THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH AND SOCIAL WELFARE

MEDICALLY ASSISTED TREATMENT FOR OPIOID DEPENDENCE

A Clinical Guide For Zonal And Regional Referral Hospitals




Dar es Salaam, May 2010

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FOREWORD

In recent years, opiate misuse in Tanzania has increased substantially. The misuse of heroin has not only increased, but its route of use has changed, from almost exclusively by smoking to high rates of intravenous use. Heroin misuse is associated with rapid development of dependence that has enormous socio-economic and health consequences, including employment problems, family disruptions, legal complications, as well as high risk of HIV infection, especially among those injecting drugs. WHO evidence, local data and that from other African countries, show a strong association between injecting drug use (IDU) and HIV infection. About 30% of HIV infections in sub-Saharan Africa and up to 80% of cases in some countries in Eastern Europe and central Asia, is associated with injecting drug use.

Despite limited data to characterize HIV among IDUs in Tanzania, there is evidence of high rates of both injecting and non-injecting drug use and the emergence of HIV among drug-using populations. The emerging epidemic of HIV among injecting drug users, presents challenges to act quickly to prevent further spread of HIV. Epidemics of HIV among IDUs, have been characterized by rapid and explosive growth, sustained high prevalence and geographic spread over time, from the epicentre to other regions within the country.

Development of this clinical guide is timely and is in line with the National Strategy for Growth and Poverty Reduction (MKUKUTA) and the vision 2025, the National Health Policy 2007, Health Sector Strategic Plan (HSSP) III 2009-2015, National Primary Health Service Development Strategy (2007-2017 -known in its Kiswahili acronym as MMAM), Mental Health Policy Guideline 2006, National Guidelines for the management of HIV and AIDS and the Non-Communicable Diseases Strategy - 2008.

The treatment of heroin dependence, can help the drug user have an opportunity to see his or her problems from a different perspective, improve his/her self-reliance, empower the individual to seek and effect life changes, improve self-esteem and give realistic hope. In most cases, treatment is a long term program that aims not only to reduce or stop opioid use, but also, to improve the health and social functioning of the patient, thus avoid more serious consequences of opioid use.

Methadone assisted therapy is available in Tanzania, and is designed to provide relief by reversing the acute symptoms of heroin withdrawal. It is being piloted in Dar es Salaam, to develop local experience. Symptomatic treatment, using simple medicines like promethazine and diazepam, will now be found in the guide for screening and brief intervention of substance misuse, at level one health care setting, and will be combined with on-going counselling sessions. Thus improve the health and social wellbeing of the patients. Scaling up the recently introduce pilot project of MAT in Dar es Salaam will eventually increase the chances of wider coverage in the country, thus improve accessibility of these services and reduce the burden of drug addiction in Tanzania..

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ABBREVIATIONS

AA	Alcoholic Anonymous
ADHD	Attention-deficit hyperactivity disorder
AIDS	Acquired immune deficiency syndrome
ARVs	Antiretroviral Therapy
CD4	Cluster of differentiation 4
CSAT	Center for Substance Abuse Treatment
DSM IV-TR	Diagnostic and Statistical Manual, Fourth Edition, Text Revision
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
MAT	Medically Assisted Treatment
NA	Narcotic Anonymous
NAS	Neonatal abstinence syndrome
TB	Tuberculosis

DEFINITIONS OF TERMS

Aftercare	Is the follow-up care provided after a medical procedure or treatment programme.
Brief Intervention	Is the process of applying screening tools to identify a disorder and give feedback as well as brief advise
Co-morbidity	Coexistence of psychiatric and medical conditions or diseases
Detoxification	Is a pharmacological management of substance
Drug overdose	The use of any drugs in such an amount that exceed therapeutic limit and cause harm to the users
Opiates	Any of a group of alkaloids derived from opium poppy (*Papaver somniferum*) such as morphine and codeine, including their derivatives, such as heroin.
Opioid	A generic term applied to opiates and their synthetic analogues, with actions similar to those or morphine, in particular the capacity to relieve pain
Pharmacology	Study of the effects of the drugs on the body (pharmacodynamics), and the effect of the body on the drugs such as absorption, metabolism, distribution, and excretion (pharmacokinetics).
Pharmacotherapy	treatment by using pharmacological drugs
Poly-substance dependence	Dependent disorders caused by more than one drugs
Psychosocial interventions	Therapeutic intervention that uses cognitive, behavioural, behavioural and social supportive interventions to relieve pain or condition
Screening	Screening is a preliminary assessment that indicates probability that a specific condition (e.g. alcohol use) is present.
Withdrawal Symptoms	Symptoms that occur to a dependent individuals when there is a reduction drugs in the body

EXECUTIVE SUMMARY

The clinical guidelines for medically assisted treatment for opioid dependence in Tanzania describes clinical steps for detoxification and maintenance of opioid dependent individuals using methadone and buprenorphine treatment. The document is divided into four main chapters which include introduction, intake procedures, treatment procedures and special considerations for specific groups and settings.

Introduction; This chapter introduces the problem of opioid dependence and its effects and describes opioid dependence as a chronic relapsing medical condition. It also states the purpose of the guide, methods to increase effectiveness of MAT services and what is recorded and how to keep those records.

Intake procedures: The chapter provides step by step procedures for screening, assessment and diagnosis for opioid dependence and associated medical conditions; criteria for inclusion and exclusion from MAT services; treatment planning, treatment options and ethical consideration during treatment. Health care providers obligations are also highlighted.

Treatment Procedures: The pharmacology, induction, stabilization, maintenance and withdrawal from methadone and buprenorphine is described in this chapter. Issues of urine screening and considerations of some special clinical situations such as missed doses, Vomited doses, split doses, overdose, frequency of visits, length of treatment and how to deal with remandees and incarcerated individuals is discussed. Furthermore, the need for psychosocial services in conjunction with MAT services is stressed.

Special Considerations for specific groups and conditions: This chapter considers how to manage people with specific conditions such as patients with HIV/AIDS, hepatitis and TB; Adolescents, Women and especially those with pregnancy or breastfeeding, the newborns, people with psychiatric co-morbidity , poly-substance dependence, people using other drugs that increase overdose with methadone or buprenorphine or those using drugs that do not increase overdose with methadone or buprenorphine and patients with acute and chronic pain

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CHAPTER 1

1 INTRODUCTION

1.1 Background Information

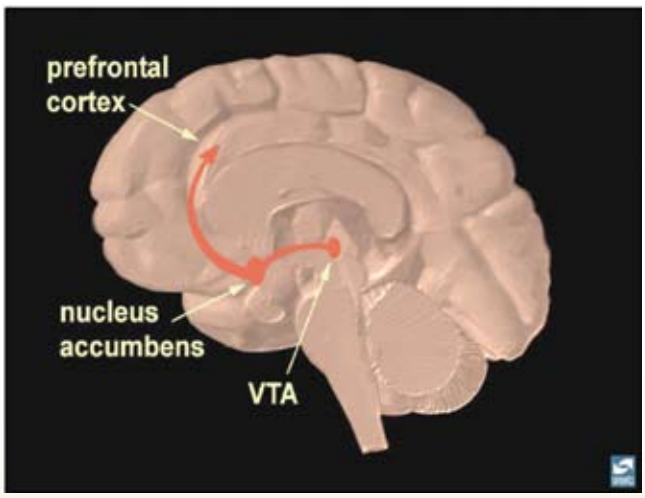
1.1.1 Opioid Dependence

Opioid dependence is characterised by a cluster of cognitive, behavioural and physiological features. The international classification of Disease (IDC-10) identifies six features:

- Strong desire or sense of compulsion to take opioids
- Difficulties in controlling opioid use
- Physiological withdrawal state
- Tolerance
- Progressive neglect of alternative pleasures or interests because of opioid use
- Persisting with opioid use despite clear evidence of overly harmful consequences

1.1.2 Neurobiology of opioid dependence[1]

When heroin, oxycodone, or any other opioid is taken, it travels through the bloodstream to the brain and attach to specialized proteins, called *mu* opioid receptors, on the surfaces of opioid-sensitive neurons (brain cells). The linkages of these chemicals with these receptors triggers the brain process that reward people with feeling of pleasure. One of the brain circuits that is activated by opioids is the mesolimbic (midbrain) reward system. This system generates signals in a part of the brain called ventral tegmental area (VTA) that result in the release of the chemical dopamine (DA) in another part of the brain, the nucleus accumbens (NAc). This release of DA into the NAc causes feelings of pleasure. Other area of the brain creates a lasting record or memory



1 NIDA (2002) Research Reviews – The Neurobiology of Opioid Dependence: Implication for Treatment

that associates these good feelings with the circumstances and environment in which they occur. These memories, called conditioned associations, often lead to the craving for drugs when the abuser reencounters those circumstances and/ or environments.

Repeated exposure to escalating dosages of opioids alters the brain so that if functions more or less normally when the drugs are present and abnormally when they are not. Two clinically important results of this alteration are opioid tolerance (the need to take higher and higher dosages of drugs to achieve the same effects) and drug dependence (susceptibility to withdrawal symptoms). Withdrawal symptoms occur only in patients who have developed tolerance leading to daily drug use to avert the unpleasant symptoms of drug withdrawal. The intensely dysphoric withdrawal symptoms from opioid include watery eyes, runny nose, yawning, sweating, diarrhoea, increased blood pressure, chills, cramps and muscles aches which can last up to seven days or longer.

1.1.3 Opioid Dependence as a Medical Condition[2]

Historically, opioid dependence was often seen as a disorder of willpower, reflecting poorly on the character of an individual. However, with recent advances in the understanding of the biological mechanisms behind dependence and its implications, it has now been widely accepted that, regardless of the reasons for opioid use, the neurological changes that occur with opioid dependence constitute a brain disorder. Therefore, opioid dependence is considered as a medical condition, with complex sociological and individual determinants.

1.1.4 Treatment of Opioid Dependence

Treatment of opioid dependence is a set of pharmacological and psychosocial interventions aimed at reducing or ceasing opioid use, preventing future harms associated with opioid use and improving quality of life and well-being of the opioid-dependent patient. Treatment of drug dependence can serve a multiple of purposes. Beyond reductions in drug usage, it can help the drug user to see his or her problems from different perspective, improve self-reliance, and empower the individual to seek and effect changes in their life; it can even confer self-esteem and give hope. In most cases, treatment will be required in the long term or even throughout the life. The aim of treatment services in such instances is to not only reduce or stop opioid use, but also to improve health and social functioning and to help patients avoid some of the more serious consequences of drug use.

1.3 Purpose of these guidelines

These guidelines are developed in response to an identified need for Medically Assisted Treatment (MAT) of opioid dependence in Tanzania. MAT for opioid dependence is defined in this document as utilization of (Methadone,

2 WHO (2009) Guidelines for Psychosocially Assisted Pharmacological Treatment of Opioid Dependence

Buprenorphine and/or Morphine) medications to improve addiction treatment related outcomes. Generally, MAT aims to reduce the harm to the individual and the community that is associated with alcohol and other drug abuse.

These guidelines are intended for use by accredited clinics and the staff who will provide MAT to opioid dependent individuals . MAT has demonstrated efficacy in reducing the morbidity and mortality of opioid dependent individuals , reducing the transmission of HIV, HCV and HBV, reducing crime and improving the socio-economic status of the patient and their families. MAT for the treatment of opioid dependence consists of methadone and/or Buprenorphine for adults and the utilization of morphine for neonatal opioid abstinence syndrome. Naloxone, as an opioids antagonist, will be utilized here to reverse symptoms of opioid intoxication or overdose.

