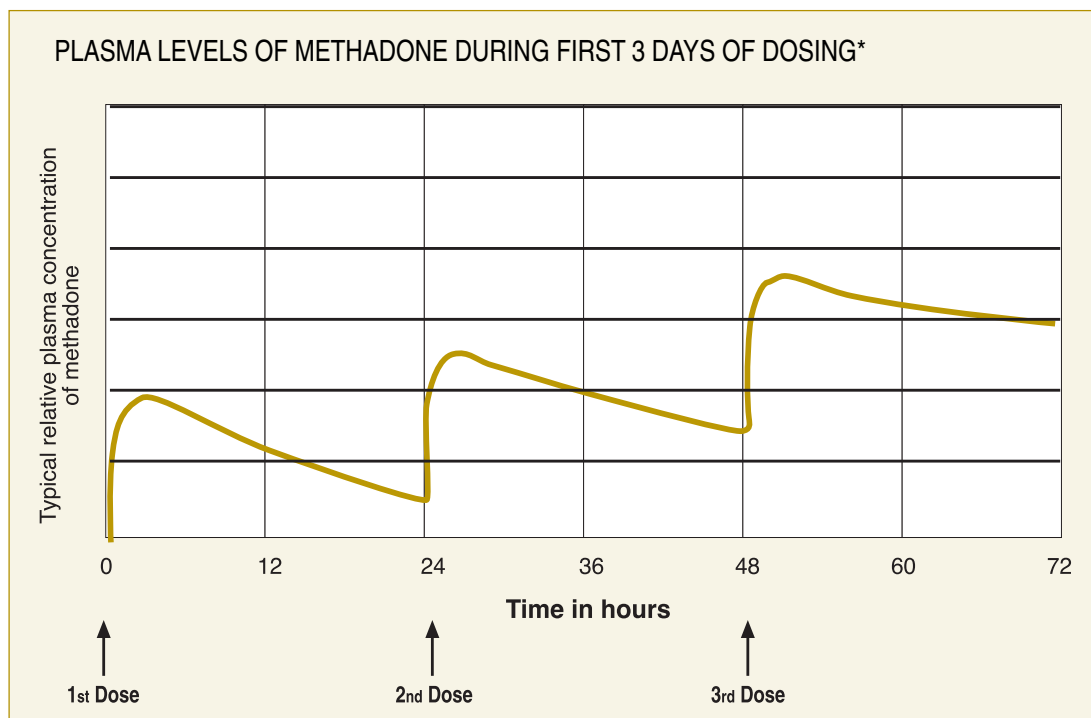
Methadone is fat soluble and binds to a range of body tissues including the lungs, kidneys, liver and spleen such that the concentration of methadone in these organs is much higher than in blood. There is then a fairly slow transfer of methadone between these stores and the blood. **Because of its good oral bioavailability and long half life, methadone is taken in an oral daily dose.**

Methadone is primarily broken down in the liver via the cytochrome P450 enzyme system. Approximately 10% of methadone administered orally is eliminated unchanged. The rest is metabolised and the (mainly inactive) metabolites are eliminated in the urine and faeces. Methadone is also secreted in sweat and saliva.

Pharmacokinetics

There is wide individual variability in the pharmacokinetics of methadone but in general, blood levels rise for about 3-4 hours following ingestion of oral methadone and then begin to fall. Onset of effects occurs approximately 30 minutes after ingestion. The apparent half life of a single first dose is 12 – 18 hours with a mean of 15 hours. With ongoing dosing, the half life of methadone is extended to between 13 and 47 hours with a mean of 24 hours. This prolonged half life contributes to the fact that methadone blood levels continue to rise during the first week of daily dosing and fall relatively slowly between doses.

FIGURE 1



*Preston A (1999) The New Zealand Methadone Briefing. Used with permission.

Methadone reaches steady state in the body (where drug elimination equals the rate of drug administration) after a period equivalent to 4-5 half lives or approximately 3-10 days. Once stabilisation has been achieved, variations in blood concentration levels are relatively small and good suppression of withdrawal is achieved. For some, however, fluctuations in methadone concentrations may lead to withdrawal in the latter part of the inter-dosing interval. If dose increases or multiple dosing within a twenty four hour period do not prevent this, other agonist replacement treatment approaches such as buprenorphine should be considered.

Onset of effects	30 minutes
Peak effects	Approx 3 hours
Half life (in MMT)	Approx 24 hours
Time to reach stabilisation	3-10 days

Withdrawal Syndrome

The signs and symptoms of the opioid withdrawal syndrome include irritability, anxiety, restlessness, apprehension, muscular and abdominal pains, chills, nausea, diarrhoea, yawning, lacrimation, piloerection, sweating, sniffing, sneezing, rhinorrhoea, general weakness and insomnia. Signs and symptoms usually begin two to three half-lives after the last opioid dose, ie. 36 to 48 hours for long half-life opioids such as methadone, and 6 to 12 hours for short half-life opioids such as heroin and morphine.

Following cessation of heroin, symptoms reach peak intensity within 2 to 4 days, with most of the obvious physical withdrawal signs no longer observable after 7 days. The duration of methadone withdrawal is longer (5 to 21 days). This first, or acute, phase of withdrawal may then be followed by a period of protracted withdrawal syndrome. The protracted syndrome is characterised by a general feeling of reduced well-being. During this period, strong cravings for opioids may be experienced periodically.

The opioid withdrawal syndrome is rarely life-threatening. However, completion of withdrawal is difficult for most people. Untreated methadone withdrawal symptoms may be perceived as more unpleasant than heroin withdrawal, reflecting the more prolonged nature of methadone withdrawal. Factors that have been identified as having the potential to influence the severity of withdrawal include the duration of opioid use, general physical health, and psychological factors, such as the reasons for undertaking withdrawal and fear of withdrawal. Buprenorphine appears to have a milder withdrawal than other opioids.

Drug Interactions

Toxicity and death have resulted from interactions between methadone and other drugs. Some psychotropic drugs may increase the actions of methadone because they have overlapping, additive effects (e.g. benzodiazepines and alcohol add to the respiratory depressant effects of methadone). Other drugs interact with methadone by influencing (increasing or decreasing) metabolism (See Appendix 1). Drugs which induce the metabolism of methadone can cause a withdrawal syndrome if administered to patients maintained on methadone. These drugs should be avoided in methadone

patients if possible. If a cytochrome P450 inducing drug is clinically indicated for the treatment of another condition seek specialist advice. Cytochrome P450-3A inhibitors can decrease the metabolism of methadone and cause overdose.

A full list of drugs which interact with Methadone appears at Appendix 1

Safety

The long term side effects of methadone taken orally in controlled doses are few. Methadone does not cause damage to any of the major organs or systems of the body and those side effects which do occur are considerably less harmful than the risks of alcohol, tobacco and illicit opiate use (see Section 4.1). The major hazard associated with methadone is the risk of overdose. This risk is particularly high at the time of induction to MMT and when methadone is used in combination with other sedative drugs. The relatively slow onset of action and long half life mean that methadone overdose can be highly deceptive and toxic effects may become life threatening many hours after ingestion. (see section 4.2). Because methadone levels rise progressively with successive doses during induction into treatment, most deaths in this period have occurred on the third or fourth day of treatment.

Formulations

Two preparations are available for methadone maintenance treatment in Australia:

- Methadone Syrup® from Glaxo Smith Kline. This formulation contains 5 mg/ml methadone hydrochloride, sorbitol, glycerol, ethanol (4.75%), caramel, flavouring, and sodium benzoate.
- Biodone Forte® from McGaw Biomed. This formulation contains 5mg/ml methadone hydrochloride and permicel-red colouring.

2 Entry into methadone treatment

2.1 Entry into Methadone Maintenance Treatment

Note: Jurisdictional requirements stipulating eligibility for entry to MMT may vary from state to state and from time to time. These guidelines are an attempt to present the clinical basis for MMT. If in doubt consult your jurisdictional policy.

Indications

Methadone maintenance treatment is indicated for those who are dependent on opioids and who have had an extended period of regular opioid use.

The diagnosis of opioid dependence should be made by eliciting the features of opioid dependence in a clinical interview (See Section 2.2 Assessment for treatment with methadone). The definitional criteria of *The diagnostic and statistical manual of mental disorders, 4th edition* (DSM-IV) are useful to diagnose dependence.

Diagnostic Definition of Opioid Dependence (DSM IV)

Dependence is defined as “A maladaptive pattern of substance use leading to clinically significant impairment or distress as manifested by three or more of the following occurring at any time in the same 12 month period.”

- **Tolerance as defined by either of the following:**
 - A need for markedly increased amounts of opioids to achieve intoxication or desired effect;
 - Markedly diminished effect with continued use of the same amount of opioids.
- **Withdrawal as manifested by either of the following:**
 - The characteristic withdrawal syndrome for opioids (see section 1.1).
 - Opioids or a closely related substance are taken to relieve or avoid withdrawal symptoms.
- **Opioids are often taken in larger amounts or over a longer period than was intended.**
- **There is a persistent desire or unsuccessful attempts to cut down or control opioid use.**
- **A great deal of time is spent in activities necessary to obtain opioids, use opioids, or recover from their effects.**
- **Important social, occupational, or recreational activities are given up or reduced because of opioid use.**
- **The opioid use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.**

NOTE: A person diagnosed as opioid dependent may or may not be physically dependent on opioids at the time of presentation. If there is no current physical dependence MMT will not usually be appropriate. For those not physically dependent at the time of presentation, the prescribing practitioner must clearly document that the potential benefits to the individual's health and social functioning outweigh the disadvantages of MMT.

- **The patient will usually be at least 18 years of age.** The prescribing doctor should seek a second or specialist opinion before treating anyone under 18 years of age. However, methadone treatment should not be precluded on the grounds of age alone.
- **The patient must be able to provide proof of identity** – a requirement for treatment with any S8 medication.
- **The patient must be able to give informed consent to treatment with methadone.**

Suitability for Methadone Treatment

opioid dependent

18 years or older

proof of identity

capable of informed consent

Contraindications

The following categories of patients are not suitable for treatment with methadone.

- Patients with severe hepatic impairment (decompensated liver disease) as methadone may precipitate hepatic encephalopathy.
- Generally treatment other than methadone should be considered for a person under the age of 18 years, however, methadone treatment should not be precluded solely on the grounds of age. The prescribing doctor should check jurisdictional requirements regarding age limits for MMT.
- Where patients are unable to give informed consent due to the presence of a major psychiatric illness or being underage, the prescribing doctor should consider relevant secondary consultation and check jurisdictional requirements regarding obtaining legal consent.
- Patients who are hypersensitive to methadone or other ingredients in the formulation.
- Other contraindications *identified by the manufacturers of methadone* include severe respiratory depression, acute asthma, acute alcoholism, head injury and raised intracranial pressure, ulcerative colitis, biliary and renal tract spasm, and patients receiving monoamine oxidase inhibitors or within 14 days of stopping such treatment. It is recommended that specialist advice be sought in these cases.

