Guidelines for South Australian Pharmacists Dispensing Medication Assisted Treatment for Opioid Dependence (MATOD)

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Drug and Alcohol Clinical Advisory Service (DACAS): Phone (08) 8363 8633

Available 24 hours a day 7 days a week, for clinicians seeking advice on management of their patients with alcohol and drug related problems. If you have any concerns and are unable to contact DASSA clinics or the community prescriber, then DACAS can provide advice.

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This document is the result of input from a team of people. The contributions of the following to this current revision are acknowledged:

Associate Professor Linda Gowing, Principal Research Officer, Evidence-Based Practice, Drug and Alcohol Services South Australia

Ms Carolyn Hills, Pharmacist, Acting Community Pharmacy Program Manager, Drug and Alcohol Services South Australia

Dr Chris Holmwood, Addiction Medicine Specialist, Director Clinical Consultation Liaison and Standards, Drug and Alcohol Services South Australia

Mr Martin Hurley, Senior Pharmacist, Drug and Alcohol Services South Australia

Dr Phuong-Phi Le, Community Pharmacy Program Manager, Drug and Alcohol Services South Australia

Ms Susan O'Neill, Coordinator – Opioid Dependence Substitution Program, Drugs of Dependence Unit, Food and Controlled Drugs Branch, SA Department for Health and Ageing

Ms Katherine Reid, Senior Pharmacist, Drugs of Dependence Unit, Food and Controlled Drugs Branch, SA Department for Health and Ageing

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Currently under review

Table of contents

Table of contents ii
Introduction 1
Chapter 1. Unsanctioned opioid use and dependence 2
1.1. Unsanctioned opioid use 2
1.2. Harmful effects of unsanctioned opioid use 3
1.2.1. Overdose 3
1.2.2. Problems related to injecting 3
Trauma and/or infection of injection sites 3
Systemic bacterial or fungal infections 3
Transmission of blood-borne viruses 3
1.2.3. Social and economic harms 3
1.2.4. Harm minimisation 4
1.3. Nature of dependence 5
1.3.1. Why do people use drugs? 5
1.3.2. What is the effect on the brain? 5
1.3.3. Genetic factors in drug dependence 6
1.3.4. Substance use and mental health disorders 6
1.4. Defining opioid dependence 7
1.4.1. ICD-10 7
1.4.2. Legal Basis of Drug Dependence in South Australia 7
Chapter 2. Interventions for opioid use and dependence 8
2.1. Goals of treatment 8
2.2. Types of treatment 9
2.2.1. Screening and brief intervention 9
2.2.2. Detoxification 10
2.2.3 Substitution treatment (agonist maintenance) 10
2.2.4 Relapse prevention 11
2.2.5 Living skills development 12
2.3. Psychological factors in treatment 12
2.3.1. Pre-contemplation stage 13
2.3.2. Contemplation stage 13
2.3.3. Preparation stage 13
2.3.4. Action stage 13
2.3.5. Maintenance of change 14
2.3.6. Relapse 14
2.4. Opioid pharmacology 14

Currently under review

2.4.1. Tolerance and withdrawal 15
2.4.2. Opioid withdrawal syndrome 16
2.4.3. Side effects of opioid drugs 16
Nausea and vomiting 17
Drowsiness, dizziness, confusion 17
Dry mouth 17
Constipation 17
Histamine release 17
Excessive sweating 17
2.5. Methadone 17
2.5.1. Pharmacokinetics 17
2.5.2. Dose 18
2.5.3. Safety 18
2.5.4. Side-effects 18
2.5.5. Interactions 19
2.5.6. Preparations 19
2.5.7. Diversion 19
2.5.8. Non-supervised methadone doses 20
Diluting take-away doses 20
Diluents 21
Exceptions 21
Storage of take-away doses 21
2.6. Buprenorphine 21
2.6.1 Pharmacokinetics 22
2.6.2 Dose 22
2.6.3 Safety 22
2.6.4 Precipitated withdrawal 23
2.6.5 Side-effects 23
2.6.6 Precautions 23
Hepatic impairment 23
Pregnancy 23
Lactation 24
2.6.7 Interactions 24
Buprenorphine and naloxone combination – Suboxone® 24
2.6.8 Preparations 24
2.6.9 Diversion 25
2.6.10 Supervised dosing procedure for buprenorphine/naloxone film 25

Currently under review

2.6.11 Non-supervised buprenophine 26
2.8 Safety considerations for opioid substitution treatment 26
2.8.1 Contraindications to opioid use 26
2.8.2 Precautions to Opioid Use 27
2.8.3 Interactions with Opioids 27
2.8.4 Overdose 27
2.9 Special cases 28
2.9.1 Pregnancy 28
Special entry 28
Foetal Withdrawal 29
Breast feeding 29
2.9.2 HIV/AIDS 29
2.9.3 Prison release 30
2.9.4 Treatment of pain in MATOD clients 30
2.9.5 Pain clients 30
Pain authorities vs dependence authorities 30
2.10 Naltrexone 31
2.10.1 Pharmacokinetics 31
2.10.2 Dose 31
2.10.3 Starting treatment with naltrexone for opioid addiction 32
2.10.4 Side-effects 32
2.10.5 Contraindications 32
2.10.6 Precautions 32
2.10.7 Interactions 33
2.10.8 Safety 33
2.10.9 Antagonist-induced (“rapid”) withdrawal 33
2.11 The treatment alliance 33
2.11.1 Prescriber’s role 33
2.11.2 Client’s role 34
Client perspective: the treatment journey 35
2.11.3 Pharmacist’s role 36
Chapter 3. Pharmacist responsibilities 37
3.1 Dosing clients 37
3.1.1 Supervised dosing 37
3.2 Non-supervised or takeaway doses 38
3.2.1 Policy for six non-supervised doses per week 40
Admission criteria for one supervised dose per week: 40
Criteria for continuation of one supervised dose per week: 41
3.2.2 Split dosing 41

Currently under review

3.3 Valid prescription 42
3.3.1 Interstate Scripts 42
3.3.2 Replacement of methadone liquid or sublingual buprenorphine products or doses 43
3.4 Recording 43
3.5 Storage in the pharmacy 44
3.6 Returns to the drug of dependence unit 44
3.7 Transferring between pharmacies 44
3.8 Confidentiality 44
3.9 Lawful disclosure 45
3.9.1 Investigators 45
3.9.2 Solicitors 45
3.9.3 Criminal behaviour 45
3.9.4 Child protection 45
3.9.5 Research 45
3.10 Preventing problems 45
3.10.1 Contracts 46
3.10.2 Response to client intoxication 46
Recognising symptoms of intoxication 47
Breath Alcohol Levels (BAL) 47
3.10.3 Response to missed doses 48
3.10.4 Response to diversion 48
3.10.5 Response to behavioural problems 48
Personality disorders 49
3.10.6 Dispensing errors 49
Overdoses 49
Under-doses 50
Avoiding Errors 50
3.10.7 Communication with locum pharmacists 50
3.10.8 Communication with other health professionals 50
3.10.9 Managing pharmacy payment 51
3.10.10 Prescriptions for other drugs 51
Appendix 1: Glossary of terms and abbreviations 53
Appendix 2: Contacts 55
Drugs of Dependence Unit 55
Drug and Alcohol Services South Australia 55
Community Pharmacy Program 55
DASSA Central Service 55
DASSA Southern Service 55
DASSA Northern Service 55

Currently under review

Information services 55
Drug & Alcohol Clinical Advisory Service (DACAS) 55
Alcohol and Drug Information Service (ADIS) 55
Health Services 56
Prison Opioid Substitution Program 56
Family and Youth Services 56
Family Drug Support 56
Mental Health Service 56
Poisons Information Line 56
Intravenous drug misuse 56
Hepatitis SA 56
Needle Clean Up Hotline 56
Appendix 3: Client/pharmacy contract 57
Appendix 4: Measuring methadone liquid 59
Pumps 59
Syringes 59
Conical measures 59
Pipettes and autopipettes 59
Appendix 5: Detection time for selected drugs in urine 60
Appendix 6: Dispensing paperwork 61
Methadone calculator for methadone 5mg/mL liquid 61
Biodone Forte® Client Record 62
Methadone Syrup® Client Record 63
Suboxone® Film Client Record 64
Subutex® Tablet Client Record 65
Appendix 7: Standard operating procedure for pharmacists dispensing methadone or buprenorphine 66
Appendix 8: Quality Care Pharmacy Program (QCPP) Checklist for pharmacists dispensing methadone or buprenorphine 67
Appendix 9: References 68

Currently under review

Currently under review

Introduction

Medication Assisted Treatment for Opioid Dependence (MATOD) is prescribed by doctors to some clients with illicit opioid and other drug problems. It is a combination of medication and psychosocial support. MATOD treatments include methadone, buprenorphine (also known as opioid substitution treatment) and naltrexone (for relapse prevention). The medication controls withdrawal or cravings and blocks the euphoric effects of further opioid use, while psychosocial support refers to the many ways in which the psychological health and the social environment of the opioid user can be addressed to help improve both the quality and duration of life. MATOD improves the health and well-being of clients and assists them to adjust to the responsibilities and realities of everyday life.

This guideline has three chapters and is intended to provide the background knowledge needed by a pharmacist involved with dispensing MATOD medications. Chapter 1 provides information on unsanctioned opioid use and dependence. It includes a description about the harmful effects of unsanctioned opioid use, the nature of dependence and how opioid dependence is defined. Chapter 2 covers interventions for opioid use and dependence. It outlines the goals and types of treatments as well as the psychological factors which can impact on treatment. Chapter 3 details pharmacist's legal responsibilities in supervised dosing and dispensing of methadone liquid, buprenorphine/naloxone film and buprenorphine tablets. It also provides practical tips and suggestions on how to best manage the opioid substitution treatment program in a community pharmacy.

The Appendices at the end of these guidelines provide useful templates for community pharmacies as well as organisational contact details. This includes example contracts, dispensing paperwork, the standard operating procedure and check list for pharmacists dispensing methadone and buprenorphine. Further information can be found on the SA Health website under Community Pharmacy Program (www.sahealth.sa.gov.au/DASSAprograms)

Currently under review

Chapter 1. Unsanctioned opioid use and dependence

1.1. Unsanctioned opioid use

Problems with opioid drugs do not only stem from illicit heroin use, but also from the misuse of prescribed opioid medication and over-the-counter codeine preparations. The term “unsanctioned opioid use” reflects this mix of illicit heroin and the use of pharmaceutical preparations that are being used in an unsanctioned way. The prevalence of unsanctioned opioid use in the general population is low, making it difficult to determine accurately, but there are indications in Australia and globally of increasing prevalence of unsanctioned use of pharmaceutical preparations and decreasing prevalence of heroin use.

The 2013 National Drug Strategy Household Survey[1] recorded a small but significant fall in recent use of heroin, from 0.2% of the adult population in 2010 to 0.1% in 2013. The proportion of survey participants reporting injecting drug use also fell, from 0.4% in 2010 to 0.3% in 2013. At the same time unsanctioned use of pharmaceutical preparations increased, with 3.3% of participants in the 2013 survey reporting the use of pain-killers or analgesics (eg. paracetamol, over-the-counter and prescription codeine combination products) while less than 1% reported the unsanctioned use of methadone, buprenorphine or other opiates (not including heroin).

Heroin remains the opioid that is used most commonly by people seeking treatment for drug and alcohol problems, and for clients accessing MATOD. In 2013, MATOD clients were twice as likely to record heroin as their primary source of opioid drug of dependence than that of all other opioid pharmaceuticals combined.[2]

There has been a small but noticeable increase in clients requesting treatment in South Australia for opioid dependence as a result of overuse of over-the-counter codeine-based products. The opioid dependence results in large amounts of ibuprofen and paracetamol being consumed. Excessive amounts of paracetamol in particular can cause intestinal, renal and hepatic problems that can be life-threatening. Ibuprofen overuse can also result in gastric erosions, ulcers and anaemia. It is difficult to gauge the full extent of the problem as most clients only present for treatment when they develop complications from their excessive medication use. However, there have been increases in some specific types of hospital presentations relating to the over-use of ibuprofen, such as renal tubular acidosis.

Although the number of opioid users is quite small, the problems that their drug use causes to themselves, their families, communities and to society as a whole are considerable. Details of these impacts will be further expanded on in the following section. The prominence of such users and their isolation from mainstream society make the use of opioid substances, and particularly heroin, a very topical and emotive issue.

Currently under review

1.2. Harmful effects of unsanctioned opioid use

1.2.1. Overdose

In 2007 the Australian *Burden of Disease* study found that 1.3% of deaths were attributable to illicit drug use. These include deaths from hepatitis C, self-inflicted injuries, and heroin and other drugs. An estimated 46,257 disability-adjusted-life-years (lost years of healthy life) were attributed to illicit drug use.[1]

The estimated mortality rate (from all causes) for heroin users is approximately 1–2% per annum. Regular heroin users are at considerably greater risk (estimated at between 10 and 20 times) of death than age and gender matched controls in the community.

The majority of heroin-related overdoses occur following the use of heroin and other sedatives, such as benzodiazepines and/or alcohol. A minority (18%) of heroin-related overdoses were due to heroin alone.

Most heroin-related deaths occur in 'older' male heroin users (late twenties and thirties) with several years of drug use experience. Only a very small minority of heroin-related deaths occur in individuals with limited experience with opioid drugs.

1.2.2. Problems related to injecting

Trauma and/or infection of injection sites

Frequent injecting, poor injecting technique and the injection of adulterants can cause a number of local lesions, including scarring, venous thrombosis, thrombophlebitis, and cellulitis.

Systemic bacterial or fungal infections

These include septicaemia, infective endocarditis, pneumonia, osteomyelitis and renal complications (including glomerulonephritis).

Transmission of blood-borne viruses

The transmission of Human Immunodeficiency Virus (HIV) among injecting drug users in Australia has been well contained thus far. Prevalence rates are less than 3% among injecting drug users in most Australian capital cities.

The spread of the Hepatitis C Virus (HCV) has not been contained. Current estimates suggest that approximately 50% of drug users have been infected with HCV within four years of regular injecting drug use and 60–70% HCV antibody positive at treatment entry.

The incidence of Hepatitis B virus amongst injecting drug users is between 5 and 15%.

1.2.3. Social and economic harms

There are numerous 'social' harms for the individual and the community associated with heroin use. Much of this relates to:

- financial problems arising from the expense of illicit heroin use (daily habits of $50 to $200 are common) and disrupted employment history;
- legal problems, due to the illicit behaviour that many individuals must engage in to sustain their drug use, including drug dealing, property crime, sex work, and the illicit nature of heroin use;
- impaired functioning or retraction from other activities, such as work, parenting, study, friendships; and

Currently under review

> the stigma for individuals, their families and friends associated with heroin use.

Approximately 10% of the prison population had been convicted of drug-related offences and many more convicted of other offences which can be related to drug use, e.g. property offences (37% attributable to drug use), violence (34% attributable to drug use).

The economic cost of drug use to the community is enormous. The Australian Institute of Health and Welfare estimated the cost of illicit drug use in Australia to be $8.2 billion for 2004-05.[3] The estimate included the cost of crime, lost productivity and healthcare. Illicit drug use accounted for 2.0% of Australia's total burden of disease in 2003. A significant factor in this was hepatitis C, which is commonly contracted by risky injecting practices.

1.2.4. Harm minimisation

In response to growing concerns about a potential HIV/AIDS epidemic amongst injecting drug users and the broader community and concerns regarding substance misuse (including heroin abuse), in 1985 the Commonwealth Government instigated a policy of harm minimisation. The aim of this policy is to reduce the adverse consequences of drug use for both the individual and society. It involves a balance between three basic concepts:

> reducing demand for drugs

> reducing the supplies of drugs available

> reducing the harm caused by drug use.

A variety of approaches has been taken to achieve these aims, including:

> health promotion campaigns

> school-based education packages about drugs

> increased resources for customs services

> improved liaison between federal and state law enforcement agencies

> provision of sterile injecting equipment

> provision of safe injecting places

> drug court diversion programs to keep users out of jail

> support for non-government and community-based programs

> therapeutic communities

> opioid substitution programs.

Harm minimisation does not imply any support for illegal or risky behaviour. Rather it acknowledges that, where they occur, there is a responsibility to develop, implement and promote measures designed to minimise the harm that such behaviour can cause.

Opioid substitution programs have consistently been shown to:

> reduce heroin, and other illicit drug use

> reduce injecting

> reduce infections with blood-borne viruses

> reduce criminal behaviour

> improve social functioning, including employment

> reduce mortality rates from all causes.

Currently under review

1.3. Nature of dependence

1.3.1. Why do people use drugs?

The reasons why people start taking alcohol and other drugs are diverse. Initial and ongoing use is influenced by a range of risk and protective factors that are biological, sociological and psychological in nature. With repeated drug use biological factors become important in determining vulnerability to dependence. It is estimated that genetic factors account for between 40 and 60% of a person's vulnerability to addiction.[4]

The age of first use, route of administration and individual response to drug use are all factors that influence the likelihood of initial drug use progressing through regular use to dependence. Many drugs are capable of producing drug dependence but not all people who try those drugs will become dependent. The proportion that do become dependent varies from drug to drug (eg. very few cannabis users become dependent whereas many cigarette smokers become dependent on nicotine).

The properties of drugs which are perceived by users as beneficial vary from drug to drug, and from person to person. For example, opioid drugs produce euphoria, relief of physical pain, and relief of emotional pain. Any one of these, or a combination of them, can cause a person to want to continue to use opioid drugs.

1.3.2. What is the effect on the brain?

Drugs of dependence affect a system in the brain that is involved in determining what we learn and what we are motivated to do. In effect, it indicates that a significant event has occurred which is worth remembering and repeating. It is normally associated with subjective sensations of pleasure or relief of suffering, indicating strong survival advantage for the behaviour which produces those sensations. For example, sexual activity and eating are two behaviours which would be expected to activate these pathways. It is referred to as the brain reward system.

The key areas of the brain involved in the reward system are the ventral tegmental area, nucleus accumbens and the prefrontal cortex. The main neurotransmitter system implicated is dopamine. Drugs of dependence directly or indirectly activate brain reward pathways by increasing dopamine release or inhibiting dopamine re-uptake.

Physical dependence occurs when the nervous system adapts to the presence of certain drugs. It is a homeostatic response to the regular presence of a drug which disturbs normal activity. The response of the brain is to:

- reduce the number of receptors
- desensitise the receptors
- decrease the production or release of neurotransmitters and
- change cellular signalling pathways.

Physical dependence is manifested in two ways:

1. tolerance, where higher doses of the drug are needed to achieve the same effect; and
2. a withdrawal syndrome which develops if drug taking is reduced or stopped abruptly.