Methadone: Methadone assisted treatment involves the daily oral administration of methadone over an extended period of time as a treatment for heroin or other opioid dependence. Methadone is a long acting full *mu* opioid agonist and has a long history of safe and efficacious use throughout the world. Once an individual has been stabilized on methadone, subsequent daily doses cause neither sedation nor euphoria.

Buprenorphine: Buprenorphine assisted treatment involves sublingual administration of buprenorphine over an extended period of time as a treatment for heroin or other opioid dependence. Buprenorphine is a partial *mu* opioids receptor agonist and as such is easier to taper than methadone, it has milder withdrawal symptoms, and a wider margin of safety than full *mu* opioid receptor agonists. However, it is relatively more expensive compared to methadone.

Morphine: Morphine assisted treatment is utilized for the structured treatment of neonatal opioid abstinence syndrome in newborns of opioids dependent mothers. Morphine is a short-acting full *mu* opioid receptor agonist.

***Naloxone*:** Naloxone is a medication used to reverse the respiratory and central nervous system effects of opioid overdose. Naloxone is a *mu-receptor* antagonist. As an antagonist, there is no liability for abuse among opioid dependent patients.

1.4 Optimizing benefits of MAT treatment

The benefits of MAT are optimized when programs are readily accessible, entry into treatment is prompt and retention in treatment is high. Other factors include extended opening hours at clinics, provision of medically appropriate doses, clinicians with high morale and non-judgmental attitudes as well as easy access to allied medical, psychological and social welfare services.

1.5 Patient records

Clinical record keeping within MAT programs is essential to patient safety and good clinical outcomes. The MAT programme must ensure that each patient has an individual file which is secured and the contents of which remain confidential.

All entries in the file must be legible and written by staff authorized by the program and are signed and dated appropriately (with designation and name printed).

The file shall contain the following:

1. Unique record number
2. Full name
3. Telephone number
4. Address
5. Date of birth
6. Gender
7. Language spoken,
8. Current medications taken (e.g., ARVs, anti-TB, etc)
9. Person(s) to notify in an emergency,
10. Relevant drug and alcohol history
11. Medical history,
12. Psychiatric history,
13. Family history,
14. Social considerations
15. Physical and mental state examination
16. A treatment plan which addresses the patient's addiction, mental, and physical health.
17. 'Alert' notations for conditions such as allergic responses, adverse drug reactions and infection risks (these should be readily apparent)
18. Summary sheet to be completed at the time of discharge.

CHAPTER 2

2 INTAKE PROCEDURES

2.1 *Screening and Admission*

The aim of screening is to identify individuals with opioid dependence that would benefit from MAT. Screening for opioid dependence will follow standard criteria for the diagnosis of opioid dependence using DSM IV-TR, plus clinical evaluation of the patient, and urine toxicology. Key criteria for admission into MAT services should include the continued use of opioids despite the negative consequences (e.g., acquisition of HIV and/or hepatitis C), engagement in illegal activity to support opioids use (e.g., sex work, theft), and an inability to cease opioids use despite several attempts. The clinical evaluation should focus on the presence of fresh track marks suggestive of recent injection and the evaluation for opioid withdrawal. The presence of opioid positive urine toxicology can be used as supportive data to admit a patient to MAT; however, opioid urine toxicology alone without any of the key criteria listed previously is insufficient for admission. Those individuals with serious medical conditions that are the consequence of opioid dependence (e.g., cardiac disorders such as endocarditis, HIV, hepatitis C) and pregnant women should be considered as priorities for treatment because stabilization of these patients is necessary to improve health outcomes in their medical conditions.

2.2 *Exclusion*

All individuals seeking treatment who are not opioid dependent will be excluded from MAT. These individuals will be referred to appropriate programs to address their ongoing substance use.

2.3 *Assessment and Diagnosis*

A focused medical and psychosocial assessment should be completed prior to the beginning of treatment. The purpose of the assessment is to document the patient's dependence on opioids, evaluate the complications related to drug use, and assess psychiatric and medical problems and high-risk behavior in order to recommend a comprehensive and practical treatment plan to the patient. The assessment process consists of the following steps:

Document the patient's history; this must include:

- Reason(s) for presenting at the current time
- Documentation of screening measures including urine toxicology and breathalyzer.

- Documentation of clinical justification and for admission and the specific criteria utilized (e.g., the patient has tolerance, withdrawal, and use despite the negative consequences).
- Drug use history included the choice of drug(s) and the amounts taken, route of administration and duration of dependency
- History of use of other substances including tobacco and ethanol use
- Past addiction treatment, outcomes of treatment – i.e. was it a previously successful treatment
- High risk behaviours e.g., unsafe sex, injection practices, criminal involvement, and poly-substance use (including alcohol use).
- Medications,
- Allergies
- Past medical history
- Past psychiatric history, including current suicidal ideation
- Social history including custody of children and partner's substance use history
- Contraceptive practices
- Family history, including medical and addiction history of family members
- Vocational/Educational history
- Current involvement with the judicial and/or criminal justice system (e.g., pending criminal charges or under probation).

A focused physical examination should be performed prior to starting a patient on MAT. Special attention should be given to: signs of opioid withdrawal, malnutrition, jaundice, hepatosplenomegaly, presence or absence of heart murmurs, pupil size, signs and symptoms of chronic liver disease, signs of HIV infection, needle tracks, and abscesses.

A urine drug screen and breathalyzer are to be completed during the assessment phase, the results of which should generally be interpreted prior to initiation of MAT. However, if a patient meets criteria listed above, urine toxicology result should not unnecessarily delay access to treatment. As a general rule, the validity of the urine screen increases if the sample collection is done under supervision. Initial laboratory testing should include TB test, HIV, Hepatitis B and C serology, liver function tests such as albumin and transaminases as indicated. Screening for opportunistic infections and CD4 count if found to be HIV positive.

2.4 Treatment Plan

After detailed history and diagnosis the individual treatment plan will depend on the identified needs as follow:

- Plans for the identified patient's MAT dosage (e.g., dose initiation, dose stabilization, maintenance dose, dose reduction)
- Plan for the identified drug use problems (including alcohol and tobacco)
- Plan for the identified risk behaviours (e.g., needle sharing, overdose

and sexual risk)
- Plan for the identified major medical, psychiatric and psychosocial problem areas.

2.5 *Treatment Options*

Methadone Assisted Treatment is the most appropriate treatment for most opioid-dependent people, provided patients seek treatment voluntarily and request methadone treatment after being fully informed about the treatment and other treatment options for opioid-dependent people including alternative pharmacotherapies such as buprenorphine and morphine. Morphine will be utilized solely for the treatment of neonatal opioids abstinence syndrome. All medically assisted treatments benefit from patient involvement in self-help groups such as AA, NA and other psychosocial and counseling services.

2.6 *Informed Consent*

When a health care provider or program requires a patient to sign a treatment agreement, it is important that the patient receive clear information about the MAT rules and expectations. Issues such as the take-home policy, urine screens and appointment frequencies should be specified. The reasons for discontinuation of methadone, should it become necessary, are to be specified. It is important to advise patients about the services or resources that are available to them either in the MAT and/or the community in conjunction with the prescribing of MAT. The following acknowledgements/statements should be discussed and agreed to in a comprehensive treatment agreement and are the basis of informed consent for a patient (*See annex 4 for methadone treatment agreement form*).

- The patient has considered the treatment options for opioid dependence as explained by the physician, and that these options are acceptable to the patient.
- MAT services involve the use of methadone, buprenorphine or morphine are opioids in nature and hence may cause dependence. If the patient abruptly discontinues the medication, opioid withdrawal symptoms will likely result.
- MAT is generally a long-term (or life time) treatment option.
- During the stabilization period, sedation and/or withdrawal symptoms may be present. Driving automobile or operating machinery during the stabilization period of MAT maintenance may be dangerous. These dangers can also arise again during dose adjustments or periods of instability.
- Illicit drug or ethanol use with MAT can be dangerous, therefore the clients should refrain themselves from these substances. The use of other substances including prescribed or non-prescribed medications while taking MAT should be discussed with the physician, as drug interactions may occur. For example, some HIV medications cause withdrawal.

- For reasons of safety, the MAT dose may be withheld if the patient appears to be intoxicated.
- After three missed days of MAT (methadone in particular), a patient needs to be reassessed by the physician because of the risk of overdose if the original prescribed dose is given at this time.
- MAT assists in the stabilization of the patient physically and emotionally so that the counseling and lifestyle changes necessary for recovery may occur.
- The average daily dose of MAT (methadone in particular) may result in death if taken by a person not dependent on opioids.
- Side effects from MAT can include constipation, sweating, fatigue, decreased libido and weight gain.
- Fertility frequently improves with stabilization on MAT, so patients should consider this factor during family planning.
- A baby born to a mother on MAT (methadone in particular) may experience symptoms of opioid withdrawal after birth; neonatal opioid withdrawal may be delayed 1-2 weeks postpartum. The symptoms are treatable and have not been shown to result in long-term developmental or physical problems.
- It is the obligation of the patients to inform any physician if they have received a narcotic (pethidine or morphine) from another physician within the preceding 30 day period - otherwise a patient will have committed the offence of double doctoring.
- The patient may voluntarily withdraw from the MAT treatment program at any time after discussing with health care provider the plan for methadone/buprenorphine tapering.

2.7 The health care provider's obligations to his/her patients

- To provide professional, respectful and reliable services to patients
- To provide back-up coverage for holidays and periods when the health care provider is on vacation or unavailable
- To provide appropriate notice to the patient should a health care provider choose to leave this area of practice
- To assist in the transfer of patients to other methadone prescribing health providers to ensure continuity of treatment.
- To either provide or facilitate patient access to services related to recovery, this includes counseling, vocational support services, primary health care, etc.
- To remain current in practices and standards for MAT and the treatment of opioid dependence.

CHAPTER 3

3 TREATMENT PROCEDURES

3.1 Methadone Assisted Treatment

3.1.1 Pharmacology

Methadone is a synthetic pure *mu* opioids agonist with good oral bioavailability. It is highly effective for the treatment of opioid dependence and can be administered once daily due to its protracted half-life of 15 to 22 hours. This means that steady-state of methadone will be achieved between three to five days after changing a dose; therefore, dose adjustments should occur no sooner than every 3 to 5 days (the exceptions are in Stage 1 and Stage 4 when faster titration may be warranted). Daily dosing (same time) maintains constant blood levels and suppresses withdrawal symptoms from opioids for up to 36 hours and thereby facilitates normal activity of an individual. As a full opioid agonist it remains a potent analgesic.

3. 1.2. General Comments on Methadone Dosing

Methadone assisted treatment consists of four steps with respect to dosing. These steps are:

Removal of withdrawal symptoms:
The goal of this stage is to remove symptoms of opioid withdrawal that the patient may experience from inadequate dosing of methadone. This stage is typically a faster titration upwards to alleviate the symptoms of methadone withdrawal. This stage should occur over the first several weeks of treatment.

Therapeutic dose assessment/Dosage Stabilization:
The goal of this stage is to ascertain the correct therapeutic dose for the patient. Once the patient is no longer in active withdrawal (i.e., successful completion of the previous stage), a slower titration upwards to the correct dose that will be required for maintenance is needed. This titration should occur no faster than 10 mg every 7 days. Dose change should be based upon patient report of ongoing drug craving, drug dreams, ongoing use, trouble sleeping, waking in the morning feeling uncomfortable, etc. This stage should occur over the first two months of treatment.

