



UNODC

United Nations Office on Drugs and Crime

METHADONE MAINTENANCE TREATMENT

1



INTERVENTION TOOLKIT

PREVENTION OF TRANSMISSION OF HIV AMONG
DRUG USERS IN SAARC COUNTRIES
(RAS/H13)

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METHADONE MAINTENANCE TREATMENT INTERVENTION TOOLKIT

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- 4) **Maldives:** Department of Public Health and Department of Medical Services, Ministry of Health, Government of Maldives
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Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
CTN	Clinical Trial Network
COWS	Clinical Opiate Withdrawal Scale
DOT	Direct Observation Treatment
HIV	Human Immunodeficiency Virus
ICD	International Classification of Disease
ICTC	Integrated Counselling and Testing Centre
IDUs	Injecting Drug User
LAAM	Levo Alpha Acetyl Methadol
MMT	Methadone Maintenance Treatment
MSJE	Ministry of Social Justice and Empowerment
NACO	National AIDS Control Organizations
NAS	Neonatal Abstinence Syndrome
NGO	Non-Governmental Organisation
ORW	Outreach Workers
OST	Opioid Substitution Treatment
PE	Peer Educator
PM	Project Manager
SAARC	South Asian Association for Regional Cooperation
SHG	Self-help Group
STI	Sexually Transmitted Infections
TI	Targeted Interventions
UNODC ROSA	United Nations Office on Drugs and Crime Regional Office for South Asia
WHO	World Health Organization

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BACKGROUND

The project “*Prevention of transmission of HIV among drug users in SAARC countries*” (Project RAS/H13) is executed by UNODC as part of a joint UN initiative between UNODC, UNAIDS, and WHO in South Asia. The overall goal of this project is to reduce the spread of HIV among drug using populations in SAARC countries. In doing so, the project assists governments and communities to scale-up comprehensive prevention and care programs for drug users, especially injecting drug users (IDUs), and their regular sex partners.

Under its current phase (Phase II), the project is designed to demonstrate the effects of comprehensive harm reduction interventions which were initiated in Phase I and place the evidence for consideration by national governments to scale up programmes for significant coverage with quality services. The project is presently working in seven countries (Bangladesh, Bhutan, India, Nepal, Maldives, Pakistan and Sri Lanka) and has four key components:

- 1) Advocacy to support change in policy and practice
- 2) Demonstrate the effectiveness of comprehensive risk reduction approaches to reduce HIV transmission among drug users, especially IDUs, and their sex partners
- 3) Scaled up risk reduction approaches to reduce HIV transmission among drug users, especially IDUs, and their regular sex partners and
- 4) Efficient project management

A number of tools have been developed by UNODC to build the capacities of service providers, institutions, as well as policy makers on

various aspects linked to HIV prevention among drug users. The tools have been tailor-made, keeping in mind the strategic gaps in capacities and service delivery, to ensure quality, and to ensure standardization of services which are cost effective and can be replicated.

Accordingly, a set of six intervention tool kits were developed by UNODC during Phase I of the project. These toolkits were field tested through implementation at the demonstration sites developed under the project’s Phase I (2003-2007). They have been extensively used by the countries and finalized drawing from the implementation experiences.

Two toolkits on Opioid Substitution Treatment (OST) i.e., one each on buprenorphine and methadone substitution have been of particular significance in this context and specially in assisting countries with their scale-up plans. Since the inception of the project and development of the toolkits, four out of the seven SAARC countries have initiated OST. The choice of medicines has been different in different countries. While Bangladesh and Maldives have initiated Methadone maintenance treatment alone, India and Nepal have initiated OST with both Buprenorphine and Methadone. Bhutan too has demanded the initiation of OST interventions. The rich experiences gained over the years on OST implementation in the SAARC region have been drawn upon to revise and update this intervention toolkit on Methadone Maintenance Treatment.

This toolkit therefore has been developed with the aim of assisting policy makers and program implementers to initiate, strengthen and scale-up OST interventions for opioid dependent drug users (and specially those who inject drugs) based on lessons learnt elsewhere and the cumulative weight of scientific evidence.

INTRODUCTION

In South Asia, opioid use and in particular heroin use is on the increase. The diffusion of injecting drug use is causing concern in the region (UNODC and MSJE, 2004). Heroin and other opioid dependence cause significant morbidity and mortality; it is a chronic and enduring condition that often requires long-term treatment and care. An adequate access to a range of treatment options should be offered to respond to the varying needs of people with heroin/opioid dependence.

Substitution maintenance treatment is an efficacious, safe and cost-effective modality for the management of opioid dependence. Such treatment is a valuable and critical component of the effective management of opioid dependence and the prevention of HIV among IDUs. Scientific evidence suggests that substitution treatment can help reduce criminality, infectious diseases and drug-related deaths as well as improve the physical, psychological and social well-being of dependent users (Gibson et al. 1999). Provision of substitution maintenance treatment should be integrated with other HIV preventive interventions and services, as well as with those for treatment and care of people living with HIV/AIDS (WHO, UNODC and UNAIDS, 2004). A recent review recommended that the provision of substitution treatment for opioid dependence should be supported both in countries with emerging HIV and injecting drug use problems as well as in countries with established populations of IDUs (Gowing et al. 2004).

Pharmacological agents used as substitution substances in the management of opioid dependence are: methadone, buprenorphine, levo alpha acetyl methadol (LAAM), dihydrocodeine and tincture of opium (laudanum). Methadone is the most employed agent in

Drug substitution means replacing, under medical supervision, the drug which the drug user is taking with a similar substance. It may also mean using the same drug but taking it in a different way, for example, sublingual buprenorphine to replace injecting of buprenorphine. Substitution treatment comes either with or without psychosocial support.

substitution treatment around the world. Buprenorphine is emerging as a useful complementary or alternative option to methadone as there have been increasing doubts about the safety of LAAM because of the related cardiac risk.

The first methadone study was performed in late 1963 and early 1964 at The Rockefeller Institute for Medical Research by Drs Vincent Dole and Nyswander (Dole and Nyswander, 1965; Dole and Nyswander, 1966). Their research concluded that methadone prevented opioid withdrawal symptoms, blocked the euphoria of heroin, and decreased cravings in opioid-dependent individuals; and thereby confirmed methadone as a maintenance medication with efficacy for opioid dependence. Dr Robert Halliday from Vancouver set up what is believed to be the first Methadone Maintenance Treatment (MMT) program in the world. Since then, opioid agonist treatment with MMT has become an effective treatment option for opioid-dependent individuals worldwide. Many European countries such as France, Holland, Germany, Spain, Finland, Greece and

Australia currently operate large-scale methadone programs. In Asia, a scaled-up program with methadone is operational in Hong Kong, the Republic of China and Malaysia. Further, countries such as Indonesia, Thailand, Myanmar, Vietnam, Cambodia, Nepal, Bangladesh and Maldives offer methadone substitution treatment to opioid dependents. Pilot projects have been initiated in five sites in India.

Methadone is an opioid falling under the same category as other synthetic and naturally-occurring opioids such as pethidine, heroin, morphine, codeine, etc. Although all these substances produce tolerance and dependence on repeated administration, the user becomes tolerant to opioids and not to any specific opioid. This makes it possible to preclude the euphoric and other effects of all opioids by establishing a high degree of tolerance through the prescribing of methadone. One can also prevent withdrawal symptoms among individuals who have a long history of heroin use by prescribing appropriate doses of methadone. And that, in essence, is the pharmacological basis for the use of methadone for long-term 'maintenance' (Byrne and Newman, 1999). Methadone has ideal properties for a maintenance agent: it is orally active and long-acting (one dose suppresses symptoms of opioid withdrawal for 24-36 hours without producing euphoria, sedation and analgesia). This enables patients to function normally (i.e., without impairment) and experience normal pain and emotional responses. Another advantage of methadone is the ability to suppress craving (Lowinson et al. 2006).