The withdrawal syndrome and its immediate relief following re-administration of the drug are important factors in continuing drug use.

Currently under review

1.3.3. Genetic factors in drug dependence

There are genetic factors involved in the individual vulnerability to developing drug problems which have been shown in studies of people dependent on alcohol and nicotine. The examination of exactly what factors are inherited is in its early stages but a few characteristics are known.

The A1 allele of the dopamine D2 receptor gene appears to confer an increased risk of alcohol and drug dependence, apparently due to reduced dopaminergic function. Individuals affected by this are sometimes referred to as 'reward deficient'.

There are also drug-specific traits which are inherited. The best known example is the protective effect for alcohol dependence of reduced aldehyde dehydrogenase activity. The high acetaldehyde levels consequently produced when alcohol is consumed have a repellent action on those affected. A similar outcome is seen with nicotine, where reduced nicotine metabolism means that affected individuals experience stronger nicotine effects and so smoke fewer cigarettes.

1.3.4. Substance use and mental health disorders

The misuse of alcohol and other drugs is more common among people with mental illness compared with the general population. Studies have also consistently found that mental health disorders are more common in people who misuse alcohol and other drugs. While it is clear that there is an association between substance use and mental health disorders, the reasons for the association are complex. Some risk factors (social and biological) are shared across both substance use and mental disorders. Mental health disorders may increase sensitivity to the effects of psychoactive substances, and people with mental health disorders may use psychoactive substances for perceived beneficial effects in alleviation of the symptoms of the mental health disorder. Substance use may also be a precipitating factor in the development of mental health disorders.

A very high rate of mental health conditions accompanies opioid dependence. These include depression, social phobia and other anxiety disorders. Many opioid users (especially females) exhibit symptoms of anxiety and depression at the time of presentation for treatment. Sometimes depression and anxiety resolves with treatment, but in some patients, specific treatment of the mental health symptoms may be required.

Most, but not all, studies link psychiatric distress to poorer treatment outcome. Depression has been found to predict poor psychosocial functioning and to increase the risk of relapse to opioid use in the event of life crises.

Multiple studies have indicated that opioid substitution treatment can reduce levels of psychiatric distress with improvement apparent within weeks of commencement of treatment. All patients should be screened again for psychiatric disorders once stabilised on substitution treatment.

Currently under review

1.4. Defining opioid dependence

1.4.1. ICD-10

Opioid dependence is defined in the current International Classification of Diseases (ICD 10) as a maladaptive pattern of drug use, showing as three or more of the following in the same 12 month period:

- a strong desire to take opioids
- difficulties in controlling opioid-use
- withdrawal
- evidence of tolerance
- progressive neglect of alternative pleasures or interests because of opioid use
- persisting with opioid use despite harmful consequences.

This is the definition usually followed in assessing whether a person is suitable to receive opioid substitution treatment[5]. The salient point in this definition is the continued use of opioid drugs despite the recognition of harm being caused by their use.

Although physical dependence need not be present to meet these criteria, careful thought is needed before prescribing opioid substitution treatment to people who do not already have a physical dependence.

1.4.2. Legal Basis of Drug Dependence in South Australia

In South Australia, the *Controlled Substances Act 1984* (SA) outlines a legal basis for dependence. For the purpose of Section 18A (2) of the *Controlled Substances Act 1984* (SA) a person is dependent on drugs if:

- the person:
    - has acquired, as a result of the repeated administration of prescription drugs or controlled drugs, an overpowering desire for the continued administration of such drugs; and
    - is likely to suffer mental or physical distress or disorder on cessation of the administration of such drugs; or
- the person has a history of consuming or using prescription drugs or controlled drugs in a quantity or manner that
    - in the case of drugs lawfully supplied to the person—is contrary to the prescribing practitioner's instructions relating to consumption or use of the drug; and
    - in any case—presents a risk to the person's health.

Currently under review

Chapter 2. Interventions for opioid use and dependence

2.1. Goals of treatment

Most people taking action to modify their drug use behaviour do not successfully maintain their gains on their first attempt. For example, with tobacco smoking, successful self-changers make an average of three to four attempts before they become long-term abstainers; relapses occur frequently. Follow-up studies indicate a similar pattern for opioid drugs. People who are dependent may continue to use opioids for decades. Among these users, periods of daily use are interrupted by detoxification, drug treatment and incarceration for drug-related offences. It is this pattern of use, cessation and relapse that causes opioid dependence to be regarded as a chronic relapsing condition.[6]

The proportion of people who achieve enduring abstinence from opioid drugs after any treatment encounter is small but it increases with time and age. The Australian Treatment Outcome Study followed three cohorts of heroin users from the time of entry to treatment (opioid substitution treatment with methadone or buprenorphine, detoxification, or residential rehabilitation) and a comparison group of heroin users who were not in treatment when they were recruited to the study. Over a three year period 99.3% of study participants had been exposed to some form of treatment (including 92.9% of the "no treatment" comparison group). At baseline 99% reported using heroin in the month prior to interview, compared to 35% at 24-month and 36-month follow-up interviews. One month abstinence from heroin was associated with having spent more time in opioid substitution treatment and residential rehabilitation, but was unrelated to time spent in detoxification.[7]

The broad goal of treatment for opioid dependence is to reduce the health, social and economic harms to individuals and the community arising from unsanctioned opioid use.

The community expectation of "treatment" of drug dependence is, in general, that it will result in drug users achieving a drug-free lifestyle. Abstinence is an important long-term goal, but this viewpoint of treatment does not adequately reflect the complexities of drug dependence, or the extended treatment period required by some people.

An emphasis on abstinence to some extent devalues the other achievements that can be made through treatment. For most people entering treatment, short-term achievable goals are important, such as:

- staying alive;
- reducing unsanctioned drug use;
- reducing risk of infectious disease;
- improving physical and psychological health;
- reducing criminal behaviour;
- reintegration in the labour and educational process; and
- improving social functioning,

without necessarily ceasing drug use.

These goals represent steps along a continuum, extending from chaotic drug use, to

Currently under review

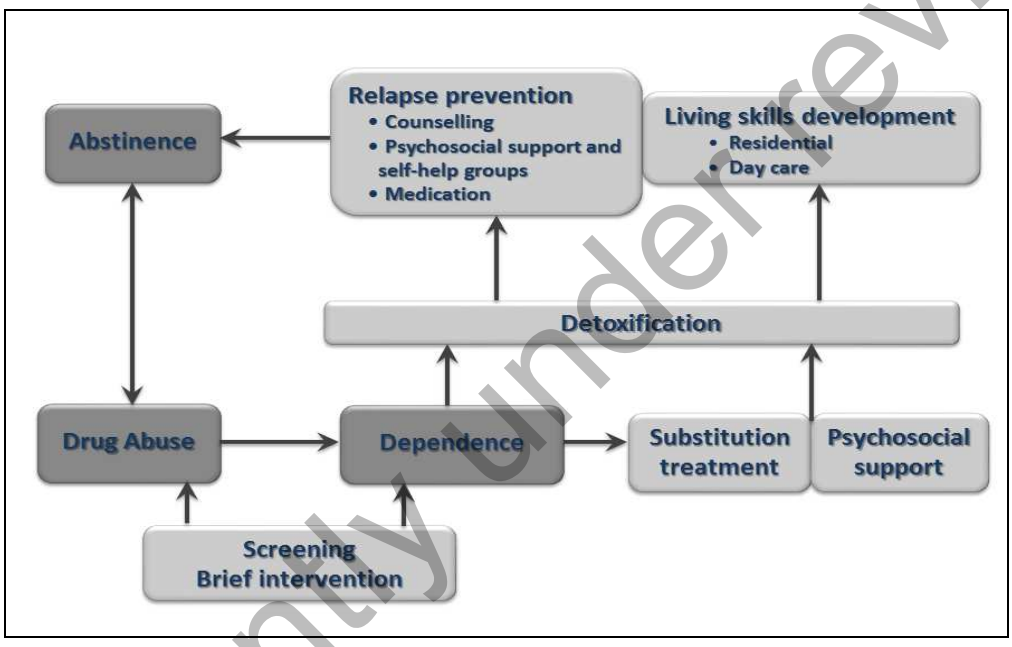
reduced, safer use, through to abstinence. Reduced or controlled use, stable relationships, employment or better health are all important changes that may encourage abstinence in the future.

'Slip ups' or lapses are a normal part of changing any human behaviour. Every time they occur, a person can learn from the experience and develop better ways of dealing with a similar situation in the future. It may be only through a number of unsuccessful attempts at controlled use that a person decides on a goal of abstinence.

2.2. Types of treatment

Figure 1 represents the broad range of treatment options, related to the stage of dependency. The nature of these options is outlined in the following sections.

Figure 1: Treatment framework



2.2.1. Screening and brief intervention

Drug users are often reluctant to enter treatment. They may lack insight into the negative consequences of their use of drugs, and they may be in a state of denial about their level of use. Contact with primary health care services, police, the criminal justice system, and outreach activities provide opportunities for the delivery of brief interventions to this group of users.

Brief interventions are structured therapy of a limited number of sessions, usually one to four, sometimes requiring no more than five minutes, and sometimes up to two hours in total. Such interventions can provide information about drug use, particularly through approaches to reduce the risks of drug use, both to the individual and the general community. Brief interventions also aim to increase awareness of the negative aspects of drug use and reasons for ceasing use, to motivate users to take action to modify their drug using behaviour and to encourage them to engage in treatment.

Brief interventions on their own can promote behavioural change, particularly for people whose drug and alcohol use is at levels associated with low to moderate risk of harm, or

Currently under review

can be the first stage of more intense treatment. Brief interventions are appropriate for individuals from a wide range of cultures and backgrounds and can be used in a variety of settings, both opportunistic and within specialised drug and alcohol treatment.

Open access services are important components of this level of intervention and encompass “drop-in”, community outreach, telephone helplines, support groups and general support services. These services can encourage individuals to take action to reduce their drug use without formal treatment, they can provide interventions such as access to clean needle and peer education programs to reduce the harms of drug use and the risk of overdose, and they can act as entry points to more formal treatment approaches.

2.2.2. Detoxification

Chronic use of alcohol and other drugs is associated with physiological changes that comprise physical dependence. Users who are dependent must undergo detoxification if they are to become abstinent. Withdrawal occurs when the drug of dependence is eliminated from the body, and any physical adaptation that has occurred as a consequence of dependent drug use is reversed. The nature and severity of withdrawal depends on an individual’s drug use history and the pharmacology of drugs used.

People may experience withdrawal in a variety of settings, including general hospitals, specialist drug and alcohol units, outpatient and home. Detoxification entails the provision of interventions to ensure that the withdrawal process is completed with safety and minimal discomfort. Many drug users cease use without assistance from detoxification services; others may be supported by family members or other services.

Because detoxification addresses only the physical adaptation, and not the social dimension of dependence, detoxification is not in itself a treatment for dependence. Rather, detoxification is a necessary stepping stone to drug-free treatment.

Rates of relapse following detoxification tend to be high. Given that tolerance is reduced by detoxification, there is also a high risk of overdose associated with relapse in the period after detoxification. Nonetheless, detoxification provides a limited opportunity for interventions which may encourage users to move towards the next stage of change, and at least a period of respite from the risks associated with regular use of alcohol and other drugs as well as promoting engagement in further treatment.

A specialist drug and alcohol withdrawal service is operated by DASSA at Glenside Health Services, offering inpatient treatment for people withdrawing from drugs or alcohol. Assessment for admission is triaged through the Alcohol and Drug Information Service (see *Contacts* in Appendix 2 pg 55). Similar services are offered by a few private providers; in particular Adelaide Clinic, Gilberton offers inpatient withdrawal with follow-up support services provided by Kahlyn Private Hospital, Magill.

2.2.3 Substitution treatment (agonist maintenance)

Substitution treatment involves the prescription of a drug with similar properties to the drug of dependence, but with a lower degree of risk. The value of substitution treatment lies in the opportunity it provides for dependent drug users to reduce their exposure to risk behaviours and stabilise in health and social functioning before dealing with the physical dimension of dependence.

The main forms of substitution treatment are prescribed methadone or buprenorphine for opioid dependence. Psychosocial support, at various levels, is an integral part of opioid substitution treatment[5].

In South Australia the state government opioid substitution treatment program is run by

Currently under review

Drug and Alcohol Services South Australia (DASSA) which operates three services in the metropolitan area:

> Central Service
  92 Osmond Terrace, Norwood SA 5067
  Tel: (08) 8130 7500, Fax: (08) 8130 7575

Central Service will relocate to new premises on 18 April 2016
91 Magill Rd, Stepney SA 5069
Tel: (08) 7425 5000 Fax: (08) 7425 5015

> Northern Service
  22 Langford Drive, Elizabeth SA 5112
  Tel: (08) 8252 4040, Fax: (08) 8287 0050

> Southern Service
  209 Main South Road, Morphett Vale SA 5162
  Tel: (08), 8325 8111, Fax: (08) 8325 8177

Opioid Substitution Treatment is also accessible through a number of private prescribers, who have had specific training in addiction treatment and who have an interest in this area. In addition, all willing medical or nurse practitioners are able to prescribe through the Suboxone® Opioid Substitution Program. An up-to-date list of community prescribers is available from the Alcohol and Drug Information Service (ADIS) or the Drugs of Dependence Unit (see *Contacts* in Appendix 2 pg 55).

Medical officers employed by the South Australian Prison Health Service (SAPHS) are approved to prescribe methadone and buprenorophine/naloxone to prisoners for the period of their imprisonment. The aim of the program is to allow continuation of treatment, or for methadone or buprenorphine/naloxone treatment to be commenced during their incarceration if required. Some prisoners may commence opioid substitution treatment a few weeks prior to their release if they have previously been opioid dependent and are at risk of resuming illicit opioid use when released, even if they do not have a current opioid dependence. This strategy works to reduce the risk of the post release opioid overdose.[8]

Prior to release from prison, appointments will be made with DASSA or a community-based prescriber and the dosing pharmacy will be organized for the inmate. All pharmacy payments are the responsibility of the client. The prison medical officer will usually write a continuation script for inmates to last until the first appointment with the new prescriber. Prison medical officers will not write any further prescriptions. Prescriptions from the prison will always be faxed and then the original sent via post to the new pharmacy, the client will not present a prescription.

If there are any concerns contact the prison involved and ask for the Health Centre who have a nurse present 7 days a week, or contact the Corrections office on (08) 7002 3100.

2.2.4 Relapse prevention

Relapse prevention and rehabilitation programs are designed to change the behaviour of patients to enable them to regain control of their urge to use substances. It is an important component of opioid substitution treatment, and is integral to naltrexone treatment.

Counselling and psychosocial support, including self-help groups, are important components of relapse prevention approaches. Psychological interventions help patients to identify and address the reasons for drug use, the negative consequences of their drug use, and the benefits associated with changing drug user behaviour. Relapse prevention interventions comprise skills to recognise cues and risk factors for drug use, and the development of strategies to resist drug use.

Currently under review

2.2.5 Living skills development

Problematic substance use is a complex condition combining social, psychological, behavioural and physiological dimensions. It is often a symptom of underlying social, psychological or behavioural issues which need to be addressed if recovery is to occur.

Psychological and social support interventions change drug using behaviour and address the various emotional issues, practical needs (housing, employment, financial management) and social interaction (family issues, building networks unrelated to drug use) for recovering drug users. Psychological treatment is also an important part of medicated treatment for supporting compliance with the prescribed treatment and minimising unsanctioned drug consumption. Concepts and definitions of recovery abound, but a consistent theme is recovery as a process, spanning years rather than weeks and months, and encompassing personal change, maximisation of health and well-being and participation in the rights, roles and responsibilities of society. This understanding of recovery allows for several pathways, including through medication-assisted treatment.

The aspects of recovery that are encompassed in the phrase “living skills development” are perceived as:

- requiring establishment or renewal of personal values, such as honesty, self-reliance, and responsibility to self and others;
- involving learning or re-establishing the behavioural skills, attitudes and values associated with community living; and
- involving personal development and lifestyle change consistent with shared community values.

This aspect of recovery is most commonly addressed through residential rehabilitation. Residential rehabilitation is based on the principle that a structured drug-free residential setting provides an appropriate context to address the underlying causes of addictive behaviour. These programs assist the patient to develop appropriate skills and attitudes to make positive changes towards a dependence-free lifestyle. Therapeutic communities represent a subset of residential rehabilitation defined by an emphasis on accepting personal responsibility for decisions and actions, and assigning residents tasks of “everyday living” as part of their treatment.

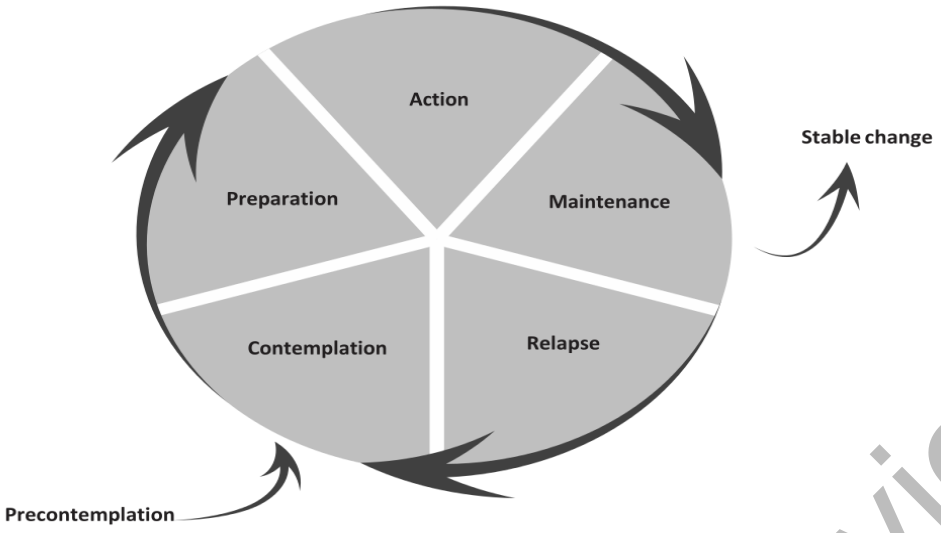
2.3. Psychological factors in treatment

The ‘stages of change’ model[9] is useful in understanding of the processes involved in behaviour change (see Figure 2). The model is based on the concept that individuals (may) pass through a number of stages during behavioural change.

Motivation to change is not a ‘fixed’ state in a person, but rather is subject to many forces, including the intervention of health workers. The health worker can assist patients to move from one stage to the next and to learn from unsuccessful attempts to control their drug use.