Maintenance treatment:
The goal of this stage is to maintain the patient on the appropriately ascertained dose of methadone and to now focus on the psychosocial services necessary

to help the patient achieve the life goals for which they started treatment (e.g., becoming a productive member of his/her family/community). Understanding the importance of regulating the neurobiological mechanisms involved in opioid dependence, this stage will be the longest stage of treatment and should be tailored to maximize clinical benefits to the individual patient. Although methadone doses do not often need to be adjusted during this phase, occasions will arise where doses must be changed. Examples include:

- Patient life stressor which rekindles craving and drug use (e.g., victimization)
- Polysubstance use requiring methadone dose reduction to avoid overdose
- Medication interactions that require dose increases (e.g, neviripine, efavirenz, and rifampicin).

Withdrawal from methadone:
The goal of this stage is to assist the patient in a slow, structured taper off methadone to avoid relapse to opioids. This stage should only be considered once the patient has demonstrated maximal clinical benefit from the previous stage of maintenance that will often be after approximately two years of maintenance treatment. Abrupt withdrawal of methadone can be severe and protracted (i.e., for months); therefore, abrupt removal from methadone should be avoided. Ideally, methadone should be tapered slowly over time to avoid rapid changes in brain biochemistry that would stimulate craving and relapse to use. A dose reduction of 2 mg per week is low enough that many patients are able, with appropriate psychosocial support, to taper off.

3.1.2 Stage Specific Guidelines

Stage1. Dose Initiation and Removal of Withdrawal Symptoms

- The initial dose of methadone will be 15 to 30 mg on the first day (exact dose will be determined by the health care provider responsible for methadone at that site).
- The first two weeks of methadone initiation is when the patient is at greatest risk of overdose as the methadone dose is titrated upwards in the setting of ongoing opioid use by the patient. Overdose and death can occur from increasing a dose before the full effects of the current dose are known. It is critical for health care providers to inform patients of the risks of overdose during this titration.
- Some patients may be difficult to ascertain an initial dose or titration schedule. In this situation, an initial safe dose can be administered and the patient re-evaluated three to four hours later to assess the response to that dose. If necessary, an additional dose can be provided and the next day's dose adjusted accordingly. However, no more than 30 mg can be administered to a patient on the first day of treatment.
- Once it has been established that the initial dose is well tolerated the

methadone dose is gradually increased until the patient is comfortable and refrains from heroin and other illicit opioids.

Stage2. Therapeutic Dose Assessment/Dose Stabilization

- Criteria for dose increases include:
  - Signs and symptoms of withdrawal (objective and subjective)
  - Amount and/or frequency of illicit opioids use not decreasing
  - Persistent cravings for opioids (e.g., drug dreams, intrusive thoughts, etc.)
- During the stabilization phase, the key phrase is "start low – go slow". Stabilization will occur over the following months
- Dose adjustments during the stabilization period are typically in the 5 to 10mg range. While during the stabilization phase, dose adjustments no more frequently than every three to five days are recommended.

Stage3. Methadone Maintenance

Optimal Dose:

- The optimal methadone dose is that dose which relieves withdrawal symptoms, blocks the euphoria from short acting opioids and ameliorates drug cravings without sedation or other significant side effects.
- With experience from other countries, the optimal dose for the majority of clients can be established within eight weeks of methadone initiation.
- Health care providers should focus on the clinical presentation of the individual client and prescribe as much or as a little methadone as necessary for the patient to meet his/her treatment goals. The health care providers should remain cognizant of the evidence that higher doses of methadone (>60 mg) result in better retention in treatment and less heroin use than lower doses (<40 mg).

Methadone Maintenance/Dose reviews:
Dose reviews should occur regularly for all patients, including those who appear to be progressing well. *Although the frequency of patient review will be determined by the stability of the patient, all patients should be reviewed at least four times a year by an experienced clinician.*

Changes in the patient's goals or plan of treatment that may occur after these reviews should be documented in a modified treatment plan. The review of treatment progress should document:

- Any patient requests, current issues or concerns
- Treatment mechanics, e.g., take-home doses
- Adequacy of methadone dose and any pharmacological issues (side effects, or interactions)
- Recent drug use — prescribed and other (including alcohol and tobacco)
- Physical and psychological health

- Social functioning
- Review of risky behaviors such as criminal offences, ongoing injection use and sexual risk taking which may place the patient at risk of HIV, hepatitis B and hepatitis C infection
- Renewal of prescription of methadone at stabilized dose or at new dose based upon this assessment preparations for the patient's eventual structured withdrawal from the methadone program, including strategies to enhance psychosocial supports for the patient which will be needed after discharge.

Methadone Maintenance/Avoiding hazards of methadone treatment

Hazards associated with methadone treatment include overdose, accidental poisoning of someone other than the patient and illegal diversion and trafficking of methadone.

To minimize these hazards:

- Health care providers should be adequately trained in providing methadone treatment
- Methadone treatment should be voluntary and received only by those individuals assessed as suitable by an approved methadone prescribing doctor
- Generally, methadone should be consumed under supervision and techniques to verify dosage consumption should be employed (such as talk to patient before he leaves the counter).
- Methadone treatment should occur in an environment that is safe for patients, staff and the community.

Methadone Maintenance/ Take-home Dosing

The following criteria should be assessed prior to initiating take-home dosing. These criteria should be re-assessed regularly with regards to continuing take-home privileges and/or increasing/decreasing the number of take-home doses:

- Clinical stability- the client demonstrates clinical stability when, in the judgment of the program health care provider the patient is refraining from ongoing drug use and is appropriate for take-home dosing and demonstrates the social, cognitive and emotional stability necessary to assume responsibility for the care of the medication and to use it as prescribed
- Social stability – the patient demonstrates the social stability when, in the judgment of the program health care provider the patient is in good standing with the policies and procedures of the clinic, does not have any current involvement with the criminal justice system, is involved in a stable support system and activities and regular attendance at the services as planned. Patients with unstable living arrangements, such as those living on the street or in hostels without storage facilities may not be appropriate to receive take-homes; however, this is not an absolute contraindication to take-home privileges among those with unstable living

arrangement. Patients should be informed that a locked container for their carries is advisable in situations where other individuals (especially children) may have access to the carries or in the circumstance of shared accommodation with other drug users.

- The length of time in methadone treatment – The greater the length of sobriety while on the methadone, the less risk that take-home doses will be inappropriately used. Patients will become eligible for their first take-home dose after a minimum of 30 days with no active drug use.
- Ability to safely store medication - All take-home doses shall be dispensed in childproof bottles. One bottle will be dispensed for each day's dose of methadone. However, childproof containers are insufficiently secure in the home setting and all patients must guarantee they will safely store the medication in an inaccessible location (e.g., locked cabinet).

Number and frequency of takeaway doses

Months in Treatment	Maximum Number of Eligible Take-home Doses in a Week*
3	1
6	2
9	3
12	6
24	13

*At 24 months of sobriety, the patient is eligible for 13 take-home bottles in a 14 day period.

Reassessment and/or Reduction of Take-home Privileges

Reassessment occurs through several important mechanisms. First, ongoing meetings with counselling and the doctor to review clinical progress, random urine toxicology and breathalyzers, and evaluations of the patient's overall progress in treatment will assist in ascertaining those who are continuing to do well with take-home privileges. Second, a bottle recall process must be included in the clinic's policies and procedures. The recall policy allows for the clinic staff to call a patient and request that patient with take-home bottles return to the clinic within 24 hours to inspect the take-home bottles. This is utilized in situations where there are concerns of tampering with the take-home bottles. Upon notification, the patient is to report to the clinic in 24 hours for inspection. If the patient does not report or there is a problem with the inspection, the patient's take-home privileges may be reduced or eliminated. Third, a reassessment and possible reduction of a patient's take-home privileges should be undertaken when the patient engages in risky behaviour that is not consistent with recovery from addiction. For example: Patient failed to maintain clinical stability as previously outlined.

- Continued problematic drug or alcohol use.
- Patient is not meeting agreed upon goals and objectives.
- Patient has failed repeatedly to leave a urine sample for drug screening in

the required manner as agreed upon in the treatment plan. Patients have tampered with their urine sample.
- Patient has either diverted their methadone or there is a strong suspicion that methadone has been diverted or used in an inappropriate way (not as prescribed).
- Patient consumes take-home dose early, or reports lost or stolen take-home dose should have their level of take-homes doses re-assessed.

When a patient has a sustained relapse:
- Patients who remain clinical stable: Reduce one take-home dose per week for each illicit opioid positive urine (typically tested once per month).
- Patients who are clinically unstable such as those who demonstrate sustained use and/or other forms of clinical instability should have all take-home doses discontinued.
- Return take-home doses to the previous level at a rate no greater than an increase of one take-home dose per week for each illicit opioids negative urine (typically tested once per week), provided that the patient is otherwise stable and meets the criteria

Exceptions to Take-home Privileges

All exceptions to the carry schedule must have clear documentation of their necessity and can never exceed 13 take-home bottles at one time. Exceptions may be due to a medical necessity that prevents the patient from attending the clinic, a social situation which prevents transport to the clinic (e.g., travel out of the area), or other condition or event which two physicians are in agreement that the patient is medically stable and able to responsibly self-administer methadone provided in take-home bottles.

1. Medical Necessity
   - A consensus of two health care providers who know the case may decide to initiate or increase take-home doses to a patient who otherwise does not qualify if they suffer from a medical condition that significantly interferes with their ability to attend the clinic.
   - Every effort should be made to have some supervision of the methadone consumption in these cases.
   - For medical conditions of a temporary nature, the requirement for take-home doses should be re-assessed once the patient's ability to attend the clinic is established.
   - It should be recognized that the medical condition that necessitates carries might involve pain and clinical situations that trigger increased substance abuse.

2. Social situations that prevent transport such as travel outside of a region. Verification of travel arrangements should be obtained as part of the clinic's due diligence and no more than 13 take-home bottles can be dispensed at one time.

3. Although a positive urine toxicology would typically make a patient ineligible for take-home privileges, there are special circumstances in which take-homes could be provided even in the setting of positive urine toxicology. Patients in this category may receive more than one carry per week if the following conditions are satisfied:
    - A specific medical diagnosis has been made that warrants the use of the medication to treat the symptoms of the condition.
        - Chronic benzodiazepine use as second line drugs for treatment of panic disorder or specific anxiety disorders.
        - Stimulant use for ADHD (i.e., Ritalin)
        - Opioids use for conditions of chronic pain.
    - The patient is clinically stable and meets other carry criteria.
    - Consideration given for a referral to a physician knowledgeable in addiction medicine who has supported the use of the medication.

4. For prescription medications it is important that the physician prescribing has full knowledge of the current prescribed medications and the patient's past addiction history. Benzodiazepine abuse correlates the onset of action of the medication – faster acting benzodiazepines have a greater abuse liability (e.g. valium) than those with a slower onset of action. The risk of abuse, however, is increased in a patient who has already demonstrated a history of substance abuse and/or dependence.

5. Health care provider must recognize that it is difficult to monitor supplemental and non-prescribed drug use in a patient to whom a drug with abuse potential has been prescribed.

Stage 4: Withdrawal from Methadone Assisted Treatment
Voluntary withdrawal from methadone treatment

1. Patients who leave methadone treatment voluntarily after a gradual withdrawal from methadone are least likely to relapse into illicit opioid use. The decision to withdraw voluntarily from methadone should ideally be made collaboratively between the patient and attending health care providers. When all agree about the timing and method of withdrawal from methadone, patients tend to be more successful in their methadone reduction.