Major observational studies have indicated that MMT reduces illicit drug use and criminal activities (Ball and Ross, 1991; Hall et al. 1998). Scientific evidence suggests that substi-

tution treatment with methadone can help reduce criminality, infectious diseases and drug-related deaths as well as improve the physical, psychological and social well-being of dependent users (Gibson et al. 1999; Davestad et al. 2009). Patients stabilized on adequate doses of methadone can function normally, hold jobs, avoid crime and violence of the street culture, and reduce their exposure to HIV by stopping or decreasing injecting drug use and drug-related high risk sexual behaviour (NIDA/NIH, 1999). A Cochrane Review (Mattick et al. 2009) of 11 randomized clinical trials found that methadone was more effective than non-pharmacological treatments with respect to the outcomes of treatment retention and suppression of heroin use. The great majority of trials were with heroin users. Literature on the effectiveness of MMT in the treatment of prescription opioid addiction is sparse. Banta-Green et al. (2009) reported that prescription opioid users can be treated at least as effectively as heroin users with MMT. The cost effectiveness of treatment with methadone has been examined and found to be efficient (Zaric et al. 2000; Doren et al, 2003). There is also evidence about the safety of MMT (Bell and Zador, 2000). The treatment also reduces the number of fatal overdose deaths due to illicit drug use (Grönbladh et al. 1990; Caplehorn et al. 1996).

The beneficial role of methadone maintenance in HIV prevention among IDUs has good scientific evidence to support it (Metzger et al. 1993; Dolan et al, 1996; Ward et al, 1998; Gibson et al. 1999; Kerr et al. 2004). Rapid access to treatment and a more aggressive policy facilitating the availability of methadone to reduce opioid drug use is urgently needed to contain HIV among opioid injectors across the world (Bruce, 2010). Implementation of

Introduction

MMT in China is considered as one of the most important public health initiatives in the past decade (Schmacher et al. 2007); it has reduced drug use, risky injecting and sexual behaviours among participants (Qian et al. 2008; Yin et al. 2010). In Malaysia, patients receiving adequate dose of methadone (around 80 mg and above) were better retained in the treatment programs (Mohamed

et al. 2010). MMT contributes to more rapid initiation and subsequent adherence to anti retroviral therapy (ART) among opioid-using HIV-infected IDUs (Uhlmann et al. 2010; Wolfe et al. 2010). In addition, MMT increases favourable HIV treatment outcomes among HIV/HCV co-infected IDUs (Palepu et al. 2006).

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AIM

The following are the aims of the methadone module:

- To outline the effectiveness of methadone in the management of heroin and other opioid dependence and in preventing HIV amongst injecting opioid users.
- To describe the guidelines and procedures for methadone maintenance treatment (MMT) for opioid dependence.
- To discuss issues relating to dispensing of methadone and a rollout plan for methadone substitution clinics.
- To understand the quality assurance indicators in the operation of the methadone clinics.

3

WHAT NEEDS TO BE IN PLACE BEFORE INITIATING METHADONE SUBSTITUTION

Steps to be Taken before Initiating Opioid Dependence Treatment in Methadone Clinics

- Establish policies and procedures for MMT (outpatient delivery in supervised settings)
- Plan for staff education and training
- Plan backup coverage for the absence or leave of the medical doctor/core team
- Assure privacy and confidentiality of addiction treatment information
- Develop linkages with other drug treatment services that will accept referrals for other forms of treatment (e.g., abstinence oriented approaches; psychosocial interventions)
- Develop a referral network of medical specialists
- Conduct timely physical examinations
- Develop linkages with medical treatment facilities, including HIV treatment and care
- Develop linkages with addiction and psychiatric treatment programs (e.g., detoxification centres, psychiatric clinics)
- List community referral resources, including specific self-help groups that would welcome patients on methadone substitution

Regulatory rules

As methadone is a controlled narcotic drug, the central authority¹ in each country will be responsible for procuring methadone for the substitution program. Besides, it is necessary to follow other regulatory processes related to narcotic drugs in each country. So, it is recommended that the Methadone Maintenance Treatment Program should be undertaken under the guidance of the central authority of any given country.

Assessment of the agencies' capacity

The capacity of the agencies that will be establishing the methadone substitution clinics has to be assessed. Given the nature of the treatment and the regulatory procedures, it is important that the services are provided, to begin with, by clinics at the medical colleges, university hospitals, major government hospitals and recognized services offering drug treatment. The box in this subsection lists procedures that need to be established in methadone clinics at the outset.

¹ Examples of central authority: In Bangladesh, Nepal and Pakistan - Narcotic Control Division/Department, Ministry of Home Affairs; in India, Narcotics Control Bureau, Ministry of Finance; and in Sri Lanka, National Dangerous Drug Control Board.

Decision on low threshold and high threshold methadone programs

It is preferable to consider low threshold methadone programs as they are most suited for preventing HIV among injecting drug using populations.

Low threshold programs	High threshold programs
Easy to enter	Difficult to enrol
Harm reduction oriented	Aims at abstinence
Objective to treat withdrawals Stop craving Suppress further use of illicit opioids	Abstinence is the objective Strict urine controls Discharge patients who are using illicit opioids
Flexible treatment options	No flexible treatment approaches;
Voluntary psychosocial interventions	Compulsory psychological interventions

Adopted from Methadone Guidelines from Verster and Buning, 2000

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IMPLEMENTATION

The implementation of methadone substitution is organized into five subsections. Subsection 4.1 on clinical pharmacology provides information on the effectiveness of methadone. Subsection 4.2 deals with the assessment of opioid dependent individuals for methadone treatment. Subsection 4.3 describes the guidelines and procedures for MMT. Subsection 4.4 discusses the issues relating to the administration of methadone and the rollout plan for delivering methadone to the patients. Final subsection 4.5 focuses on training needs and ongoing support.

-
- **Clinical pharmacology**
 - **Assessing patients for treatment with methadone**
 - **Guidelines and procedures for maintenance treatment**
 - **Roll-out plan for methadone administration**
 - **Training and support**
-

4.1 Clinical Pharmacology

In this subsection, the following will be discussed:

- i) About methadone pharmacology
- ii) Adverse effects and toxicity
- iii) Drug interactions

i) About methadone pharmacology

Methadone is an opioid agonist² and the action results from binding to the opioid receptors in the brain. Oral methadone is well absorbed from the gastrointestinal tract, and it is fat soluble. Methadone is eliminated from the body in the form of metabolites resulting from biotransformation and by excretion of the drug itself in urine and faeces. Familiarity with the following characteristics of methadone is important for the safe and effective use of methadone.

- Peak plasma concentration occurs 1 to 5 hours after oral dosing
- Long half-life³
- Low therapeutic index⁴ (the risk of overdose is high during the first few days of treatment)
- Repeated dosing leads to accumulation

² Drugs that have affinity for and stimulate physiologic activity at opioid cell receptors (mu, kappa, and delta) and are normally stimulated by naturally occurring opioids. Repeated administration often leads to dependence and addiction.

³ Half-life: time taken for half of the drug to be metabolized in the body. After a single first dose of methadone, the apparent half-life is shorter than in extended use; with a single first dose, the half-life is 15 hours and after the first few days of methadone, the half-life is 25 hours.

⁴ There is an overlap of toxic and therapeutic blood levels, and the risk of overdose is high in the first few days of treatment. Methadone gets distributed in the tissues considerably and there is gradual equilibration between these tissues and blood in the first few days of treatment.