Currently under review

Figure 2: 'Stages of change' model of behavioural change



2.3.1. Pre-contemplation stage

Not all drug users want to stop using drugs. In the pre-contemplation stage, drug users will not have allowed any concerns they may have about their drug use to influence their actions. They will often not immediately recognise problems they are having as resulting from their drug use. Motivational interviewing is an appropriate technique to help users not yet contemplating change to explore the advantages and disadvantages of current patterns of drug use.

During pre-contemplation the user perceives the benefits of drug use as outweighing the disadvantages, and the disadvantages of change outweigh the advantages. Family, friends, health and social workers may be concerned about some consequences of the person's drug use, but the drug user may accept this as collateral damage.

Commonly, there is resistance to 'action oriented interventions' and explanations about how to 'give up', but relevant information about risks, and how to avoid or minimise them, may be well received. For example, a heroin user may be keen to get advice on how to avoid overdose and blood-borne viruses.

2.3.2. Contemplation stage

The person has realised that their drug use is doing harm and is weighing up the benefits and the costs of continuing to use. The balance of costs and benefits begin to shift, although there is still ambivalence about change. This ambivalence is best explored using motivational interviewing.

2.3.3. Preparation stage

The balance has shifted. The person is preparing to take action and has confidence in their capacity to change. Change is seen as worthwhile; this is often a planning stage. Goal setting, identifying internal and external supports or resources and identifying strategies to support change can help.

2.3.4. Action stage

The person is taking steps to change. Support and specific skill training can be provided. Review initial reasons that led to the decision to change. The person is implementing strategies to change their drug use pattern. They usually spend the least time in this

Currently under review

stage as they are waiting to enter treatment, relapsing and returning to thinking about stopping, or on the way to maintenance.

2.3.5. Maintenance of change

The person has succeeded in stopping their harmful drug use and is concentrating on continuing that progress. An intervention technique known as relapse prevention teaches strategies for dealing with the pressures to relapse. Encourage patients to articulate the positive reasons for maintaining change to reinforce their decisions.

Changes in behaviour maintained for six months or more are usually associated with substantial improvements in the quality of life. Without such changes, the effort to change may not seem worthwhile and relapse becomes more likely. Quality of life includes factors such as employment, the quality of relationships, financial security, housing and spiritual support (variously defined). Drug and alcohol treatment services cannot be expected to address all these factors, but may be able to facilitate access to a range of advice and support services. These might include, but are not limited to housing services, financial support services, legal advice, employment, education and training.

2.3.6. Relapse

Relapse should not be seen as a treatment failure, but as a common characteristic of therapy. Most users will work through this cycle several times in their drug-using careers. Relapse may occur for any number of reasons. It could be a reasoned choice about the benefits of returning to drug use or it could be a slip related to a variety of emotional or social triggers. Relapse may take the user into any of the other stages of behaviour. The stages of change model highlights the relapsing-remitting nature of addiction.

2.4. Opioid pharmacology

Opioid analgesics mimic endogenous opioids by attaching to and activating opioid receptors in the central and peripheral nervous systems. They reduce the release of neurotransmitter substances and also reduce the activity of post-synaptic neurones in the spinal cord, preventing the transmission of the pain impulse.

Opioid receptors are classified into three main types: mu (μ), kappa (κ) and delta (δ).

- Activation of mu receptors produces analgesia, respiratory depression and constipation. This is the most studied receptor type, and it is mu receptors that appear to have the greatest role in mediating opioid effects.
- Kappa receptor activation produces analgesia (mainly in spinal cord nerves), meiosis (pupil constriction), dysphoria (feeling unwell) and respiratory depression.
- Delta receptor activation is likely to contribute to analgesia in humans.

Opioid agonists include:

- Alfentanyl
- Codeine
- Dextropropoxyphene
- Fentanyl
- Heroin (diacetylmorphine, diamorphine)
- Hydromorphone
- Methadone
- Morphine

Currently under review

- Oxycodone
- Pethidine
- Sufentanil
- Tramadol

Drugs that are mu opioid agonists bind to and activate mu opioid receptors. Activation of mu opioid receptors results in the following actions:

- Central nervous system: analgesia, sedation, changes in mood, respiratory depression, miosis, nausea and vomiting, cough suppression;
- Gastrointestinal: decreased gastrointestinal motility, increased biliary tract pressure;
- Endocrine: stimulate prolactin release, reduce glucose tolerance;
- Cardiovascular: peripheral vasodilatation, decreased blood pressure (not usually significant).

Opioid antagonists are described as drugs that bind to, but do not activate, mu opioid receptors. In binding to mu opioid receptors, antagonists block the mu receptors and prevent opioid agonists from binding to and activating these receptors. Examples of mu opioid antagonists are naloxone and naltrexone.

In the absence of opioid drugs, opioid antagonists have no observable effects. In opioid intoxication, opioid antagonists will reverse opioid effects. In the presence of opioids in a person who is physically dependent on opioids, opioid antagonists will precipitate withdrawal or worsen the opioid withdrawal syndrome.

2.4.1. Tolerance and withdrawal

Prolonged, regular use of opioids leads to a down-regulation of the opioid receptors in the brain and a decrease in sensitivity to the effects of opioids. This is probably due to a reduction in the number of receptors. When regular opioid use is reduced or stopped suddenly, the lack of receptor activity is manifested as withdrawal symptoms. These symptoms generally are opposite in effects to the pharmacological effects of the drugs.

Opioid agonists (morphine, heroin, methadone etc.) display cross-tolerance, which is:

- using any one of these drugs will produce tolerance to the effects of any other; and
- any of these drugs will suppress the withdrawal symptoms from any other.

Giving a gradually increasing dose of methadone above the dose equivalence of the opioid they are dependent on will increase the level of tolerance to opioid effects. This higher level of tolerance has important benefits:

- It has a protective effect in terms of opioid overdose. Individuals will be less sensitive to opioid effects, so large doses of heroin are less likely to produce an overdose;
- Continuing heroin use will yield less of a ‘high’, reducing the positive reinforcement of continuing heroin use.

A long-term opioid user will become accustomed to their tolerance level and make allowances for it in the quantity of drugs they use. Any sustained period of abstinence from opioids will reduce their tolerance and increase the danger of overdose if drug use is then resumed. This effect has been noted in particular among prisoners released from jail and among people who have been maintained on the opioid antagonist drug, naltrexone (see section 2.10 pg 31). Both groups have been subject to a high incidence of fatal opioid overdoses.

Currently under review

2.4.2. Opioid withdrawal syndrome

Withdrawal occurs when the drug of dependence is eliminated from the body, and any physical adaptation that has occurred as a consequence of dependent drug use is reversed. Opioid withdrawal is associated with a well-defined pattern of withdrawal symptoms, as indicated in Table 1.

The opioid withdrawal syndrome can be very distressing but does not present a direct danger to health in physically fit people, provided adequate hydration and electrolyte levels are maintained. Completion of withdrawal is difficult for most people.

Table 1: Common withdrawal symptoms according to time of last heroin use

Time since last heroin use	Common symptoms
6 to 12 hours	Runny eyes and nose, sneezing, yawning Sweating
12 to 24 hours	Agitation and irritability Goosebumps Sweating, hot and cold flushes Loss of appetite
More than 24 hours	Strong urges (cravings) to use heroin Stomach cramps, diarrhoea Poor appetite, nausea, vomiting Back pain, pain in joints, legs or arms, headache Poor sleep Lethargy, fatigue Restlessness, irritability, agitation Poor concentration Hot and cold flushes, increased sweating
2nd to 4th days	Symptoms reach their peak
5th to 7th days	Most physical symptoms begin to settle down; appetite returns
Second week	'Physical' discomfort subsiding; may have ongoing problems with poor sleep, tiredness, irritability, cravings, low mood
Weeks to months	Improvements in sleep, levels of activity and mood, and general health; reduced cravings

The duration of methadone withdrawal is longer (5 to 21 days) than withdrawal from heroin or other short acting opioids. 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.

2.4.3. Side effects of opioid drugs

The reported side effects of methadone and buprenorphine are qualitatively similar to those of other opioid drugs. Most people who have used heroin or other opioids will experience few side effects from opioid substitution treatment. The most common side effects are discussed below.

Currently under review

Nausea and vomiting

Common, particularly in the first few days of treatment. Prophylactic use of an anti-emetic (e.g. metoclopramide) may be necessary but should be reviewed within a few days as tolerance to this effect develops swiftly. Reduction of opioid dose should be considered if nausea and vomiting is persistent.

Drowsiness, dizziness, confusion

Clients should be warned not to drive or operate machinery, particularly in the first few days of treatment and after dose increases. If daytime drowsiness persists, a dose decrease may be necessary. The use of sedative and other drugs by the patient should be reviewed.

Dry mouth

Reduced salivary flow exposes clients to the risk of dental problems. They should be advised to take particular care of their teeth, to avoid acidic drinks (eg. cola, fruit juice) and to chew sugar-free chewing gum to increase saliva if necessary.

Constipation

Increasing dietary fibre, maintaining an adequate level of fluid intake (mainly water) and fibre supplements can assist in maintaining healthy bowel function. Acute constipation may be relieved with an osmotic (sorbitol, lactulose) or stimulant (eg. docusate sodium with senna) laxative. Tolerance does not generally develop to opioid-induced constipation.

Histamine release

Common following administration of morphine, heroin and some other opioids, causing urticaria, itching, hypotension and flushing.

Excessive sweating

Particularly troublesome with methadone, but likely to be present with all opioids.

2.5. Methadone

Methadone is a synthetic opioid originally developed as an analgesic. It was first used to treat opioid dependence in the USA in the 1960s and in Australia in 1969. Its use became widespread in the mid-1980s when harm minimisation policies were first implemented. It is generally available as a racemic mixture, of which levo-methadone is the active isomer. Methadone acts primarily as a mu opioid agonist. The long, mostly successful history of methadone prescribing in dependence treatment make it the gold standard for therapeutic interventions for opioid dependence.

2.5.1. Pharmacokinetics

Methadone is rapidly and extensively absorbed from the gastrointestinal tract. It can be detected in plasma after about 30 minutes and peak plasma levels occur after about 2–4 hours. It is widely distributed among the tissues and 60-90% of the methadone present in plasma is protein bound.

The main route of elimination is hepatic metabolism, predominantly by the cytochrome P450 system, in particular CYP3A4. The main metabolic paths are N-demethylation and cyclisation. The importance of this enzyme system makes the metabolic processing of methadone vulnerable to interference due to drug interactions either inducing or competitively inhibiting methadone metabolism. There may also be some auto-induction,

Currently under review

resulting in declining methadone plasma concentrations over time.

The metabolites have no significant pharmacological activity and are eliminated in bile and urine, together with some unchanged drug. Methadone remains detectable in urine for about three days with commonly used drug screening tests. The elimination half-life of methadone averages about 35 hours but there are wide variations; as much as 15–60 hours. Accumulation occurs with repeated administration, necessitating careful adjustment of doses. Steady-state plasma levels are achieved about 5 days after dose adjustments. The main route of elimination is hepatic metabolism.

2.5.2. Dose

Maintenance methadone doses used to treat opioid dependence vary widely. Starting doses are chosen on the basis of assessment of the levels of opioid use and of tolerance; usually 15–30mg daily. Commencement doses higher than 30mg/day of methadone should be highly scrutinised and the cause for such a high dose should be confirmed with the prescriber and documented in pharmacy records. Alteration to doses should always be made on the basis of assessment by a qualified and experienced clinician. Daily doses can be gradually increased until withdrawal symptoms are successfully suppressed and the client no longer feels cravings to use opioids.

The initial dose stabilisation period is usually a week or more, but further increases are often needed in the following weeks and months. The average maintenance dose is about 60–80mg but some clients require much higher doses. Doses of at least 60mg a day have been associated with better outcomes in terms of reduced illicit drug use, reduced criminal activity and improved retention in treatment programs. Clients may pressure clinicians for higher starting doses and to increase doses more quickly but the desire to retain them in treatment must be balanced against the significant overdose risk.

Authorities issued by the Drugs of Dependence Unit in South Australia to prescribe liquid methadone for the treatment of opioid dependence cap the daily methadone dose at 150mg.

2.5.3. Safety

In opioid-naïve individuals as little as 40mg of methadone may constitute a fatal overdose, even less in children. The risk of overdose is markedly increased if other depressant drugs are also present, particularly alcohol and benzodiazepines.

The period of highest risk to maintenance clients is the first two weeks of treatment, this may be due to:

- uncertain level of opioid tolerance
- excessive methadone doses being prescribed or too rapid dose increases
- insufficient methadone dose causing client to use other drugs to counteract withdrawal symptoms.

2.5.4. Side-effects

See also *Side-effects of opioid drugs* in section 2.4.3 pg 16.

- Endocrine system – hypoadrenalism has been demonstrated.
- Sexual function – serum testosterone has been shown to be reduced by 43%, with associated impairment in sexual performance and potency. Gynaecomastia, which occurs occasionally, may also be associated with this effect.
- Pain at injection site – unsanctioned injection of methadone has been reported to cause

Currently under review

pain at injection sites. Inadvertent subcutaneous injection can cause local irritation and induration. The injection of methadone syrup is less likely if takeaway doses are diluted.

2.5.5. Interactions

A number of prescription medications are known to, or may potentially result in clinically significant interactions when used in combination with methadone. Such interactions should be avoided if possible, or patients should be monitored and drug regimens adjusted if necessary.

- Fluvoxamine inhibits methadone metabolism with possible toxicity when starting fluvoxamine, and withdrawal symptoms on cessation of fluvoxamine. Fluoxetine may have a similar but lesser effect.
- Medications that induce metabolism of methadone, reducing plasma levels and causing withdrawal symptoms, include phenytoin, rifampicin, phenobarbitone, carbamazepine, ritonavir, nevirapine, and efavirenz. Clients prescribed these drugs may require an increased dose of methadone.
- Methadone may also affect the metabolism of other prescribed medications. An example is zidovudine – methadone decreases metabolism of zidovudine leading to increased plasma levels of zidovudine. Symptoms of zidovudine toxicity can be misinterpreted as opioid withdrawal.

2.5.6. Preparations

1. Biodone Forte® – McGaw Biomed Australia Pty Ltd., 200mL and 1L – contains:

- methadone 5 mg/mL
- permicol red (food colouring)
- water

2. Methadone Syrup® – Aspen Pharma Pty Ltd., 200 mL and 1L – contains:

- methadone 5 mg/mL
- sorbitol
- alcohol/ethanol
- sodium benzoate
- glycerol
- caramel
- SC345280 anise spice
- Water purified

Both methadone preparations are listed on the Pharmaceutical Benefits Scheme as Section 100 items, for the treatment of opioid dependence.

2.5.7. Diversion

A street market for diverted methadone has developed, with prices up to $1 per milligram of methadone having been reported. This has resulted from a shortage of treatment places, inadequate doses being prescribed and temporary shortages in heroin supplies. A proportion of the diverted methadone is injected, to achieve a more intense high. Injecting an oral preparation has important implications for the health of users because:

- the solutions are not sterile.

Currently under review

> the syrup is hypertonic.

> sorbitol injected in large quantities can cause death from cardiac arrhythmia resulting from metabolic acidosis, hypophosphataemia, hypoglycaemia and hyperuricaemia.

Other dangers of methadone being diverted are:

> accidental ingestion by children or people other than the client

> use by non-tolerant individuals resulting in overdose

> legal problems for the client if caught selling methadone

The use of Biodone Forte® is recommended in preference to the syrup formulation to prevent some of the potential harms of injection.

2.5.8. Non-supervised methadone doses

Non-supervised or takeaway doses of methadone should be supplied in opaque bottles with child-resistant closures. Each day's dose should be supplied in an individual bottle, labelled with the date on which it is to be taken (see example). In cases where split dosing (two doses per day) is authorised e.g. pregnancy, two individual bottles should be supplied for each day.

The warnings on the second label are obtainable on labels produced by Bagot Press. Cautionary label number 1 (drowsiness) must also be attached.

Methadone..... mg Take the contents of this bottle as a single dose on .....(date) at .....(time). Client's name..... Prescription number ..... Date dispensed..... Pharmacy name, address, phone..... Keep out of reach of children

To be taken by mouth by the person named on the label on the day stated on the label. DO NOT INJECT May cause death or serious injury if injected or taken by another person.

Diluting take-away doses

Take-away doses should usually be supplied diluted[5]:

> doses greater than 25 mg should be diluted to 100 mL

> doses less than 25 mg should be diluted to 50 mL

Diluting doses has a few advantages:

> reduction in the value of diverted methadone;

> discouraging injection;

> reduction in the chance of an entire dose being accidentally swallowed by someone other than the client, with possibly fatal consequences.

Currently under review

Diluents

The Biodone Forte® brand of methadone may be diluted with purified water.

Methadone Syrup should be diluted with a preservative solution containing:

> sodium benzoate 0.05%

> citric acid 0.1%

> purified water to 100 mL

Exceptions

In some circumstances it may be necessary to provide undiluted non-supervised doses, but this should only be done in consultation with the prescriber and with written approval from the Drugs of Dependence Unit. Undiluted take-away doses may be justified for pregnant women and others having trouble with vomiting due to the larger volumes but written approval is still required from the Drugs of Dependence Unit.

Storage of take-away doses

Diluted take-away doses may be stored at room temperature for up to five days. They must be kept in a locked cupboard/box. They should not be stored in a refrigerator, near food or where children may be able to access them. A Methadone Buprenorphine not for kids handout leaflet is available at www.sahealth.sa.gov.au

2.6. Buprenorphine

Buprenorphine is often called a mixed agonist/antagonist drug but is more accurately described as a partial opioid agonist with high receptor affinity. It is a semi-synthetic opioid drug, which acts mainly as a partial agonist at mu opioid receptors. It also binds to delta and kappa receptors, acting as an antagonist at kappa receptors. It has a high affinity for mu and delta receptors but only low intrinsic activity. Buprenorphine has actions similar to the full agonist drugs but with less efficacy such that increases in dose have progressively less increase in effect. In practice, buprenorphine does display opioid actions, but has a weaker effect than the full agonists like methadone, morphine or heroin.

In the absence of other opioids, partial agonists have similar effects to agonists, although the maximal effect is less. In the presence of opioids which are full agonists, partial agonists may precipitate a withdrawal syndrome (depending on the level of full agonist present). The significance of this is that buprenorphine

1. produces less opioid effects than a full agonist can, irrespective of how big a dose is given; and
2. exerts a blocking action on the receptors, preventing other opioids from binding to them.