2. Take a flexible approach to dose reduction in voluntary methadone withdrawal. The aim is to maximize the patient's chances of completing the methadone treatment program in a manner that minimizes the risks of relapse into opioids use. This requires individualizing reduction regimens to best suit each patient. Even at slower rates of reduction it is common for patients to experience some withdrawal discomfort at times. It may be appropriate to maintain a patient at a constant dose at times during the reduction until the patient is better prepared to reduce further. If relapse is likely, or has occurred, further reductions in methadone dose may need to be suspended or an increase in dose considered.

3. In general, the slower the rate of tapering, the lower the probability of relapse due to recurrence of craving due to dramatic changes in brain chemistry. Where slow tapers are possible, the patient should be encouraged to consider no more than 2 mg per week. In situations where patients are unable to do a slow taper (e.g., impending incarceration), larger dose reductions are appropriate at higher doses, with smaller changes at lower doses. For example, individuals on doses greater than 80 mg can tolerate reductions of 10 mg/week until they reduce to about 70 mg–80 mg. whereas; individuals whose daily methadone dose is between 40 mg and 80 mg will generally tolerate a dose reduction of 5 mg/week.

4. Individuals vary greatly and it is best to allow patients to control the frequency and amounts by which their dose is reduced during voluntary reduction. During the withdrawal period, patients will usually benefit from increased psychosocial support. Throughout the reduction phase, accurate information about what the patient is experiencing, along with supportive counseling (orientated towards preventing relapse), can enhance the likelihood of a successful outcome.

Involuntary termination of methadone treatment

1. It is sometimes necessary to discharge a patient from treatment for the safety or wellbeing of the patient, other patients or the staff. At the beginning of methadone assisted treatment, patients should be provided in writing with the conditions under which they may be involuntarily discharged. Situations that may warrant this action include:
    - Violence or threat of violence against staff or other patients
    - Property damage or theft from the methadone program
    - Drug dealing on or near methadone program premises
    - Repeated diversion of methadone.
2. If it is possible to safely transfer the patient to another methadone program, this should be undertaken to avoid methadone withdrawal and relapse to drug use.
3. If the patient is to be involuntarily withdrawn from methadone treatment, reduction in dosage should be gradual. However, rapid dose reduction or abrupt cessation of treatment is warranted only in cases of violence, assault or threatened assault.
4. In general, involuntary withdrawal from methadone should not take less than 21 days. Patients should be advised of other treatment options, including detoxification. Because tolerance changes during detoxification, patients should be warned of their increased risk of overdose during withdrawal from methadone.

The place for adjunctive pharmacotherapy during maintenance and withdrawal phases

1. Sleep disturbances are common among people who withdraw

from almost any psychoactive drug, including methadone. This information should be clearly explained to patients. Training in non-pharmacological strategies to help them cope with disturbed sleep should be provided.

2. Other psychotropic medication (in particular, hypnotics and sedatives) is ***not*** recommended for patients taking methadone maintenance and during monitored withdrawal, except when indicated for patients with diagnosed psychiatric co-morbidity.
3. If it is considered medically necessary to prescribe sedative/hypnotic medication, it should be at a low dose for a specified short duration (3–5 days), with prior explanation of the reason for its prescription, the associated risks of taking such medication and the intended short duration of this treatment. Provide ongoing supervision in all cases and restrict the quantity of tablets to 1–2 days' requirements for reasons of safety

Avoiding secondary alcohol and sedative/hypnotic problems during the withdrawal phase

During and after withdrawal from opioids, over-indulgence in alcohol and the inappropriate use of sedative/hypnotic medication is common. This should not necessarily be construed as indicating a long-term shift to alcohol and other drug dependence, but the clinician should remain vigilant to the possibility that alcohol consumption or other drug use may be increasing to hazardous or harmful levels and provide appropriate intervention.

Readmission to treatment

When relapse occurs some time after leaving treatment and the patient seeks readmission to a methadone program, this should be offered expeditiously and without recrimination. Provided that the person is clinically suitable for methadone treatment, there should be no barriers to readmission after leaving the program.

Failure to attend for treatment

A patient who has not presented to pick up their methadone dose for three or more consecutive days should not receive methadone without consultation with the prescribing doctor. A patient who fails to attend for seven or more consecutive days may be withdrawn from methadone treatment with no penalty should the patient seek readmission in the future.

Aftercare

Aftercare refers to structured interventions that assist patients who have completed treatment to remain drug free and improve their psychosocial functioning. Aftercare is aimed at reducing the rate of relapse after methadone treatment.

Clinicians working in methadone programs should, whenever acceptable to the patient, offer scheduled aftercare support services themselves or by referral.

Such services might include skills training (e.g., relapse prevention, problem solving skills or vocational skills training), social support services (e.g., self-help groups such as Narcotics Anonymous), or booster motivational counseling sessions. Providing such aftercare to those who are highly motivated will enhance the overall efficacy and cost effectiveness of treatment.

Transferring Patients

When a patient exits treatment entirely, or transfers between doctors, a Treatment Exit Form (not included) must be completed and should be received at the dosing point within five days of the patient terminating treatment.

In addition, to avoid the potential for double dosing, the prescribing doctor should notify the dosing site and have them cancel all dosing instructions for that patient.

If a patient has not changed his/her prescribing doctor but indicates that he/she wishes to transfer between dosing sites, the other dosing site to be notified by phone or other immediate means to effect a change.

3.2 Buprenorphine Assisted Treatment

3.2.1 Pharmacology

Buprenorphine is a thebaine derivative, leading to its legal classification as opioids. Buprenorphine is a partial agonist and it has high affinity for the *mu* opioid receptor thus competes with other opioids and blocks their effects. It has high potency as a parental analgesic. It has a long duration of action when used for the treatment of opioid dependence which contrasts with its relatively short analgesic effects.

3.2.2 The Induction and Stabilization Phase

During Induction phase buprenorphine is administered when an opioid-dependent individual has abstained from using opioids for 12–24 hours and presents with early signs and symptoms of opioid withdrawal.

Usually, 2–4 mg of buprenorphine is administered sublingually on first day of treatment, and then the patient is monitored for a maximum of 2 hours. If withdrawal symptoms are not relieved, repeat the dose of 2 to 4 mg of buprenorphine up to a maximum of 8 mg in the first 24 hours. On day two, if the patient returns experiencing withdrawal symptoms, continue dose increases by 4 to 8 mg and observe for a maximum of two hours. If the withdrawal symptoms are not relieved continue dose increase up to a maximum of 16 mg on day 2. However, a target dose of 12–16 mg of buprenorphine per day by the end of the first week is recommended. If the patient returns experiencing withdrawal symptoms on subsequent induction days, verify patient's appropriate sublingual technique and consider dose increases as per the schedule shown above, up to a maximum of

32mg of buprenorphine per day. However more recent clinical data suggest that daily doses above 24 mg of buprenorphine do not provide additional therapeutic benefit to the vast majority of patients.

3.2.3 Maintenance dose

Once the patient is stabilized on a single daily dose, he/she may continue a single daily dose or may shift to alternate-day dosing (e.g., every other day or Monday, Wednesday, Friday) (Amass et al., 2001). In the setting of alternate day dosing, providers can increase the dose on the dosing day by a minimum of 8 mg and a maximum of the amount not received on intervening days. For example, if the patient stabilizes on 8 mg daily, and every-other-day dosing is desired, then the provider may change the dosage to 16 mg on Monday, 16 mg on Wednesday, and 24 mg on Friday (to provide medication coverage for the 2-day weekend).

During maintenance phase the patients should be seen by physician no less frequently than every 12 weeks.

3.2.4 Withdrawal from treatment

The patient's buprenorphine dose should be tapered slowly at a rate that both the prescriber and the patient consider acceptable. Patients commonly want to taper more quickly, so helping patients set realistic goals at the outset is important. Some patients will ask to proceed directly from stabilization to medically supervised withdrawal. However, unless there is a compelling reason to discontinue buprenorphine quickly (e.g., travel), a slow taper is usually encouraged, because it is associated with a higher likelihood of treatment success (CSAT, 2004).

3.3 Urine Drug Screening

- Results of urine drug screens may provide valuable information and can be used as an aid in documenting baseline drug use and periods of abstinence
- Verifying self report of drug use
- Aiding in assessing functional stability
- Minimizing possible drug interactions
- Assisting in evaluating compliance with methadone by detecting presence or absence of methadone and/or metabolites
- Assisting in assessing appropriate carry status
- Adjusting methadone dosage
- Reevaluating treatment goals

The design and implementation of urine collection, testing and interpretation should be done in a way that maximizes patient retention, compliance, monitoring, positive treatment outcomes, and the safety of the patient and others. Results of the urine drug screens should be interpreted by the physician in conjunction with functional stability. Patients not willing to comply with urine testing as directed should not be allowed to have take-home privileges unless the patient is medically incapable of providing a urine toxicology screen.

3.3.1 Urine Collection

Ideally, urine samples should be obtained on a random schedule under the direct observation of personnel trained in the collection of urine samples. The validity of a test can be increased further by measuring the temperature of the sample immediately after collection, bluing of the toilet water and ensuring no access to running water in the collection area. It is important that personnel act in a professional and respectful manner towards patients and that sensitivity and privacy be exercised during the urine collection process. If direct observation is not possible or if there is any question about the reliability of the urine drug screen results, other methods should be employed. If tampering is suspected the physician should be notified and whenever possible a second sample should be collected the same day so results can be compared.

3.3.2 Frequency of Urine Testing

At least one urine drug screen should be collected and interpreted prior to initiation onto methadone. However, urine toxicology must not be allowed to delay access to treatment unnecessarily. Thereafter, urine testing should be done on a random schedule at least one urine toxicology done on all patients per month. More frequent screening may be necessary in the setting of ongoing substance abuse or other medically necessary conditions. Ongoing reassessment of the frequency of urine screens is based on the physician's assessment of the patient and their pattern of drug use, validity of the patient's self-report and functional stability. It is important that the urine drug screening results not be utilized in a punitive manner.

Typically urine specimens are initially screened using an enzyme immunoassay. At a minimum, urine toxicology screening should include opioids, benzodiazepines, methadone and cocaine. Depending on local drug use patterns and clinical judgment, other substances may need to be added to the urine toxicology panel.

3.4 Alcohol screening

Additionally, ethanol should be screened utilizing a breathalyzer on all patients who present intoxicated. In addition, patients should have random breathalyzers done at the time of urine toxicology at the physician's clinical discretion, but at least twice a year.

3.5 Special Clinical Situations

3.5.1 Missed doses

Methadone

- Missed one to two days – full dose can be given
- Missed three days – half dose given and then the next day a full dose.
- Missed four or more days – half dose given and then a build-up of 10 mg a day back to maintenance dose.

These dosing parameters assume that the patient is not taking any substance that interacts with methadone and also presumes the patient is not ingesting other substances which could lead to overdose (e.g., benzodiazepines and alcohol).

Buprenorphine – if patient has not relapsed to opioid use, the patient is given half a dose on the first day and a full dose the next day regardless of the number of days missed (up to 7 days as the patient is discharged past 7 days).

3.5.2 Vomited doses

This is for doses vomited on the premises and witnessed by someone from the program. Opioids such as methadone and buprenorphine can cause nausea and vomiting as a side effect.