Methadone’s pharmacological profile makes it useful as a substitute opioid medication as it allows for oral administration, single daily dosage and achievement of steady-state plasma levels after repeated administration with no opioid withdrawal during usual one day dosing interval.

ii) Adverse effects and toxicity

Adverse effects

The adverse effects of methadone are similar to those for other opioid analgesics:

- Nausea and vomiting, dizziness, drowsiness, light-headedness, dry mouth, sweating (especially at night); methadone users may get used to these effects over a period of time
- Respiratory depression, particularly when combined with the use of other central nervous system (CNS) depressants like alcohol, benzodiazepines
- Occasional reports of hypotension (low blood pressure), collapse and oedema
- Spasm of biliary and renal tracts
- Change in menstruation
- Dependence

Opioid Poisoning Triad

1. Pinpoint pupils (meiosis)
 2. Respiratory depression
 3. Coma
-

Drug interactions

Drugs	Drug interactions
Abused drug	Pharmacokinetic interactions
Alcohol	Increased sedation Increased respiratory depression
Other opioids (e.g., heroin)	Increased respiratory depression
Benzodiazepines	Increase the risk of respiratory depression
Tricyclic antidepressants, such as amitryptaline	Increase the risk of overdose

Toxicity

The toxicity of methadone following an overdose resembles that of the usual opioid poisoning triad. Slurred speech, unsteady gait, poor balance, drowsiness, retarded movement and stupor usually precede the triad. Overdose is a medical emergency and needs to be attended to urgently. Unattended, it can lead to death.

iii) Drug interactions

Almost all methadone-related deaths occur in the presence of other CNS depressants, and patients who abuse or depend on other drugs may be at greater risk of methadone toxicity. Methadone levels are affected by the regular high intake of more than four alcoholic drinks per day. When blood levels of ethanol are acutely elevated (>150mg/dl), increased levels of methadone can be anticipated.

Methadone is metabolized in the liver by the cytochrome P450-related enzyme systems (mostly the CYP3A4 and, to a lesser degree, the CYP2D6, CYP2B6, and CYP1A2 systems) to two biologically inactive metabolites, a pyrroline and a pyrrolidine. There is potential for pharmacokinetic interaction between methadone and drugs that inhibit or induce methadone metabolism by hepatic enzymes.⁵ Drug-drug interactions with methadone have been well-documented, in particular with HIV drugs, anti-TB medication (rifampicin) and anti-epileptic drugs (phenytoin). Alfa-2b interferon given

⁵ Methadone is metabolized by the hepatic enzyme system (cytochrome P450 3A4).

Drugs that increase methadone metabolism	Drugs that decrease methadone metabolism
HIV drugs (nevirapine, efavirenz, ritonavir and lopinavir-ritonavir)	Selective serotonin reuptake inhibitors (SSRIs), including sertraline and fluvoxamine
Anti-tuberculosis drugs (rifampicin)	Antifungals, including fluconazole
Anti-epileptic drugs (carbamazepine, phenytoin)	Antihistamines, including cimetidine
<i>Increase methadone dose in case of withdrawal symptoms</i>	<i>Decrease methadone dose in case of symptoms of intoxication</i>

as treatment for Hepatitis C does not appear to have any clinically significant interaction in terms of subjective or objective effects,

Drugs that inhibit the hepatic enzymes⁶ and drugs that induce the hepatic enzymes⁷ (cytochrome P450 3A4 system) alter methadone metabolism (see table above).

4.2 Assessing Patients for Treatment with Methadone

To determine the appropriateness of methadone substitution treatment, a comprehensive patient assessment is essential. A candidate for methadone treatment should have an objectively ascertained diagnosis of opioid dependence. In this subsection, how to assess and diagnose opioid dependence through history, examination and laboratory investigations is outlined first, followed by the criteria to determine the suitability of patients for MMT. Additional information on appropriateness of methadone treatment is given in Annexure.

i) How to assess and diagnose opioid dependence?

A) History of substance use:

Reason for presentation

- In crisis (health or economic or legal crisis)

- Brought in by a concerned parent/relative/spouse/employer/friend/outreach worker (ORW)
- Want help for their drug use and motivated to change their behaviour
- Usual source of drugs not available
- Referred by another medical practitioner
- Pregnant

Past and current drug use (last four weeks)

- The age of starting drug use (including alcohol and nicotine)
- Types and quantities of drugs taken (including concomitant alcohol misuse)
- Frequency of use, including routes of administration
- Experience of overdose
- Periods of abstinence
- What triggers a relapse?

History of injecting and risk of HIV and hepatitis

- Past history
- Present usage and why patient changed to injecting
- Supply of needles and syringes
- Sharing habits, including lending and borrowing injecting equipment/paraphernalia
- Does the patient know how to inject safely?
- How does the patient clean equipment?
- How does the patient dispose of the used equipment/paraphrenalia?

⁶ Medications that inhibit this enzyme system will potentially increase blood levels of methadone.

⁷ Medications that induce the enzyme system will potentially decrease the blood levels of methadone. Avoid commencing any drug that inhibits or induces the activity of the hepatic enzymes during induction into treatment with methadone. When commencing methadone in patients who use medications that inhibit the hepatic enzymes, prescribe conservative doses, review the patient carefully for signs of toxicity during induction, and advise the patient on the possibility of drug interaction.

- Has the patient thought of or tried any other method of use?
- Knowledge of HIV, Hepatitis B and C issues and transmission
- Use of condoms

Medical history

- Complications of drug use – abscesses, thromboses, viral illnesses, chest problems
- Hepatitis B, C status, if known
- HIV status, if known
- History and/or diagnostics for STIs
- Last menstrual period
- Operations, accidents and head injury
- Any current medication

Psychiatric history

- Any psychiatric consultations?
- Any overdoses (accidental or deliberate)?

Forensic history

- Any outstanding charges?
- Past imprisonment?
- Past custodial lock-ups?

Social history

- Family situation
- Employment situation
- Housing situation
- Financial situations, including debts

Past contact with treatment services

- Previous efforts to reduce or stop taking drugs
- Contacts with doctors, addiction services, social services, community services
- Previous admissions, how long they lasted and the cause of relapses

B) Assessing motivation for change

Is the patient motivated to stop or change his/her pattern of drug use or to make other changes in life? Patients have different levels of motivation for changing their substance use. The five stages of Prochaska and DiClemente (1983) are listed in the box below.

HISTORY

Tip: TRAPPED

Treatment History

Route of administration

Amount of drug used

Pattern of use

Prior abstinence

Effects (medical, psychiatric, social)

Duration of use

Welsh, 2003

Stages of Change

1. Precontemplation: “I don’t desire to stop”
2. Contemplation: “I may want to think about stopping, some day”
3. Preparation (determination): “I am planning to stop soon”
4. Action: “I have just stopped using drugs”
5. Maintenance: “I have been away from substances (drugs) for several months”

Prochaska and DiClemente, 1983

C) Examination

- Assessing general health
- General – Anaemia, nutritional status, dentition and overall hygiene
- Skin - Needle marks, tattoo, skin abscesses and open wounds
- Route specific – Injecting (abscesses, cellulitis)
- Drug related – (*See Annexure for assessing medical syndromes associated with opioid use*)
 - ◆ Side effects (e.g. constipation)
 - ◆ Overdose (e.g. respiratory depression)
 - ◆ Withdrawal (e.g. irritability, pain) – (*See Annexure for opiate withdrawal scale*)
- Current medication – what drugs? If HIV status known, whether on HIV drugs?
- Mental status examination – co-existing psychiatric problems

D) Special investigations with full informed consent

- Haematological investigations
 - ◆ Haemoglobin
 - ◆ Liver function tests
 - ◆ HIV
 - ◆ Hepatitis B and C

Urine assessment: Opioids persist in the urine for up to 24 hours

Diagnosis

The International Classification of Diseases-10 (ICD-10) provides criteria for establishing the diagnosis of substance dependence.