There is some evidence that kappa opioid receptor overactivity is involved in affective and psychotic conditions. The kappa antagonist activity of buprenorphine may indicate a possible role as an antidepressant or antipsychotic, but more research is needed before positive recommendations can be made.

In opioid dependence, buprenorphine reduces withdrawal symptoms and cravings for opioids. It is indicated for use in maintenance treatment and also to assist in opioid withdrawal.

For the treatment of opioid dependence buprenorphine is available:

> as a single agent preparation (as Subutex® sublingual tablets) with restrictions (see

Currently under review

Preparations in section 2.6.8 pg 24);

- combined with naloxone in a 4:1 BPN-NLX ratio (as Suboxone® sublingual film). This is intended to discourage misuse by injecting.

2.6.1 Pharmacokinetics

Buprenorphine is absorbed orally but has a large first-pass effect, making this route impractical. It is absorbed rapidly by the sublingual route, having an absolute bioavailability of an average 13.6% (range 5.1–24.9%). Following sublingual administration, therapeutic effects are first noticed after 30–60 minutes and peak plasma levels are achieved after about 1–2 hours. Plasma levels then fall again quite rapidly as it is distributed around the body; distribution half-life is 2–5 hours. Buprenorphine is mainly eliminated in the faeces by biliary excretion of the glucuronide conjugate (70%), the rest is eliminated in the urine.

Several factors contribute to buprenorphine having prolonged action (the terminal elimination half-life averages 35 hours):

1. Buprenorphine has a high affinity for mu opioid receptors; the receptor-drug complex dissociates only slowly;
2. It is highly lipophilic - buprenorphine is stored in body fat;
3. Enterohepatic cycling - the conjugated metabolite (glucuronide) is hydrolysed in the intestines, and reabsorbed.

Plasma levels do not correlate well with opioid activity. Despite the short duration of significant blood levels, buprenorphine has a relatively long duration of action:

- 8–12 hours for low, single doses - 4 mg or less
- up to 48–72 hours for higher, repeated doses - more than 16mg.

When administered sublingually, naloxone has a bioavailability of about 3%.

2.6.2 Dose

When used in analgesia, buprenorphine is used sublingually in doses of about 0.2–0.4mg and when used subcutaneously or intravenously, 0.3–0.6mg.

Doses used in opioid dependence are always given sublingually and should be tailored to the individual client and their response to buprenorphine. Initial dose is usually 2–8mg; most clients achieve stability with doses between 8mg and 24mg daily.[7] The recommended maximum dose is 32mg daily. It is unlikely that higher doses will give any further effect as the opioid receptors will be virtually saturated at this point. This is also the maximum dose currently approved by the Drugs of Dependence Unit in South Australia for authorities to treat opioid dependence.

Outside of pregnancy and confirmed allergy, the use of the buprenorphine requires authority approval from the Drugs of Dependence Unit.

2.6.3 Safety

Buprenorphine displays a ceiling effect in its dose-response curve, so high doses (above 16mg daily) don't have a significantly greater effect than lower doses (8–12mg). Even in overdose, clinically significant respiratory depression is unlikely. Most of the fatal overdoses reported in clinical use overseas have resulted from illicit injection of buprenorphine or the combination of buprenorphine with other CNS depressants.

Buprenorphine overdoses are difficult to reverse with naloxone. It has been suggested that doses of naloxone as high as 10mg or more may be needed.

Currently under review

2.6.4 Precipitated withdrawal

Buprenorphine has a higher affinity for opioid receptors than opioid agonists like morphine and methadone but it has a lower activity than these drugs. If enough buprenorphine is given to a person already under the influence of an agonist, the agonist will be displaced from the receptors. It is likely that the person will experience mild-to-moderate withdrawal symptoms, beginning 1-4 hours after the first buprenorphine dose and continuing for up to 12 hours. Providing no other opioids are consumed, it is unlikely that the second or subsequent doses will precipitate further withdrawal symptoms.

Precipitated withdrawal is the major concern when considering the change-over from methadone to buprenorphine. Change over from higher methadone doses should be attempted with caution, beginning with small doses of buprenorphine (see Table 2).

Table 2: Converting from methadone to buprenorphine

Last methadone dose	**Buprenorphine dose**	
	Day 1	**Day 2**
1-10mg	2mg	2-4mg
10-20mg	4mg	4-8mg
20-40mg	4mg	6-8mg
>60mg	Transfer is likely to result in significant withdrawal symptoms	

To minimise the chances of precipitated withdrawal, the initial buprenorphine dose should be taken at least 24 hours after the final methadone dose.

Warning the client about the possibility of precipitated withdrawal, how to minimise the chance of it occurring and what to do about it if it does occur, will help them to cope with any symptoms which do develop.

2.6.5 Side-effects

See also *Side-effects of opioid drugs* in section 2.4.3 pg 16.

Headache is common early in treatment, particularly if high doses are used. Treat with NSAIDs or paracetamol. In some cases the headache can persist beyond the initial stages of treatment and require a review of treatment options.

2.6.6 Precautions

Hepatic impairment

Elimination of buprenorphine may be reduced. Use a lower initial dose and titrate dose according to clinical effects. Buprenorphine is contraindicated in hepatic failure.

Pregnancy

Buprenorphine and methadone are both listed as Category C drugs by the Australian Drug Evaluation Committee (ADEC). Withdrawal symptoms may occur in the neonate at birth following exposure to methadone or buprenorphine during pregnancy, but outcomes for mother and child are consistently better from opioid substitution treatment during pregnancy than is the case with the continued use of illicit opioids. Overall methadone and buprenorphine are both effective in pregnancy. If buprenorphine is used in pregnancy the single agent preparation (Subutex®) is preferable. While the absorption of naloxone is minimal when the combination product (Suboxone®) is administered sublingually, the

Currently under review

effect of long term low level naloxone exposure on the fetus is unknown. It is recommended not to attempt transfer from methadone to buprenorphine during pregnancy because of the risk of precipitated withdrawal.[7]

Further information about dosing pregnant clients is described in section 2.9.1 pg 28).

Lactation

Contact Drugs in Pregnancy & Lactation Information Service, Women's & Children's Hospital, Telephone (08) 8161 7222.

2.6.7 Interactions

Buprenorphine is metabolised by the cytochrome P450 isoenzyme CYP3A4. Combined use with other drugs which induce or inhibit this enzyme may result in changes of plasma levels. The risk of respiratory depression in overdose is lower with buprenorphine compared to methadone and hence the risks associated with increased plasma levels due to drug interactions are lower with buprenorphine.

Opioid analgesics - treatment of a client who suffers from severe pain may be difficult due to the receptor blocking effect of buprenorphine.

Buprenorphine and naloxone combination – Suboxone®

Naloxone is added to buprenorphine to reduce the risk of the preparation being injected. Naloxone is a pure opioid antagonist which has no significant effects if administered sublingually. However if it is injected, it will attenuate the agonist effects of the injected buprenorphine for 30-60 minutes, reducing the attractiveness of injection. This decreases the value of the product on the black market and thus the risk of diversion.

2.6.8 Preparations

Subutex® sublingual tablets, available as 0.4mg, 2mg and 8mg of buprenorphine. They are packed in boxes of 7 tablets, in foil covered plastic strips. The tablets are packed under nitrogen to minimise oxidative breakdown, so do not remove from foil packaging until dose is required.

Suboxone® sublingual films contain naloxone in a ratio of 4:1 (buprenorphine to naloxone). The available strengths of Suboxone® films are 2mg/0.5mg and 8mg/2mg. These films are moisture sensitive and should not be removed from their packaging until dosing. If a film is accidentally dropped, damaged or becomes wet before being given to the client, it should be destroyed or kept for destruction and a new dose dispensed. This must comply with the legislative requirements for destruction of S8 drugs. The sachet that they are packed in is considered child resistant. The films are orange in colour with the strength printed in white (N2 or N8), and have a lime flavour.

All three strengths of Subutex® and the two strengths of Suboxone® films are listed on the Pharmaceutical Benefits Scheme as Section 100 items, for the treatment of opioid dependence in accordance with the law of the relevant State or Territory.

Buprenorphine alone in the form of Subutex® sublingual tablets is only available to be prescribed in South Australia for patients who are pregnant or have a proven allergy to naloxone. All other patients must be prescribed Suboxone® sublingual films.

A short course of treatment with the 0.4mg sublingual tablets may also be authorized for patients undergoing a slow dose taper, who cannot tolerate cessation of the last 2mg of buprenorphine as Suboxone® films should not be cut. This requires written approval by the Drugs of Dependence Unit and is generally limited to 6 weeks in duration.

Currently under review

2.6.9 Diversion

Since buprenorphine prescribing has become wide-spread in Australia, reports of diversion and misuse have become common. Take-away doses and supervised doses that are diverted may be sold or injected in an attempt to achieve a greater opioid effect.

There are significant risks associated with this behaviour which all clients should be warned about:

- clients not consuming their full buprenorphine dose are more likely to continue illicit drug use;
- injection is associated with risk of thrombophlebitis, thrombosis, local or systemic infections. The risk of infection is increased where buprenorphine tablets or film have been diverted after being held in the mouth for some time;
- diversion to other people can result in overdose (particularly when combined with other drugs). Extended exposure to illicit prescription opioids, such as buprenorphine, can result in the development of dependence in other people;
- diversion to a person on methadone or other opioids can cause them to experience precipitated withdrawal which may encourage more urgent drug seeking and more risky behaviour.

To minimise the chances of diversion and the time needed for properly supervised dosing, it is recommended that buprenorphine tablets be crushed before being given to the client. A proprietary pill crusher is suitable and the crushed tablets can be tipped into a disposable plastic spoon. Fine powder can be difficult to manage in the mouth so roughly crushed tablets are a good compromise. The client must be supervised until the powder has dissolved (about 3–5 minutes).

Suboxone® films adhere within seconds to the oral mucosa and are difficult to remove after 30 to 60 seconds, thus allowing for a shorter observation time. In situations where ongoing buprenorphine diversion is a problem, it may be necessary to transfer the client to methadone, which is more easily supervised.

2.6.10 Supervised dosing procedure for buprenorphine/naloxone film

- Prior to dosing: Advise client not to eat immediately before dosing, as it may interfere with absorption. Offer a sip of water to moisten mouth. Ensure client's hands are clean and dry as the film may stick to wet hands and make it difficult to place them correctly in the mouth.
- Collect films needed to make up dose and check against prescription. Films should not be cut-up to manipulate dose (e.g. half a 2/0.5mg film to achieve a 1/0.25mg dose). Clarify with the prescriber in such an event.
- Open all packages (cut or tear along the long side and tear across the top to make separating the foil easier) and offer the open packages to the client, who removes films from packages one at a time to place in their mouth.
- Offer 8mg films first to allow for a longer supervision period as they are thicker and require longer to adhere completely.
- Observe correct placement of films. The client should place films sublingually one at a time. If multiple films are needed, the first two are placed under the tongue either side of the frenulum, and the rest are placed onto the inside of the cheeks (although buccal administration is an off-license method of use, the bioavailability is similar for sublingual and buccal use). Advise client not to attempt to move the films once they have been placed in the mouth, nor to chew or swallow until the films are fully dissolved (generally

Currently under review

2 to 5 minutes). If films accidentally stick on top of the tongue or to the teeth, reassure the client that buprenorphine will still be absorbed and to keep the mouth closed with mucous membranes in contact with the films as they dissolve.

- Films adhere to mucous membranes within seconds and are difficult to remove within 30 to 60 seconds, so under normal circumstances, post-dose supervision does not need to exceed one minute. Discourage the client from overlapping films when placing in the mouth, as this impairs adherence to the mucosa, prolongs the time required for supervision, and increases the risk of diversion.

No active drugs will remain on the inside of the packaging under normal circumstances. Empty sachets should be discarded discretely in the normal rubbish.

2.6.11 Non-supervised buprenophine

Buprenorphine/naloxone is the preferred preparation for non-supervised or take-away doses. Film should be dispensed in their original foils and packed into a tablet box with appropriate labelling. The films are temperature and moisture sensitive; their stability cannot be guaranteed out of their original packaging.

Example labelling is shown below. Cautionary label number 1 (drowsiness) MUST be attached. Please ensure that the dates to be taken are clearly indicated.

Buprenorphine 2mg/naloxone 0.5mg (Suboxone®) .....films

Allow film(s) to dissolve under the tongue daily.

Dose for ..... (date).

Client's name .....

Date dispensed .....

Pharmacy name, address, phone .....

Keep out of reach of children

Do NOT inject. May cause death or serious injury if injected or taken by another person

Clients should be advised to store film/s in a secure, cool place below 25°C. For example, do not leave in a car's glove box on a hot day. Do not remove film/tablet from packaging until you are ready to use them. Also, the appearance of the films may be attractive to children so keep take-away doses away from reach of children.

2.8 Safety considerations for opioid substitution treatment

2.8.1 Contraindications to opioid use

- Respiratory impairment – generally opioids are contraindicated in severe respiratory depression. The risks in terms of potentially worsening lung function must be carefully weighed against the expected benefits. Buprenorphine is less risky than methadone, heroin or morphine in this situation.
- Biliary tract disorders – opioids may cause spasm of the sphincter of Oddi, raising intrabiliary pressure and exacerbating biliary disorders.
- Phaeochromocytoma – risk of pressor response due to histamine release occurs with morphine.
- Untreated raised intracranial pressure – although opioids can be used in headache due

Currently under review

to brain tumour where the potential benefits outweigh the risks.

2.8.2 Precautions to Opioid Use

- Careful titration of dose of opioids is required where there are uncorrected endocrine abnormalities, hypothyroidism, adrenocortical insufficiency, head injury, convulsive disorders, acute alcoholism, or myasthenia gravis.
- Hepatic impairment – Liver disease does not preclude use of opioids but dose adjustment may be required. Hepatic impairment is common among injecting drug users, due to excessive alcohol consumption and the large proportion infected with Hepatitis B and C.
- Prostatic hyperplasia, hypotension, shock, inflammatory or obstructive bowel disorders are conditions in which opioids should be used with caution.
- Elderly – Opioid dose requirement decreases with age due to pharmacokinetic and pharmacodynamic changes associated with ageing. Use a lower initial dose in the elderly and titrate upwards.
- Pregnancy and lactation – See section 2.9.1 pg 28.
- Labour – Opioids given during labour can cause respiratory depression in the neonate. Babies born to mothers on maintenance treatment are likely to have developed tolerance to the depressant effects of their mother's normal dose. They will still require close monitoring as they may have problems metabolising the opioid once separated from the mother's circulation.

2.8.3 Interactions with Opioids

Also see *Interactions* in section 2.5.5 pg 19.

- CNS depressants will have an additive depressant effect when used concurrently with opioids, increasing the risk of overdose. CNS depressants include benzodiazepines, non-benzodiazepine hypnotics, tricyclic antidepressants, and sedating antipsychotics and antihistamines.
- Caution is required if medications affecting methadone metabolism (hepatic CYP450 system) are to be prescribed to clients receiving methadone. Reduced metabolism of methadone may result in increased plasma levels of methadone resulting in an increased risk of overdose. Buprenorphine is also metabolised by the CYP450 system, but there appear to be fewer clinically relevant drug interactions with buprenorphine compared to methadone.
- Naloxone, naltrexone – precipitate withdrawal, or reverse toxicity when given in opioid overdose.
- Monoamine oxidase inhibitors – serious and possibly fatal reactions have occurred when pethidine has been given with MAOIs (including moclobemide and selegiline). Avoid using any opioid in patients on MAOIs or within 14 days of stopping them.

2.8.4 Overdose

Large doses of opioids produce respiratory depression and hypotension, with circulatory failure and deepening coma. Death may occur from respiratory depression. Pulmonary oedema after overdose is a common cause of fatalities among people who are opioid dependent.

Currently under review

2.9 Special cases

2.9.1 Pregnancy

Both methadone and buprenorphine are ADEC category C3. They 'have caused, or are suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible.' Opioids can cause respiratory depression and withdrawal symptoms in the newborn.

Methadone has been used extensively in pregnancy with positive impacts on pregnancy outcomes. Buprenorphine has been used in pregnancy in some limited trials with similar outcomes to methadone. The use of the combined preparation containing naloxone is not recommended (see *Precautions* in section 2.6.6 pg 23).

Special entry

Pregnant women will usually be considered for priority entry to an opioid substitution treatment program and should be referred for specialist obstetric services.

Continuing use of illicit opioids during pregnancy endangers the health of the woman and her foetus through:

- continually changing blood opioid levels;
- exposure to a diverse range of drugs and contaminants;
- infections due to injecting drug use.

Opioid withdrawal during pregnancy may induce abortion, premature labour or foetal distress particularly before the 14th week or after the 32nd week. Withdrawal is a regular feature of the lives of heroin users as they seek their next hit. Each episode puts the pregnancy at risk. Opioid substitution treatment will smooth out the highs and lows of opioid effects, so even if the mother continues to use some illicit opioids, her withdrawal is unlikely to be severe.

Due to lifestyle factors associated with opioid dependency, pregnant women in this population do not usually have adequate nutrition, necessary rest or sufficient antenatal care. Enrolling a woman in an opioid substitution treatment program will provide opportunities for interventions aimed at ensuring a relatively trouble-free pregnancy.

Opioid substitution treatment in pregnancy:

- avoids periods of drug withdrawal that may be associated with miscarriage early in the pregnancy or foetal growth retardation and stillbirth late in pregnancy
- reduces the incidence of prematurity
- reduces the incidence of intra-uterine growth retardation
- increases attendance for antenatal care.

Doses in pregnancy

During pregnancy dose requirements for opioids, particularly methadone, may increase due to several factors:

- increased volume of distribution;
- increased hepatic metabolism;
- increased glomerular filtration; or
- increased metabolism by placenta and foetus.

These factors may make any dose reduction by the pregnant woman difficult. Reductions

Currently under review

to a level at which the woman experiences significant withdrawal puts her at risk of returning to uncontrolled illicit drug use, and therefore puts the pregnancy at risk.

The increased metabolic rate can be partially counteracted by giving the daily dose of methadone in two halves (split dosing), usually one half supervised in the morning, the second half as a take-away dose to be taken 12 hours later.

As with any deviation from standard guidelines, approval for this approach should be negotiated between the client, the prescriber and the Drugs of Dependence Unit.

Pregnant women who are experiencing morning sickness may experience withdrawal symptoms because they vomit their methadone dose. In these cases, it may be necessary to split their dose or to allow the client to slowly sip her dose. In severe cases, anti-nausea drugs may be given prophylactically before methadone dosing.