Methadone

- If emesis occurs greater than 20 minutes after dosing, the patient has absorbed sufficient methadone and no additional methadone is given.
- If emesis occurred less than 20 minutes after dosing, but did not occur immediately after dosing, the patient is given half a dose which will prevent withdrawal and avoid any concerns that the patient may have ingested sufficient amounts of methadone to overdose when combined with the new dosing.
- If emesis occurs immediately after dosing, a full dose can be re-administered.
- The nursing staff should alert the medical staff of the patient's emesis as the patient may need evaluation as to the etiology of the patient's symptoms.

Buprenorphine

- Re-dosing with half the dose. Although a full dose could be given, opioids such as buprenorphine can cause nausea and vomiting. Half the dose will be sufficient to avoid withdrawal symptoms and may provoke less nausea.

3.5.3 Concurrent drug use

General

- Ongoing drug use is common in methadone maintenance clinics for a variety of reasons. This may be the result of patients operating in a pre-contemplative stage regarding their other drug use. It may also be the result of self-medication of an underlying mental illness. Patients should not be discharged because they are struggling with other substance abuse. Rather, more intensive services should be offered to ascertain how best to meet the patient's needs.

Methadone

- Polysubstance use in the setting of methadone is concerning because of the

increased risk of respiratory depression and overdose.

- For patients who present intoxicated to the clinic, the patient must be assessed to ascertain if the patient is safe to have any methadone administered on that day. Because methadone has long half-life, the patient does not have to be given methadone on a day in which he/she is too intoxicated to safely be given methadone.
- Because the timing of illicit substance ingestion may be unclear (e.g., were drugs ingested 8 hours prior or 30 minutes prior), it is wise to have intoxicated patients who present to the clinic be observed for an hour to see if they become more or less intoxicated. Those who have increasing intoxication likely should not be medicated. Those with a decreasing level of intoxication may be medicated at the discretion of the treating physician.
- Patients who are medicated with some level of intoxication should be observed for one hour post dosing to insure that the patient remains clinically stable.

Buprenorphine

- Buprenorphine causes far less respiratory depression compared with methadone.
- However the lack of additive respiratory depression is relative and therefore precaution should be exercised in prescribing buprenorphine in combination with sedative use like benzodiazepines and alcohol.
- If a patient has ongoing opioid use while on buprenorphine, this suggests the buprenorphine is inadequate to treat the patient's opioid dependence and the patient should be placed on methadone assisted treatment to help the patient obtain control over his/her heroin addiction.

3.5.4 Split doses

Methadone

- Split doses are utilized in two settings: 1) Rapid methadone metabolizers who require more frequent dosing and 2) Patients hoping to have improved pain control with methadone.
- Split dose patients must be eligible for take-home dosing privileges and the treating physician must believe the patient fits into one of the two settings above.

Buprenorphine

- Although not pharmacologically necessary, many buprenorphine patients wish to take buprenorphine twice daily. This occurs because of the patient's concerns about waking up in the morning in withdrawal.
- Patients meeting buprenorphine take-home privileges should be allowed to administer the medication twice daily if so desired.

3.5.5 Overdose

- Overdose risk is greater in methadone patients than in buprenorphine patients because methadone is a full opioid agonist. Therefore, particular attention should be made to methadone patients at risk for overdose.
- Overdose risk during methadone treatment is greatest during Stages 1 and 4 when tolerance will be changing. Patients should be clearly informed of these risks.

  Poly drug users of other respiratory depressants such as alcohol and sedatives (e.g., benzodiazepines) are at greatest risk of overdose. These patients should be targeted for risk reduction measures to help moderate the risk of overdose. Such risk reductions measures should include the distribution of naloxone to prevent overdose

3.5.6 Frequency of visits

- Health care provider visits will begin with the admission to treatment and a follow-up visit during the first 8 weeks of treatment. Thereafter the physician should see the patient at least quarterly to ascertain that the patient's health status during treatment.
- Nursing visits will consist of daily evaluations at the time of dosage administration.
- Counseling visits should be more intensive in the beginning of treatment. Specifically, the counseling visits should be weekly for the first 8 weeks and then should spread out to twice a month for 3 months and then monthly thereafter. In times of relapse or worsening clinical status, the counseling visits should be increased in frequency.

3.5.7 Length of treatment

- Medically assisted treatment (MAT) should be provided to the patient for as long as the patient continues to have positive health benefits as a result of treatment. That is, for as long as the benefits of ongoing MAT outweigh any risks associated with ongoing MAT.
- However for many injection drug users with protracted heroin use, the length of treatment on MAT should be for at least two years.

3.5.8 Inpatients

- Patients on MAT should continue to be provided MAT within inpatient settings such as hospitals, residential drug treatment, and other inpatient clinical settings.
- If patients are admitted to inpatient settings, MAT should continue to be made available to those patients during the course of their hospitalization. Either the MAT program should continue to provide MAT to the patient while inpatient or the inpatient facility should assume the responsibility for dosing of MAT for the duration of the inpatient stay.
- Clear coordination for dosing and ongoing treatment will need to occur

between the inpatient medical staff and the MAT medical staff to insure that MAT treatment does not interact or interfere with ongoing treatment in the inpatient stay. This is especially important in hospitalized settings where patients may be started on new medications that may interfere with MAT.

3.5.9 Remandees and incarcerated

- Patients on MAT should continue treatment in pre-trial detention and in prison where such treatment is feasible. Either the MAT program should continue to provide MAT to the patient while incarcerated, or the correctional facility should assume the responsibility for dosing of MAT.
- Ongoing MAT within correctional facilities reduces the risk of illicit drug use within correctional facilities.
- For individuals who are sentenced and in prison, long-term methadone may not be feasible within a correctional setting. For those patients, a slow taper off methadone in accordance with guidelines regarding tapering off methadone is most appropriate.
- Opioid dependent patients who are being released from prison back to the community should be considered for restarting of methadone or buprenorphine prior to release to reduce the probability of relapse to heroin use upon release.

3.5.10 Psychosocial interventions

Psychological interventions

- In the first 4 weeks of treatment, the focus should be on motivational enhancement therapy to increase the patient's confidence in continuing with treatment.
- Thereafter, the specific psychosocial intervention(s) should be based upon counseling and Health Care Provider staff assessment of the best treatment plan with the consent of the patient.

Social interventions

- Multiples social interventions have proven successful in helping drug users obtain sobriety, therefore MAT programme should strive to provide these services on site or by referral.

CHAPTER 4

4 SPECIAL CONSIDERATIONS FOR SPECIFIC GROUPS AND CONDITIONS IN TREATMENT

4.1 Patients with HIV/AIDS, hepatitis and TB

- Methadone and buprenorphine can be safely utilized in patients with HIV, hepatitis, and tuberculosis.
- Some pharmacological interactions are of concern between HIV therapies and methadone/buprenorphine (see appendix for table describing the important interactions).
- Patients with hepatitis can be normally dosed with methadone and buprenorphine. Patients with cirrhosis who are being started on MAT will require lower doses than those individuals with normal liver function. In this patient population, starting low and going slowly will be important.

4.2 Adolescents

- The goal of treatment in the adolescent is, as with the adult, long term sobriety from opioids.
- The adolescent, however, may benefit from shorter periods of MAT due to the likely shorter time period of previous opioids use.

4.3 Women

- Women are often victims of violence and female drug users may have been victims of male drug users – all of whom are attending the same MAT program. Therefore, MAT clinics must be sensitive to the needs of women and insure that all women have a safe place to obtain MAT.
- Because heroin suppresses ovulation, many women who are starting MAT will begin to ovulate again and may become pregnant. Family planning services should be discussed and ideally provided to female patients attending the MAT program.

4.4 Pregnancy/breastfeeding

- Pregnant patients should have easy access to MAT services as starting MAT has clear benefit for both the mother and the fetus.
- Methadone and buprenorphine are both safe in pregnancy; however, methadone remains the standard for treating the opioid dependent

pregnant woman.

- The co-formulated buprenorphine/naloxone cannot be utilized in pregnancy because of concerns regarding naloxone's effect on the fetus. Women who are maintained on buprenorphine/naloxone who become pregnant must be changed to the buprenorphine mono-formulation.
- Women can safely breastfeed during treatment though methadone and buprenorphine will be secreted in the breast milk; however, the levels are low and children born to these women will already have tolerance to the presence of the opioids given *in utero* exposure.

4.5 *The newborns*

- Treatment of neonatal abstinence syndrome (NAS) has 3 goals
    - o Prevent seizures
    - o Normalize sucking and improve feeding
    - o Control withdrawal symptoms
    - o For infants exposed only to opioids, opiates appear to be the most effective therapy for achieving these goals
    - o Morphine is the recommended at a dose of 0.04mg/kg
- Initial: 0.03-0.1 mg/kg by mouth every 4 hours, increase as needed by 0.02-0.04 mg/kg PO until abstinence scores are <8 (Refer Fennegan score annex: 7)
- Maintenance dose: 0.03-0.1 mg/kg by mouth every 4 hours
- Once scores stabilized for 3-5 days; gradually wean by 20% every other day
- Discontinue when total single dose is <0.08 mg.

4.6 *Psychiatric co-morbidity with opioid dependence*

- If patients relapse to drug use or appear to be struggling in adherence to treatment, the first consideration should be that the patient has an undiagnosed mental illness; therefore providers should be vigilant to look for possible mental illness.
- The most prevalent psychiatric co-morbidity among opioid dependent patients is major depressive disorder. Brief mental health screening instruments for psychosis are available (See Annex: 9). Patients who are identified and started on appropriate pharmacotherapy can have dramatic improvements both in their mood as well as their sobriety from illicit drugs.

4.7 *Poly-substance dependence*

- The poly-substance user is a more complicated patient than the individual with pure opioid dependence and is classified into two categories: poly use of drugs that increase overdose risk and those drugs that do not increase the risk of overdose.

4.8 *Use of drugs that increase overdose with methadone or buprenorphine:*

- Alcohol and sedatives such as benzodiazepines when combined with opioids such as methadone/buprenorphine can increase the risk of overdose.
- Individuals with ongoing alcohol or sedative use should be maintained at lower doses of methadone. Buprenorphine is less likely to combine with alcohol/sedatives and result in overdose (with the exception of midazolam and rohypnol).
- Use of opioid agonists like methadone is contraindicated in patients with acute alcohol intoxication exhibiting depressed vital signs. If the breathalyzer reading exceeds 0.05 methadone should be withheld.

4.9 *Use of drugs that do not increase overdose with methadone or buprenorphine:*

- Stimulants and cannabis, when combined with opioids, do not increase the risk of respiratory depression. No dose reduction of methadone/ buprenorphine, therefore, is necessary in patients abusing these substances with MAT.

4.10 *Patients with acute and chronic pain*

Acute pain is defined as pain of less than or equal to 6 months while chronic pain is pain that occurs for greater than 6 months.