After completing a comprehensive assessment of a candidate for treatment, the physician should be prepared to:

- Establish the diagnosis or diagnoses
- Determine appropriate treatment options for the patient
- Make initial treatment recommendations

Dependence Syndrome

Presence of three or more of the following during the past 12 months:

1. Evidence of tolerance
 2. A physiological withdrawal state when substance use has ceased or reduced
 3. A strong desire or sense of compulsion to take the substance
 4. Difficulties in controlling substance-taking behaviour in terms of its onset, termination or levels of use
 5. Progressive neglect of alternative pleasures or interests
 5. Progressive neglect of alternative pleasures or interests
 6. Persisting with substance use despite clear evidence of overtly harmful consequences
-

- Formulate an initial treatment plan
- Plan for engagement in psychosocial treatment
- Ensure that there are no absolute contraindications to the recommended treatments
- Assess other medical/psychiatric conditions that need to be addressed

The physician then decides about the appropriateness of methadone treatment for the patient. (*See Annexure for methadone treatment appropriateness checklist*)

Criteria to determine suitability for treatment with methadone

Patient Selection Criteria

- Age above 18 years
- Opioid dependent individuals (satisfying the criteria for opioid dependence as defined by ICD -10 or DSM IV)
- Persons willing to undergo oral substitution treatment with methadone (provide informed consent for treatment)

Contraindications

- Hypersensitivity to methadone
- A history of respiratory depression, especially acute asthma attack
- Acute alcoholism
- Head injury, raised intracranial pressure
- Treatment with Monoamine oxidase (MAO) inhibitors
- Acute abdomen (active ulcerative colitis or Crohn's disease)
- Severe liver impairment
- Biliary and renal tract spasm

Precautions

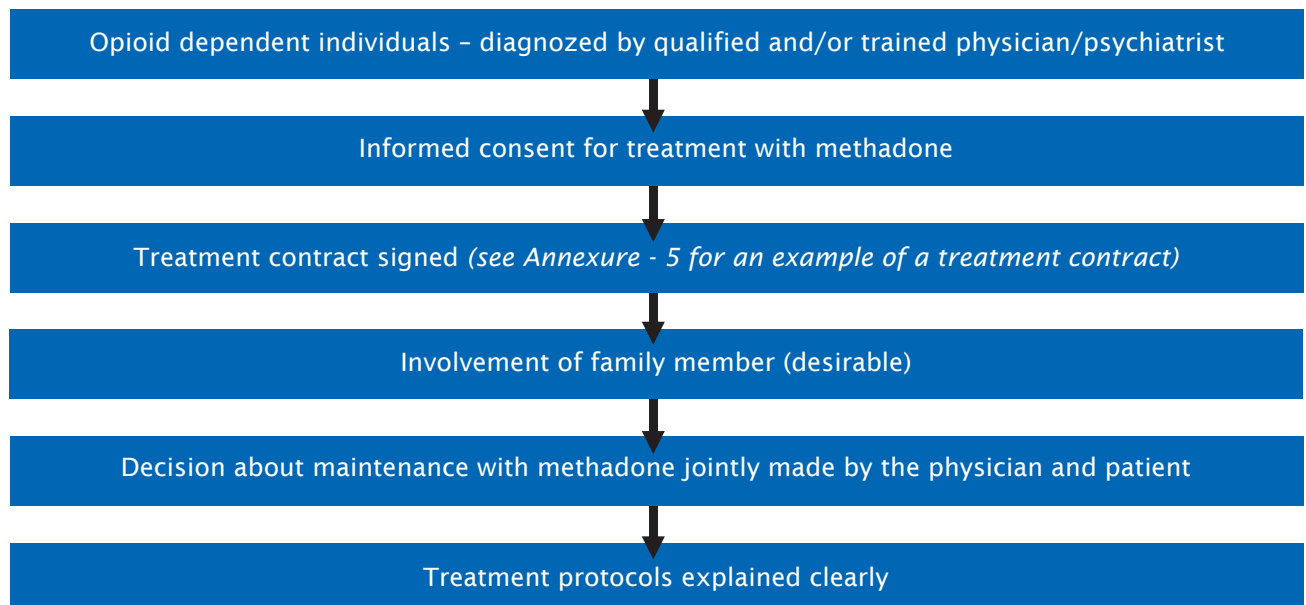
- Elderly persons
- Liver impairment

Further Considerations

Programmatically speaking, methadone substitution should be started and continued through examining various other psychosocial aspects of the patients. These aspects include, but are not limited to the following:

- Admissions to methadone substitution should be restricted to persons who are dependent on opioid substances.
- Persons with history of unsuccessful attempts of methadone substitution should not be excluded from methadone maintenance treatment, if she/he fits the eligible criteria.
- Confidentiality of the persons on methadone substitution should always be maintained.
- The patient and doctor should jointly decide the duration of treatment.
- The patients who are not suitable or less likely to benefit with non MMT treatment interventions can be considered for MMT.
- Initial urine drug screening facilitates objective corroboration of the patient history of opioid drug use, but it is not necessary to make this mandatory as urine testing is unavailable in several settings in South Asia.

Intake Process



4.3 Guidelines and Procedures for Maintenance Treatment

Physicians who use methadone to treat opioid dependence must consider the entire process of treatment, from induction to stabilization and then maintenance. At each stage, many different factors must be considered if the physician is to provide comprehensive and maximally effective opioid addiction care. The following issues are dealt with in this subsection:

- i) Induction
- ii) Methadone dose stabilization
- iii) Maintenance dosing
- iv) Missed doses
- v) Split dosing
- vi) Vomited dose
- vii) Frequency of visits
- viii) Take-home dose
- ix) Withdrawal from methadone
- x) Methadone during pregnancy and lactation
- xi) Retention in treatment
- xii) Detoxification using methadone
- xiii) Transfer from buprenorphine maintenance to methadone

i) Induction

Having established that the patient is suitable for methadone treatment, determine

The initial dose of methadone

Patient Factor	Dose
No risk factors	≤ 30mg
Higher risk for methadone toxicity	≤ 20 mg
Recent abstinence from opioids	≤ 10 mg

The important thing in induction is to START LOW AND GO SLOW. The initial dose should be 15-30 mg of methadone per day for the first three days.

an initial dose that will be comfortable and safe for the patient. An initial dose should usually be 15-30 mg per day. It is unusual for patients to require doses higher than 30 mg, but patient review may show evidence of opioid withdrawal during the first few days of methadone treatment. Give initial doses higher than 30 mg only if you are confident that the patient has a high degree of tolerance to opioids, is at low risk of abusing other substances, and has good liver function. Commence patients with a low level of tolerance on a dose of less than 20 mg. If the patient has a low level of physical dependence or you are unsure of the degree of tolerance, commence with a low dose (less than 20 mg) and adjust the dose after reviewing the patient soon after commencing treatment. Before the third or fourth dose, titrate the dose according to the patient's symptoms (suggesting either opioid withdrawal or methadone toxicity) and his/her continued use of opioids and other CNS depressants. Adopt a cautious approach to dosing (with careful review during the first week of treatment) for patients who you identify as being at high risk of methadone toxicity, including those on medication that inhibits hepatic enzyme activity.

Factors determining the initial dose

- Degree of tolerance to opioids
- Concurrent medical conditions, including impaired hepatic function
- The time since the patient's last drug use
- The patient's state of withdrawal or intoxication
- Interactions with other prescribed medications

- Use of alcohol, prescription sedative drugs, prescription opioids or illicit drugs
- Body weight

Patient Factors Contributing to High Methadone Toxicity

- Alcohol-dependent patients or those consuming heavy amounts of alcohol
- Recent benzodiazepine use
- Use of other sedatives
- Age >60 years
- Respiratory illnesses
- Taking drugs that inhibit methadone metabolism
- Lower opioid tolerance
- Recent discharge from inpatient drug use treatment/rehabilitation centre
- Recent incarceration
- Severe liver disease

In single-dose overdose cases, death has been reported with methadone doses as low as 50 mg in non-tolerant individuals. The ratio between the maximum recommended initial dose (30 mg) and a potentially fatal single dose is exceedingly low compared to other medications. Methadone blood levels contin-

ue to rise for five days after starting or raising a dose. Death by accumulated toxicity may result from increasing a dose before the full effect of the current dose is known.

ii) Methadone Dose Stabilization

Once the initial dose of methadone is well tolerated, the dose should be gradually increased until the patient is comfortable and not using heroin or other illicit opioids. The rate of increase should be individually assessed, and should generally be in the range of 5-15 mg every few days.