Foetal Withdrawal

Some infants born to opioid-dependent women will experience withdrawal symptoms, known as Neonatal Abstinence Syndrome (NAS). The symptoms usually manifest within 72 hours of birth and commonly include agitation, restlessness and poor sleeping, but in severe cases can include vomiting, diarrhoea or convulsions. Severely affected babies may be given oral morphine solution at a reducing dose, or occasionally phenobarbitone, to help them through withdrawal.

Logically there would be expected to be a greater incidence of NAS among babies born to mothers on higher doses of methadone. However, there is no proven correlation between methadone dose at delivery and occurrence of NAS.

Opioid detoxification during pregnancy is not usually recommended. The advantages of methadone in pregnancy gained in the antenatal period should be weighed against the disadvantages encountered in the neonatal period. Evidence[10,11] suggests that substituting illicit opioids with methadone or buprenorphine during pregnancy provides the best outcome for mother and child. Some clients prefer to be drug-free at the time of delivery, but there is a risk of relapse to injecting drug use once they have withdrawn from opioids, and of potential problems with the pregnancy if they experience withdrawal process.

Breast feeding

For lactating women who are taking methadone, the medication is present in their breast milk but in small quantities. It is for this reason that women should not feel discouraged about whether or not to should breast feed her child; unless the mother's dose is more than 100mg. There is a theoretical chance of the baby experiencing some withdrawal symptoms when breast feeding ceases.

For lactating women who are taking buprenorphine, the medication is present in their breast milk in small quantities. Buprenorphine has poor oral bioavailability, thus its use is safe for a breast feeding mother.

In cases where a lactating women taking either methadone or buprenorphine is breast feeding, the infant should be monitored closely for increased drowsiness, weight gain and developmental milestones.

2.9.2 HIV/AIDS

Injecting drug use represents a risk for transmission of HIV. In the interests of public health, some providers will consider HIV-positive clients for priority entry to a maintenance program.

Currently under review

2.9.3 Prison release

There is a high incidence of opioid overdose and death in the first few weeks after release from prison. Prisoners will probably have reduced or stopped their opioid use while in prison, resulting in reduced tolerance. Therefore resumption of use at their usual dose may result in toxicity.

In response to this, a pre-release MATOD program has been instigated. More recently, MATOD programs in prisons have been extended to continue treatment of prisoners started before being sentenced and to initiate treatment for prisoners considered at risk while in prison.

For those not started in prison, an argument can be made to start them on MATOD when they are released, despite not having a current addiction. In this situation, dosing with methadone or buprenorphine must be very conservative in the initial stages.

2.9.4 Treatment of pain in MATOD clients

There is a growing body of evidence that people on opioid substitution treatments may be hypersensitive to some types of pain and do not respond well to standard analgesic doses of opioids. Also, buprenorphine will at least partially block the effect of opioids.

- In mild-to-moderate pain, non-opioid analgesics, such as paracetamol or NSAIDs are the preferred option.
- Clients suffering chronic pain should be referred to a pain clinic or specialist.
- Severe, acute pain is best dealt with by an anaesthetist or experienced pain specialist. Treatment may require large doses of opioids and possibly, sedation.

It is important for clients seeking treatment for severe, acute pain to advise the treating health professional of their maintenance program, as they may require larger than usual doses of analgesics.

2.9.5 Pain clients

There is a growing group of people who have become dependent on opioid drugs through legal treatment for painful conditions.

- In some cases the drugs prescribed have been inadequate to properly control the pain. The patient begins to obtain drugs from elsewhere, either from other doctors or from illicit sources.
- A doctor treating a person with opioids to control pain becomes alarmed at the amount of opioid needed and withholds or reduces treatment.

These clients represent a separate group from the mainstream MATOD clients. Their primary problem is judged to be the pain but their dependence is a major management problem.

They tend to be treated differently to mainstream clients, with less supervision and use of drugs which are more appropriate to pain treatment, such as slow-release preparations of morphine and oxycodone. Long-term treatment will still require approval from the Drugs of Dependence Unit.

Pain authorities vs dependence authorities

Treating drug dependence requires an authority from the State Minister (DDU) prior to commencement of the treatment; it is an offence to prescribe or supply medication for this purpose without an authority for any period.

Currently under review

In the case of a chronic physical condition, eg. pain, not dependence, it is an offence to prescribe or supply (including administering from the prescribers' own supply), drugs of dependence for regular use for a period exceeding two months without authority from the Minister. This now also includes alprazolam, which was rescheduled on the 1st of February 2014 to a drug of dependence by the Therapeutic Goods Administration (TGA).

Treatment provided by other prescribers must be considered when calculating the two-month period. Some exceptions apply i.e. for persons over 70 years of age (treated with drugs other than pethidine) and notified palliative care patients (NPCP). Please contact the DDU if you require more details. They are available during business hours on ph: 1300 652 584.

2.10 Naltrexone

Naltrexone is a long acting opioid antagonist approved for use in Australia for relapse prevention in alcohol dependence and opioid dependence. It is a PBS benefit only for the treatment of alcohol abuse and is not covered by the PBS for the treatment of opioid dependence.

In people with alcohol dependence, it has been shown to reduce relapses and to reduce the amount of alcohol consumed in each relapse.

In the management of opioid dependence, as an opioid antagonist, it blocks all the effects of opioids including analgesia, euphoria and respiratory depression. It is used as security against relapse. With regular treatment at normal doses, the blocking effects persist for a few days after stopping use. It has no effect on the craving for opioids although the recognition by the user of their lack of vulnerability may impact on perceived cravings.

Long-term abstinence relying on oral naltrexone alone is uncommon. Retention rates are low and relapse to opioid use is widespread. It has not been shown to reduce mortality rates. It is only likely to be useful for clients who are highly motivated to stop using opioids, eg. professionals whose careers depend on maintaining abstinence and those with a strong support network.

Long-acting depot preparations are undergoing clinical trials and may improve adherence to treatment and hence improved abstinence rates. Sustained release and implant preparations of naltrexone are currently not registered in Australia and remain experimental.[5]

2.10.1 Pharmacokinetics

Naltrexone is rapidly absorbed from the gastrointestinal tract but undergoes first-pass metabolism and possibly enterohepatic recycling. Peak plasma levels of naltrexone and its major metabolite, 6-beta-naltrexol, occur about one hour after an oral dose. It has a relatively short half-life of about 4 hours and 6-beta-naltrexol (which also has some opioid antagonist activity) has a half-life of about 13 hours. The opioid-blocking effect continues for a much longer period, probably up to a few days.

2.10.2 Dose

Initial dose is 25mg (half a tablet) daily; if there are no withdrawal symptoms, increase to 50mg daily. If taking naltrexone daily creates difficulties, try dosing 3 times weekly, ie. 100mg on Monday and Wednesday, 150mg on Friday.

Support is a major component of treatment for opioid users. Consider getting a friend or relative to observe administration.

Currently under review

2.10.3 Starting treatment with naltrexone for opioid addiction

It is important to ensure that withdrawal has been completed before a client begins taking naltrexone. If not, the opioid molecules will be displaced from receptors, precipitating a withdrawal syndrome which may be severe and persistent. To avoid precipitated withdrawal, delay commencement of naltrexone until at least 7 days after the last dose of a short-acting opioid or 10 days after the last methadone dose.

Short-term buprenorphine treatment allows more rapid naltrexone initiation, with initial doses possible two days after the last buprenorphine dose, or even while buprenorphine doses are still being reduced. Some withdrawal is likely in this situation.[7]

Some clinicians will administer an injected dose of the short-acting opioid antagonist, naloxone, commonly referred to as a naloxone challenge. If this dose does not produce withdrawal symptoms, then naltrexone can be safely started. An alternative is to give a small test dose of naltrexone. If there is no response to a quarter of a tablet (12.5mg) after an hour, the rest of the tablet can be taken.

Smaller doses (eg. 6.25mg) are sometimes prescribed to initiate treatment. Crushed tablets can be dissolved in water and aliquots measured out as needed. The resulting solution is likely to remain stable for at least five days.

2.10.4 Side-effects

Common side effects reported by more than 10% of patients include:

- insomnia
- anxiety
- nausea
- headache
- fatigue
- sleepiness
- hepatotoxicity (rare)

A number of clients may report transient symptoms suggestive of opioid withdrawal, including muscular aches and pains, abdominal cramps and diarrhoea. These symptoms should subside after one to two weeks.

Reduced potency and ejaculatory difficulties have also been reported.

Rare side effects include skin rashes, thrombocytopenia, and a risk of hepatocellular damage (with high doses).

2.10.5 Contraindications

- Naltrexone should be avoided in clients taking opioids for painful conditions.
- Current dependence on opioids or acute withdrawal.
- Acute hepatitis, liver failure, liver enzyme levels more than three times upper limit of normal.

2.10.6 Precautions

- Naltrexone should be ceased at least 48 hours before elective surgery, including dental procedures, which may require opioid analgesia.
- When opioid analgesia is needed in other situations, larger doses than usual will be needed, with an increased risk of respiratory depression and other adverse effects.

Currently under review

- Use with caution in cases of hepatic dysfunction. Monitor liver function (especially total bilirubin) before starting treatment, then at monthly intervals for the first 3 months, then 3 monthly.
- The safety and efficacy of naltrexone in pregnancy is not established – naltrexone is category B3 under the system established by the Australian Drug Evaluation Committee (ADEC). For more advice contact Drugs in Pregnancy & Lactation Information Service, Women's & Children's Hospital, Tel: 8161 7222.

2.10.7 Interactions

Opioid drugs: Effects are blocked by naltrexone – see above.

Disulfiram (Antabuse®): Both agents can cause hepatotoxicity. Avoid the combination.

2.10.8 Safety

Abstinence from opioids and regular dosing with naltrexone will reduce opioid tolerance. Any relapse to opioid use will expose the user to a high risk of overdose. A number of deaths due to overdose have already been reported in this group.

Clients should be advised that attempts to overcome the blockade with large doses of opioids could also result in fatal overdose. It is very important that pre-treatment counselling includes warnings about this risk and that it be reiterated at follow- up and review sessions.

2.10.9 Antagonist-induced ("rapid") withdrawal

Naltrexone has been used experimentally in a number of programs to accelerate withdrawal from opioids. This is not an approved indication so practitioners have more than usual responsibility to ensure candidates are fully informed of the risks and of alternative approaches.[5]

2.11 The treatment alliance

2.11.1 Prescriber's role

The prescriber must obtain an authority must from the Minister responsible for the *Controlled Substances Act 1984* (SA), through the Drugs of Dependence Unit to prescribe maintenance pharmacotherapy for each individual client, before the commencement of treatment. An authority is a legal document granted by delegates of the Minister for the *Controlled Substances Act 1984* (SA) (the Act). Officers at the Drugs of Dependence Unit (DDU) are such delegates. An authority, issued under Section 18A of the Act allows prescribers to treat dependence in an individual with specified drugs of dependence. An authority is not intended to provide clinical endorsement and treatment remains the responsibility of the treating health professionals. An authority under the Act is not the same as an authority issued by Medicare Australia. Medicare Australia authorities are for financial purposes and allow for subsidised supply of medications under the Pharmaceutical Benefits Scheme (PBS).

The authority to prescribe and supply Schedule 8 drugs to treat opioid dependence is granted by the Minister responsible for the *Controlled Substances Act 1984* (SA) and issued and regulated by the Drugs of Dependence Unit under Section 55 of the *Controlled Substances Act 1984* (SA).

In order to prescribe methadone or buprenorphine alone (Subutex®) for opioid

Currently under review

dependence, the prescriber must undertake special training. This will endorse them to prescribe under the rules of the Opioid Dependence Substitution Program (ODSP). A training day, exam and clinical attachment are required before the medical practitioner is considered for authorisation to prescribe methadone or buprenorphine alone. There is an ongoing review process, through the Opioid Dependence Prescriber Review Committee, to ensure that treatment standards are maintained.

Since 2011 any registered practitioner may provide treatment for opioid dependence with Suboxone® film for up to 5 clients, without any specialised training, once an authority is obtained. While this program is restricted to the use of buprenorphine with naloxone in sublingual film form, all other program policies and rules remain.

A prescriber who is to be unavailable for some time should make arrangements for a locum or another member of their practice to continue treatment of their clients in an opioid substitution treatment program. If problems arise, the Drugs of Dependence Unit should be contacted for advice.

The prescriber is expected to:

- assess drug use to determine suitability for treatment;
- obtain authorisation to prescribe prior to the commencement of any dosing;
- supply valid, legal prescriptions as required;
- communicate with pharmacists to organise supply arrangements;
- arrange transfers between pharmacies if necessary;
- withdraw or terminate clients from the program as appropriate.

2.11.2 Client's role

To access referral or treatment services, Alcohol and Drug Information Service (ADIS) provides a telephone counselling and information service for the general public:
Tel: 1300 13 1340, 8.30am-10pm, 7 days per week

The service offers:

- information and publications on alcohol, illegal drugs and some prescription drugs;
- counselling and professional assistance in helping you deal with and understand your own or another's problem with alcohol or other drugs; and
- referral options if ongoing assistance is required.

ADIS is the first point of contact for drug users and concerned others seeking assistance with alcohol and other drug problems. Clients should initially contact who will carry out an initial assessment by phone and arrange an appointment for a more comprehensive assessment. The assessment procedure will:

- determine the course of action best suited to an individual's situation (eg. inpatient or outpatient withdrawal, substitution treatment, counselling);
- identify priority issues that need to be addressed;
- give advice about safer drug use practices; and
- provide referrals where appropriate.

Assessments may also be carried out by DASSA community workers located in metropolitan or country areas.

MATOD clients are expected to:

- comply with program rules and contracts;

Currently under review

> act towards treatment providers and other clients with respect; and

> ensure in-date script maintained for treatment.

A sample client/pharmacy contract can be found in Appendix 3 pg 57.

Client perspective: the treatment journey

On average, MATOD clients are getting older; in 2013, 11% were less than 30 years of age, down from 28% in 2006, and 19% were 50 years or more, up from 8% in 2006. In both 2013 and 2006, 69% of MATOD clients were aged between 30 and 49 years.[2] Around two-thirds (65%) of MATOD clients are male, and almost one in 10 (9%) clients identify as Aboriginal or Torres Strait Islander people.

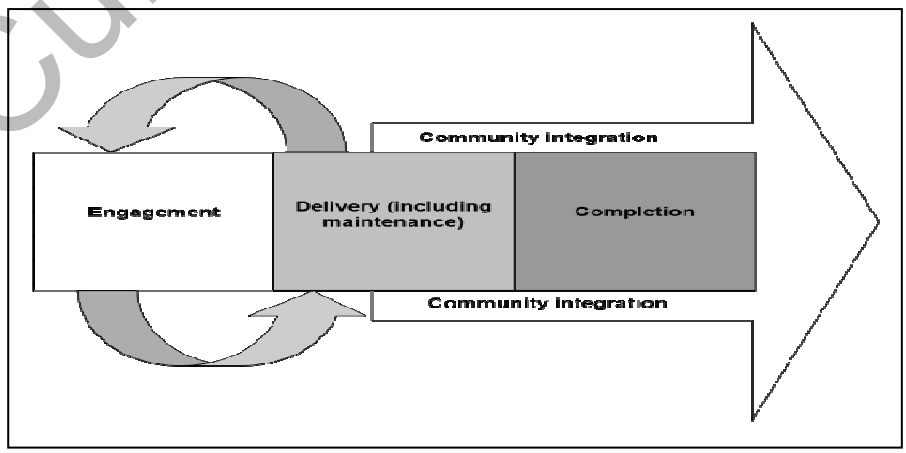
Dependent alcohol and other drug users may express a strong desire to be abstinent but remain ambivalent about treatment and about ceasing use. As the negative consequences of alcohol and drug dependence escalate, the individual becomes increasingly conflicted about continuing use. This conflict will move some individuals to contemplate and take action to change their behaviour. Drug users commonly present for treatment when they are in crisis.

Clinical experience and research have repeatedly demonstrated that motivation to remain abstinent is often short-lived. There is strong evidence that longer-term treatment is associated with a greater likelihood of long-term abstinence than are shorter periods of treatment. Stability and consequent improvements in drug use and psychosocial stability gained as a result of opioid substitution treatment tend to become significant after three months of treatment, or more, with the majority of benefit gained after one year (benefits may be sustained beyond this point with continued treatment). However this is seldom what clients or their families wish to hear at the time of entering treatment.

The chronic relapsing nature of drug dependence, and individual variability in personal circumstance indicates a need for services that are sufficiently varied and flexible to respond to the needs of patients, their severity of dependence, personal circumstance, motivation and response to interventions, and that will support their progression through the different stages of behavioural change.

As treatment progresses, patient needs change making it necessary to continually assess and modify an individual's treatment and services plan. Furthermore, treatment journeys are not linear (see Figure 3), but there is progression through stages with relapses common[12]. An individual may require varying combinations of services and treatment components during the course of treatment and recovery from drug dependence.

Figure 3: The treatment journey



Currently under review

2.11.3 Pharmacist's role

Dispensing and administration of maintenance pharmacotherapy drugs must be carried out by a pharmacist, not delegated to an assistant. All pharmacists involved in the program are expected to have a thorough understanding of the use of methadone and buprenorphine in dependence treatment.

The pharmacist is expected to carry out a number of duties including the following:

- ensure positive identification of the patient before administering a dose. Refer to the patient's photograph or photographic identification;
- check for messages which may have been received from the prescriber;
- examine the prescription to verify the dose and to ensure the prescription is in-date;
- prepare the dose as authorised by the prescriber;
- determine that it is safe to administer a dose:
    - determine when the previous dose was administered, contacting the previous dosing point when necessary;
    - do not dose if three or more consecutive days have been missed (for clients on daily dose) or missed two consecutive doses (for clients on alternate daily dose) and contact the prescriber;
    - assess the client for signs of possible intoxication and withhold dose and contact prescriber if there are signs of intoxication;
- ensure the dose is consumed with minimal possibility of diversion:
- for methadone, observe that the client takes the dose, and have the client speak to demonstrate that they swallowed the dose;
- for buprenorphine, ensure the dose has dissolved under the tongue or that films have been placed sublingually, adhered and not stacked;
- ensure the prescriber is advised of irregularities in a client's attendance, behaviour or condition. Fill out an incident form if this is required to document events. It is recommended to take a pro-active role in your interaction with MATOD prescribers;
- ensure the necessary information is readily available to all pharmacists. Ensure client records, records of administration and details of communications with the prescriber are clearly and consistently maintained. Also, ensure MATOD program guidelines are readily available for reference.

Refer to the Standard Operating Procedure (Appendix 7 on page 66) and the following chapter for further details on pharmacist responsibilities.