Precautions

Particular caution should be exercised by prescribers when assessing individuals with the following clinical conditions as to their suitability and safety for treatment with methadone. Concomitant medical and psychiatric problems and other drug use increase the complexity of management of patients on MMT and may also increase the risk of overdose and death. The prescribing doctor should seek specialist advice or assistance in such cases.

- *High risk poly drug use*: all opioid substitution treatments should be approached with caution in individuals using other drugs, particularly those likely to cause sedation such as alcohol, as well as benzodiazepines and antidepressants in doses outside the normal therapeutic range. Particular attention should be given to assessing the level of physical dependence on opioids, co-dependence on other drugs and overdose risk. (see Sections 4.2 and 4.9).
- *Co-occurring alcohol dependence*: due to the significant management problems presented by this group, consideration should be given to concurrent disulfiram or acamprosate therapy. If disulfiram or acamprosate are used, a methadone liquid formulation that does not contain alcohol should be considered to reduce the risk of reactions.
- *Recent history of reduced opioid tolerance*: after a period of treatment with naltrexone, or having recently completed a period in prison or an opioid withdrawal program, the patient can be expected to have reduced tolerance to opioids and is at significant risk of overdose if they use opioids (see Section 3.1).
- *Psychiatric illness* (see also Section 4.12):
 - *People whose mental state impairs their capacity to provide informed consent* (e.g. those with an acute psychotic illness, cognitive impairment or a severe adjustment disorder) should receive adequate treatment for the psychiatric condition so that informed consent can be obtained before initiation of MMT. (Note: at entry to methadone most patients exhibit some degree of depression which usually resolves quickly with MMT. Most of these patients do not require antidepressant treatment before commencement of methadone).
 - *High risk of self-harm* Individuals at moderate or high risk of suicide should not be commenced on methadone in an unsupervised environment and specialist consultation should be sought.
- *Chronic pain* – refer for specialist assessment first
- *Concomitant medical problems*

A significant proportion of methadone related deaths involve individuals who were in poor health and had other diseases (particularly hepatitis, HIV and other infections) which may have contributed to their death. This emphasises the importance of giving consideration to concomitant medical problems.

- *Head injury and increased intracranial pressure*: This is generally seen only in the hospital emergency setting.
- *Phaeochromocytoma*: aggravated hypertension has been reported in association with heroin use.
- *Asthma and other respiratory conditions*: In such patients even usual therapeutic doses of opioids may decrease the respiratory drive associated with increased airways resistance.
- *Special risk patients*: Methadone should be used with caution in the presence of hypothyroidism, adrenocortical insufficiency, hypopituitarism, prostatic hypertrophy, urethral stricture, shock and diabetes mellitus.
- *Poor compliance*: patients who exhibit poor compliance with treatment for major intercurrent illness such as asthma or diabetes pose a particular challenge in MMT.

EXERCISE CAUTION

with patients in any of the following categories

high risk polydrug use

co-occurring alcohol dependence

history of reduction in opioid tolerance

psychiatric illness

concomitant medical problems

2.2 Assessment for treatment with methadone

Initial assessment procedures are similar for all opioid users seeking treatment. A comprehensive assessment of the patient's drug use, medical, psychological, and social conditions, previous treatment history and current treatment goals should be conducted and documented. Specific attention should be given to assessment of dependence and tolerance, and the indications, contraindications, and precautions for methadone treatment (see section 2.1). Obtain corroborative evidence of identity and aspects of the history relating to drug use, medical and psychiatric conditions to clarify any inconsistencies between physical examination findings and reported history. Accuracy of clinical assessment may be improved by using corroborating evidence such as urine tests and examination of veins for evidence of injecting drug use.

Corroborative evidence of dependence should also be obtained. The best evidence is observed signs of opioid withdrawal (spontaneous or precipitated by naloxone challenge), or a verifiable history of previous treatment for opioid dependence (detoxification or maintenance).

The initial assessment will result in an initial management plan which can be implemented directly. However, extra information will also need to be gathered at subsequent reviews so that more comprehensive treatment plans can be developed.

Key features of the assessment

- **Opioid use**
 - Opioids used, quantity, frequency, route of administration, duration of current episode of use, time of last use and use in the last 3 days
 - Severity of dependence (see Section 2.1, Appendix 3)
 - Age of commencement, age of regular use, age of dependence, timing and duration of periods of abstinence
 - Episodes of overdose
- **Other drug use** including alcohol, illegal and prescribed drugs, current medications.
- **Health status**
 - Diseases from drug use (blood borne viruses, other)
 - Intercurrent health conditions (psychiatric, general)
- **Psychosocial status**
 - Legal
 - Social – employment, education/vocational skills, housing, financial, family.
 - Psychological – mood, affect, cognition.
- **Past treatment**
 - Where
 - When
 - Periods of abstinence
 - Degrees of success/acceptance of treatment
- **Selection of treatment**
 - Motivation for treatment
 - Trigger for seeking treatment
 - Patient goals for treatment episode
 - Stage of change (see Appendix 6 for further reading)
- **Physical examination**
 - Observation of clinical signs related to drug use (needle track marks, intoxication, withdrawal – (See Appendices 2 & 3)
 - Evidence of medical problems (eg liver disease – jaundice, ascites, encephalopathy).
- **Investigations**
 - Urine drug screening tests may be indicated if there are concerns about the accuracy of the drug history and diagnosis and may also be useful to confirm benzodiazepine and other drug use.
 - Investigations for HIV and hepatitis B and C if indicated.

2.3 Informed consent and patient information.

Obtain informed consent to methadone treatment in writing from the patient before commencing treatment. For patients to make a fully informed decision, they should be provided with written information about:

- The nature of methadone treatment
- Other treatment options
- Program policies and expectations
- Consequences of breaches of program rules
- Recommended duration of treatment
- Side effects and risks associated with taking methadone (see Section 1)
- Risks of other drug use
- The potential impact of methadone on their capacity to drive or operate machinery
- The availability of further information about treatment

Methadone may affect the capacity of patients to drive or operate machinery during the early stages of treatment, after an increase in dose, or when patients are also taking other drugs. Warn patients about this effect before entry into treatment, when the dose of methadone is increased, or when the use of other drugs is suspected.

A number of excellent patient information resources are available which can be provided to patients or a program specific patient information booklet can be prepared. (See Appendix 5 for details of suitable resources).

2.4 Meeting legislative requirements

Methadone is a registered Schedule 8 medication that is approved for the purpose of treating opioid dependence and withdrawal. Each jurisdiction is responsible for a system for authorising medical practitioners to prescribe methadone for the purpose of treating addiction. Prescribers must obtain authority for each patient. Check your jurisdictional policy for details of authorisation procedures (See Appendix 7 for contact details)

- Patient identity must be verified at the time of assessment.
- Patients must not begin methadone treatment until approval has been obtained from the jurisdictional authority.

Once authorisation has been obtained, commencement of methadone treatment should not be delayed. Successful commencement and continuation of treatment is enhanced by prompt program access.

2.5 Coordinated Care

- The relationship between the prescriber and dispenser of methadone requires ongoing communication to ensure consistency in the overall treatment program. This communication can be facilitated by the development of coordinated care plans.
- The prescriber and dispenser and other members of the therapeutic team have a duty of care to the patient that may necessitate sharing of information despite professional obligations to maintain patient confidentiality.
- The dispenser is legally required to assess whether a dose of methadone is appropriate and can withhold treatment if necessary.
- There are jurisdictional requirements regarding child protection and notification of at risk children. Occasionally staff may experience a conflict between their duty of care to the patient and their jurisdictional responsibilities.

3

Guidelines for maintenance treatment (MMT)

3.1 Induction to methadone treatment

Commencing methadone from heroin use

Objectives during induction to methadone are to retain individuals in treatment by reducing the signs and symptoms of withdrawal and to ensure their safety. This can be achieved by careful explanation regarding intoxicating effects and withdrawal during the induction and maintenance phases of methadone treatment, establishment of a therapeutic relationship, safe dosing and repeated observation of patients.

It is particularly important to clearly explain that it takes time to complete induction onto methadone and that patients will experience increasing effects from methadone over the first few days of treatment even if the dose is not increased.

There is a need to achieve a balance between adequate relief of withdrawal symptoms and the avoidance of toxicity and death during the induction phase of MMT. The aim is to minimise the symptoms and signs of withdrawal while simultaneously minimising the risks of sedation and toxicity. While doses of methadone which are too high can result in toxicity and death, inadequate commencement doses may cause patients experiencing withdrawal symptoms to “top up” the prescribed dose of methadone with heroin, benzodiazepines or illicit methadone. This can also have potentially lethal consequences.

For most patients withdrawal symptoms will be alleviated but not entirely eliminated by doses less than 30mg.

Deaths during the induction phase of methadone treatment have been related to:

- Concomitant use of other drugs (particularly sedatives such as alcohol and benzodiazepines);
- Inadequate assessment of tolerance;
- Commencement on doses that are too high for the level of tolerance;
- Lack of understanding of the cumulative effect of methadone;
- Inadequate observation and supervision of dosing;
- Individual variation in metabolism of methadone.

Size of the first dose

The first dose of methadone should be determined for each patient based on the severity of dependence and level of tolerance to opioids.

- The history of quantity, frequency and route of administration of opioids, findings on examination, corroborative history and urine testing together provide an indication of the level of tolerance a patient has to opioids, but do not predict it with certainty.
- A defined period of observation for signs and symptoms of opioid toxicity and withdrawal is a more accurate method of assessing opioid tolerance than history alone. In circumstances where there is doubt about the degree of tolerance, a review of the patient at a time when withdrawal symptoms are being experienced may help to resolve uncertainty about a safe starting dose.
- Prescribers should make every effort to communicate with other practitioners who may have seen the patient previously in order to corroborate significant elements of the patient's history and to assist in decision making about commencing treatment.
- New patients should be dosed with caution. Deaths in the first two weeks have been associated with doses in the range 25-100 mg/day, with most occurring at doses of 40-60 mg/day.
- If at all possible, patients should be observed 3-4 hours after the first dose (ie. at the time of peak effect) for signs of toxicity or withdrawal. (See Appendices 2 and 3)
 - If the patient is experiencing persistent withdrawal symptoms at 4 hours, a supplementary dose of 5mg can be considered.
- When deciding on the commencing dose, also consider:
 - Where dosing is to occur.
 - Are staff and facilities available for observation and assessment of the patient before and after dosing?
 - Who will assess withdrawal/intoxication prior to dosing? (see Section 4.3)
 - Time since last opioid use.
 - Concomitant use of benzodiazepines or alcohol. (See also Sections 4.2, 4.9)
 - The risk of overdose increases most markedly when other central nervous system depressants are also used.
 - If the patient shows signs of intoxication with benzodiazepines or alcohol, the dose should be withheld or reduced.
- Induct morphine, codeine and oxycodone users as if they were heroin users

- **A dose of less than or equal to 20 mg for a 70kg patient can be presumed to be safe, even in opioid-naïve users as this is the lowest dose at which toxicity has been observed.**
- **Caution should be exercised for starting doses of 30mg or more.**
- **Exercise extreme caution if an initial dose of methadone exceeding 40mg is considered necessary. Specialist consultation may be advisable.**

Stabilisation

During the first two weeks of MMT the aim is to stabilise the patient so that they are not oscillating between intoxication and withdrawal. This does not necessarily mean that the patient will reach an optimum maintenance dose in that time and further dose adjustments may be required after the patient has been initially stabilised.