Typical Reasons for Dose Increase

1. Signs and symptoms of withdrawal
2. Amount and/or frequency of opioid use not decreasing
3. Persistent craving for opioids
4. Failure to achieve a dose that blocks the euphoria of short acting opioids

iii) Maintenance Dose

As with the drug treatment of other medical conditions, dose is an important determinant of effectiveness. The prescription should not focus on reducing the dosage to a level to minimize the risk of adverse effects or decrease dependence, but rather on effectively controlling the patient's craving for and continued use of illicit opioids.

The stabilization phase of methadone

Patient Factor	Dose and Frequency
No risk factors	10-15 mg every 3-5 days
Higher risk for methadone toxicity	5-10 mg every 3-5 days
Recent abstinence from opioids	10-15 mg every 5 days or more

Dose adjustment during the period of stabilization is 10 mg (range 5-15 mg) every few days.

Dosage of Methadone

For what?	Methadone dose
Managing withdrawal symptoms	10-30 mg
Craving	40-80 mg
Suppressing further use of heroin/illicit opioids	80 mg and above

- The maintenance dose should be individualized to the patient's needs.
- Evidence indicates that high doses of methadone (>60 mg) result in better retention in treatment and less heroin use than lower doses (<40 mg).
- Doctors should prescribe effective doses of methadone and be prepared to increase the dose if patients are still using illicit opioids
- Clinicians should encourage patients to use high doses (60-120 mg) and not reduce their dose, particularly when they are still using illicit opioids.

High doses of methadone may be associated with increased risk of QT prolongation. Clinicians should ask patients whether there is any history of structural heart disease, arrhythmia and syncope. Clinicians should be aware of interactions between methadone and other drugs that possess QT interval-prolonging properties or slow the elimination of methadone. The risk of QT-related adverse effects is probably smaller than the benefits of high methadone doses. This is supported by the evidence for lower mortality risk for patients on high methadone doses.

Maintenance doses below 60 mg are justified for patients who have no unauthorized opioid use, report no significant withdrawal symptoms or cravings, are at high-risk for methadone toxicity, or who have been only using low doses of synthetic opioids such as injectable buprenorphine, pentazocine or proxyvon.⁸

In Asia, a majority of patients require a methadone maintenance dose of about 80 mg every day.

⁸ Experience from Nepal and Bangladesh indicates that the methadone dose requirement of persons using injectable synthetic opioids such as buprenorphine and pentazocine may be less. Rigorous studies, however, are needed to confirm this.

iv) Missed Doses

A clinically significant loss of tolerance to opioids may occur within as little as three days without methadone. For this reason, after a period of three days without methadone, it is recommended that the physician consider reducing the methadone dose to ensure that any loss of tolerance does not result in a "single-dose" overdose of methadone. After tolerance to the first dose is demonstrated, the dose can be rapidly increased over a period of days in proportion to the previous dose for that person. After missing five or more days of methadone, the body has eliminated the drug, and so the most prudent course is to restart methadone at 30 mg or less. After assessing response to the initial dose over three days, the dose may be safely increased relatively quickly toward the previous stable dose of methadone.

v) Split Dosing

Split dosing is commonly used during the management of pregnancy or in patients on medications that induce rapid metabolism of methadone.

vi) Vomited Dose

Vomited methadone doses are not replaced unless a methadone team member directly observes emesis. If the vomiting was witnessed by a staff member, and it occurred less than 15 minutes after consumption, the dose can be replaced at no more than 50% of the regular dose.

vii) Frequency of Visits

When a patient is initiated on methadone, he/she should be seen every 3-4 days to adjust the dose. After a stable dose has been reached, it is recommended that the patient and the physician (or other member of the treatment team) meet every 1-12 weeks, depending on the patient's stability. The patient should see a physician more frequently during times of relapse or unusual stress.

viii) Take-home Dose

The following three criteria should be assessed prior to initiating take-home.

1. Clinical stability – The patient demonstrates clinical stability when the dose has reached a stable level. Also he/she demonstrates this stability by stable housing, support system and activities and regular attendance at clinic appointments.
2. Time spent in methadone treatment – Take-home is not recommended during the first two months of treatment.

Risks of Take-away Doses

- Hoarding and deliberate overdose of self or others
- Use in dangerous combination with other drugs
- Self-administration by injection
- Diversion of methadone for illicit use
- Trafficking to provide funds for heroin purchase
- Accidental overdose (e.g., by children)
- Sharing of dose with drug-using friends

3. Ability to safely store medication – It is not appropriate to give take-home doses to patients with unstable living arrangements, such as those living on the street or in places without storage facilities. Ensure children don't have access to the medicine.

ix) Withdrawal from Methadone

Patients may wish to cease treatment for a variety of reasons. Discourage premature withdrawal and warn the patient of the high risk of relapse, particularly if there is rapid reduction of the methadone dose. The decision to withdraw and the rate of withdrawal may be determined by agreement between the patient, doctor and others in the treatment team. Closely monitor the patient, and if he/she experience difficulties, decrease the rate of dose reduction until he/she stabilizes. The majority of patients tolerate the following rate of withdrawal:

Methadone dose rate of withdrawal (per week)

1. Over 50 mg: 5 mg
2. 30-50 mg: 2.5 mg
3. Less than 30 mg: 1-2 mg

(Source: Bell and O'Connor, 1994)

Reasons for Terminating Maintenance Treatment with Methadone

- Violence, threats or abuse to staff or other clients
- Diversion of methadone from the clinic
- Confirmed drug dealing or other illegal activities around the clinic
- Continued use of dangerous quantities of other CNS depressant drugs
- Trafficking in take-away doses

x) Methadone and Pregnancy

Methadone metabolism is significantly accelerated in the third trimester of pregnancy, and methadone doses often need to be increased at that time to prevent withdrawal symptoms and drug-seeking behaviour (Pond et al. 1982). During pregnancy, methadone may need to be given twice daily (in divided doses) due to differences in elimination, absorption and clearance (Jarvis et al. 1999). Breastfeeding is safe for women in MMT and their babies.

Methadone-exposed newborn infant is at risk of manifesting signs of neonatal abstinence syndrome (NAS). Neurologic excitability, gastrointestinal dysfunction and autonomic signs of methadone withdrawal are typically observed within 48–72 hours after birth (Seligman et al. 2010). Untreated NAS can cause considerable distress to infants and, in rare cases, can cause seizures. Cochrane Collaboration reviews indicate that opioids and barbiturates are more effective than placebo or benzodiazepines, with opioids probably more effective than barbiturates.

xi) Retention in Treatment

There is a positive dose-response relationship between methadone dose and client retention. Patients with doses >80 mg of methadone are more likely to adhere to treatment (Mohamad et al. 2010). It has been found in Asia that MMT clinics affiliated with local health departments have more clients and higher retention rates. Longer operating hours and incentives for compliant clients facilitate treatment adherence. Psychosocial support and peer support play a critical role in retaining patients in treatment.

xii) Detoxification Using Methadone

Suggested Methadone Dosing to Manage Opioid Withdrawal

Day	Dose in milligrams
1–4	30
5–8	35
9	30
10	25
11	20
12	15
13	10
14	5
15	0

There can be flexibility in the regimen shown in the table, depending on the symptoms exhibited by the person experiencing withdrawal.

xiii) Transfer from Buprenorphine Maintenance to Methadone

A patient can be transferred from buprenorphine to methadone under the following circumstances:

- Patient is experiencing intolerable side-effects due to buprenorphine
- Patient shows inadequate response to buprenorphine treatment
- Patient is transferred to a program where buprenorphine is unavailable

Prior to the transfer, the patient should be stabilized on daily doses of buprenorphine. The buprenorphine dose should be reduced to 16 mg or less for several days prior to transfer. Methadone can be commenced 24 hours after the last dose of buprenorphine. The initial methadone dose should not exceed 30 mg. Patients being transferred from lower doses of buprenorphine (4 mg or less) should be commenced on lower doses of methadone. Care should be taken not to increase the dose of methadone too quickly.