- Methadone and buprenorphine have different analgesic properties. Methadone as a full opioid agonist has greater analgesic properties compared to buprenorphine which is a partial agonist. In addition, buprenorphine's high binding affinity results in a blockade of opioids that might be utilized for analgesia. Methadone and buprenorphine dosed once daily for opioid dependence is inadequate for acute and chronic pain control.
- Acute pain treatment may require the utilization of short acting opioids. Because methadone and buprenorphine block the access of opioids to receptor sites and therefore dampen the analgesic properties of these medications, a short acting opioid may need to be added at a higher dose to overcome this blockade. More frequent follow-up visit will be necessary to re-evaluate the level of pain control in these patients to insure that adequate analgesia is provided.
- Chronic pain treatment should avoid the utilization of short acting opioids and should focus on longer acting opioids that may provide better long-term analgesia. For patients on methadone, consideration of split dosing in the patient eligible for take-home doses (see take-home dose described earlier) will improve chronic pain analgesia. Dose increases of methadone or the introduction of additional opioids may be required to achieve adequate analgesia in these patients. Because buprenorphine is inferior

to methadone in the treatment of chronic pain, it may be necessary to move buprenorphine patients to methadone in order to provide improved analgesia.

REFERENCES

1. Amass, et al (2001). Thrice-weekly supervised dosing with the combination buprenorphine-naloxone tablet is preferred to daily supervise dosing by opioid-dependent humans. *Drug and Alcohol Dependence, 61*(2), 173–181.
2. APA (2008). Diagnostic Statistical Manual IV-Text Revised
Center for Substance Abuse Treatment
3. CSAT (2004) *Clinical guidelines for the use of buprenorphine in the treatment of opioids addiction.* Treatment Improvement Protocol (TIP) Series 40. DHHS Publication No. (SMA) 04-3939. Rockville, MD:
4. Bruna Brands and John Bruna, (1998). Methadome Maintanance: A Physician's Guide to Treatment; CAMH,Toronto, ON M55 281
5. Douglas R. et al (2007). Clinical Care of the HIV-Infected Drug User; Yale University AIDS Program, Yale University School of Medicine,135 College Street, Suite 323, New Haven, CT 06510, USA
6. Gabriele F. (2005), Management of Pregnant Drug Users; Targeting reproductive & sexual health of IDU women in New States of European Union & Neighboring Countries; Medical University Vienna, Austria
7. Hendree E.(2008).Treatment of opioid-dependent pregnant women: Clinical and Research Issues: Journal of Substance Abuse Treatment; Department of Psychiatry, Medical University of Vienna, Vienna, Austria
8. NACO, (2008). Standard Operating Procedure for Oral Substitution Therapy with Buprenorphine: 9Floor, Chandralok Building 36, Janpath New Delhi – 110001
9. SAMHSA, (2009). Buprenorphine: A Guide for Nurses Technical Assistance Publication (TAP) Series: 1 Choke Cherry Road: Rockville, MD 20857
10. Sarz Maxwell, MD, Marc Shinderman, MD, (1999). Journal of Psychoactive Drugs: Vol-31 #2
11. Thomas F. et al (2009).Medication Assisted Treatment in the Treatment of Drug Abuse and Dependence in HIV/AIDS Infected Drug Users: Department of Psychiatry, University of California, San Francisco, USA

ANNEX 1: Intake Assessment Module For MAT

This module is designed to document key areas and stages to follow during client assessment. It is designed to be used by ticking boxes to record key findings and writing the details in the lines nearby.

MAT PROGRAM CLIENT ASSESSMENT FORM

PHOTO	Record No

A. Particulars

Name _____

(First) (Middle) (Last)

Gender: Male _____ Female _____

Date of Birth (day/month/year) _____

Age (Years) _____

Marital status_____

Tribe _____

Place of residence_____

District _____

Address (Detailed physical address) _____

_____

Phone no _____

Emergence contacts

1. Name and relationship_____

Address *(Details physical address)*_____

Phone no _____

2. Name and relationship _____
Address *(Details physical address)* _____
Phone no _____

B. Presentation

Presenting date and time _____
Reasons for Presentation _____
_____
Referral from _____

C. Drug use history

Brief outline _____
_____
_____

D. Drug use summary

Drug used	No of days used in last month	Frequency used per day	Estimated amount used daily	Routes of administration	Date/time of last use *(hours)*	Age at start of regular use *(yrs)*

E. Previous Alcohol/other drug use treatment (Please tick the appropriate response)

1. In patient detoxification	2. Outpatients Detoxification	3. MAT treatment
4. Counseling/psychotherapy	5. Alcoholic anonymous	6. Narcotics anonymous
7. Others (specify)_____		

F. History of Alcohol/drug treatment

Treatment *(Drug treated)*	When *(Year)*	Duration *(months)*	Name of provider

G. Problems related to Alcohol/drug use *(Please tick the appropriate response)*

Relationships		ANY COMMENTS
Family		
Social		
Medical		
Psychological		
Financial		
Legal		
Overdoses		
Others		

H. Medical History

System	Conditions	Comments
Gastrointestinal	Hepatitis (B or C), liver disease, peptic, bowel habits, others	
Cardiovascular	Hypertension, endocarditis, other current symptoms	
Respiratory	Asthma, bronchitis, tuberculosis, other current symptoms	
Neurological	Seizures, head injury, other current symptoms	
Genito-urinary	Pregnancy, STD's including HIV status, sexual dysfunction, menstrual abnormalities, contraception, other current symptoms	
Endocrine	Diabetes, thyroid disease *(toxic goiter, hypothyroidism)*, other current symptoms	
Other	Chronic pain, musculoskeletal (*trauma, arthritis),* dermatological, other current symptoms	
Current drug prescribed	List all	

I. Key conditions (*Summarize after complete history taking*)

I. Pregnant	II. HIV-positive	III. Hepatitis C Positive
IV. Hepatitis B infection	V. Hepatitis B infection	VI. Liver disease
VII. Cardiovascular disease	VIII. Respiratory disease	IX. Renal disease
X. Chronic pain	XI. Drug allergies	XII. Contraceptive use
XIII. Others		

J. Infectious Risk Behaviors

1. Frequency of needle sharing in last three months	Average no per day	Average no per week	Average no per month	Any comments
2. Use of bleach to clean needles before re-use 3.	Always	Sometimes	never	Any comments
4. Needle sharing partners in last three months	Number using needle before	Number using needle after		Any comments
5. Number of sexual partners in last three months		Any comments		
6. Number of penetrative vaginal sex partners for unprotected penetrative sex in last 30 days		Any comments		
7. Number of penetrative anal sex partners in last 30 days		Any comments		

K. Family History

Disorder	Yes/No	Details information
Psychiatric Disorders		
Medical conditions		
Drug or Alcohol Problems		
Problem family Relationship		
Suicides attempts/committing in the family		

L. Personal and Social History

Current stressors	**Yes/No**	**Details information**
Losses		
Problems with relationships		
Financial		
Legal		
Employment		
Accommodation		
Others		
Others		
Past Significant life events		
History of abuse		
Loss of significant others		
Other Traumatic events		
Current social situation and significant relationships		
Single		
Married		
Separated or divorced		
Abusive partner		
Drug-using cohabitants		
Supportive Friends		
Supportive relatives		
Children, separated		
Dependant children		
1. Others		

Formal Qualifications and Skills		
Primary education		
Form four education		
Form six education		
Certificate/Diploma		
Advanced Diploma		
Degree		
Masters degree and above		
Others		
Employment status		
Current employment		
Past employments *a) Job 1* *b) Job 2* *c) Job 3*		
Current average income per month	*(Tshs)*	
Legal History		
Currently facing charges		
Past convictions		
Time spent in jail		

M. Mental State Examination

Parameters	Components	Remarks
General Appearance and Behavior	Attire, grooming, movements *(agitated, retarded)*, speech, attitude to examiner,	
Speech	Tone, speed, logic	
Mood	Elated, depressed, normal	
Affect	Euphoria, happy, normal, sad, crying	
Thoughts	Tempo, form, contents, delusions suicidal, homicidal Thoughts disturbances – *broadcasting, insertion, withdrawal, echo*	
Perceptions	Hallucinations, illusion, perceptual distortion	
Cognitive function	Orientation, memory, attention, concentration Abstract thinking, judgment	
Insight	Good, poor, partial	
Other findings		
MSE - Conclusion	Mentally Stable, mentally unwell , provisional Diagnosis	

N. Physical Examination

System	Parameters	Remarks
General Appearance	Pallor, cyanosis, dehydration status, dyspnoea, pedal oedema, skin scratching marks, PPE, scabies, fungal lesions,	
Vital sigs	Temp _____ ^{o}C Pulse _____ /Min BP _____mm/Hg	
Head and neck	Lymphadenopathy, Ears, nose, eyes *(pin pointed pupils)*, mouth *(oral thrushes, ulcers)*	
Cardiovascular	Precordial observation, movements, percussion and auscultation,	

Respiratory	Chest observation, movements, percussion and auscultation,	
Abdominal	Abdomen observation, palpation for organomegaly, percussion and auscultation	
Neurological exam	Central nervous system, Peripheral nervous system, Local neurological exams	
Other findings		
Summary of findings	Provisional Diagnoses	

Evidence of injecting drug use	**Yes/No**	**Indicate sites, size, and other details**
Needle marks		
Venous scarring		
Phlebitis		

O. Physical Investigations

Baseline Investigations	**Yes/No**	**Results Summary**
FBP		
ESR		
RBG		
Serum electrolytes		
Liver Function Tests		
Renal Function Test		
Chest X-ray		
Sputum for AFB		
Urinalysis		
Stool analysis		
Others		

Specific Investigations		
Urine test for opioids		
Hepatitis serology		
HIV test		
Others		

P. Check list

Patient information given	**Yes/No**	**Remarks**
Treatment aims		
Treatment plan		
MAT effects and adverse effects		
Consequences of non compliance		
Warnings		
Overdose and intoxications		
Control of vehicles		
Patient routine obligations		
Appointments/collections		
Report use of other drugs		
Report withdrawal symptoms		
Provide urine tests		
Attend counseling		

Involuntary discharge conditions		
Violence		
MAT diversion		
Failure to collect doses		
Drug dealing		
Others		
Patient requested to obtain ID photos		
Support services available		
Review and appeal process		
Reducing infectious risk behavior		
Documents given to patient		
Printed IEC materials		
Copy of informed consent to treatment given		
Treatment sheet with doctor's instructions and/or prescriptions		

Q. Management Plan

Components		
Starting dates		
Initial dose		
Early monitoring arrangements		
Initial harm reductions actions		
Case Management arrangements		
1. Others		

ANNEX 2: Opioid Dependence Screening Tool

In the past 12 months (if yes score 1):

a) Have you needed to use more [insert main drug] to get the desired effect, or has taking your usual amount had less of an effect than it used to?
b) Have you felt sick or unwell when the effects of [insert main drug] have worn off, or have you taken more of it, or a similar drug, to relieve or avoid feeling unwell?
c) Have you used [insert main drug] in larger amounts or for a longer period of time than you intended?
d) Have you had a persistent or strong desire to take [insert main drug] or have you had problems cutting down, or controlling how often or how much you use?
e) Have you spent a large amount of time obtaining, or using, or recovering from the effects of [main drug]?
f) Have you given up work, recreational, or social activities as a result of your [insert main drug] use?
g) Have you continued to use [insert main drug] despite having physical or psychological problems as a result?

Total score = _____

If total score is 3 or more, dependence is diagnosed

ANNEX 3: MAT Treatment Checklists

1. Does the patient have a diagnosis of opioid dependence?
2. Are there current signs of withdrawal?
3. Is the patient interested in MAT?
4. Does the patient understand the risks and benefits of MAT?
5. Can the patient be expected to adhere to the treatment plan?
6. Is the patient psychiatrically stable? Is the patient actively suicidal or homicidal?
7. Is the patient pregnant?
8. Is the patient currently dependent on or abusing alcohol?
9. Is the patient currently dependent on benzodiazepines or barbiturates?
10. Is the patient taking other medications that may interact with MAT?
12. Does the patient have medical problems that will complicate treatment?
13. Are the patient's psychosocial circumstances sufficiently stable?