Monitoring during the first two weeks.

- **Patients should be observed daily prior to dosing** and an assessment made of intoxication. If any concern they should be seen by a doctor before the dose is administered.
- Because of the pharmacology of methadone, to ensure safety, **it is desirable that patients are reviewed at least once, and preferably twice by an experienced clinician** (doctor or nurse) in the first week with a view to assessing intoxication from methadone.
- **Dose increases should only be considered subject to assessment by the prescriber.** Assessment should include withdrawal severity (see Appendix 3), intoxication (see Appendix 2), other drug use (see Section 4.9) side effects and patient perception of dose adequacy, and adherence to dosing regime.

Dose titration.

- Stabilisation is about titrating the dose against needs of the individual patient.
 - Do not increase the methadone dose for at least the first 3 days of treatment unless there are clear signs of withdrawal at the time of peak effect (i.e 3-4 hours after dose) as the patient will experience increasing effects from the methadone each day.
 - Consider dose increments of 5-10mg every 3 days subject to assessment.
 - Total weekly increase should not exceed 20mg.
 - The maximum dose at the end of the first week should typically be no more than 40mg.
 - Patients should be warned not to drive or operate machinery during periods of dose adjustments.

Transfer from other pharmacotherapies

Prescribers may need to seek specialist advice when prescribing for patients who are transferring from other pharmacotherapies with which they are unfamiliar.

Buprenorphine

(See also “National guidelines and procedures for the use of buprenorphine in the treatment of heroin dependence”)

- Consideration should be given to transferring a patient from buprenorphine to methadone under the following circumstances:
 - Patient experiencing intolerable side effects to buprenorphine;
 - Inadequate response with buprenorphine treatment;
 - Transferring to a program where buprenorphine is not available.

- Patients should be stabilised on daily doses of buprenorphine and their buprenorphine dose reduced to 16mg or less for several days prior to transfer.
- Methadone can be commenced 24 hours after the last dose of buprenorphine.
- The initial methadone dose should not exceed 40mg.
- Patients transferring from lower doses of buprenorphine (4 mg or less) should be commenced on lower doses of methadone.
- Care should be taken not to increase the dose of methadone too quickly.

Naltrexone

- Transfer will generally be considered because of relapse to opioid use following cessation of naltrexone.
- After a short period, possibly only a few days, on naltrexone the patient loses tolerance to opioids. Consequently, patients transferring from naltrexone should be treated as if they were naïve to opioids and non tolerant to their effects unless the clinical circumstances clearly indicate a return to regular, heavy heroin use.
- Do not administer methadone until at least 72 hours after the last dose of naltrexone.
- Extreme caution should be exercised with commencing doses of methadone which should be no greater than 20mg.

3.2 Maintenance dosing

Dose Levels

Doses should be determined for individual patients but generally a higher dose is required for maintenance than is required for initial stabilisation. Typically effective maintenance doses are greater than 60mg/day.

There is a dose response relationship between maintenance doses of methadone, retention in treatment and continued use of heroin.

- Methadone doses in excess of 60 mg/day are associated with higher retention rates and less heroin use. This has been demonstrated in both randomised controlled trials and cohort studies.
- Cross tolerance to heroin increases as a function of increasing methadone dose and results in blockade of the euphoric effect of concurrent heroin use. A daily methadone dose of 60mg or greater should be sufficient to ensure a substantial level of tolerance to effects of heroin in the majority of individuals.

Maintenance doses for effective MMT are typically 60-100mg/day.

Doses in excess of 100mg/day may be necessary to achieve successful maintenance with patients who have a fast methadone metabolism but there is no evidence from treatment outcome studies to suggest that routine dosing at levels in excess of 100mg/day results in any additional benefit for the majority of patients.

Changing dose level

Patient input to treatment decisions, including determination of dosing levels, promotes a good therapeutic relationship by enhancing patient trust and responsibility. When making decisions about changes in dosage the following should be taken into consideration.

- Concurrent use of illicit opioids and continued injecting use may indicate the need for a higher dose;
- Individual variation in methadone metabolism.
- Use of other medications (See Appendix 1).
- Pregnancy (See Section 4.8).
- Polydrug use (See Section 4.9).

Compliance

- Daily administration of methadone is recommended to ensure that plasma methadone levels are maintained and to avoid withdrawal symptoms.
- If plasma levels are not maintained, cross tolerance to heroin will be lessened, reducing the capacity of MMT to moderate the euphoric effect of heroin. Reduced compliance is therefore associated with an increased risk of relapse to heroin use.

Monitoring Drug Use

Reasons

- Assessment of drug use enables monitoring of progress in treatment and can give useful information for making decisions on clinical management. Monitoring can also be used to support contingency management approaches.
- Concurrent use of other drugs with methadone by patients may threaten their safety (see also Appendix 1)
- Monitoring drug use can also provide a basis for program evaluation.
- There is little evidence to support the use of drug monitoring as a deterrent against unsanctioned drug use.

Options

- Self report, urine testing and clinical observation are currently available monitoring approaches. Hair analysis, saliva and sweat analysis may be an option in the future.

Self report

- Self report can be a reliable guide to drug use in settings where no negative consequences result from disclosure. However, in the clinical situation there are always contingencies which patients may perceive as punitive. Consequently, caution should be exercised when making clinical decisions based solely on self-reported drug use. The best information is usually obtained from a combination of self-report and urinalysis.

Urine testing

- Urinalysis is an objective measure of drug use, however:
 - urinalysis may not be a reliable indication of drug use if collection is not observed. Observed urines are demeaning to both patients and staff. Reliability of unobserved urines may be increased by checking the temperature of the urine sample.
 - Urinalysis will only detect recent drug use. The actual time frame varies depending on the drug being measured and will also depend on the threshold level set by the testing laboratory. The table at Appendix 4 can be used as a guide.
 - False positives and false negatives do occur.
 - Research literature suggests that urine testing does not reliably reduce drug use.
 - Methadone programs should not be punitive.
- Urinalysis is most useful in the following circumstances:
 - Patients in the early stages of treatment.
 - Where clarity of drug use is required for diagnostic purposes
- Frequency of urinalysis
 - Medicare allows for a maximum of 21 urinalysis tests per patient per year.
 - It is expected that the average number of tests will be significantly lower than this maximum and will decrease the longer a patient has been in treatment.

3.3 Adjunct Treatment

There is compelling evidence that treatment factors other than an adequate dose of methadone contribute to improved outcomes. In particular, the quality of the therapeutic relationship between treatment providers and client is important. Where clients are treated respectfully, with regard to their dignity, autonomy and privacy, the outcomes of treatment are likely to be improved. In addition, some formal processes are of value.

Social Services

- Multiple social problems are common among opioid dependent people.
- A history of physical, sexual and emotional abuse is prevalent among opioid dependent people, particularly for female clients and may have a negative impact on treatment outcome.
- Providing reinforcement and referral to vocational, financial, housing and family assistance contributes positively to the progress of treatment.

Counselling

- Counselling should not be mandatory within methadone programs, however, there is evidence that access to counselling as an adjunct to MMT improves the effectiveness of MMT and is associated with greater retention in treatment and reduced use of illicit opioids.
- Therapeutic tools such as motivational interviewing, relapse prevention and social skills training have been associated with improved outcomes.
- All ancillary services should be provided on the basis that the patient freely consents to be involved.

NOTE: For further information on counselling strategies see Jarvis T, Tebbutt J & Mattick R (1995) Treatment Approaches for Alcohol and Drug Dependence. Sussex, England: John Wiley and Sons.

3.4 Takeaway doses

The takeaway policy for methadone is determined for each jurisdiction in line with the National Policy on Methadone Treatment.

The benefits of takeaway doses include:

- Enhancement of integration into the community, through reduction of time and associated travel costs for the patient;
- Promotion of patient responsibility for treatment;
- Reduced inconvenience of regular attendance for the patient thereby enhancing retention. Studies have indicated that programs which have takeaway policies have better retention rates than programs which restrict takeaways;
- Reduced inconvenience and cost of daily dispensing for the pharmacist or clinic.

Concerns regarding takeaway doses of opioid medications include:

- Risk of deliberate or accidental overdose by the patient or others, particularly through the use of the takeaway dose by children and other non tolerant individuals and/or use in combination with other sedative drugs.

- Injection of takeaway medication, resulting in overdose, damage to veins or other health consequences. All patients in receipt of takeaway doses should have an inspection of their veins at regular clinical review. People with evidence of continued injection should have takeaway doses suspended until they show evidence that injecting has ceased.
- Diversion of takeaway doses resulting in poor outcomes for the patient (poor compliance with the treatment regime) and abuse by other individuals.

Uncontrolled access to takeaway doses is associated with greater diversion and adverse consequences including bringing the program into disrepute. The safety of takeaway doses of methadone is increased by:

- Careful selection of patients suitable for takeaway methadone (requiring close monitoring by the prescriber and dispenser.)
- Education of the patient.

Takeaway doses for interstate or overseas travel must be organised through the jurisdictional authority responsible for controlling methadone and the Commonwealth Department of Health and Ageing.

- Prescribers should consult the National Policy on Methadone Treatment and jurisdictional policy documents for details.

The International Methadone Users Network provides information and advice on import regulations for methadone and on the possibilities of maintaining treatment abroad in over 150 countries as well as a range of other topics related to international travel by methadone patients. The information is aimed at both patients and doctors and is available on the world wide web at <http://www.indro-online.de/nia.htm>
To contact the network email INDROeV@t-online.de

3.5 Missed doses and reintroduction

When patients miss methadone doses they may use other drugs including other central nervous system depressants such as alcohol or benzodiazepines. When methadone doses are missed for 3 or more days, tolerance to opioids may be reduced placing patients at increased risk of overdose when methadone is reintroduced.