Currently under review

Chapter 3. Pharmacist responsibilities

3.1 Dosing clients

Pharmacists should dose clients in a discreet manner, preferably away from mainstream customers. Clients must not be allowed to enter the dispensary. Pharmacists who intend to specialise in MATOD would be well advised to make suitable modifications to the pharmacy to facilitate safe and confidential dosing.

3.1.1 Supervised dosing

The primary basis of MATOD is supervised dosing. With health and lifestyle improvements, non-supervised doses may be introduced after some time but it is vital that doses prescribed to be supervised are supervised properly, to ensure that the client is remaining compliant with the program.

A pharmacist dosing a client with MATOD must be satisfied that all supervised doses are actually being consumed by the person intended, at the time intended. To ensure this, certain precautions should be taken.

- Dose one person at a time. Don't allow others to approach the dosing area until you are satisfied that the dosing has been completed appropriately.
- For methadone, make sure the client speaks before leaving the dosing area. This is to ensure that the dose is not held in the mouth and then transferred to a hidden container. Diluting the dose with water or another liquid can be useful if there are any doubts on this point.
- Do not allow the client to drink from their own container immediately after taking the methadone dose. The cup containing the methadone dose should be rinsed out at least once, using either water or another drink and then should be discarded.
- For buprenorphine tablets, crush tablets and ensure that the client remains in the dosing area for 3-5 minutes.
- For buprenorphine film, watch the placement of films carefully, don't allow them to turn away, fold the film or stack them on top of one another. Films should be spread around the mouth, with the first two under the tongue and others on the cheeks. Providing a mirror may help with placement. Make sure the client speaks before leaving the dosing areas as compromised ability to speak may be an indication of possible diversion.
- Do not allow clients to place films on the teeth, as they can be easily removed later. Stacking or rolling of film into a lump by an individual's tongue can also reduce absorption.
- A client who demonstrates changed behaviour, seems nervous, or reluctant to speak or who mumbles, may be trying to divert; in particular, they may have extraneous material in their mouth to shield the film from the saliva (eg. plastic wrap in the cheeks to prevent adhesion) or even false teeth to hide films in.
- Film dosing, requires monitoring of the client for 30-60 seconds after placement of films; pharmacist should be vigilant during this process.
- Do not delegate dosing to pharmacy assistants, students or unsupervised interns.
- Any dose not consumed under supervision is considered a take-away dose. In

Currently under review

exceptional circumstances a prescriber may, with approval from the Drugs of Dependence Unit, agree that some doses be collected for later consumption, in excess of normal take-away restrictions.

> Another person will not normally be allowed to collect a client's dose. The Drugs of Dependence Unit and the prescriber would need to approve any such arrangement.

There may be situations whereby the pharmacy is requested to prepare doses for clients to receive their supervised dose in custody. South Australian Police Officers are considered Authorised Officers under Section 50 of the *Controlled Substances Act 1984* (SA), authorising them to transport and store controlled substances in accordance with policies and procedures of SAPOL. This includes obtaining methadone or buprenorphine from a pharmacy for supply to patients within SAPOL holding cells. This would be considered as a supervised dose. The standard regulations around not replacing doses, client missed doses, intoxication and appropriate recording all need to be considered before supplying any medication. Medication needs to be clearly labelled as outlined above and any unused medication must be returned to the pharmacy to prevent extra take-away doses being given. Provide only the minimum necessary number of doses as a client will usually only be in police custody until they appear in court. A pharmacist can supply medication only if they believe it is in the best interest of the client. Pharmacists are encouraged to record the officers' details in the pharmacy records and provide some guidance on supervision, and possible adverse outcomes ie. intoxication, diversion, allergy.

3.2 Non-supervised or takeaway doses

All doses of drugs used to treat addiction should be supervised, in order to allow assessment before dosing and to minimise harm from drug diversion, abuse and overdose. The gradual introduction of non-supervised doses can be a valuable reward for treatment progress (see Table 3).

The rules governing the prescribing and dispensing of non-supervised (take-away) doses are set out below.

1. All new admission patients should complete their first month at a seven-day pharmacy wherever possible.
2. Unstable patients should continue at a seven-day pharmacy to prevent access to take-away doses.
3. Take-away doses must be handed directly to the patient unless prior approval has been granted by the Drugs of Dependence Unit for an agent to collect the drug.
4. Take-away introduction schedule:

> No take-away doses may be supplied during the first two months of treatment. Non-supervised doses are allowed on Sundays and public holidays at six-day pharmacies.

> For the first nine months of treatment, the take-away allowance must not exceed six doses per month at seven-day pharmacies or two doses per month plus Sundays & public holidays at six-day pharmacies.

> For the period nine to eighteen months, the take-away allowance must not exceed twelve doses per month (three per week) at a seven-day pharmacy or eight doses per month plus Sundays and public holidays at six-day pharmacies.

> After eighteen months, and with evidence of lifestyle improvement and abstinence from

Currently under review

unsanctioned drug use, take-away doses may be increased gradually. There must be a minimum of three supervised doses per week for methadone or two supervised doses per week for buprenorphine.

5. The maximum number of take-away doses to be given at one time should not exceed *four* consecutive days' doses for methadone or *five* consecutive days' doses for buprenorphine.
6. Regardless of daily dosing, second or third day dosing (buprenorphine) or missed doses there must be a minimum of *three* supervised doses per week for methadone or *two* supervised doses per week for buprenorphine, unless prior approval has been given by the Drugs of Dependence Unit.
7. All take-away doses for methadone must be diluted (methadone liquid dispensed for non-supervised dosing should be diluted to a volume of: 100mL for doses above 25mg of methadone and 50mL for doses of 25mg methadone or less).
8. Patients must be advised to provide adequate security to prevent theft, loss or damage of take-away doses. Requests for replacements should be refused and access to future take-away doses reviewed.
9. Pharmacists should report to the medical practitioner with regards to:

> missed doses for those clients on daily dosing, if they have missed 3 consecutive days (or more than ten days in a 30 day period),

> missed doses for those clients on alternate doses, if they have missed 2 consecutive doses (or 5 doses in a 30 day period)

> if the client presents intoxicated

> if they have any concerns about the client's treatment.

When considering take-away privileges, it is important to first consider the amount of supervised doses the patient must have. Also, take-away doses should be immediately preceded by a supervised dose. I.e. a patient has their supervised dose and asks for multiple take-aways, the client should not be back into the pharmacy until the next supervised dose is scheduled. Clients are not to change the day that their take-aways are consumed once supplied. Pharmacists should not take returns of take-aways not even if they are to be supplied on a different day to the same client.

Note: Increased take-away privileges may be authorised for going away on holiday; the DDU will provide written verification to the prescriber in this case.

Currently under review

Table 3: Restrictions on unsupervised (take-away) methadone and buprenorphine dosing

	Dosing at a **six-day** pharmacy		Dosing at a **seven-day** pharmacy	
Month	daily dosing	alternate day dosing buprenorphine	daily dosing	alternate day dosing buprenorphine
1	**ZERO** take-away doses (except Sundays & public holidays) Seven-day pharmacy if possible	**ZERO** take-away doses (except Sundays & public holidays) Seven-day pharmacy if possible	**ZERO** take-away doses	**ZERO** take-away doses
1 to 2	**ZERO** take-away doses (except Sundays & public holidays)	**ZERO** take-away doses (except Sundays & public holidays)	**ZERO** take-away doses	**ZERO** take-away doses
3 to 9	**SIX** take-away doses/month	**THREE** take-away doses/month	**SIX** take-away doses/month	**THREE** take-away doses/month
10 to 18	**12** take-away doses/month	**FIVE** take-away doses/month	**12** take-away doses/month	**FIVE** take-away doses/month
> 18	**METHADONE** **18** take-away doses/month	**SEVEN** take-away doses/month	**METHADONE** **18** take-away doses/month	**SEVEN** take-away doses/month
	BUPRENORPHINE **22** take-away doses/month		**BUPRENORPHINE** **22** take-away doses/month	

3.2.1 Policy for six non-supervised doses per week

Some clients that have been on the program for many years may be entitled to increased take-away doses, under strict circumstances. These clients may be entitled to six non-supervised doses per week with the requirement to have one weekly supervised dose. Both the prescriber and pharmacist must support the application for such a request. Each member of the team must complete an application form and forward to the DDU for consideration (available on the SA Health web site). The DDU will write to both the pharmacist and prescriber if approved. The DDU may refuse an application where concerns are held for the client, community, or other particular members of the public.

Admission criteria for one supervised dose per week:

1. The client must be under the care of an Accredited Prescriber. Clients treated through the Suboxone® Only Substitution Program are ineligible (non-accredited prescribers).
2. The client has consulted one medical practitioner and one pharmacy continuously for a minimum of six months.
3. Three random urinalyses have been conducted, with Gas-Chromatography Mass-Spectrometry (GCMS) confirmation for all substances including norbuprenorphine, buprenorphine, and oxycodone. Samples must be separated by two to six weeks over the previous 6-12 months, confirming stability and absence of unsanctioned drug/substance use. If there have been other urinalyses conducted during this time results must also demonstrate stability and absence of unsanctioned drug/substance use. Results of three urinalyses are to be submitted to the DDU by the medical practitioner along with the application form.
4. The client's initial contact/enrolment in an opioid pharmacotherapy program was ten or more years ago. If treatment was initially interstate, confirmation is required.

Currently under review

5. The client has been maintained continuously on an opioid pharmacotherapy program for five or more years in the community setting. If treatment was initially interstate, confirmation is required. Treatment within correctional settings exceeding two months does not contribute to the five year period. Opioid pain treatment is excluded when calculating the five year period.
6. The client is maintained on buprenorphine with naloxone or a daily methadone dose of less than 100mg. Split-dosing of methadone is not permitted unless an application is made to and approved by the DDU. Buprenorphine without naloxone is not permitted unless the client becomes pregnant.
7. There have been no reports or allegations of lost, stolen or damaged prescriptions or doses.
8. There have been no reports or allegations of diversion or drug misuse.
9. There have been no reports of criminal activity, and the client's social circumstances are stable.
10. The client is engaged in employment or other meaningful activity (eg. volunteering, active-parenting).
11. The client has verifiable financial support.
12. The client's use of prescribed medicines is stable.
13. There is no unauthorised use of potentially hazardous or illegal substances or drugs (e.g. alcohol, benzodiazepines, over-the-counter analgesics, cannabis, or heroin etc.).
14. The client has signed a valid agreement for release of their personal information held by Medicare Australia and the form has been submitted to that Commonwealth agency.

Criteria for continuation of one supervised dose per week:

- There is a continuous absence of intravenous drug use, unauthorised drug use or hazardous substance abuse, including alcohol consumption.
- Continued satisfaction of all admission criteria.
- A short break in treatment, not exceeding two months, will not adversely affect continued access to six non-supervised doses per week providing all other criteria is fulfilled.

3.2.2 Split dosing

Split dosing or twice daily dosing of methadone (where the second dose is not supervised) is considered a take away dose and requires written authorisation from the Drugs of Dependence Unit.

It may be required:

- in pregnancy during the 3rd trimester due to faster metabolism. In this case the prescriber will be reluctant to increase the dose due to possible effects on the foetus, so splitting the dose 50:50 or 70:30 can overcome this problem;
- in people who are ultra-rapid metabolisers. Kinetic studies must be undertaken to demonstrate a methadone half-life of less than 14 hours in that client;
- a patient with acute pain may, under special circumstances, require split dosing. Although methadone can maintain therapeutic blood levels and prevent withdrawal symptoms for 24 hours, multiple daily doses may be required to provide analgesia for 24 hours. In a small number of patients experiencing acute pain, split methadone doses

Currently under review

may be required for one to two weeks. Application to the Drugs of Dependence is still required.

3.3 Valid prescription

It is an offence under the *Controlled Substances Act 1984* (SA) to dispense any drugs of dependence without a valid and current prescription. An initial MATOD prescription should be accompanied by photographic identification. All prescriptions for drugs of dependence, including methadone liquid and sublingual buprenorphine products must satisfy all the requirements listed in Regulation 34 of the *Controlled Substances (Poisons) Regulations 2011* (SA) prior to dispensing including:

- name, address and date of birth of client;
- signed in the prescriber's own hand;
- contact number and details for the prescriber;
- the maximum total quantity of drug to be dispensed, in words and numerals;
- the maximum number of doses to be given
- a prescription starting date and expiry date;
- instructions for daily administration under supervision with number of non-supervised doses if allowed; and

It is the client's responsibility to ensure they have a valid prescription. Prescribers are not permitted to, nor should they be expected to, back-date prescriptions to include doses dispensed against an out-of-date prescription. It is unlawful to dispense on an expired prescription.

Any variation in conditions (e.g. additional supply of non-supervised doses) must be authorised in writing by the Drugs of Dependence Unit. Pharmacists do not have the authority to permit additional take-away doses.

If a client wishes to transfer to another pharmacy they must obtain a replacement prescription from their prescriber. MATOD prescriptions should not be handed back to clients. They must be retained by the pharmacy and sent to the Drugs of Dependence Unit with the monthly Schedule 8 (S8) prescription return. Prescriptions should be dispensed through the usual dispensary software to record the prescription and get a serial number for the S8 return.

3.3.1 Interstate Scripts

Interstate scripts are valid as long as they fulfil all legal requirements. They do not need to be authorised by the South Australian DDU, but the pharmacist does need to verify the legitimacy of the script by contacting the prescriber as well as the interstate DDU equivalent.

There is no time limit on temporary interstate transfers, but a maximum of four weeks is suggested due to a lack of medical supervision. This should give the client sufficient time to organise a local prescriber if they wish to extend their stay.

If you are unsure please contact the South Australian DDU on 1300 652 584 or DrugsofDependenceUnit@health.sa.gov.au

Currently under review

3.3.2 Replacement of methadone liquid or sublingual buprenorphine products or doses

Some clients may attempt to obtain additional supplies of drugs to replace doses they claim to have lost. Reasons given may include:

- vomiting their dose;
- non-supervised/take-away doses being lost or stolen;
- take-away doses being confiscated by the police; or
- spilt or leaking take-away containers.

Replacement doses cannot be supplied under any circumstances unless the client's prescriber provides an additional prescription and accompanying letter from the Drugs of Dependence Unit authorising the further supply. Missed doses cannot be supplied at a later date.

3.4 Recording

It is recommended that a separate record is maintained for each client so all necessary information is readily available to the administering pharmacist when the client attends. Separate records, for example in drop-folders, can help ensure that information relating to one client is not visible to others. Avoid large, bold lettering of client's names on the covers of folders that might be visible to other customers, and keep documents out of public sight.

The current prescription and client photograph should be readily available. It is recommended that these be prominently located in the client records.

The client should sign, date and record the time of dosing to confirm receipt of each dose, including take-away doses, on a Pharmacy Attendance Sheet. The pharmacist must also countersign to confirm the identity of the dispenser as well as record the exact dose given. For signing sheet template examples, see *Dispensing Paperwork* in Appendix 6 on pg 66.

The dispensing pharmacist must maintain a separate record showing the exact quantity of each drug dispensed. Depending on client numbers and circumstances, this may be a computerised record or a daily or weekly recording sheet. Record sheets should be tallied regularly (daily, or at least, weekly) and corresponding entries made in the S8 drugs register. Normally the dose will be recorded in milligrams, with a conversion to millilitres for completion of the Controlled Drugs Register.

The Controlled Drugs Register must be balanced at least monthly in line with legal requirements, but it is good practice to calculate a balance every time an entry is made. This requires pharmacists to physically measure the amount of methadone remaining in the safe, including opened bottles or counting the actual number of films. Dosing records must be retained for two years.

Currently under review

3.5 Storage in the pharmacy

The Therapeutic Goods Administration schedules drugs and poisons federally and lists methadone and buprenorphine as a Schedule 8 poison. Methadone and buprenorphine are drugs of dependence, and must be stored in an approved safe. Keep the bottle in use in a secure location and return it to the safe when it is no longer being used and overnight. Details of storage requirements can be found in the Code of Practice for the Storage and Transport of Drugs of Dependence (www.sahealth.sa.gov.au)

3.6 Returns to the drug of dependence unit

Prescriptions for all drugs of dependence must be forwarded to the Drugs of Dependence Unit monthly prior to the 7th day of the following month

The return must include:

- a photocopy or duplicate of all prescriptions for drugs of dependence including those with repeats
- a true copy of the original prescriber's prescription is required, ie. a photocopy, not a copy of a repeat authorization; if a methadone/buprenorphine prescription is valid for more than one month, a copy must be sent in each month that it is valid (not just when the prescription expires)
- any schedule 4 pseudoephedrine prescriptions.

Each prescription forwarded must have all the original information from the prescription. Pharmacies are also requested to send an electronic monthly return. Details can be found on the SA Health website or contact the Drugs of Dependence Unit for further instructions.

3.7 Transferring between pharmacies

The prescriber or other responsible health worker must be included in discussions of transfers between pharmacies. A new script is required when clients transfer to a new pharmacy. Any outstanding issues involving money owed to the original pharmacy should be resolved before agreeing to a transfer.

3.8 Confidentiality

The stigma attached to drug addiction and its treatment makes confidentiality a very important issue. Pharmacists are governed by a professional responsibility and duty of care under common law, statutory law and codes of professional practice. Pharmacy staff should be informed of their obligations and the rights of all clients and customers to privacy. Provision of information to any other person without the client's express permission could result in civil action or a charge of professional misconduct.

However, not communicating in circumstances where health or safety could be compromised is also a cause for concern. For this reason, as a requirement for obtaining an authority prescription, clients agree when entering into the treatment program that communication between health professionals involved with their care is permitted when in the interest of their health and/or safety.

Currently under review

3.9 Lawful disclosure

In some circumstances, disclosure may be required by law. Ensure that legal documents demanding information are authentic. Tell the client about the disclosure.

3.9.1 Investigators

Police and officers authorised by the Minister responsible for the *Controlled Substances Act* (SA) have powers to examine and seize documents in certain circumstances. Officers will produce documentation and will explain their powers. Sections, 50, 51 & 52 of the *Controlled Substances Act 1984* (SA) has full particulars.

Information about a specific client under investigation may also be released at the discretion of the pharmacist as long as they can justify their reasons and maintain records about those reasons. Reasons may include a perceived danger to the client or the general public.

3.9.2 Solicitors

Solicitors acting for a client will produce the client's written consent for the provision of any information about that client or their treatment. Solicitors acting for other parties will provide the client's written consent or a subpoena.

3.9.3 Criminal behaviour

Pharmacists involved in maintenance programs retain the right to inform the police of any suspected illegal behaviour involving clients, including threats, shop stealing, drug diversion and drug dealing.