ANNEX 4: Sample Methadone Treatment Agreements

Client Name: _____

I _____agree to enter into a program of methadone maintenance treatment offered by [NAME OF YOUR PROGRAM]. This treatment is specifically designed to help me deal with my problems of opioid dependence and will assist me in dealing with the psychological and social difficulties that often accompany

problems of addiction. The main purpose of this program is to help me make positive changes in my life related to the use of opioids and other substances.
I am seeking help to stop use of illicit drugs and other substances like alcohol and prescription drugs. I am interested in gaining assistance in overcoming my problems with drug use and any associated psychosocial difficulties.

I understand [NAME OF YOUR PROGRAM] offers a range of services in conjunction with methadone maintenance treatment, which can assist me in achieving my goals. Medical care pertinent to my methadone treatment will be provided. In addition, a range of counseling services are encouraged and available on a voluntary basis. Counseling options include support groups, relapse prevention groups, individual counseling and crisis support as well as referrals to other community services.

I understand that this treatment is likely to help me but if not other clinical care will be discussed with me.

I understand that, as a participant in this treatment program, I am agreeing to the following:

1. Methadone treatment
Methadone is an opioid and, as such, its prescribing and dispensing are regulated by a number of legal guidelines. I understand that my receipt of methadone depends on the following:

- I agree to pick up my medication during normal clinic dispensing hours and to take the medicine according to the health care provider's directions.
- I agree to notify program staff of all prescription and non-prescription medications that I am taking. I will bring my prescriptions or medication bottles to the pharmacy so that the exact drug and dosage can be noted. The treatment team will advise me, in consultation with my prescribing physician, of any drugs that I am taking that are inconsistent with my treatment plan. I will then refrain from taking these drugs while I am receiving treatment on this program.
- I understand that on some days I may be required to leave a supervised urine sample before obtaining my methadone dose. If I am unable to provide the required sample, staff may ask me to wait. Upon providing the urine sample, I will be able to obtain my methadone.
- I understand that tampering with urine samples is a serious program violation. I understand that as I progress in the program, I may request methadone take-home doses that reduce the number of days I have to attend the clinic.
- I understand that I may request to have my methadone dose reduced or increased at any time by discussing this with my physician.
- I am aware that the treatment team will check to ensure that I am taking my methadone and that I am providing my own urine samples.

2. *Initial Assessment/Treatment Progress Reviews*

- I understand that upon entry to the program, I will receive an initial comprehensive assessment that will be used to help me develop a personal action plan based on my specific needs and goals. In the event that I am unable to attend the scheduled initial assessment meetings, I will notify the program's staff as soon as possible, preferably at least 24 hours in advance. Program staff will accord me with the same courtesy should they be unable to attend a scheduled session.
- I will be offered a range of counseling options that I can elect to engage in. I understand that the continued eligibility in most counseling services depends on regular attendance.
- I understand that I will be expected to attend periodic meetings to have my methadone prescription renewed and to review my treatment progress.

3. *Medical Care*

- I will be provided with an initial assessment by a physician affiliated with this program. The assessment for the purpose of determining if methadone is appropriate and safe for me.
- I understand that [NAME OF YOUR PROGRAM] is a specialized addictions service. I agree to sign a consent form allowing health care provider in the program to exchange medical information relevant to my care.
- If another physician or dentist proposes to prescribe opioids (i.e. narcotics) to me I will inform him or her that I am receiving methadone. Obtaining narcotics from more than one physician or dentist could be dangerous to my health and is illegal.

4. *Clinic Environment*

- I understand that that [NAME OF YOUR PROGRAM] is committed to maintaining a clinic environment that is safe for clients, visitors and staff and to maintaining positive, respectful behavior. Such behavior does not include threats, violence or destructive behavior. I agree to uphold these standards.
- I understand that if I have any concerns, I may approach health care provider immediately and if I am not satisfied with the response there is a problem resolution procedure that I may follow.

5. *Confidentiality*

- My privacy will be respected. Confidentiality of my health record will be protected in the same way that it is in other health facilities. No release of information from my health record will be given without my written consent or as required by law.
- I understand only in certain situations, the treatment team may be required by law to give out information without my consent. This involves situations where the treatment team perceives my behavior to be of risk to myself or to other people (such as where child neglect or abuse is suspected).

- Because my participation in the program will bring into contact with other opioid users, I expect other clients to be respectful of my rights, confidentiality and treatment goals, and I will respect the rights, confidentiality and treatment goals of other clients.

My signature below indicates that I have discussed this treatment agreement with a counselor and understand and agree to all of the above. Should I fail to meet my responsibilities as a participant in this program, I understand that this will result in a re-assessment of the treatment plan and a consideration of my continued involvement in the program.

Client Signature ----------

Name ----------

Address----------

Date----------

Signature of health care provider----------

ANNEX 5: Interactions Between Antiretroviral And Methadone And Buprenorphine

NRTI				
Medication	**Effect On Methadone**	**Effect On BUP**	**ARV**	**Comments**
Abacavir (ABC)	↑ clearance	Not studied	↓ C_{max}	Unclear if ↑ in M clearance is caused by ABC ↓C_{max} not clinically relevant.
Didanosine (ddI)	No effect	Not studied	↓ ddI AUC by 57% for buffered tablet partially corrected by EC capsule to within range in historical controls	EC capsule recommended for methadone patients
Emtriva (FTC)	Not studied	Not studied	Not studied	
Lamivudine (3TC)	No effect	Not studied	Not studied	AZT/3TC co-formulation studied only
Stavudine (d4T)	No effect	Not studied	↓d4T AUC_{12h} by 23% and C_{max} by 44%.	Changes unlikely to be clinically significant.
Tenofovir (TDF)	No effect	Not studied	Not studied	
Zalcitabine (ddC)	Not studied	Not studied	Not Studied	
Zidovudine (AZT)	No effect	No effect	↑ AZT AUC by 40%	Watch for AZT related toxicity (symptoms and laboratory)
NNRTI				
Medication	**Effect On Methadone**	**Effect On BUP**	**ARV**	**Comments**
Delavirdine (DLV)	↑ AUC by 19%; ↑Cmax by 10%	> 4 fold increase in BUP AUC, but without clinical effect	No effect by either BUP or methadone	Likely not clinically relevant, but should be used with caution as long-term effects (greater than 7 days) unknown.

Efavirenz (EFV)	Significant effect – mean ↓methadone AUC by 57%	↓in AUC of buprenorphine by 50%, but no clinical effect	No effect by either BUP or methadone	Opiate withdrawal common. Methadone dose increase necessary
Nevirapine (NVP)	Significant effect – mean ↓ methadone AUC by 46%	Not studied	No effect from methadone	Opiate withdrawal common. Methadone dose increase necessary.
PI				
Medication	**Effect On Methadone**	**Effect On BUP**	**ARV**	**Comments**
Amprenavir (AMP)	↓ AUC of R-methadone by 13%	Not studied	↓ AUC by 30%	Decreases in AUC do not appear to be clinically significant
Atazanavir (ATV)	No effect	Questionable oversedation	No effect	No dose adjustments necessary for methadone. Consider slower titration in buprenorphine
Fosamprenavir (fAMP)	Not studied	Not studied	Not studied	As a pro-drug of amprenavir, will likely have the same interactions noted above.
Indinavir (IND)	No effect	Not studied	↓C_{max} between 16 to 28% and↑ C_{min} between 50 to 100%	Differences do not appear to be clinically significant
Lopinavir/ritonavir (LPV/r)	↓ AUC by 26-36%	No clinical effect	Buprenorphine increased LPV AUC by 16%	↓AUC of M caused by lopinavir. One study reported opioid withdrawal symptoms in 27% of patients. Methadone dose increase may be necessary in some patients.

Nelfinavir	↓AUC by 40%	No significant clinical effect	↓AUC of active M8 metabolite by 48% in methadone; No changes in NFV of M8 were observed	Despite ↓ M AUC, clinical withdrawal is usually absent and *a priori* dosage adjustments are not needed. Decrease in AUC of M8 unlikely to be clinically significant. TDM may be useful in patients with good adherence and virologic failure.
Ritonavir (RTV)	↓ AUC by 37% in one study and no effect in another (see text)	↑AUC by 57% without clinical effect of oversedation	Buprenorphine had no effect on RTV pharmacokinetics	No dosage adjustment
Saquinavir (SQV)	↓ AUC by 20-32%	Not studied	Not studied	Saquinavir boosted with ritonavir studied. Despite↓ M AUC, clinical withdrawal was not reported.
Tipranavir (TPV)	↓ methadone by 50%**	Not studied	Not reported	Methadone may need to be increased

NRTI = nucleoside reverse transcriptase inhibitors
NNRTI = non-nucleoside reverse transcriptase inhibitors
PI = protease inhibitor
AUC = area under curve
TDM = therapeutic drug monitoring
See text for references

Table 1. Interactions between antiretrovirals and methadone and buprenorphine.

NRTI			
Medication	Effect on methadone	Effect on buprenorphine	ARV
Abacavir (ABC)	No dose change	Not studied	No ARV dose change when combined with methadone
Didanosine (ddI)	No dose change	No dose change	Do not use buffered tablet with methadone. Only EC capsule
Emtriva (FTC)	Not studied	Not studied	Not studied
Lamivudine (3TC)	No dose change	No dose change	Not studied
Stavudine (d4T)	No dose change	Not studied	No ARV dose change when combined with methadone
Tenofovir (TDF)	No dose change	No dose change	Not studied
Zalcitabine (ddC)	Not studied	Not studied	Not studied
Zidovudine (ZDV)	No dose change	No dose change	Methadone increases ZDV, some cases of ZDV toxicity in methadone-maintained. No significant effect in buprenorphine-maintained or naltrexone-maintained.
NNRTI			
Medication	Effect on methadone	Effect on buprenorphine	ARV
Delavirdine (DLV)	Increased methadone exposure; no toxicity observed	No dose change	No ARV dose change when combined with methadone or BUP
Efavirenz (EFV)	Opiate withdrawal common Increased methadone doses needed	Decreased buprenorphine plasma concentrations, but no opiate withdrawal	No ARV dose change when combined with methadone or BUP
Etravirine (ETV)	No dose change (only 100 b.i.d. of etravirine used)	Not studied	No ARV dose change when combined with methadone
Nevirapine (NVP)	Opiate withdrawal common Increased methadone doses needed	No dose change	No ARV dose change when combined with methadone
PI			
Medication	Effect on methadone	Effect on buprenorphine	ARV
Amprenavir (AMP)	No dose change	Not studied	No ARV dose change when combined with methadone
Atazanavir (ATV)	No dose change	Possible sedation; slow titration recommended	No ARV dose change when combined with methadone or BUP
Darunavir (DRV)	Opioid withdrawal may occur.	Not studied	No ARV dose change when combined with methadone
Fosamprenavir (fAMP)	As a pro-drug of amprenavir, will likely have the same interactions noted above.		
Indinavir (IND)	No effect	Not studied	No ARV dose change when combined with methadone
Lopinavir/ritonavir (LPV/r)	Opioid withdrawal may occur; methadone dose increase may be necessary in some patients	No dose change	No ARV dose change when combined with methadone or BUP
Nelfinavir	Decreased methadone plasma concentrations, but few cases of withdrawal, clinical monitoring advised in methadone-treated patients	No dose change	No ARV dose change when combined with methadone or BUP
Ritonavir (RTV)	No dose change	No dose change	No ARV dose change when combined with methadone or BUP
Saquinavir (SQV)	No dose change	Not studied	No ARV dose change when combined with methadone
Tipranavir (TPV)	Opioid withdrawal possible; may need to increase dose	Decrease in norBUP	No ARV dose change when combined with methadone. TPV may be less effective with BUP-administration
Entry inhibitors			
Medication	Effect on methadone	Effect on buprenorphine	ARV
Maraviroc (MVC)	Not studied	Not studied	Not studied
Enfurvitide (T20)	Not studied	Not studied	Not studied
Integrase inhibitors			
Medication	Effect on methadone	Effect on buprenorphine	ARV
Raltegravir (RAL)	Not studied	Not studied	Not studied

ARV, antiretrovirals; NRTI, nucleoside reverse transcriptase inhibitors; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor. Adapted with permission [44].