4.4 Rollout Plan for Methadone Substitution Clinics

Methadone is an opioid and its use is regulated. Clinicians should take special precautions in the prescribing, handling, dispensing and storage of the medication. Certain procedures have to be followed before administering the drug to the patients. Government commitment is critical for a rational, evidence-based approach to the treatment of drug users.⁹ Methadone treatment should be part of a comprehensive treatment and care service for opioid dependents; and in order to achieve this, government-run community based methadone clinics should work in close collaboration with non-governmental agencies as well as hospitals.

i) Transport of methadone

Methadone bottles will be brought from the central store for program participants on a weekly basis. Transport of methadone from the central store to each MMT clinic will occur on scheduled days within specific time periods. A nurse accompanied by a member of the central store staff will transport bottles to each facility. One or two people at each site (preferably a nurse) will be designated to be responsible for accepting the methadone bottles, cataloguing their receipt, storing them in a locked cabinet, and returning empty bottles from the previous week.

ii) Procedures prior to administering the dose of methadone

A psychiatrist at the substitution clinic or a physician trained in methadone treatment shall prescribe methadone. Once the treating physician has stabilized the dose, a pharmacist or nurse or a community health nurse can administer the drug subsequently. Prior to administering the medication, the staff must:

- Establish the identity of the patient

- Confirm that the patient is not intoxicated
- Check the quantity of the drug in the prescription
- Check that it is a valid current prescription
- Record the dose in the recording system

iii) Administering methadone

To prevent possible diversion of methadone, directly supervise the patients when they take the dose, and engage them in conversation to ensure they have consumed the dose. It is recommended that methadone doses are administered in disposable containers, or that the clinic has some appropriate means of sterilizing glasses or similar dosage vessels. The aim is to ensure a satisfactory standard of hygiene. Observe the patient for signs of methadone or other drug toxicity; and do not dose them if they appear intoxicated. The doctor should be notified if the dosing administrator has concerns that patients may be attempting to divert their medication.

iv) Rollout plan for methadone substitution

The following are required to operate a methadone substitution clinic serving about 300 regular patients with opioid dependence:

1. Program manager
2. Doctor
3. Nurse
4. Counsellor
5. Outreach Workers (ORW)
6. Peer Educators (PEs)
7. Office Support Staff: guard, office boys, etc.

Apart from ensuring optimal dose, the effectiveness of the substitution treatment is dependent on the length of time in treatment and linkages with other services. In order to ensure that patients enrolled receive uninter-

⁹ In Hong Kong, the government recognized the usefulness of methadone substitution programs in the early 1970s and sustained the program. The Government of Hong Kong supports additional ancillary services for drug users through significant involvement of the non-governmental sector.

rupted medication, it is important that the substitution programs are supported and endorsed by the respective governments. Sudden interruptions in the supply of maintenance medication can potentially do more harm to the users. Long-term plans should be made for establishing and maintaining substitution programs. Community-based clinics are more attractive to drug users; hence, the government-sponsored methadone clinics should be community based. Both the government (involved in the supply of substitution medication and monitoring of regulatory procedures) and the non-governmental organizations (NGOs), involved in community-based services, psychosocial care and support services for drug users, should become partners in the delivery of treatment. The substitution program should be integrated to existing drug

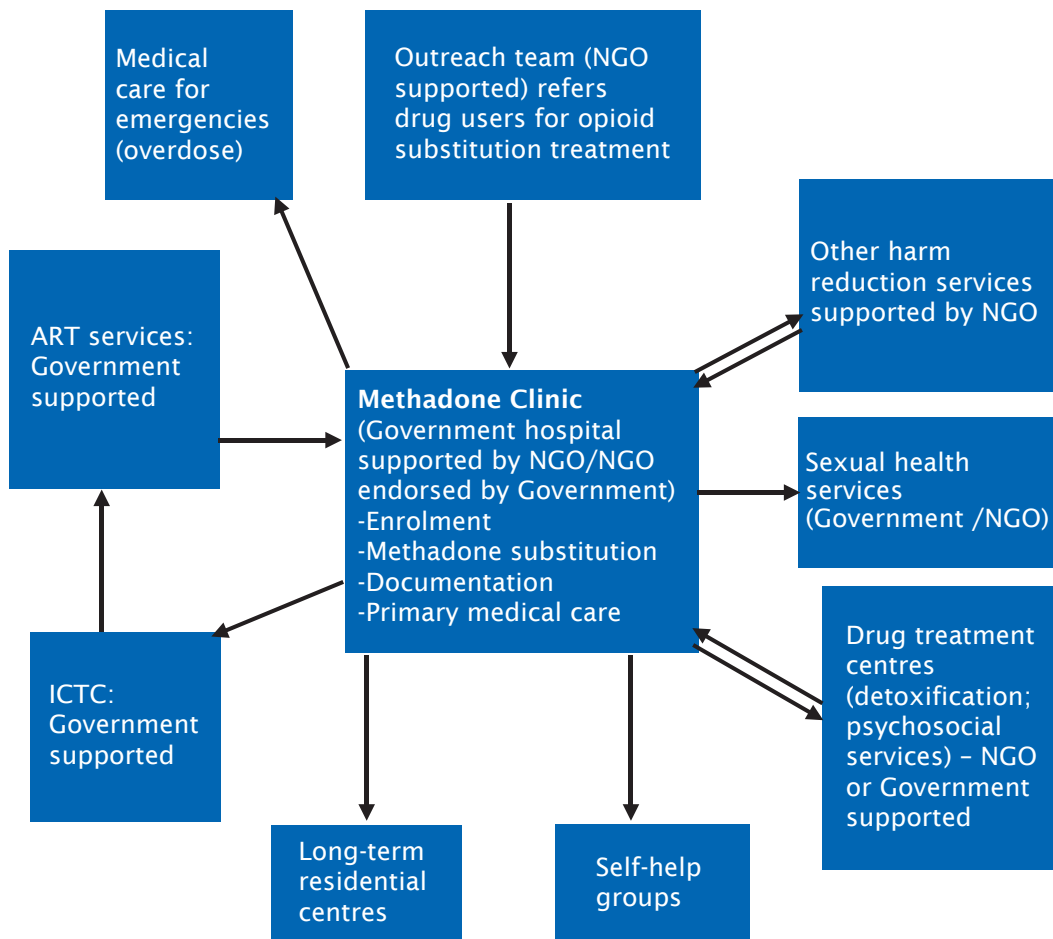
treatment/rehabilitation services and should be part of a comprehensive and continuum of care for drug users. In places with high potential for HIV transmission among injecting opiate users, substitution treatment should become a key component of HIV prevention strategies for IDUs. The proportion of problem opioid users to be covered by the substitution (coverage) can be reviewed periodically in different geographical locations.

v) Information to be provided to the patient

The following information should be provided to the patients:

- The dynamics of stabilization (starting slow and going slow)
- The hazards of poly drug use, particularly in the first week of treatment

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- The effects and side effects of methadone use
- Program guidelines and conditions
- Expected behaviour from the patients on MMT
- Risks and symptoms of an overdose

4.5 Training and support

The staff at the clinics needs to be trained, and the training should be organized before the clinics are operational. Proper training on the use of methadone will be the key to the successful implementation of methadone substitution. There should be provision for ongoing support for the staff. The training for the staff can be assisted with the help of

- a) Training module
- b) One to five-day-long training workshops
- c) Clinical placement in an existing methadone clinic

Apart from the initial workshops, there should be a provision for follow-up training. A comprehensive training module should be developed; it can be field-tested and widely used in the region. It is likely that pilot projects will be established in many countries in South Asia before large-scale methadone programs supported by respective Governments, become operational. The staff participating in the pilot projects can be brought together for a central-

ized workshop. The workshop for the medical doctors can address issues specifically related to patient assessment for methadone treatment, clinical pharmacology – dosing, drug interactions – and, methadone in the context of dependence care and HIV services. For the core team members from a state/province, an initial training program conducted centrally within that state/province can address several issues relating to maintenance treatment, patient care, administrative issues, confidentiality, regulatory issues, documentation, liaison services and linkages. Clinical placements are extremely useful; and even after establishment of projects, there could be exchange visits. Attendance at Harm Reduction Conferences and Drug Treatment Workshops should be encouraged for the methadone clinic team members. The core team members, who have been trained at the state/province level training workshops, can train new members of the team with the help of local consultants periodically. At the minimum, the program manager, doctor, nurse and the counsellor should have received central training and the outreach staff should have been trained by the program staff of the MMT centre.