Reintroduction

- Patients should be assessed for signs of intoxication and withdrawal before dosing is recommenced after missed doses (see also Section 4.3, Appendices 2 and 3).
- If the dose has not been collected for 3 or more consecutive days the dose should be withheld or reduced until the patient has been assessed by the prescriber.
- In general the following schedule can be presumed to be safe and effective.
If the patient has missed
 - One day:** No change in dose.
 - Two days:** If no evidence of intoxication administer normal dose.
 - Three days:** Administer half dose in discussion with the prescriber.
 - Four days:** Patient must see prescriber. Recommence at 40mg or half dose whichever is the lower.
 - Five days or more:** regard as a new induction.

3.6 Cessation of methadone maintenance treatment

Voluntary withdrawal

Factors that motivate patients to consider detoxification include lifestyle issues, tangible and intangible personal rewards, and perceptions and attitudes directed towards methadone.

Length of time in treatment

Studies have found the length of time in treatment is predictive of an improved treatment outcome. This relationship was evident for durations between 3 months and 2 years and was linear.

- A significant reduction in heroin use after treatment was only observed for those who spent more than 1 year in MMT.
- Significant reductions in criminality were only observed while patients remained in treatment.
- The findings of multiple observational studies indicate that it is a combination of treatment duration and behaviour change (ceasing heroin use, stable relationship, employment) during treatment which predicts positive post treatment outcomes.

It is recommended that patients be encouraged to remain in treatment for at least 12 months to achieve enduring lifestyle changes.

Management of withdrawal from MMT

- **Dose reductions should be made in consultation with the patient.** Continued reduction in the face of distress is usually counterproductive. It may be appropriate to maintain a patient at a reduced dose for a prolonged period until the patient feels comfortable recommencing the reduction regime.
- During this phase **the aim of any intervention is to ensure that the withdrawal process is completed with safety and comfort.**
- When a regime of reducing doses of methadone is used to manage withdrawal from heroin or methadone, typically **signs and symptoms of withdrawal will begin to rise as the methadone dose falls below 20mg/day**, with peak symptoms occurring two to three days after cessation of methadone. Subsidence of the symptoms is slow with studies reporting withdrawal scores not falling below baseline until 10 to 20 days after the cessation of methadone, depending on the duration of the methadone taper.
- **Clonidine offers no benefit as an adjunct to a regime of reducing doses of methadone**, primarily because of a high incidence of hypotensive side effects when clonidine is used in this way. Clonidine can be given after cessation of methadone.

Voluntary Withdrawal Schedule

- Recommend reducing dose by 10mg/week to a level of 40mg/day, then 5mg/week. Rates of reduction should be negotiated with patients, and dose changes should occur no more frequently than once a week.
- Abrupt cessation of methadone could be considered from 40mg/day in conjunction with clonidine and symptomatic medications to manage withdrawal signs and symptoms.

Other approaches to the management of opioid withdrawal that have been the subject of research in recent years include the use of buprenorphine to ameliorate the signs of symptoms of withdrawal, and the use of opioid antagonists to induce withdrawal. The efficacy of these approaches to manage withdrawal from MMT remains uncertain.

Risk of relapse

- Longer duration and greater intensity of pre treatment opioid use is associated with an increased probability of relapse to opioid use after leaving treatment.
- The likelihood of a patient maintaining abstinence after leaving treatment is increased in people who have established drug-free social supports, are in stable family situations, employed, and with good psychological strengths.

Supportive care / after care

- There is evidence from randomised controlled trials that structured after care (compared with assistance on request) reduced the risk of relapse, self reported crime and helped unemployed patients find work.
- Supportive care should be offered for at least 6 months following cessation of methadone.
- For recently discharged patients an automatic fast track for readmission to MMT should be available if needed.

Involuntary withdrawal

It is sometimes necessary to discharge a patient from treatment for the safety or well being of the patient, 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 methadone program.
- Drug dealing on or near program premises
- Repeated diversion of methadone.

Interruption to treatment may also occur as the result of a change in the patient's situation such that they are no longer able to access methadone.

Management of involuntary discharge from MMT

- In some instances problems may be resolved by transferring the patient to another program rather than discharging them from methadone.

- Abrupt cessation of methadone or rapid dose reduction may occasionally be warranted in cases of violence, assault or threatened assault against staff or patients.
- Where treatment is interrupted for less severe breaches of clinic rules or for other reasons, patients should, where possible, be withdrawn to 40mg/day according to the above voluntary withdrawal schedule.
- Patients being discharged must be warned about the risks of illicit drug use and informed of other treatment options.

Transfer to Naltrexone

- Administration of naltrexone to a patient who is physically dependent on opioids will precipitate a severe withdrawal syndrome.
- MMT patients being transferred to naltrexone should undergo methadone detoxification (see management of detoxification) followed by a 14 day drug free period to allow stored methadone to be eliminated from the body.
- Seek specialist advice if it is not possible to follow this regime.

See the National Naltrexone Guidelines for further information or seek specialist advice

Transfer to Buprenorphine

Buprenorphine has a higher affinity for mu receptors than methadone, but has a weaker action at these receptors. Consequently when methadone patients take a dose of buprenorphine, methadone is displaced from the mu receptors.

Patients on low doses of methadone (<30mg) generally tolerate this transfer with minimal discomfort.

Patients on higher doses of methadone may find that replacement of methadone with buprenorphine precipitates transient opioid withdrawal.

Very low doses of buprenorphine (eg 2 mg) are generally not adequate to substitute for methadone while high doses (8 mg or more) are more likely to precipitate withdrawal.

Buprenorphine should not be dispensed within 24 hours of last methadone dose. The first dose of buprenorphine should be delayed as long as possible and ideally until there are signs of withdrawal (lacrimation, rhinorrhoea, and piloerection). Increasing the interval between the last dose of methadone and the first dose of buprenorphine reduces the incidence and severity of precipitated withdrawal. It is important the patient is aware of the reason for the delay in dosing and does not supplement the buprenorphine dose with other opioids (especially heroin) as this will further exacerbate withdrawal.

See the National Buprenorphine Guidelines for further information or seek specialist advice.

4 Common management issues

4.1 Side effects

Sleep disturbance

A number of resources are available for patients experiencing sleep problems which include guidance regarding sleep hygiene and simple relaxation techniques. (See Appendix 5).

Patients on methadone appear to be at increased risk of sleep apnoea and the use of hypnotic drugs may therefore paradoxically worsen sleep, by exacerbating sleep apnoea.

Teeth problems

All opioids including methadone reduce the production of saliva while illicit use is associated with poor nutrition and poor dental hygiene. Consequently dental problems are common at entry to MMT.

It is common for patients to blame methadone for their dental problems.

Salivary flow can be increased by chewing. Encourage patients to improve dental hygiene.

Reduced libido and sexual dysfunction

Reduced dose may help but needs to be balanced against the risk of return to heroin use.

Lethargy

Elucidate the cause. The methadone dose may need to be reduced.

Excessive sweating

Try reducing the dose although this may not alleviate the symptoms. Sweating can also be a prominent symptom in withdrawal and so careful history taking and observation of the patient prior to dosing may be necessary to assist in making the distinction.

Constipation

People rarely develop tolerance to the constipating effects of opioids and so patients may experience chronic constipation.

Encourage patients to consume plenty of fruits and vegetables and non alcoholic fluids each day.

4.2 Overdose

In Australia, more than 90% of deaths during stabilisation on methadone involved other drugs, in particular, alcohol, benzodiazepines and antidepressants. Patients should be warned of the risks associated with using other drugs with methadone. (See also Sections 4.3 and 4.9)

Death following methadone induction often occurs at home during sleep, many hours after peak blood methadone concentrations have occurred. Typically overdose occurs around the third or fourth day of methadone induction.

- Given that many deaths occur during sleep, administration of methadone in the morning will ensure peak methadone concentrations occur when patients are normally awake and other people may be around if overdose should occur.
- Naloxone, which promptly reverses opioid induced coma, should be given as a prolonged infusion when treating methadone overdose. A single dose of naloxone will wear off within one hour leaving patients at risk of relapse into coma due to the long lasting effects of methadone.
- Patients who are thought to have taken a methadone overdose require prolonged observation.
- Family members should be warned that deep snoring during induction to treatment could be a sign of dangerous respiratory depression and should be reported to the prescriber. Heavy snoring during maintenance treatment may be associated with sleep apnoea and should also be reported.

Signs and Symptoms of Methadone Overdose

- Pinpoint pupils
- Nausea
- Dizziness
- Feeling intoxicated
- Sedation/ nodding off
- Unsteady gait, slurred speech
- Snoring
- Hypotension
- Slow pulse (bradycardia)
- Shallow breathing (hypoventilation)
- Frothing at the mouth (Pulmonary Oedema)
- Coma

NOTE: Symptoms may last for 24 hours or more. Death generally occurs from respiratory depression

4.3 Intoxicated presentations

Patient safety is the key consideration in responding to those who present for methadone administration while intoxicated due to opioids, alcohol or other drugs.

- Patients should always be assessed by the person dispensing the dose (nurse or pharmacist) before the dose is given
- The assessment should ensure that the patient is not showing evidence of intoxication due to opioids, alcohol or other drugs. (See Appendix 2 Assessment of Intoxication).
- Patients who appear intoxicated with CNS depressant drugs should not be given their usual methadone dose or a takeaway dose at that time. The patient can be asked to re-present later when they are no longer intoxicated.
- If intoxication is evident but appears mild the patient may be given a reduced dose but only after being reviewed by the prescriber.

4.4 Incorrect dose administered

A patient who receives a methadone dose in excess of that prescribed is at risk of overdose.

To prevent accidental methadone overdose:

- Establish procedures for easy and accurate identification of patients to minimise the risk of inappropriate dosing.
- Ensure patients are informed of the risks and signs and symptoms of overdose.

In the case of an accidental overdose, the critical issues which determine how clinicians should respond are the patient's level of tolerance and the amount of methadone given in error.

- Patients in the first 2 weeks who receive an overdose of any magnitude require observation for 4 hours. If signs of intoxication continue, more prolonged observation is required. This may require sending the patient to an Emergency Department.
- Patients who have been on a dose >40mg/day consistently for two months will generally tolerate a dose double their usual dose, without significant symptoms. For an overdose with greater than double the usual daily dose the patient will require observation for at least 4 hours. If signs of intoxication are observed, more prolonged observation must be maintained.
- If patients are receiving regular take-away doses, or if they do not attend daily, it cannot safely be assumed that they have been taking their daily dose and have a known level of tolerance. Therefore, such patients require observation in the event of overdose of >50% of their usual dose.
- Patients in whom the level of tolerance is uncertain (dose <40mg/day, or in treatment for <2 months) require observation for at least 4 hours if they are given a dose >50% higher than their usual dose.