3.9.4 Child protection

Pharmacists are mandated notifiers of child abuse. This means that a failure to report suspected physical or mental abuse or general neglect of any child may have legal and professional repercussions. Reports should be made to the Family and Youth Services Child Abuse Report Line (Tel: 131 478). The identity of the informant is kept confidential.

3.9.5 Research

Client permission is needed for the disclosure of any information for research purposes. The bona fides of a research project should be confirmed before cooperation and information is provided. Legitimate research projects must be approved by an ethics committee to ensure the client's interests are not compromised.

3.10 Preventing problems

It is possible to run a successful MATOD program in a community pharmacy. Some pharmacists report concerns with having to deal with difficult clients or difficult situations. However, with planning, staff training and consistency it is possible to run a program with minimal difficulties.

At the initial visit, provide clients with information about their medication, how it is to be administered as well as outline the details of your client/pharmacy contract. It is recommended to provide the client with a copy of the signed client/pharmacy contract. These other strategies may assist in preventing problems or miscommunication:

- Each point on the agreement should be explained fully prior to treatment commencement.

Currently under review

- All infractions should be pointed out and the appropriate action taken.
- Address problems as they arise to build an understanding of acceptable behaviour.
- Provide reminders when required.
- Be consistent with all clients to ensure fair treatment amongst all clients.
- Do not allow credit, unless you are willing to deal with unpaid debts.
- Ensure all pharmacy staff are conversant with procedures set for the program management, particularly to the adherence of client privacy.

3.10.1 Contracts

It is strongly recommended that a contract be signed by each new client before they commence opioid substitution treatment dosing at a pharmacy (see Appendix 3 pg 57 for suggested client/pharmacy contract template).

The contract should cover such details as:

- the fee charged, payment schedules and credit policy (if applicable);
- what constitutes unacceptable behaviour and the consequences of such behaviour;
- an understanding that medically relevant information may be communicated to the prescriber or to other medical staff involved in the client's care; and
- the important elements of the dosing procedure (e.g. methadone doses being diluted).

3.10.2 Response to client intoxication

Most opioid-related overdose deaths occurring in opioid substitution treatment clients are the result of a combination of drugs being taken. While a pharmacist cannot control what their client does after being dosed, they should be confident that the client is not intoxicated state at the time of being dosed.

Intoxication is impairment from a substance which can be observed such as unsteadiness, slurred speech, excessive sleepiness, uncharacteristic garrulousness or occasionally, irritability and aggression (refer to Table 4 for more details).

A client who presents in an intoxicated state should not be given a dose. This is one of the issues which should be made absolutely clear at the time of commencement. Intoxication suggests that either their dose is excessive or that they have taken another drug. In either case it would be dangerous to give them a potent drug like methadone or buprenorphine.

- In all cases the prescriber should be contacted and then a decision made if the client needs to go back to their prescriber for a review.
- A severely intoxicated client should always be referred to a hospital emergency department for assessment, or if they refuse, arrangements made for a responsible person to look after them.
- In cases of mild or moderate intoxication the client could be advised to return either later that day, or the next day, to be dosed.
- There are many medical conditions which may resemble intoxication, such as head injuries, hypoglycaemia or acute hepatic failure. They all require urgent assessment by a doctor.

Currently under review

Recognising symptoms of intoxication

Assessment of intoxication is a specialist subject best handled by experienced professionals; however, gross intoxication is usually obvious to any casual observer. The most common symptoms likely to be noticed with the main drugs of concern are detailed in Table 4 below.[5]

Table 4: Signs of intoxication and overdose

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, alprazolam, flunitrazepam)	Disinhibition Sedation Drooling Incoordination Slurred speech Lowered blood pressure Dizziness	Stupor/coma Ataxia Confusion Respiratory depression
Stimulants (e.g. 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 inflammation	Paranoid psychosis Confusion Agitation Anxiety/panic Hallucinations

Currently under review

Breath Alcohol Levels (BAL)

An increasing number of pharmacies have breath alcohol testing machines to be used with their MATOD clients. These can be useful if a client has a concurrent alcohol dependence problem.

In the case of a client having significant tolerance to alcohol it may be difficult to tell from their behaviour or appearance how much they have had to drink. An alcohol dependent person may appear normal even with a very elevated BAL (may not appear intoxicated). There is also no specific BAL which indicates that there will be a dangerous interaction with their dose and it is difficult to determine what level (if any) is safe. One patient will be

able to tolerate far more than another.

Due to this uncertainty, if a prescriber has specifically requested that BALs be taken and a positive reading is returned, regardless of whether the patient appears intoxicated or not, the prescriber should be contacted to determine the action to be take. Any client who registers three positive readings within a week (or 10 in a month) should be referred back to their doctor for review. This would be easiest to monitor if recording of BALs is on the client signing sheet. Clients who require BALs are not recommended to have alternate day dosing.

It is not considered standard practice to alcohol test MATOD clients unless requested by the doctor. If you have reason to think a client is alcohol affected, the safest option is to report the intoxication and not rely on a breath alcohol level to try and decide on their level of intoxication.

If a previous prescription has requested BALs be done prior to dosing, but it is not requested in a new prescription, continue with regular testing, and check with the prescriber regarding their intentions.

3.10.3 Response to missed doses

Pharmacists should not dose clients and contact the prescriber in the following situations:

- for clients on daily dosing, if they have missed 3 consecutive doses (or missed ten days in a 30 day period),
- for clients on alternate doses, if they have missed 2 consecutive doses (or 5 doses in a 30 day period.

In either case, dosing should only continue on the explicit instructions of the prescriber.

Pharmacists should also report to the prescriber when a client has missed a large number of consecutive doses and has appeared to cease the program (eg. a week of dosing). Otherwise a prescriber may not become aware that a client has ceased the program until the client misses a medical appointment, which could be up to three months later.

3.10.4 Response to diversion

In all cases of suspected diversion, attempted diversion or confirmed diversion, the pharmacist should report the incident to the prescriber and the Drugs of Dependence Unit. An incident report form is available from the Drugs of Dependence Unit directly or from their website (http://www.sahealth.sa.gov.au/drugsofdependence).

Diversion includes not consuming the dose to the complete satisfaction of the dispensing pharmacist, as well as supplying a take-away dose to another person. Clients are required to consume their medication as prescribed.

Fraudulent changes to the prescriptions, such as change of dose, change in the number of takeaways or impersonating the prescriber to change dispensing arrangements, is a serious breach and is considered confirmed diversion. Fraudulent changes to the prescription must be reported to the Police in addition to the prescriber and the Drugs of Dependence Unit.

3.10.5 Response to behavioural problems

A client may become aggressive for a variety of reasons and it is important to deal with this effectively and defuse the situation to avoid losing control. Building a good relationship with the client reduces the chances of such behaviour occurring. Remain

Currently under review

client-oriented and try to address the problem. If you don't feel your safety is at risk, escort the client to a quiet area away from other customers and staff to defuse the situation. Do not try to resolve major issues at times of stress as this may inflame the situation.

Next time the client presents, try to address the issue of expected behaviour. Serious or repeated incidents should be reported to the prescriber or caseworker. You are not expected to tolerate unacceptable behaviour and such incidents may be grounds to withdraw from your contract to supply methadone/buprenorphine. If you perceive a genuine threat, do not hesitate to call the police or to seek other advice from either DASSA or the DDU. The Drugs of Dependence Unit should also be informed of serious offences and an official report form can be obtained from the Unit or from their website.

Personality disorders

A significant percentage of the drug-using population can be characterised as having a personality disorder. The presence of such a condition suggests that they may have difficulties in interpersonal relationships. Treatment for these people is usually a long-term project, involving behavioural containment and support rather than pharmacotherapy alone.

Personality disorders are rigid, inflexible, maladaptive patterns of behaviour, of sufficient severity to cause significant impairment in functioning or internal distress. They are lasting and persistent styles of behaviour and thought, not atypical episodes.

Clients with personality disorders can often exhibit impulsive 'acting out' behaviours, which may be a learned response to earlier abuse or trauma. They may assume certain roles, which may prompt other another person to take a complementary role (eg. you can be either the rescuer or the persecutor to their victim).

These people will often seek prescribed or illicit drugs in an attempt to:

> alleviate the symptoms of the disorder;

> improve feelings of low self-esteem;

> decrease feelings of guilt; or

> improve feelings of diminished individuality;

3.10.6 Dispensing errors

Dosing errors could go undetected before possible harmful effects develop because the dose is normally consumed immediately after being measured (or counted). It is essential that procedures are in place to minimise the chances of errors occurring. Dispensing errors and other incidents should be reported to the prescriber.

Overdoses

Unintentionally giving a client a higher dose than prescribed is a real cause for concern. However, in most cases, prompt action will avoid any long-term consequences. Suspected errors should be reported as soon as possible to the client and to the prescriber. The level of the overdose and the client's known tolerance to opioids will determine the action to be taken. Advice should be sought from ADIS Tel: 1300 13 1340, or from one of the DASSA clinics (see *Contacts* in Appendix 2 pg 55).

An overdose of less than 50% of the usual dose given to a client who is opioid-tolerant has a low risk of causing problems. In the absence of obvious symptoms, the client should be advised to ask a responsible adult to stay with them for up to six hours after the dose. This person should be made aware of the symptoms of overdose (especially

Currently under review

excessive drowsiness, vomiting, and shallow breathing) and advised to seek medical attention if these symptoms occur.

Clients with an uncertain level of tolerance, or clients showing signs of intoxication following a large overdose (greater than 50% of usual dose) require immediate admission to hospital for observation and for treatment if needed. If the client loses consciousness, an ambulance must be called. Intoxication may be reversed with the emergency administration of naxolone by intravenous or intramuscular injection. Because of the long action of methadone and buprenorphine, this procedure is likely to have to be repeated, or an infusion given in hospital. If respiration ceases CPR should be commenced *immediately*, pending the arrival of the ambulance.

Under-doses

A single episode of under-dosing is unlikely to have severe consequences due to the long action of methadone and buprenorphine. Continued under-dosing may cause the client to experience withdrawal symptoms, which may cause them to seek other opioids to relieve these symptoms. A loss of opioid tolerance may also develop over time, potentially causing toxicity if the correct dose is then resumed.

Avoiding Errors

- For methadone, one of the most common, and potentially dangerous, sources of error is the milligram–millilitre confusion. Clients may not recognise the distinction and talk about 'mills' meaning milligrams. Doses on prescriptions and in records should be expressed in milligrams or in both milligrams and millilitres. There have been numerous instances of five-times dosing errors causing serious complications arising from this confusion.
- Failure to notice dose changes on a prescription and simply continuing dosing at the same dose level. It is important to check the prescription each time a dose is supplied. A day book or diary can be used to record such changes and to pass on important information to other staff.
- Ensure that proper identification including an authorised photograph is included in each client's record card.
- If you have clients with similar names or a client is on a large or unusual dose, attach a warning note to their records.

3.10.7 Communication with locum pharmacists

A source of possible problems arises if locums employed in a pharmacy are not practiced in dosing maintenance clients. It is the regular pharmacist's responsibility to ensure that:

- important issues relating to particular clients are clearly set out in a written form, preferably in the client's record folder or book;
- relevant paperwork is up-to-date and unambiguous;
- instructions for using measuring devices are accessible;
- phone numbers of prescribers are accessible; and
- there is access to the Standard Operating Procedure for Pharmacists Dispensing Methadone/Buprenorphine (see Appendix 7 pg 66).

3.10.8 Communication with other health professionals

Circumstances that suggest a problem with a client's treatment include:

- changes in mood or behaviour, like agitation, aggression, depression;

Currently under review

- rapid weight changes;
- presenting intoxicated;
- obtaining prescriptions for psychoactive drugs from other prescribers;
- attempted diversion of doses; or
- non-attendance or erratic attendance.

This type of information, which may have a bearing on the safety of clients or others, should be reported to the prescriber, preferably with the client's consent, but if necessary, without their consent.

3.10.9 Managing pharmacy payment

Methadone and buprenorphine are supplied free of charge to pharmacies for clients on an approved maintenance program, under the Section 100 Scheme with the Commonwealth Department of Health and Ageing. They are not part of the general Pharmaceutical Benefits Scheme. At present there is no mechanism for pharmacists to be reimbursed for their time, expertise and the expenses involved in running a maintenance program. This expense is the direct responsibility of the client. Charges should be agreed upon before the client begins at a new pharmacy and specified in the client/pharmacy contract. Many pharmacies charge a particular fee per day or per dose, with an extra charge for take-away doses to cover containers and labels. Others charge a flat weekly rate and give discounts for payment in advance. Payment for doses are a subject between the client and their pharmacist.

Problems have been encountered when clients have been allowed credit by their well-meaning pharmacists. Once the client is in arrears, it is very difficult to rein it in. Soon the debt becomes unmanageable, leaving the pharmacist with a choice of either refusing to dose the client or simply waiving the debt. It is suggested that once a debt reaches $30, further action should be taken.

Public program clients who are in this position should be referred back to the prescribing clinic, who will attempt to negotiate a fair conclusion. As a last resort, the client will be dosed at a DASSA clinic but will have their dose reduced until they are off maintenance treatment or have repaid the debt. If the debt is not repaid, further treatment will not be provided. It is the policy of the public program that clients are not allowed to transfer between pharmacies while they owe money for MATOD to the original pharmacy.

Clients of private prescribers should be referred back to their prescriber. Private clients do not have the option of being referred back to DASSA pharmacy dosing sites.

It is recommended that pregnant clients do not have their dose reduced or refused for financial reasons. If there is a financial problem with a pregnant client, please refer them back to their prescriber immediately to make suitable arrangements.

3.10.10 Prescriptions for other drugs

Pharmacists have the right, and indeed a professional obligation, not to dispense a prescription if they think it may present a danger to the client. If a client presents a prescription for a medication that may potentiate the effects of their MATOD drug, written by another prescriber, it is the pharmacist's responsibility to contact both prescribers to inform them of the interaction. When a client is issued an authority to receive MATOD they are informed that they must not consult other doctors with the aim of obtaining other opioids or drugs that may potentiate their MATOD. For further professional guidance, contact the Drugs of Dependence Unit or the authorised prescriber.

Currently under review

Currently under review

Appendix 1: Glossary of terms and abbreviations

Abstinent	Drug-free or alternatively free of the substance seen as a problem.
Agonist	A substance which stimulates or activates the receptor to which it attaches to produce an effect.
Antagonist	A substance which does not activate or stimulate the receptor to which it attaches and prevents agonists from attaching and activating the receptor.
CNS	Central nervous system
DASSA	Drug and Alcohol Services South Australia
Detox	Detoxification - See Withdrawal
DH	Department of Health
Dysphoria	Unpleasant sensations, opposite of euphoria.
GI	Gastrointestinal
Gynaecomastia	Abnormal increase in the size of the male breast.
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
Hydromorphone	a morphine alkaloid – C17H19NO3 – which has narcotic analgesic effects similar to, but greater and of shorter duration, than those of morphine
MATOD	Medication-assisted treatment for opioid dependence is becoming widely used internationally as indicating the use of medication and psychosocial support in combination
Metabolites	Any substance produced by metabolism or by a metabolic process
Non-holder	Usually used in reference to people maintained on methadone. A person who experiences opioid withdrawal symptoms each day before their daily methadone dose.
NSAID	Non-steroidal anti-inflammatory drug
Opiate	Drug derived or manufactured from the sap of opium poppy e.g. heroin, morphine, codeine.
Opioid	Drug which has actions similar to opium. Includes synthetic drugs like methadone, buprenorphine and pethidine.
Opioid receptors	Central and peripheral drug receptors responsible for the opioid effects of drugs. They have been classified into numerous subtypes, the most important of which is the mu (μ) receptor.
OST	Opioid substitution treatment" refers to medication-assisted treatment using opioid agonists (methadone, buprenorphine).
Partial agonist	A substance, which has low intrinsic activity at the receptor, causing a lesser effect on cellular function. Examples of partial agonists (at the mu receptor) include pentazocine and buprenorphine.

Currently under review

PBS	Pharmaceutical Benefits Scheme
PCP	Phencyclidine, an analgesic and anaesthetic used in veterinary medicine. Used for its dissociative hallucinogenic effects.
Poly-drug use	Using/abusing multiple psychoactive drugs.
Precipitated withdrawal	Withdrawal symptoms initiated when opioid agonist drug molecules are displaced from the receptors of someone dependent on opioids.
Psychosocial	Related to a person's mental health, social status and functional capacity within a community.
Receptor affinity	How tightly a drug binds to a receptor. Drugs with high affinity bind very tightly to the receptor, taking precedence over other drugs with lower affinity.
Relapse	Return to regular use of a substance after a period of abstinence; in contrast to a lapse used to refer to a single use after abstinence.
SROM	Slow release oral morphine
Suicidal ideation	Thinking of suicide, as opposed to a suicidal gesture which may be a non-serious suicide attempt.
Withdrawal	The adjustment by the body to the lack of a substance which it has become accustomed to. May be accompanied by physical or psychological symptoms.

Currently under review

Appendix 2: Contacts

Drugs of Dependence Unit

PO Box 6 Rundle Mall SA 5000
Tel: 1300 652 584 Fax: 1300 658 447
Monday to Friday 9am-5pm

Drug and Alcohol Services South Australia

Community Pharmacy Program

On SA Health website:

www.sahealth.sa.gov.au/DASSAprograms

This website has information about:

> pharmacy legislation, guidelines and resources;

> incident reports;

> privileged circular access;

> pharmacy training; and

Enquiries to: HealthDASSAPharmacyEnquiries@sa.gov.au or Tel: 8130 7500

DASSA Central Service

92 Osmond Terrace, Norwood SA 5067
Tel: (08) 8130 7500 Fax (08) 8130 7575

Central Service will relocate to new premises on 18 April 2016
91 Magill Rd, Stepney SA 5069
Tel: (08) 7425 5000 Fax: (08) 7425 5015

Ask for Duty Counselling if you need assistance with a patient enquiry.

DASSA Southern Service

209 Main South Road, Morphett Vale SA 5162
Tel: (08) 8325 8111 Fax: (08) 8325 8177

DASSA Northern Service

22 Langford Drive, Elizabeth SA 5112
Tel: (08) 8252 4040 Fax: (08) 8287 0050

Information services

Drug & Alcohol Clinical Advisory Service (DACAS)

Phone (08) 8363 8633

Available 24 hours a day 7 days a week, for clinicians seeking advice on management of their patients with alcohol and drug related problems. If you have any concerns after hours, and can't contact DASSA clinics or the community prescriber, then this service can provide advice.