The workshops should adopt participatory training methodology and should be conducted by trainers well versed in methadone substitution. The workshop should address practical issues and enhance the skills of the participants.

Topics for a three-day training workshop for the core team

Day 1	Day 2	Day 3
Introduction to the workshop	Assessment of a patient with opioid use and criteria for methadone maintenance treatment	Directly observed treatment of methadone
Opioid dependence – concept, course and consequences	Effectiveness of MMT	Enhancing ‘quality’ in patient care
Effective treatment approaches	Regulatory procedures	Liaison services and linkages
Opioid substitution treatment – definition, benefits and risks	Documentation and record keeping	Visit to a MMT clinic

Topics for a five-day training workshop for the core team

Day 1	Day 2	Day 3	Day 4	Day 5
Overview of drugs and drug use disorders	Opioid Substitution Treatment – overview (including opioid withdrawal, intoxication and other syndromes)	OST with methadone: induction, stabilization, maintenance	Visit to MMT clinic	Referral and networking
Drug related problems and harms	Assessment and diagnosis	Special clinical situations –women; HIV; other medical conditions, dual diagnosis	Program management	Documentation and reporting
General principles of drug treatment and harm reduction	Methadone-pharmacology (including side-effects, drug interactions, contraindications)	Psychosocial interventions	—	—

5

MONITORING AND QUALITY CONTROL OF INTERVENTIONS

Description

Quality improvement is based upon measuring and monitoring the processes and outcomes of treatment, and making use of the information to improve the delivery of care. The practitioner works within a treatment system, and implements quality improvement approaches to ensure that the system delivers care in ways which are effective and accountable.

Important Tasks

- Rapid and client-centred assessment and induction
- Flexible but adequate dose of methadone after stabilization is provided
- Adequate duration of treatment
- Psychosocial services to deal with other concerns
- Trained staff
- Engaging with clients rather than punishing them for continuing illicit drug use

The project should take the following *quality assurance indicators* into consideration.

Accessibility: These programs should be community based to ensure accessibility and to keep the cost low. The NGO collaborating with the community-based methadone clinic can provide psychosocial support services; emer-

gency services such as overdose management should be provided by a hospital.

Safety: Guidelines to ensure patient safety should be laid down. Adequate training of staff is required to ensure patient referral in case of an emergency.

Preventing diversion: There is a valid basis for public health concern over inappropriate prescribing, and a need to differentiate between patients who are likely to divert drugs to the black market and those who obtain prescribed opioids for their own use. Towards this end, all the regulatory procedures must be strictly adhered to. To minimize the risks and maximize the benefits, opioids should only be prescribed in the context of a comprehensive assessment and treatment plan, with regular reviews of whether the treatment is beneficial. One of the ways of preventing diversion by clients is to have strict criteria for take-home doses.

Efficacy: An adequate dose of medicine should be given. Wherever possible, along with the maintenance drug, psychosocial intervention should be provided to the patients. Low intensity psychosocial intervention (three to four sessions in a group setting) with minimal staff investment should be planned.

Safe Methadone Use

Risks	Preventive Measures
Overdose during induction	Initial doses in the range 15-30 mg Supervised ingestion of doses
Accidental poisoning of children	Take-home doses in childproof containers
Diversion	Supervised ingestion of doses Take-home doses require a good response to treatment by patients

Intake criteria: Specific selection criteria should be laid down.

User participation: The program should be flexible and should involve patient participation at the level of planning and implementation. It should incorporate changes based on the requirement of the patient.

Cost effectiveness: The program can function with minimal staff.

Patient coverage: An outreach team supported by the NGO collaborating with the methadone clinic can facilitate referral of patients to the clinic for assessment relating to suitability for methadone substitution. By publicizing the program, adequate utilization of services can be ensured. Various methods can be adopted for this purpose, depending on their suitability for a particular community, such as street plays, advertising in local cable, television or radio, distribution of pamphlets, etc. Further recruitment can be done with the help of registered drug users using a snowball technique.

Monitoring of drug use: Assessment of drug use enables monitoring of progress in treatment and can give useful information for making decisions on clinical management. Monitoring drug use can also provide a basis for program evaluation. There is little evidence to support the use of drug monitoring as a deterrent against unsanctioned drug use. Self-report, urine testing and clinical observation are the currently available monitoring approaches.

Patient retention: This can be enhanced by using adequate doses. If plasma levels of methadone are not maintained, cross tolerance to heroin will be lessened, reducing the capacity of methadone to suppress the euphoric effect

of heroin. Reduced compliance is therefore associated with an increased risk of relapse to heroin use. In addition, having an empathetic staff, a program that is receptive to the patients' needs, flexibility in the program, and other adjunctive facilities for which a liaison with other local NGOs can be made are all necessary to improve compliance. The retention of patients in a maintenance program is related both to its "efficacy" as well as its "user friendliness".

Training of staff: The staff should be given basic information about opiates. Their training should include the concept of abuse and dependence, complications related to opioid use, history taking, psychosocial assessment, information about effective approaches and methadone maintenance. They should also be trained in identification of complications, including intoxication and overdose (see Annex), and should be aware of when to refer a case to the hospital. The training should also address issues relating to patient care – concern, empathy and user-friendly services.

Evaluation of benefits of methadone maintenance treatment

The success of MMT can be measured through outcome indicators. An independent outcome evaluation will indicate the benefits of methadone substitution. These indicators include:

- Use of illicit drugs while on methadone substitution
- Associated criminal activities while on methadone maintenance
- Incidence of blood-borne infectious diseases
- Restoration/improvement in quality of life
- Social/familial reintegration of the person

6

CHECKLIST FOR MENTOR(S)

- Number of methadone clinics in the City/State or Province/Country
- Location and type of methadone clinic
- Government – NGO partnership
- Community participation
- Training for staff
 - ◆ Proportion of trained staff
 - ◆ Qualifications/Skills
 - ◆ Ongoing training support
- Policy and procedures governing treatment delivery at the clinic in place
- Assessment and intake criteria
 - ◆ Criteria for selection defined and transparent
 - ◆ No discrimination in selecting patients for treatment
- Operational issues
 - ◆ Timing of the clinics
 - ◆ Backup coverage (for absence of key staff)
- Consent procedures
 - ◆ Informed consent
 - ◆ Treatment contracts
- Regulatory procedures
 - ◆ Strict adherence to procedures
 - ◆ Proper accounting of the medicines
 - ◆ Safe custody of medicines
- Documentation
 - ◆ Patients records (demographic, risk behaviour and treatment characteristics)
 - ◆ Confidentiality of information
- Methadone delivery
 - ◆ Range of doses
 - ◆ DOT
 - ◆ Alternate dosing schedules
- Other services provided at the clinic
 - ◆ HIV prevention education/Overdose prevention education
 - ◆ Primary medical care

Checklist for Mentor(s)

- Other psychosocial support and care services
 - ◆ Liaison with other agencies providing a range of services
 - ◆ Referral networks
- Retention rates
 - ◆ Number enrolled for treatment
 - ◆ Proportion of regular patients
- User participation in evaluation of services
 - ◆ Patient satisfaction
- Data gathered on potential outcome indicators
 - ◆ Crime rates among patients attending services
 - ◆ Employment among patients attending services
 - ◆ Risk behaviours (drug use, injection and sex related)
 - ◆ Community safety

7

COSTING IN TERMS OF MANPOWER, MATERIAL AND TRAINING

Considerations for costing related to initiating and running a MMT program is an important issue for policy makers and national program managers of a country. A template for costing along with indicative budgets are provided below, based on UNODC's experience of implementing MMT in different countries of South Asia. The various heads and sub-heads to be considered in MMT implementation are covered comprehensively. The costing is intended to provide a direction to the countries for tailoring their respective national budgets, taking into consideration the healthcare related systems in the country.