In all cases of dosing error the following procedures should be followed:

- Overdose up to 50% of the normal dose:
 - Advise the patient of the mistake and carefully explain the possible consequences.
 - Inform the patient about signs and symptoms of overdose and advise him/her to go to a hospital Emergency Department if any symptoms develop.
 - The dispenser must advise the prescribing doctor of the dosing error and record the event.
- Overdose greater than 50% of the normal dose:
 - Advise the patient of the mistake and carefully explain the possible seriousness of the consequences.
 - The dispenser must contact the prescribing doctor immediately. If the prescriber is unable to be contacted consult a drug and alcohol medical specialist.
 - If it is decided by the prescriber or drug and alcohol specialist that the patient requires hospitalisation, the reasons should be explained to the patient and they should be accompanied to the hospital to ensure admitting staff receive clear information on the circumstances.
 - If the patient has left before the mistake is realised, every attempt must be made to contact the patient.
- Caution regarding inducing vomiting:
 - Inducing vomiting may be dangerous and is contraindicated if the patient has any signs of CNS depression.
 - Emesis after the first ten minutes is an unsatisfactory means of dealing with methadone overdose as it is impossible to determine if all of the dose has been eliminated.
 - In circumstances where medical help is not readily available or the patient refuses medical care, induction of vomiting (by mechanical stimulation of the pharynx) within 5-10 minutes of ingesting the dose may be appropriate as a first aid measure only. Ipecac syrup is contraindicated as its action may be delayed.

4.5 Continued high risk drug use (see also 4.9 Polydrug use)

Continued high risk drug use is evidenced by:

- Frequent presentations when intoxicated;
- Overdoses;
- Chaotic drug using behaviour;
- Deteriorating medical or mental states due to drug use.

Continued drug use can affect patient stability and treatment progress and place the patient at risk of:

- Relationship, social and employment problems;
- Contracting infectious diseases;
- Involvement in crime.

Attempts to stabilise such patients should include:

- Review of:
 - Psychosocial interventions and supports;
 - Precipitants to continued drug use;
 - The risks of combining methadone with other drug use against the benefits of continued treatment:
 - If the patient's safety is not at risk from ongoing drug use it will generally be in the patient's interest to persist with treatment.
 - If the risks of combining methadone with other drug use outweigh the benefits to the patient of MMT arrange the patient's gradual withdrawal from methadone.
 - Medication regimes.
 - Increases in methadone dose may be helpful if this is considered safe by the prescriber.

4.6 Analgesia and anaesthesia

Analgesic requirements for patients on methadone

Consider non-opioid analgesics (NSAIDs or paracetamol). Where parenteral analgesics are required, consider ketorolac (Toradol®), or tramadol (Tramal®).

Management of acute pain in hospital for patients on MMT

- Patients on methadone who are experiencing acute pain in hospital often receive inadequate doses of opiates for serious pain.
- Analgesia should be provided to patients in MMT in the same way as for other patients. This includes the use of injectable and patient controlled analgesia.
- Because of their tolerance of opioids, patients taking methadone frequently require larger doses of opioid analgesia for adequate pain relief.
- Partial agonists such as buprenorphine should be avoided as they may precipitate withdrawal symptoms.

There is evidence of cross tolerance between methadone and anaesthetic agents and so patients on methadone may require higher doses of anaesthetic agents in the event of dental or surgical procedures.

Management of patients with chronic pain

Patients needing methadone for ongoing management of chronic pain need a comprehensive management plan. It is recommended that specialist advice be sought regarding such patients.

4.7 Diversion of methadone

Diversion of methadone to illicit use can result in opioid overdose and undermines the therapeutic rationale and effectiveness of MMT. Injection of methadone carries significant additional risks including sorbitol toxicity, bacterial infection and transmission of blood borne viruses.

- Research into methadone related deaths has consistently shown that between one third and two thirds of all methadone related deaths occurred in persons not prescribed methadone treatment.
- The major source of diverted methadone is take away doses prescribed for patients in MMT (see also Section 3.4).

The risk of diversion of prescribed methadone can be reduced by:

- Ensuring that, in general, methadone is consumed under supervision.
- Careful selection and monitoring of patients eligible to receive takeaway doses taking into account the patient's stability, reliability and progress in treatment.
- Limiting the number of consecutive takeaway doses.

4.8 Pregnancy and lactation

Pregnant women who are dependent on opioids are at high risk of experiencing complications, generally as a result of:

- inadequate antenatal care;
- lifestyle factors including smoking, poor nutrition, high levels of stress and deprivation;
- repeated cycles of intoxication and withdrawal which can harm the foetus or precipitate premature labour or miscarriage.

In most Australian jurisdictions, pregnant opioid dependent women have high priority for access to methadone maintenance programs in order to minimise the risk of complications.

- Methadone maintenance treatment:
 - enables stabilisation of drug use and lifestyle,
 - reduces or eliminates illicit opioid drug use and can help stabilise the in utero environment,
 - facilitates access to comprehensive antenatal and postnatal care,
 - does not increase the risk of congenital abnormalities in the foetus.

Methadone is classed as a Pregnancy Category C drug because of the potential risk of respiratory depression in the neonate and the likelihood of neonatal withdrawal syndrome.

- Respiratory depression is not a significant problem in babies born to opioid dependent mothers receiving methadone maintenance treatment.
- Babies born to mothers on methadone maintenance treatment may experience a withdrawal syndrome. Available evidence gives little support to the existence of a relationship between the severity of the neonatal withdrawal syndrome and maternal methadone dose at delivery, and its occurrence is unpredictable. The benefits of methadone maintenance treatment for both the mother and the baby outweigh any risks from the neonatal withdrawal syndrome.

Management in pregnancy

Opioid using pregnant women not already in treatment should be given high priority for assessment.

- Naloxone challenge should not be used in pregnant women because this may precipitate miscarriage or premature labour.

Pregnant women should be maintained on an adequate dose of methadone, to achieve stability and prevent relapse or continued illicit opioid drug use.

- Women already in methadone treatment who become pregnant can safely be maintained on their current dose.
- The bioavailability of methadone is decreased in the later stages of pregnancy due to increased plasma volume, an increase in plasma proteins which bind methadone and placental metabolism of methadone.
 - It may be necessary to divide the daily dose and possibly to increase the dose in the third trimester of pregnancy to avoid withdrawal symptoms and minimise additional drug use.

Antenatal and postnatal care should be managed in collaboration with a specialist obstetric service experienced in the management of drug dependency during pregnancy.

Dose reductions or detoxification during pregnancy.

Opioid withdrawal in the first trimester of pregnancy is thought to be associated with an increased risk of miscarriage. Opioid withdrawal in the third trimester of pregnancy may be associated with foetal distress and death. Therefore, it is important that pregnant women are not exposed to withdrawal during the first and third trimesters.

If dose reductions or detoxification are to be undertaken during pregnancy these should be implemented in the second trimester.

- Dose reductions should only occur if the pregnancy is stable.
- The magnitude and rate of reduction needs to be flexible and responsive to the symptoms experienced by the woman concerned.
- Withdrawal symptoms should be avoided as much as possible as they cause considerable distress to the foetus.
- Careful monitoring of the pregnancy and foetus should be undertaken during dose reduction.
- In most instances, dose reductions of 2.5mg-5 mg per week are considered safe.

Breastfeeding

- Breast milk contains only small amounts of methadone and mothers can be encouraged to breastfeed regardless of methadone dose provided that they are not using other drugs.
- Breastfeeding may reduce the severity of the neonatal withdrawal syndrome.
- Women receiving high doses of methadone should be advised to wean their babies slowly to avoid withdrawal in the infant.

Neonatal Withdrawal Syndrome

The occurrence and severity of neonatal withdrawal is very unpredictable. Severity of withdrawal is probably ameliorated if neonates can be kept with their mothers rather than in the neonatal intensive care nursery, which may be stressful and overstimulating. However, this is not always possible.

All babies born to opioid dependent mothers should be observed by experienced staff for the development of withdrawal signs. It is recommended that a validated scale be used to assess the presence and severity of the neonatal withdrawal syndrome (see Appendix 3).

Common signs include

- Irritability and sleep disturbances
- Sneezing
- Fist Sucking
- A shrill cry
- Watery stools
- General hyperactivity
- Ineffectual sucking
- Poor weight gain
- Dislike of bright lights
- Tremors
- Increased respiration rate

Less common signs include

- Yawning
- Vomiting
- Increased mucus production
- Increased response to sound
- Convulsions (rare).

Withdrawal symptoms usually start within 48 hours of delivery but may be delayed for 7-14 days in a small number of cases. Experience in the US suggests that in cases where withdrawal is delayed it may be because methadone was being used in conjunction with illicit benzodiazepines and the infant is withdrawing from the benzodiazepines.

Treatment of neonatal withdrawal syndrome is being considered by an expert group of Australian neonatologists and guidelines on management are being developed.

Supportive treatment involves minimising environmental stimuli and enhancing the baby's comfort and may include:

- Soothing by holding close to the body or swaddling.
- Keeping nostrils and mouth clear of secretions.
- Use of a dummy to relieve increased sucking urge.
- Frequent small feeds.

Treatment with opioids should be considered for infants who exhibit severe withdrawal symptoms.

Indications for treatment:

- Seizure
- Weight loss (poor feeding, diarrhoea and vomiting, dehydration)
- Poor sleep
- Fever

Treatment should be based on the severity of the withdrawal signs.

- Use the Finnegan Screening Instrument (Appendix 3). Treatment should be commenced when the score is 9 or more on two consecutive observations.
- Improvement should be monitored using scores on the screening tool.

Specialist advice should be sought. Treatment with opioids may depress respiration and should be used with extreme caution. Options to be considered include:

- Morphine Oral Preparation - 2 mg/ml morphine dilution (can be further diluted)
- Tincture of opium - 0.4mg/ml dilution
- Paregoric (camphorated tincture of opium)
- Methadone

Treatment with opioids should be used with extreme caution

It is recommended that neonatal care be managed in collaboration with a specialist obstetric or paediatric service which is experienced in the management of babies born to drug dependent mothers.

4.9 Polydrug use

Polydrug use is prevalent among opioid users:

- One in five patients seeking MMT are likely also to be dependent on benzodiazepines
- 5% are likely to be alcohol dependent.
- high percentages of patients are likely to be using benzodiazepines or alcohol at hazardous or harmful levels.

Patients at high risk from polydrug use:

- frequently present intoxicated or with signs of benzodiazepine or alcohol withdrawal;
- regularly use other drugs at levels above normal therapeutic doses.

It is recommended that specialist advice be sought when treating patients at high risk from polydrug use especially where sedatives are involved.

Benzodiazepines

Benzodiazepine users exhibit overall patterns of increased risk and poorer psychological functioning than other patients.

Benzodiazepine injection is associated with vascular damage as well as mortality. Injection of the gel capsule formulation of temazepam has been reported to lead to limb amputations. This formulation should not be prescribed.

Advise patients about the interactions of benzodiazepines and methadone.