ANNEX 6: Other Drugs That May Interact With Methadone

Drug	Possible effect when combined with methadone
Alcohol	Sedation, respiratory depression; may be toxic to the liver
Barbiturates	Reduces methadone levels, sedation, CNS depression
Benzodiazepines	Increased sedation
Buprenorphine	Sedation, respiratory depression
Carbamazepine	Reduced methadone levels
Chloral hydrate	Increased sedation
Chlormethiazole	Increased sedation
Cimetidine	Increase in methadone levels
Ciprofloxacin	Increased sedation, respiratory depression
Cisapride Domperidone Metoclopramide	***Theoretically*** may increase speed of onset of methadone absorption
Cyclazine and other sedating antihistamines	May cause hallucinations
Desipramine	Increased desipramine levels
Other tricyclic antidepressants	Increased sedation (dose dependent) (***theoretical***)
Disulfiram	Unpleasant side effects if combined with methadone solution which contains alcohol
Erythromycin	Increased methadone levels (***theoretical, has not been studied***)
Fluconazole	Increased methadone levels
Fluoxetine Sertraline	Increased methadone levels
Fluvoxamine	Raised plasma methadone levels
Grapefruit juice	Increased methadone levels
Indinavir	Increased methadone levels
Ketoconazole	Increased methadone levels

Drug	Possible effect when combined with methadone
MAOI (including selegiline and moclobemide)	CNS excitation, delirium, hyperpyrexia, convulsions, hypotension or respiratory depression (possible
Meprobamate	Enhanced sedative effect and respiratory depression
Naltrexone	Blocks effects of methadone
Naloxone	Blocks effects of methadone
Nifedipine	Increased nifedipine levels but no effect on methadone levels (***in vitro demonstration only***)
Omeprazole	Increased methadone levels (***demonstrated in animals only***)
Pentazocine	Enhanced sedation and respiratory depression
Phenobarbitone	Reduces methadone levels, sedation, CNS depression
Phenytoin	Reduces methadone levels
Propanolol	Enhanced lethality of toxic doses of opioids (***demonstrated in animals only***)
Rifampicin	Reduces methadone levels
Rifabutin	Reduces methadone levels
Thioridazine	Enhanced sedation which is dose dependent
Urine acidifiers (e.g. vitamin C)	Reduces methadone levels
Urine alkalisers (e.g. sodium bicarbonate)	Increased methadone levels
Zopicione	Enhanced sedative effect and respiratory depression
Other opioid agonists	Enhanced sedative effect and respiratory depression
Other CNS depressant drugs (e.g. neuroleptics, hyosine)	Enhanced sedative effect which is dose dependent

This table is based on a similar one published in Australian Government Department of Health and Aging (2003) *Clinical Guidelines and Procedures for the Use of Methadone in the Maintenance Treatment of Opioid Dependence*
This table is used with permission.

ANNEX 7: Neonatal Abstinence Syndrome Scale

Modified Finnegan Scale

This scale is used for the measurement of neonatal abstinence syndrome due to neonatal opioid withdrawal.

			Date and Time in Hours												
System	Signs and Symptoms	Score													
Central Nervous System Disturbances	High-Pitched Cry	2													
	Continuous High-Pitched Cry	3													
	Sleeps<1 hour after feeding	3													
	Sleeps<2 hours after feeding	2													
	Sleeps>3 hours after feeding	1													
	Mild Tremors Disturbed	1													
	Mod-Severe Tremors Disturbed	2													
	Mild Tremors Undisturbed	3													
	Mod-Severe Tremors Undisturbed	4													
	Increased Muscle Tone	2													
	Excoriation (specify area)	1													
	Myodonic Jerks	3													
	Generalised Convulsions	5													
Metaboli c/Vasomotor/ Respiratory Disturbances	Fever (37.3°C-38.3°C)	1													
	Fever (38.4°C and higher)	2													
	Frequent Yawning (>3.4 times)	1													
	Nasal Stuffiness	1													
	Sneezing (>3-4 times)	1													
	Nasal Flaming	2													
	Respiratory Rate > 60/min	1													
	Respiratory Rate >60/min with retractions	2													
Gastrointestinal Disturbances	Excessive sucking	1													
	Poor Feeding	2													
	Regurgitation	2													
	Projectile Vomiting	3													
	Loose Stools	2													
	Watery Stools	3													
	Mas Score:41 Total Score														
	Scorer's Initials														

Neonatal Withdrawal Scoring Chart (Term Infants)

Source: Finnegan 1980.[327]

If the baby has three consecutive scores averaging more than eight (8), the child should be treated for NAS.

ANNEX 8: Clinical Opiate Withdrawal Scale (COWS)

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is
increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.
Patient's Name:_____ Date and Time
____/_____/____:_____
Reason for this assessment:_____

Resting Pulse Rate:_____beats/minute
Measured after patient is sitting or lying for one minute
0 pulse rate 80 or below
1 pulse rate 81-100
2 pulse rate 101-120
4 pulse rate greater than 120

GI Upset: over last ½ hour
0 no GI symptoms
1 stomach cramps
2 nausea or loose stool
3 vomiting or diarrhea
5 Multiple episodes of diarrhea or vomiting

Sweating: over past ½ hour not accounted for by room temperature or patient activity.
0 no report of chills or flushing
1 subjective report of chills or flushing
2 flushed or observable moistness on face
3 beads of sweat on brow or face
4 sweat streaming off face

Tremor observation of outstretched hands
0 no tremor
1 tremor can be felt, but not observed
2 slight tremor observable
4 gross tremor or muscle twitching

Restlessness Observation during assessment
0 able to sit still
1 reports difficulty sitting still, but is able to do so
3 frequent shifting or extraneous movements of legs/arms
5 Unable to sit still for more than a few seconds

Yawning Observation during assessment

0 no yawning
1 yawning once or twice during assessment
2 yawning three or more times during assessment
4 yawning several times/minute

Pupil size
0 pupils pinned or normal size for room light
1 pupils possibly larger than normal for room light
2 pupils moderately dilated
5 pupils so dilated that only the rim of the iris is visible

Anxiety or Irritability
0 none
1 patient reports increasing irritability or anxiousness
2 patient obviously irritable anxious
4 patient so irritable or anxious that participation in the assessment is difficult

Bone or Joint aches If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored
0 not present
1 mild diffuse discomfort
2 patient reports severe diffuse aching of joints/ muscles
4 patient is rubbing joints or muscles and is unable to sit still because of discomfort

Gooseflesh skin
0 skin is smooth
3 piloerrection of skin can be felt or hairs standing up on arms
5 prominent piloerrection

Runny nose or tearing Not accounted for by cold symptoms or allergies
0 not present
1 nasal stuffiness or unusually moist eyes
2 nose running or tearing
4 nose constantly running or tears streaming down cheeks

Total Score _____
The total score is the sum of all 11 items

Completing Assessment: _____
Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

ANNEX 9: Mental Health Screening Form

Instructions: In this scale, we will ask you questions in order to identify co-occurring mental health problems in addicted individuals. However, any information you provide to us will be kept in strict confidence. It will not be released to any outside person or agency without your permission. If you do not know how to answer these questions, ask the staff member giving you this form for guidance. Please note, each item refers to your entire life history, not just your current situation, this is why each question begins - "Have you ever ...."

1. Have you ever talked to a psychiatrist, psychologist, therapist, social worker, or counselor about an emotional problem?
☐ YES ☐ NO
2. Have you ever felt you needed help with your emotional problems, or have you had people tell you that you should get help for your emotional problems?
☐ YES ☐ NO
3. Have you ever been advised to take medication for anxiety, depression, hearing voices, or for any other emotional problem?
☐ YES ☐ NO
4. Have you ever been seen in a psychiatric emergency room or been hospitalized for psychiatric reasons?
☐ YES ☐ NO
5. Have you ever heard voices no one else could hear or seen objects or things which others could not see?
☐ YES ☐ NO
6. (A1) Have you ever been depressed for weeks at a time,
☐ YES ☐ NO
(A2). Have you ever lost interest or pleasure in most of your activities?
☐ YES ☐ NO
(A3). Have you ever had trouble concentrating and making decisions?
☐ YES ☐ NO
(A4). Have you ever thought about killing yourself?
☐ YES ☐ NO
(B) Did you ever attempt to kill yourself?
☐ YES ☐ NO
7. Have you ever had nightmares or flashbacks as a result of being involved in some traumatic/terrible event? For example, warfare, gang fights, fire, domestic violence, rape, incest, car accident, being shot or stabbed?
☐ YES ☐ NO

8. Have you ever experienced any strong fears? For example, of heights, insects, animals, dirt, attending social events, being in a crowd, being alone, being in places where it may be hard to escape or get help?

☐ YES ☐ NO

9. Have you ever given in to an aggressive urge or impulse, on more than one occasion that resulted in serious harm to others or led to the destruction of property?

☐ YES ☐ NO

10. Have you ever felt that people had something against you, without them necessarily saying so?

☐ YES ☐ NO

Have you ever felt that someone or some group may be trying to influence your thoughts or behavior?

☐ YES ☐ NO

11. Have you ever experienced any emotional problems associated with your sexual interests, your sexual activities, or your choice of sexual partner?

☐ YES ☐ NO

12. Was there ever a period in your life when you spent a lot of time thinking and worrying about gaining weight, becoming fat, or controlling your eating? For example, by repeatedly dieting or fasting?

☐ YES ☐ NO

13. Have you ever had a period of time when you were so full of energy and your ideas came very rapidly, when you talked nearly non-stop, when you moved quickly from one activity to another, when you needed little sleep, and believed you could do almost anything?

☐ YES ☐ NO

14. Have you ever had spells or attacks when you suddenly felt anxious, frightened, uneasy to the extent that you began sweating, your heart began to beat rapidly, you were shaking or trembling, your stomach was upset, you felt dizzy or unsteady, as if you would faint?

☐ YES ☐ NO

15. Have you ever had a persistent, lasting thought or impulse to do something over and over that caused you considerable distress and interfered with normal routines, work, or your social relations? Examples would include repeatedly counting things, checking and rechecking on things you had done, washing and rewashing your hands, praying, or maintaining a very rigid schedule of daily activities from which you could not deviate.

☐ YES ☐ NO

16. Have you ever been told by teachers, guidance counselors, or others that you have a special learning problem?

☐ YES ☐ NO

Print client's name: _____

_____

Name of admissions counselor: _____ Date: _____

_____

Total Score: _____ (each yes = 1 point)

Source: Carroll, J. F. X., & McGinley, J. J. (2000).