Alcohol and Drug Information Service (ADIS)

Tel: 1300 13 1340 toll free

> 8:30am to 10pm, 7 days per week

> confidential alcohol/drug advice and information telephone service

> for general public and health professionals

> confidential counselling, assessment and referral service

Currently under review

Health Services

Drugs in Pregnancy or Lactation
Women's & Children's Hospital General Enquiries: Tel: (08) 8161 7000
email: druginfo@mail.wch.sa.gov.au

Prison Opioid Substitution Program

> Yatala Labour Prison – Tel: (08) 8343 0288

> Northfield Women's Prison – Tel: (08) 8343 0145

> Adelaide Remand Centre – Tel: (08) 8216 3246

> Corporate office- Tel: (08) 7002 3100

Family and Youth Services

Child Abuse Report Line Tel: 131 478

Crisis Care Tel: 131 611

Family Drug Support

Tel: 1300 368 186

Mental Health Service

Mental Health Triage Service Tel: 131 465

Poisons Information Line

Tel: 13 11 26

Intravenous drug misuse

Hepatitis SA

Info and Support Line for Hepatitis B or C Mon-Fri 9am-5pm

Tel: 8362 8443 or 1300 437 222 (regional callers), Web: www.hepatitissa.asn.au

Address: 3 Hackney Rd, Hackney, SA 5069

> Information and support

> Community information sessions

> Support groups

> Advocacy

Needle Clean Up Hotline

Tel: 1300 13 1340 (SA only, local call fee)

A state-wide service for people to report incidents of needles and syringes found in public places.

Arrangements for collection of discarded needles and syringes are made as soon as possible. Advice is also available on how to dispose of needles and syringes and how to deal with needle stick injury.

Currently under review

Appendix 3: Client/pharmacy contract

Client Name: .....

Welcome to the Opioid Substitution Treatment Program at .....

We hope that our association will be a positive experience for all involved and that you will achieve a successful outcome.

Pharmacy information

Opening hours: .....

Dosing hours: .....

Payment schedule: .....

Credit policy: .....

Your safety

Medications have the ability to effectively treat medical conditions but using more than one drug may be harmful. While receiving methadone or buprenorphine, taking other drugs (ie. alcohol or tranquilisers) can be extremely dangerous, and in some cases fatal.

Medication will not be dispensed, if in the opinion of the duty pharmacist you:

- Present as apparently intoxicated or behaving as if under the influence of alcohol and/or other drugs.
- There is a reasonable concern that misuse of the medications is likely to occur, in which case treatment may be held or withdrawn.

Agreement

- To ensure continuity of treatment I am required to pay for my treatment.
- It is my responsibility to ensure that the pharmacy has a valid, in-date prescription for dispensing.
- No dose of methadone or buprenorphine will be replaced unless authorized by my prescriber and the Drugs of Dependence Unit.
- I will need to personally contact my prescriber if I would like to request additional take-away doses.
- Pharmacists have an obligation to report any breaches of this contract or other concerns to my prescriber.

Attendance

- The substitution treatment program is a supervised dosing program and regular attendance is required.
- I am required to consume my dose within the pharmacy and in clear view of the dispensing pharmacist.
- I need a current prescription and a photograph of me certified by my prescriber, or photographic ID before a dose can be administered.
- If for any reason I am unable to attend during dosing hours, I understand that I will have to miss that day's dose.
- If I miss three consecutive doses (for daily dosing) or two consecutive doses (for alternate daily dosing), then a further dose may not be administered without being reviewed by my prescriber.

Currently under review

Communication with prescriber

The pharmacist will inform my prescriber and/or any other health professionals involved with my health care treatment if they have any concerns about my welfare or conduct. This may include:

- Getting prescriptions for medications which may affect my treatment not written by my regular prescriber.
- Suspected diversion.
- Drug dealing.

Conduct

I can expect to be treated in the same manner as any other customer. Abusive, disruptive, threatening or violent behaviour is unacceptable and may result in the cancellation of my treatment and/or police involvement.

Take-away doses

Prescribers may authorize take-away doses only for those clients who have demonstrated a reduction in their drug use and some positive changes to their lifestyle.

- I will take responsibility for storage of take-away doses by securing them in a locked cupboard that is inaccessible to children — NOT in the fridge.
- Take-away doses may be cancelled if I fail to attend regularly for supervised doses or attempt to divert any doses.
- Take-away doses are my responsibility and cannot be replaced.

Methadone administration

I must drink my methadone as per prescription and within the state guidelines. It is my responsibility to satisfy the duty pharmacist that I have swallowed my dose by:

- drinking my dose in front of the duty pharmacist;
- speaking to the duty pharmacist immediately after swallowing my dose.

Administration of buprenorphine tablets

I must take my medication as per prescription instructions and within the state guidelines. It is my responsibility to satisfy the duty pharmacist that the crushed tablet/s has dissolved by:

- placing my crushed dose under my tongue;
- waiting until the duty pharmacist says I may leave the pharmacy.

Administration of buprenorphine/naloxone film

I must take my medication as per prescription instructions and within the state guidelines. It is my responsibility to satisfy the duty pharmacist that the films have been placed appropriately under my tongue by:

- ensuring that the films have not been stacked;
- waiting until the duty pharmacist says I may leave the pharmacy.

I have read the Client/Pharmacy Contract, understand its contents and will comply with the agreement. If I fail to comply with the agreement I understand that the pharmacist has an obligation to report any breaches of this contract or other concerns to my prescriber and that my treatment may be terminated.

Client's name: .....

Signature:..... Date:.....

Address: .....

Telephone:..... Mobile: .....

A copy of this contract should be retained by both the pharmacy and the client

Currently under review

Appendix 4: Measuring methadone liquid

Pumps

For most pharmacies with more than one or two clients on methadone, a pump is the best option for accurate dose measurement.

Interpath Services
Tel: 1800 626 369

Syringes

Disposable 10 mL or 20 mL syringes with a cannula are a cheap alternative to pumps in pharmacies with only a few clients. Disposable syringes are reasonably accurate, unbreakable, cheap and easily replaced.

Conical measures

Do not measure accurately enough for methadone doses and should not be used.

Pipettes and autopipettes

Tend to be set for smaller quantities than usual methadone doses, are expensive and delicate.

Currently under review

Appendix 5: Detection time for selected drugs in urine

Times are estimates only. Detection times for an individual may vary with specific drug, dose and metabolism, and will also depend on the sensitivity of the test used.

DRUG	**TIME**
Alcohol	4-24 hours
Amphetamine-type substances including amphetamine, methamphetamine, ecstasy (MDMA)	3-4 days
Benzodiazepines Prescription dose, short acting (eg. Temazepam) Longer acting (eg. diazepam) High level abuse	 3-5 days 1-2 weeks 6 weeks
Cannabis One time use Three times a week Daily use Very heavy use (several times a day)	 2-3 days 2 weeks 2-4 weeks 4-6 weeks (up to 12 weeks)
LSD	2-3 days
Heroin Specific metabolite (monoacetylmorphine) As morphine	 12-24 hrs 2-3 days
Hydromorphone	1-2 days
Psilocybin (Magic Mushrooms)	24 hours
Methadone Single or infrequent use Daily use	 3-4 days 1-2 weeks
Buprenorphine Single use Daily use	 1 week 4 weeks
Propoxyphene Metabolites	2-3 days 3-6 days
Codeine	1-2 days
Barbiturates (eg. phenobarbitone)	2-3 weeks
Cocaine	1-5 hrs
Cocaine metabolites	2-4 days
PCP (phencyclidine)	1 week
Ketamine	2-3 days
Gamma-hydroxybutyrate (GHB)	24 hours

Currently under review

Appendix 6: Dispensing paperwork

Methadone calculator for methadone 5mg/mL liquid

mg	mL		mg	mL		mg	mL
1	0.2		51	10.2		101	20.2
2	0.4		52	10.4		102	20.4
2.5	0.5		52.5	10.5		102.5	20.5
3	0.6		53	10.6		103	20.6
4	0.8		54	10.8		104	20.8
5	1.0		55	11.0		105	21.0
6	1.2		56	11.2		106	21.2
7	1.4		57	11.4		107	21.4
7.5	1.5		57.5	11.5		107.5	21.5
8	1.6		58	11.6		108	21.6
9	1.8		59	11.8		109	21.8
10	2.0		60	12.0		110	22.0
11	2.2		61	12.2		111	22.2
12	2.4		62	12.4		112	22.4
12.5	2.5		62.5	12.5		112.5	22.5
13	2.6		63	12.6		113	22.6
14	2.8		64	12.8		114	22.8
15	3.0		65	13.0		115	23.0
16	3.2		66	13.2		116	23.2
17	3.4		67	13.4		117	23.4
17.5	3.5		67.5	13.5		117.5	23.5
18	3.6		68	13.6		118	23.6
19	3.8		69	13.8		119	23.8
20	4.0		70	14.0		120	24.0
21	4.2		71	14.2		121	24.2
22	4.4		72	14.4		122	24.4
22.5	4.5		72.5	14.5		122.5	24.5
23	4.6		73	14.6		123	24.6
24	4.8		74	14.8		124	24.8
25	5.0		75	15.0		125	25.0
26	5.2		76	15.2		126	25.2
27	5.4		77	15.4		127	25.4
27.5	5.5		77.5	15.5		127.5	25.5
28	5.6		78	15.6		128	25.6
29	5.8		79	15.8		129	25.8
30	6.0		80	16.0		130	26.0
31	6.2		81	16.2		131	26.2
32	6.4		82	16.4		132	26.4
32.5	6.5		82.5	16.5		132.5	26.5
33	6.6		83	16.6		133	26.6
34	6.8		84	16.8		134	26.8
35	7.0		85	17.0		135	27.0
36	7.2		86	17.2		136	27.2
37	7.4		87	17.4		137	27.4
37.5	7.5		87.5	17.5		137.5	27.5
38	7.6		88	17.6		138	27.6
39	7.8		89	17.8		139	27.8
40	8.0		90	18.0		140	28.0
41	8.2		91	18.2		141	28.2
42	8.4		92	18.4		142	28.4
42.5	8.5		92.5	18.4		142.5	28.5
43	8.6		93	18.6		143	28.6
44	8.8		94	18.8		144	28.8
45	9.0		95	19.0		145	29.0
46	9.2		96	19.2		146	29.2
47	9.4		97	19.4		147	29.4
47.5	9.5		97.5	19.5		147.5	29.5
48	9.6		98	19.6		148	29.6
49	9.8		99	19.8		149	29.8
50	10.0		100	20.0		150	30.0

Currently under review

Biodone Forte® Client Record

Client: .....

Month: .....

Takeaways: .....

Script expiry:.....

Dr:.....

Date	Time	Client's Signature	Payment	Dose (mg)	Vol. (ml)	Pharm Initial
1st						
2nd						
3rd						
4th						
5th						
6th						
7th						
8th						
9th						
10th						
11th						
12th						
13th						
14th						
15th						
16th						
17th						
18th						
19th						
20th						
21st						
22nd						
23rd						
24th						
25th						
26th						
27th						
28th						
29th						
30th						
31st						
			Total			

Currently under review

Methadone Syrup® Client Record

Client: .....

Month: .....

Takeaways: .....

Script expiry:.....

Dr:.....

Date	Time	Client's Signature	Payment	Dose (mg)	Vol. (ml)	Pharm Initial
1st						
2nd						
3rd						
4th						
5th						
6th						
7th						
8th						
9th						
10th						
11th						
12th						
13th						
14th						
15th						
16th						
17th						
18th						
19th						
20th						
21st						
22nd						
23rd						
24th						
25th						
26th						
27th						
28th						
29th						
30th						
31st						
			Total			

Currently under review

Suboxone® Film Client Record

Client: .....

Month: .....

Takeaways: .....

Script expiry:.....

Dr:.....

Date	Time	Client's Signature	Payment	Dose (mg)	Films (buprenorphine/naloxone)		Pharm Initial
					2mg/0.5mg	8mg/2mg	
1st							
2nd							
3rd							
4th							
5th							
6th							
7th							
8th							
9th							
10th							
11th							
12th							
13th							
14th							
15th							
16th							
17th							
18th							
19th							
20th							
21st							
22nd							
23rd							
24th							
25th							
26th							
27th							
28th							
29th							
30th							
31st							
			Total				

Currently under review

Subutex® Tablet Client Record

Client: .....

Month: .....

Takeaways: .....

Script expiry:.....

Dr:.....

Date	Time	Client's Signature	Payment	Dose (mg)	Tablets			Pharm Initial
					0.4mg	2mg	8mg	
1st								
2nd								
3rd								
4th								
5th								
6th								
7th								
8th								
9th								
10th								
11th								
12th								
13th								
14th								
15th								
16th								
17th								
18th								
19th								
20th								
21st								
22nd								
23rd								
24th								
25th								
26th								
27th								
28th								
29th								
30th								
31st								
			Total					

Currently under review

Appendix 7: Standard operating procedure for pharmacists

Identify client
Check client name and photo ID

↓

Check prescription
Check the prescription is valid and its expiry date

↓

Check last recorded dose
Check the last recorded supervised or take-away dose and any communication notes

↓

Dispense supervised dose

Intoxication
If client is noticeably affected by alcohol and/or drugs, withhold dose and contact prescriber

Missed doses
1 to 2 consecutive missed doses (for clients on daily dosing regimen): Dose as per prescription, provided not intoxicated
3 or more consecutive missed doses (for clients on daily dosing regimen): Do not dose. Refer to prescriber.
2 or more consecutive missed doses (for clients on alternate daily dosing): Do not dose. Refer to prescriber.

dispensing methadone or buprenorphine

METHADONE	BUPRENORPHINE	BUPRENORPHINE/NALOXONE
1. Check the methadone dose in mg or ml. 2. Measure the dose into a clean disposable cup. 3. Observe ingestion of dose, followed by water, cordial or another drink provided by the client – provided this is also drunk from the methadone cup. 4. Ensure the client has demonstrated to the pharmacist that the entire dose has been taken, by showing the empty cup and speaking clearly. 5. Cup to be disposed of and not taken from the pharmacy by the client.	1. Check Subutex® dose. 2. Count tablets out into the pill crusher. 3. Crush buprenorphine dose (unless otherwise authorised on the prescription) using a pill crusher into a granule-like texture. 4. Tip the crushed tablets into a plastic spoon or cup. 5. Observe the dose being placed under the tongue. 6. Supervise the client (at the pharmacy premises) for 3-5 minutes or until medication has been satisfactory absorbed.	1. Check Suboxone® Film dose. 2. Count out the required number of Films. 3. Open all packages along two sides and offer opened package to the client to be individually placed in the mouth, starting with 8mg films first. 4. Clients should hold the films by their edge and place the first two under the tongue and the rest around the cheeks, they should not be stacked. 5. Supervise the client for 1 minute post dose.

Dispense take-away dose

More than 4 take-away doses of methadone or 5 take-away doses of buprenorphine a week requires approval from the Drugs of Dependence Unit (DDU). To verify whether additional take-aways have been approved, contact the DDU.

METHADONE	BUPRENORPHINE
Check the methadone dose in mg or ml Take-away doses of methadone must be in a child-resistant bottle with a pharmacy dispensing label "Do Not Inject" and No.1 precautionary label. Methadone should be diluted unless special exemption applies. • If dose > 25mg, dilute to 100ml • If dose < 25mg, dilute to 50ml Dilute Methadone Syrup® with diluent and Biodone Forte® with purified water	Check Subutex® tablet or Suboxone® Film dose. Do not interchange Subutex (buprenorphine) and Suboxone (buprenorphine with naloxone). Take-away doses of buprenorphine must be dispensed in original manufacturers foil packaging into a box/container with a pharmacy dispensing label and No.1 precautionary label.

Recording requirements

Record the date, total dose or amount of tablets/films and any take-away doses entitlement supplied. Client must sign record.

Record dose or amount of tablets/films in each strength given in Schedule 8 drugs of dependence register.

Submit monthly Schedule 8 prescription return to DDU by the 7th day of the following month. If the prescription is still valid at the end of the month, send a copy and retain the original.

CONTACTS FOR FURTHER ADVICE OR ASSISTANCE

Private prescribers: Ensure prescribers work hours and contact numbers are up to date

Drugs of Dependence Unit (DDU)
1300 652 584 (9am-5pm Monday-Friday)

Drug and Alcohol Clinical Advisory Service
(08) 8363 8633 (24 hours)

Alcohol & Drug Information Service (ADIS)
1300 13 1340 (8.30am-10pm 7 days)

Currently under review

Appendix 8: Quality Care Pharmacy Program (QCPP) Checklist for pharmacists dispensing methadone or buprenorphine

Completing this checklist will allow pharmacists to self-evaluate their procedures and resources to dispense methadone, buprenorphine and buprenorphine/naloxone

1. Essential skills, resources and requirements

☐ Completion of specific training in opioid pharmacotherapy

☐ Participation in ongoing training in areas of substance abuse and treatment

☐ Maintain a current copy of the Guidelines for South Australian Pharmacists dispensing Medication Assisted Treatment for Opioid Dependence (MATOD)

☐ Maintain and follow a written procedure for dispensing and dosing opioid substitution treatment

☐ Have reviewed legislative, therapeutic and resource content on the SA Health, Community Pharmacy Program website including the Drugs of Dependence Unit's documents: www.sahealth.sa.gov.au/DASSAprograms

☐ Maintain accessible contact details of other referral and advice services

☐ Notebook or diary to record communication with other pharmacists, prescribing medical practitioners, case managers, pharmacists or other relevant healthcare workers

2. Appropriate equipment and pharmacy structure

☐ Discreet area within the pharmacy to permit clients to consume their supervised dose (not in the dispensary)

☐ Measuring pump or other appropriate measuring device for methadone which is serviced and maintained

☐ Disposable cups for administering methadone

☐ Drinking water (clients must not supply their own drinking liquid)

☐ Child-resistant methadone take-away bottles

☐ Tablet crusher and disposable spoon for buprenorphine tablets (if prescribed)

☐ Appropriate diluent or purified water for Methadone Syrup® or Biodone Forte® respectively

☐ Drugs of Dependence safe for storage of methadone and buprenorphine

3. Recording and reporting requirements

☐ A signed agreement with each client, to ensure they understand their obligations and rights for participating in the program

☐ Client signing sheets to record receipt for supply of supervised and take-away doses

☐ Daily or weekly recording sheets for methadone, buprenorphine and buprenorphine/naloxone; to be tallied and entered into the Schedule 8 register

☐ A recording system that has contact details of prescribers and other relevant health professionals

☐ Drugs of Dependence Registers for methadone, buprenorphine and buprenorphine/naloxone, to be tallied at least once a month.

Currently under review

Appendix 9: References

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Currently under review