Caution should be exercised in prescribing benzodiazepines in MMT. The clinical supervision of patients receiving maintenance benzodiazepines must be of the same high standard as for MMT.

4.10 HIV

Methadone treatment programs should ensure that HIV positive patients have access to specialist HIV medical care so that the patient's overall health may be monitored and appropriate treatment provided as required.

In general, patients who are HIV positive are able to comply with the requirements and conditions of the program, however, the medical, psychological and social implications of HIV infection may necessitate the provision of additional services.

Methadone doses must be monitored due to the potential for interactions between methadone and HIV medications and the effects of related illnesses.

- Higher methadone doses may be necessary if HIV medications increase methadone metabolism (see also Appendix 1).

Flexibility in dosing arrangements may be needed if patients are unable to attend for daily dosing due to illness. This may need to be negotiated with the responsible jurisdictional authority. Options include:

- Collection of daily methadone dose by a responsible adult;
- Home deliveries;
- Takeaway doses.

In the terminal stages of HIV-AIDS, methadone service providers may need to work with hospice services in managing methadone treatment and AIDS conditions.

4.11 Hepatitis B & C

Hepatitis B

Recommend hepatitis B vaccinations to all patients on the methadone program who are found to have no immunity to the hepatitis B virus.

Patients who are acutely infected or who are chronic carriers of hepatitis B should be referred to a gastroenterologist for specialist assessment and follow-up.

Hepatitis C

A high percentage of patients entering methadone programs will be hepatitis C antibody positive.

Patients should be treated in accordance with *Hepatitis C, A Management Guide for General Practitioners* (RACGP 1999).

- Patients who are hepatitis C antibody positive but who have 3 normal serum aminotransferases (ALT and AST) over 6 months should have liver function tests repeated at 6 monthly intervals and a Hepatitis C polymerase chain reaction test at 12 months.
- If the patient has 3 abnormal serum aminotransferases over 6 months referral to a gastroenterologist or liver clinic for specialist assessment and shared care is indicated.

Impaired liver function

Patients with chronic liver disease on long term methadone maintenance generally do not need dose alterations but abrupt changes in liver function might necessitate substantial dose adjustments.

4.12 Psychiatric comorbidity

Many opioid users exhibit symptoms of anxiety and depression at the time of presentation for treatment.

- Most but not all studies link psychiatric distress to poorer treatment outcome.
- Multiple studies have indicated that MMT can reduce levels of psychiatric distress with improvement apparent within weeks of commencement of treatment.
 - After stabilisation on methadone, screen all patients again for psychiatric disorders. A careful and detailed mental state examination will usually suffice.
- Psychotherapy as an adjunct to MMT may benefit patients with medium and high levels of psychiatric problems, but for those with low severity psychiatric problems the addition of psychotherapy offers no advantage.
- Depression has been found to predict poor psycho-social functioning and to increase the risk of relapse to heroin use in the event of life crises.
- Evidence of the effectiveness of antidepressants as adjuncts to MMT is equivocal with only a few studies demonstrating favourable effects on mood.
- One Australian cohort study found antidepressant use was associated with higher levels of polydrug use, poorer health and higher levels of psychiatric distress, and a greater risk of heroin overdose. The excess risk of overdose was specifically associated with tricyclic antidepressants.
 - Unless there is a particular indication for tricyclics, SSRIs are preferred.

Appendix 1

Possible drug interactions with methadone

Drug	Status of Interaction	Effect	Mechanism
Alcohol	Clinically important	Increased sedation, increased respiratory depression. Combination may also have increased hepatotoxic potential.	Additive central nervous system depression.
Barbiturates	Clinically important	Reduced Methadone levels. Increased sedation. Additive CNS depression.	Barbiturates stimulate hepatic enzymes involved in methadone maintenance.
Benzodiazepines	Clinically important	Enhanced sedative effect.	Additive CNS depression
Buprenorphine	Clinically important	Antagonist effect or enhanced sedative and respiratory depression.	Buprenorphine is a partial agonist of opiate receptors.
Carbamazepine	Clinically important	Reduced methadone levels.	Carbamazepine stimulates hepatic enzymes involved in methadone metabolism.
Chloral Hydrate	Clinically important	Enhanced sedative effect.	Additive CNS depression.
Chlormethiazole	Clinically important	Enhanced sedative effect.	Additive CNS depression.
Cimetidine	Two cases have been shown in patients taking methadone as analgesia.	Possible increase in methadone plasma levels.	Cimetidine inhibits hepatic enzymes involved in methadone metabolism.
Ciprofloxacin	Case in a patient taking methadone.	Enhanced sedative effect and respiratory depression requiring naloxone.	Probably by inhibiting hepatic enzymes involved in methadone metabolism.
Cisapride Domperidone Metoclopramide	Theoretical	Theoretically might increase the speed of onset of methadone absorption but not the extent.	Possibly by reversing the delayed gastric emptying associated with opioids.

Drug	Status of Interaction	Effect	Mechanism
Cyclazine and other sedating anti histamines. (cyclazine is not available in Australia)	Clinically important	Anecdotal reports of injection of cyclazine with opioids causing hallucinations. Reports of injections of high doses of dephenhydramine to achieve 'buzz'.	Additive psychoactive effects. Anti muscarinic effects at high doses.
Desipramine	Clinically important	Raised desipramine levels by up to a factor of two.	Unknown mechanism not seen with other tricyclic antidepressants.
Other tricyclic antidepressants	Theoretical	Enhanced sedative effect which is dose dependent.	Additive CNS depression.
Disulfiram	Avoid in combination with methadone formulations containing alcohol (check with manufacturer)	Very unpleasant reaction to alcohol which can be dangerous.	Disulfiram inhibits metabolism of alcohol allowing metabolites to build up.
Erythromycin	In theory should interact but combination has not been studied.	Increase in methadone levels	Decreased methadone metabolism.
Fluconazole	In theory the same as ketoconazole		
Fluoxetine Sertraline	Clinically important	Raised methadone levels but not as significant as for fluvoxamine	Decreased methadone metabolism
Fluvoxamine	Clinically important	Raised plasma methadone levels	Decreased methadone metabolism
Other SSRIs	Theoretical		
Grapefruit juice	Should interact in theory and there have been several anecdotal reports.	Raised methadone levels	Decreased methadone metabolism
Indinavir	Clinically important	Raised methadone levels	Decreased methadone metabolism.
Ketoconazole	Clinically important	Raised methadone levels	Decreased methadone levels
MAOI (including selegiline and moclobemide)	Severe with pethedine though unlikely with methadone and has never been described	CNS excitation, delirium, hyperpyrexia, convulsions, hypotension or respiratory depression.	Unclear, avoid the combination if possible

Drug	Status of Interaction	Effect	Mechanism
Meprobamate	Clinically important	Enhanced sedative and respiratory depressant effect	Additive CNS depression
Naltrexone	Clinically important	Blocks effect of methadone (long acting)	Opioid antagonist – competes
Naloxone	Clinically important	Blocks effects of methadone (short acting) but may be needed if overdose suspected.	Opioid antagonist – competes for opiate receptors.
Nevirapine	Clinically important	Decreased methadone levels	Increased methadone metabolism
Nifedipine	Has been demonstrated <i>in vitro</i> only.	Increased nifedipine levels. No effect on methadone levels.	Methadone increases metabolism of nifedipine.
Omeprazole	To date demonstrated only in animals	Increased methadone levels	Possibly an effect on methadone absorption from the gut.
Pentazocine		Antagonist effect or enhanced sedative and respiratory depression	Pentazocine is a partial agonist of opiate receptors with weak antagonist effect.
Phenobarbitone	See barbiturates above		
Phenytoin	Clinically important	Reduced methadone levels	Phenytoin stimulates hepatic enzymes involved in methadone metabolism
Propranolol	To date demonstrated only in animals. Significance in humans is not known. Exercise caution when co-administering.	Enhanced lethality of toxic doses of opioids	
Rifampicin	Very important. Most patients are likely to be affected.	Reduced methadone levels	Rifampicin stimulates hepatic enzymes involved in methadone metabolism
Rifabutin	Occasionally clinically important	Decreased methadone levels	Increased methadone metabolism.
Ritonavir	Clinically important	Ritonavir may decrease plasma methadone levels	Increased methadone metabolism.
Thioridazine	Clinically important	Enhanced sedative effect which is dose dependent	Enhanced CNS depression.
Other protease inhibitors	Theoretical	May raise or lower methadone plasma levels.	Inhibits methadone metabolism.

Drug	Status of Interaction	Effect	Mechanism
Urine acidifiers e.g. ascorbic acid – vitamin C	Clinically important	Reduced plasma methadone levels	Increased urinary excretion of methadone
Urine alkalisers e.g. sodium bicarbonate	Clinically important	Increased plasma methadone levels	Reduced urinary excretion of methadone
Zidovudine	Clinically important	Raised plasma levels of zidovudine. No effects on methadone levels	Unknown
Zopiclone	Clinically important	Enhanced sedative and respiratory depressant effect	Additive CNS depression
Other opioid agonists	Clinically important	Enhanced sedative effect. Enhanced respiratory depression.	Additive CNS depression
Other CNS depressant drugs (eg neuroleptics, hyoscine)	Clinically important	Enhanced sedative effect which is dose dependent	Additive CNS depression

This table is based on a similar table published in:
 Department of Health, The Scottish Office Department of Health, Welsh Office, Department of Health and Social Services Northern Ireland (1999) *Drug Misuse and Dependence – Guidelines on Clinical Management*. Her Majesty's Stationary Office. Norwich.

Appendix 2

Assessment of intoxication with methadone and other drugs

Acute intoxication states from commonly used drugs

Class of Drug	Intoxication	Overdose
Opioids (eg methadone, heroin, morphine)	Constriction of pupils Itching/scratching Sedation/somnolence Lowered blood pressure Slowed pulse Hypoventilation	Loss of consciousness Respiratory depression Pinpoint pupils Hypotension Bradycardia Pulmonary oedema
Alcohol	Relaxation Disinhibition Impaired coordination Impaired judgement Decreased concentration Slurred speech Ataxia Vomiting	Disorientation/confusion Respiratory depression Loss of consciousness Loss of bladder control
Benzodiazepines (eg diazepam, oxazepam, flunitrazepam)	Disinhibition Sedation Drooling Incoordination Slurred Speech Lowered blood pressure Dizziness	Stupor/coma Ataxia Confusion Respiratory depression
Stimulants (eg amphetamines, cocaine)	Hyperactivity Restlessness Agitation Anxiety/nervousness Great dilation of pupils Elevated blood pressure Increased pulse Raised temperature Sweating Tremor	Panic Acute paranoid psychosis Seizures Cardiac arrhythmias Myocardial ischaemia Hypertensive crisis Cerebrovascular accidents Hyperpyrexia Dehydration
Cannabis	Relaxation Decreased concentration Decreased psychomotor performance Impaired balance Conjunctival injection	Paranoid psychosis Confusion Agitation Anxiety/panic Hallucinations

Signs and symptoms to look for / enquire about

Intoxication	Toxicity
Slurred speech	Drowsiness
Unsteady gait	Shallow breathing
Drowsiness	Poor circulation
Pupil constriction	Slow pulse
Conjunctival injection	Lowered temperature
Alcoholic foetor	Nausea and vomiting
Disinhibition	Headache
Drooling	Confusion
Dizziness	
Itching/scratching	

From NSW Methadone Maintenance Treatment Clinical Practice Guidelines. Used with permission.

Appendix 3

Assessment of withdrawal from commonly used drugs

The Subjective Opiate Withdrawal Scale (SOWS)						
Date	Time	Please score each of the 16 items below according to how you feel NOW (circle one number)				
Symptom	Not at all	A little	Moderately	Quite a bit	Extremely	
1 I feel anxious	0	1	2	3	4	
2 I feel like yawning	0	1	2	3	4	
3 I am perspiring	0	1	2	3	4	
4 My eyes are teary	0	1	2	3	4	
5 My nose is running	0	1	2	3	4	
6 I have goosebumps	0	1	2	3	4	
7 I am shaking	0	1	2	3	4	
8 I have hot flushes	0	1	2	3	4	
9 I have cold flushes	0	1	2	3	4	
10 My bones and muscles ache	0	1	2	3	4	
11 I feel restless	0	1	2	3	4	
12 I feel nauseous	0	1	2	3	4	
13 I feel like vomiting	0	1	2	3	4	
14 My muscles twitch	0	1	2	3	4	
15 I have stomach cramps	0	1	2	3	4	
16 I feel like using now	0	1	2	3	4	

Range 0-64. Handelsman, L., Cochrane, K. J., Aronson, M. J. et al. (1987)

Two New Rating Scales for Opiate Withdrawal, *American Journal of Alcohol Abuse*, 13, 293-308.

Objective Opioid Withdrawal Scale (OOWS)

Sign	Measures		Score
1 Yawning	0 = no yawns	1 = ≥ 1 yawn	
2 Rhinorrhoea	0 = < 3 sniffs	1 = ≥ 3 sniffs	
3 Piloerection (observe arm)	0 = absent	1 = present	
4 Perspiration	0 = absent	1 = present	
5 Lacrimation	0 = absent	1 = present	
6 Tremor (hands)	0 = absent	1 = present	
7 Mydriasis	0 = absent	1 = ≥ 3 mm	
8 Hot and Cold flushes	0 = absent	1 = shivering / huddling for warmth	
9 Restlessness	0 = absent	1 = frequent shifts of position	
10 Vomiting	0 = absent	1 = present	
11 Muscle twitches	0 = absent	1 = present	
12 Abdominal cramps	0 = absent	1 = Holding stomach	
13 Anxiety	0 = absent	1 = mild - severe	
TOTAL SCORE			

Range 0-13

Handelsman, L., Cochrane, K. J., Aronson, M. J. et al. (1987) Two New Rating Scales for Opiate Withdrawal, *American Journal of Alcohol Abuse*, 13, 293-308

ROYAL PRINCE ALFRED HOSPITAL KING GEORGE V HOSPITAL JOHN SPENCE NURSERY			WARD _____ MRN _____ SURNAME _____ OTHER NAMES _____ DOB/SEX _____							
SYSTEM	SIGNS & SYMPTOMS	SCORE	DATE AND TIME IN HOURS							
CENTRAL NERVOUS SYSTEM DISTURBANCES	High-Pitched Cry	2								
	Continuous High-Pitched Cry	3								
	Sleeps <1 hour after feeding	3								
	Sleeps <2 hours after feeding	2								
	Sleeps <3 hours after feeding	1								
	Mild Tremors Disturbed	1								
	Mod-Severe Tremors Disturbed	2								
	Mild Tremors Undisturbed	3								
	Mod-severe Tremors Undisturbed	4								
	Increased Muscle Tone	2								
Excoriation (Specify area)	1									
Myoclonic jerks	3									
Generalised Convulsions	5									
METABOLIC/VASOMOTOR/ RESPIRATORY DISTURBANCES	Fever (37.3o-38.3oC)	1								
	Fever (38.4oC and higher)	2								
	Frequent Yawning (>3-4 times)	1								
	Nasal Stuffiness	1								
	Sneezing (>3-4 times)	1								
	Nasal Flaring	2								
	Respiratory Rate >60/min	1								
Respiratory Rate >60/min with Retractions	2									
GASTROINTESTINAL DISTURBANCES	Excessive Sucking	1								
	Poor Feeding	2								
	Regurgitation	2								
	Projectile Vomiting	3								
	Loose Stools	2								
Watery Stools	3									
TOTAL SCORE										
SCORER'S INITIALS										

MR 520
NEONATAL WITHDRAWAL SCORING CHART (TERM INFANTS)

From NSW Methadone Maintenance Treatment Clinical Practice Guidelines. Used with permission.

Withdrawal States from Commonly Used Drugs

Drug class	Onset	Duration	Symptoms
Opioids	8-12 hours (short acting). Delayed for longer acting opioids.	Peaks 2-4 days Ceases 7-10 days (short acting). Longer for long acting opioids.	Anxiety, muscle tension, muscle and bone ache, muscle cramps, sleep disturbance, sweating, hot and cold flushes, piloerection (goosebumps), yawning, lacrimation, rhinorrhea, abdominal cramps, nausea, vomiting, diarrhoea, palpitations, elevated blood pressure, elevated pulse, dilated pupils.
Alcohol	As blood alcohol falls, depends on rate of fall and hours after last drink.	5-7 days	Anxiety, agitation, sweating, tremor, nausea, vomiting, abdominal cramps, diarrhoea, anorexia, craving, insomnia, elevated blood pressure, elevated pulse, temperature, headache, seizures, confusion, perceptual distortions, disorientation, hallucinations, hyperpyrexia.
Benzodiazepines	1-10 days depending on half-life	3-6 days	Anxiety, insomnia, muscle aching and twitching, perceptual changes, feelings of unreality, depersonalisation, seizures.
Stimulants	8-36 hours	Several days, occasionally 2-3 weeks	Lethargy, depression, irritability, hyperphagia, anhedonia, dysphoria, desire for sleep increased.
Cannabis	Usually days	Weeks	Irritability, anxiety, insomnia, anorexia, sweating, muscle spasms, headaches.

From NSW Methadone Maintenance Treatment Clinical Practice Guidelines. Used with permission.

Appendix 4

Detection time for selected drugs in urine

Drug	Time
Alcohol (dose dependent)	24 hours
Amphetamines	2-3 days
Benzodiazepines (dose dependent)	
Prescription dose	3-5 days
High level misuse	6 weeks
Cannabis (tested to cut off level of 100nanograms)	
One time use	2 days
Three times per week	2 weeks
Daily use	2-4 weeks
Very heavy use	4-6 weeks (may be up to 12 weeks)
Ecstasy (MDMA)	2-3 days
LSD	2-3 days
Heroin and Morphine	3 days
Hydromorphone	1-2 days
Methadone	3-4 days
Propoxyphene	2-3 days
Propoxyphene metabolites	3-6 days
Codeine	1-2 days
Barbiturates	2-3 weeks
Cocaine	1-5 hours
Cocaine metabolites	2-4 days
Phencyclidine	1-8 days

Information supplied by the Institute of Medical and Veterinary Science, Frome Rd Adelaide.

Appendix 5

Resources for Patients

Dunlop A, Thornton D, Lintzeris N, Muhlheisen P, Khoo K, Lew R (1999) *Coming off Methadone. A guide for people considering coming off methadone.* Turning Point Alcohol and Drug Centre Inc. (booklet)

Preston A, Doverty M (1998) *The Methadone Handbook.* Australian Drug Foundation. Melbourne. (booklet)

Available from: Publications Department.
Australian Drug Foundation
PO Box 818
North Melbourne Victoria 3051.

National Drug and Alcohol Research Centre (2000) *What you need to know about Methadone and other treatment options.* NDARC UNSW Sydney (booklet).

Department of Human Services (SA) *Insomnia Management Kit.* Pharmaceutical Services Branch, Public and Environmental Health Service DHS. Adelaide.

The kit includes a general practitioner handbook and a series of self help workbooks for patients.

Drug and Alcohol Services Council (1997) *Helpful hints for healthy sleep.* Drug and Alcohol Services Council, Adelaide.(pamphlet).

Appendix 6

Further reading and references

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- Department of Health, The Scottish Office Department of Health, Welsh Office, Department of Health and Social Services Northern Ireland. *Drug Misuse and Dependence – Guidelines on Clinical Management*. Her Majesty's Stationery Office: 1999.
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- Griffith JD, Rowan-Szal GA, Roark RR, Simpson DD. Contingency management in outpatient methadone treatment: a meta-analysis. *Drug and Alcohol Dependence* 2000;58(1): 55-66.
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- Jarvis T, Tebbutt J & Mattick R (1995) *Treatment Approaches for Alcohol and Drug Dependence*. John Wiley and Sons Sussex, England
- Latowsky M. Improving detoxification outcomes from methadone maintenance treatment: the interrelationship of affective states and protracted withdrawal. *J Psychoactive Drugs* 1996; 28(3): 251-7
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- Petry NM A comprehensive guide to the application of contingency management procedures in clinical settings. *Drug and Alcohol Dependence* 2000; 58 (1):9-25.
- Preston A *The New Zealand Methadone Briefing 1999*. Drugs and Health Development Project. Wellington New Zealand: 1999
- Prochaska JO, DiClemente CC & Norcross JC (1997) In search of how people change: applications to addictive behaviours. In *Addictive Behaviours: Readings on etiology, prevention and treatment*. Edited by G A Marlatt and G R VandenBos. Washington DC: American Psychological Association, pp 671-696.
- Royal Australian College of General Practitioners. Hepatitis C. A management guide for general practitioners. *Australian Family Physician* December 1999 Volume 28 Special Issue.
- Strain EC, Bigelow GE, Liebson IA, Stitzer ML Moderate versus high dose methadone in the treatment of opioid dependence: a randomised controlled trial. *JAMA* 1999; 281(11):1000-5.
- Ward J, Mattick R, & Hall W (Eds) *Methadone maintenance treatment and other opioid replacement therapies*. Harwood Academic Publishers, Amsterdam: 1998

Appendix 7

Consultancy and support mechanisms

Australian Capital Territory

ACT Department of Health, Housing and Community Care

GPO Box 825, Canberra ACT 2601

Alcohol and Drug Program

Acting Director

Management & Administration

Telephone: (02) 6205 0947

Facsimile: (02) 6205 1180

ACT Community Care Alcohol and Drug Program

Senior Medical Officer

Telephone: (02) 6205 4545

Facsimile: (02) 6205 0951

Chief Health Officer

Telephone: (02) 6205 0883

Facsimile: (02) 6205 1884

Chief Pharmacists

Telephone: (02) 6205 9061

Facsimile: (02) 6205 0997

Policy Information

Manager

Alcohol and Drug Priorities

Telephone: (02) 6205 0909

Facsimile: (02) 6205 2037

Applications for approval to dispense methadone

Pharmaceutical Services Section

Department of Health

Telephone: (02) 6207 3974

Facsimile: (02) 6205 0961

Applications for approval to prescribe methadone

Chief Health Officer

Telephone: (02) 6205 0998

Facsimile: (02) 6205 0997

New South Wales

Alcohol and Drug Information Service

Telephone: (02) 9361 2111

Toll Free: 1800 023 599

NSW Drug and Alcohol Specialist Advisory Service

Telephone: (02) 9557 2905

Toll Free: 1800 023 687

NSW Health Drug Programs Bureau

Telephone: (02) 9391 9244

Applications for approval to prescribe and dispense methadone

Director, Chief Pharmacist

Pharmaceutical Services Branch

NSW Health Department

Building 29, Gladesville Hospital Campus

Cnr Victoria and Punt Roads

GLADESVILLE NSW 2111

Telephone: (02) 9879 3214

Facsimile: (02) 9859 5165

Northern Territory

Alcohol and Drug Service (ADIS)

Toll free 1800 131 350

Drug and Alcohol Clinical Advisory Service (DACAS)

Toll free 1800 111 092

Alcohol and Other Drugs Program, Policy and Program Development

Telephone: (08) 8999 2691

Applications for approval to prescribe and dispense methadone

Chief Poisons Inspector
Poisons Control Branch
Department of Health and Community Services
PO Box 40596
CASUARINA NT 0811
Telephone: (08) 8999 2631
Facsimile: (08) 8999 2420

Queensland

Alcohol, Tobacco and Other Drug Services

Medical Advisor
Telephone: (07) 3896 3900

Policy and Specific State Information

Senior Advisor
Alcohol, Tobacco and Other Drug Services
Telephone: (07) 3234 1700

Applications for approval to prescribe and dispense methadone

Chief Executive
Queensland Health
Locked Bag 32
COORPAROO QLD 4151
Telephone: (07) 3896 3900
Facsimile: (07) 3896 3933

Tasmania

Alcohol and Drug Service State Office

State Manager
Telephone: (03) 6233 3860

Coordinator Illicit Drugs
Telephone: (03) 6233 2269

Deputy Chief Pharmacist
Telephone: (03) 6233 3906

Alcohol and Drug Service Southern Regional Office

Manager
Telephone: (03) 6222 7511

Opiate Treatment Medical Officer
Telephone: (03) 6222 7511

Pharmacist
Telephone: (03) 6233 3906

Alcohol and Drug Service

North/North West Regional Office
Manager
Telephone: (03) 6336 5577

Opiate Treatment Medical Officer
Telephone: (03) 6233 5577

Applications for approval to dispense methadone

Opioid Pharmacotherapy Accreditation and Training Committee
C/o Alcohol and Drug Service
Department of Health and Human Services
PO Box 125
HOBART TAS 7001
Telephone: (03) 6230 7709
Facsimile: (03) 6230 3904

Applications for approval to prescribe methadone

Pharmaceutical Services
Department of Health and Human Services
PO Box 125
HOBART TAS 7001
Telephone: (03) 6233 2064
Facsimile: (03) 6233 3904

South Australia

ADIS (Alcohol and Drug Information Service)

Toll Free: 1300 13 13 40

Drug & Alcohol Clinical Advisory Service

Toll Free: 1300 13 13 40

Warinilla Clinic

92 Osmond Terrace
Norwood SA 5067
Telephone: (08) 8130 7500

Northern Methadone Service

22 Langford Drive
Elizabeth SA 5112
Telephone: (08) 8252 4040

Southern Clinic

82 Beach Road
Christies Beach SA 5165
Telephone: (08) 8326 6644

Applications for approval to prescribe and dispense methadone

Drugs of Dependence Unit
Drug Strategy and Programs Branch
Metropolitan Division
Department of Human Services
PO Box 6 RUNDLE MALL SA 5000
Telephone: (08) 8226-7166
Facsimile: (08) 8226-7102

Victoria

Victorian Drug and Alcohol Clinical Advisory Service

Exclusively for health and welfare professionals. Provides advice and information on clinical management of patients with drug and or alcohol problems, including:

- advice on recognition and management of withdrawal syndromes
 - drug use complications
 - drug information
 - prescribing information
 - assistance with cases of acute intoxication
- Metropolitan: (03) 9416 3611
country areas (toll free): 1800 81 2804

Drugs and Poisons Unit, Department of Human Services

The Unit issues permits for approved practitioners to prescribe methadone. It also approves individual medical practitioners and pharmacists to respectively prescribe or dispense methadone.

Address: PO Box 1670N, Melbourne, 3001
Telephone: 1300 364 545
Fax: 1300 360 830

Direct Line

For the general public and health and welfare professionals. Provides counselling, information and referral, including:

- needle syringe exchange and bin location
- drug and alcohol agencies and drug withdrawal beds
- methadone program contact details
- HIV/AIDS information and referral
- drink/drive education and assessment referral

Metropolitan: (03) 9416 1818
Country areas: (toll free): 1800 13 6385

Youth Substance Abuse Service

YSAS provides information, outreach and residential services for young people aged between 12 and 21 experiencing significant problems related to their use of drugs and/or alcohol.

14-18 Brunswick Street, Fitzroy 3065
Telephone: (03) 9415 8881
Fax: (03) 9415 8882
Website: <http://www.ysas.org.au>

YSASLine

YSASline provides 24 hour access to information, telephone counseling, and referral to YSAS outreach teams. The service is open to young people, their families, health and welfare workers, police and ambulance officers. Call YSASline to contact an outreach team. Access to the YSAS residential service is made by contacting your local outreach team via YSASline.

Metro: (03) 9244 2450
Country freecall: 1800 014 446

VIVAIDS: the Victorian Users Group

VIVAIDS provides information on anything and everything to do with drugs. They also provide peer support, peer education, referrals, needle exchange and advocacy to drug users, while promoting harm reduction to users and the community.

765a Nicholson Street
North Carlton 3054
Telephone: (03) 9381 2211

Specialist Methadone Services

Specialist Methadone Services provide a consultative service to methadone prescribers seeking expert opinion about the management of patients with special problems, such as psychiatric, social, medical or treatment problems. Patients may be referred by arrangement, or advice sought by contacting the service.

Turning Point Drug and Alcohol Centre

54 Gertrude St., FITZROY 3065
Administration
Telephone: (03) 9254 8061
Fax: (03) 9416 342
Clinical Services
Telephone: (03) 9254 8050
Fax: (03) 9486 9766

South Eastern Methadone Consultancy Clinic

61-69 Brighton Rd., ELWOOD 3184
Telephone: (03) 9525 7399
Fax: (03) 9525 7369

Western Hospital Drug and Alcohol Service

Gordon St., FOOTSCRAY 3011
Telephone: (03) 9317 2217
Fax: (03) 9319 6027

Austin and Repatriation Medical Centre Specialist Methadone Service

Studley Rd., HEIDELBERG 3084
Administration
Telephone: (03) 9496 5000
Pharmacy
Telephone: (03) 9496 4999
Fax: (03) 9459 4546

Eastern Region Specialist Methadone Service

Whithorse Community Health Service
65 Carrington Street, BOX HILL, 3128
Telephone: (03) 9890 2220

Royal Women's Hospital Chemical Dependency Unit

For women who are pregnant and use drugs. The unit provides a direct service for women who live within a 25 km radius, and secondary consultation for other women. Midwives and social workers are available for consultation.

264 Cardigan Street
Carlton 3053
Telephone: (03) 9344 2363

Health Insurance Commission.

The HIC provides information about medical consultations and pharmaceutical benefits obtained through its Doctor Shopper Hotline. It is also able to provide this information if the patient signs a privacy release form authorising the HIC to provide this information. Forms and explanatory letters are available from the HIC.

Health Insurance Commission
134 Reed Street
Tuggeranong ACT 2900

**Doctor shopper hotline (free call):
Telephone 1800 631 181**

Hepatitis C information

Hepatitis C Support Line

Hepatitis C Council

The Hepatitis C Council has produced a booklet "**Hepatitis C Contact**" which provides information, and answers frequently asked questions.

Carlow House, Level 9
289 Flinders Lane
Melbourne 3000
Telephone: (03) 9639 3200
Country Calls: 1800 703 003

Hepatitis C Helpline

Telephone: (03) 9349 1111
Country Calls: 1800 800 241
TTY: 1800 032 665
Vietnamese Line: 1800 456 007

Department of Human Services.

DHS pamphlet "**Hepatitis: the Facts**" available from the Department of Human Services, or on the internet at: <http://www.dhs.vic.gov.au/phd/9904043/index.htm>

The Department of Human Services has produced a booklet "**Management, Control and Prevention of Hepatitis C: Guidelines for Medical Practitioners**". It is available from the Department.

Health care providers can obtain information and assistance with counselling from the Hepatitis C Educator (03 9288 4127). Advice on notification of hepatitis C can be obtained from the Infectious Diseases Unit.

AIDS information

AIDSLINE

Telephone: (03) 9347 6099
Country Calls: 1800 133 392
TTY: 1800 032 665

Melbourne Sexual Health Centre

580 Swanston Street, Carlton 3053
Telephone: (03) 9347 0244
Country Calls: 1800 032 017

Needle and Syringe Exchange Programs (NSEPs).

Contact details of Victorian NSEPs is available: On the internet at <http://hna.ffh.vic.gov.au/phb/9808109/index.htm> or by calling Direct Line (see above).

Applications for approval to prescribe and dispense methadone

Drugs and Poisons Unit
Department of Human Services
GPO Box 1670N, MELBOURNE VIC 3001
Telephone: 1300 364 545
Facsimile: 1300 360 830

Western Australia

Alcohol and Drug Information Service

Telephone: (08) 9442 5000
Country Calls: 1800 198 024

Clinical Advisory Service

Next Step
32 Moore Street
EAST PERTH WA 6004
Phone: (08) 9442 5042
Country Calls: 1800 688 847

Pharmaceutical Services (Doctors and Pharmacists)

Health Department of Western Australia
Telephone: (08) 9388 4985

Applications for approval to prescribe and dispense methadone

Chief Pharmacist
Pharmaceutical Services Branch
Department of Health
PO Box 8172
Perth Business Centre WA 6849
Telephone: (08) 9388 4980
Facsimile: (08) 9388 4988.