The costs given below are for providing MMT services for 100 clients:

- A. Start-up Cost
- B. Implementation Cost

A. Start-up Cost (one-time)

Heads	Details	Cost (in USD)
Sensitization meeting	A one-day national level sensitization meeting with the policy makers, service providers, hospital authorities, and community	3,000
Training program for the service providers	A five-day induction training programme for the staff of the MMT centre at state/provincial level	4,000
	A three day refresher training programme for the staff of MMT centre at state/provincial level	3,000
Feasibility assessment	A one-day feasibility assessment to determine whether it is feasible to implement MMT at the proposed centre, as well as to recommend the necessary refurbishment required	2,000
Refurbishment of the proposed MMT centre	Necessary infrastructure changes for making the centre ready to initiate MMT	5,000
SUB-TOTAL (USD)		17,000

B. Implementation Cost (one year)

Heads	Details	Cost (in USD)
1. HUMAN RESOURCE		
1a. Clinical staff		
Medical doctor	One full-time medical doctor for diagnosis and treatment for drug related problems as well as general medical conditions (@ USD 800/month)	9,600
Nurses	Two nursing staff for daily dispensing and stock keeping (@ USD 250/month for 1 nurse)	6,000

contd...

Costing in Terms of Manpower, Material and Training

Heads	Details	Cost (in USD)
1b. Psychosocial staff¹⁰		
Counsellor	One full time counsellor for providing one-to-one and group counselling (@ USD 400/month)	4,800
Staff for conducting outreach	Two full-time ORWs and four PEs for bringing the potential clients to the MMT centre and conducting follow-ups for the MMT clients. (@ USD 400 for 2 ORWs and 4 PEs/month)	4,800
1c. Support staff		
Data manager	One full-time data manager to maintain the records at the MMT centre (@USD 200/month)	2,400
Accountant	One part-time accountant (@USD 200/month)	2,400
Other support staff	Three Staff for manning the MMT centre (@ USD 150/staff/month)	5,400
2. OFFICE RUNNING EXPENSES		
Travel-related costs	Towards travel of the psychosocial staff for outreach and home visits (if required)	1,000
Miscellaneous expenses	Towards purchase of stationery materials and other expenses such as communication and attending meetings	2,000
3. PROCUREMENT EXPENSES		
Procurement of methadone	Costs related to purchase of methadone liquid @ 60 mg/client/day (USD 35/litre methadone of strength 10 mg/ml)	8,000
Equipment and supplies	Purchase of safes (for stock-keeping), bottle top dispensers, cups, water, etc.	5,000
SUB-TOTAL		51,400
Start-up cost (USD)		17,000
Implementation cost (USD)		51,400
Grand Total (USD)		68,400

¹⁰The psychosocial staff can be part of a separate 'social support unit' (SSU) created for providing psychosocial services, or they can work as core staff of the MMT centre. In case a separate SSU is created, a program manager is also required to oversee the activities of the outreach staff. Alternatively, the services of an NGO working with drug users in the vicinity can also be used for this purpose

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ANNEXURES

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ANNEXURE-1

Criteria for Opioid Dependence

Dependence (ICD-10 [@])	Dependence (DSM-IV-TR [±])
Presence of 3 or more of the following in the last 12 months:	Presence of 3 or more of the following in the past 12 months:
1. Evidence of tolerance	1. Tolerance (marked increase in amount marked decrease in effect)
2. A physiological withdrawal state when substance use has ceased or reduced	2. Characteristic withdrawal symptoms substance taken to relieve withdrawal
3. A strong desire or sense of compulsion to take the substance	3. Substance taken in larger amount and for longer period than intended
4. Difficulties in controlling substance-taking behaviour in terms of its onset, termination or levels of use	4. Persistent desire or repeated unsuccessful attempt to quit
5. Progressive neglect of alternative pleasures or interests	5. Much time/activity to obtain, use, recover
6. Persisting with substance use despite clear evidence of overtly harmful consequences	6. Important social, occupational, or recreational activities given up or reduced
	7. Use continues despite knowledge of adverse consequences (e.g., failure to fulfil role obligation, use when physically hazardous)

[@] Adapted from WHO ICD 10 diagnostic guidelines for substance use disorders

[±] Adapted from APA DSM-IV-TR diagnostic guidelines for substance use disorders

ANNEXURE-2

Medical Syndromes Associated with Opioid Use

Syndrome (Onset and Duration)	Characteristics
Opiate intoxication	Conscious, sedated, “nodding” mood normal to euphoric Pinpoint pupils History of recent opiate use
Acute overdose	Unconscious Pinpoint pupils Slow, shallow respiration
Opiate withdrawal	
Anticipatory* (3-4 hours after last “fix”)	Fear of withdrawal Anxiety Drug seeking behaviour
Early (8 -10 hours after last “fix”)	Anxiety Restlessness Yawning Nausea Sweating Nasal stuffiness Rhinorrhoea Lacrimation Dilated pupils Stomach cramps Drug-seeking behaviour
Fully developed (1-3 days after last “fix”)	Severe anxiety Tremor Restlessness Piloerection** Vomiting, Diarrhoea Muscle spasm*** Muscle pain Increased blood pressure Tachycardia Fever, Chills Impulse-driven drug-seeking behaviour Protracted abstinence (indefinite duration)

* Anticipatory symptoms occur as the acute effects of heroin begin to subside

** Piloerection has given rise to the term “cold” turkey”.

*** The sudden muscle spasms in the legs have given rise to the term “kicking the habit”.

ANNEXURE-3

Clinical Opiate Withdrawal Scale (COWS)

For each item, circle the number that best describes the patient’s signs or symptoms. Rate only if the symptom has an 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 & Time: ____/____/____: ____

Reason for Assessment: _____

1. Resting Pulse Rate: ___ beats/minute

Measured after the patient has been sitting or lying down for 1 minute.

0 pulse rate 80 or below

1 pulse rate 81 – 100

2 pulse rate 101 – 120

4 pulse rate greater than 120

2. 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

4 pulse rate greater than 120

3. Restlessness

Observation during assessment

0 able to sit still

1 reports difficulty in sitting still but is able to do so

2 frequent shifting or extraneous movements of legs/arms

5 unable to sit still for more than a few seconds

4. GI Upset

Over last ½ hour

0 no GI symptoms

1 stomach cramps

2 nausea or loose stool

3 vomiting or diarrhoea

4 multiple episodes of diarrhoea or vomiting

5. 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

6. 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

7. 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

8. 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/muscle
- 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort

9. Runny Nose or Tearing

Not accounted for by cold symptoms or allergies

- 0 not present
- 1 nasal stuffiness or unusually moist eyes
- 4 nose constantly running or tears streaming down cheeks

10. Anxiety or Irritability

- 0 none
- 1 patient reports increasing irritability or anxiety
- 2 patient obviously irritable/anxious
- 4 patient so irritable or anxious that participation in the assessment is difficult

11. Gooseflesh Skin

- 0 skin is smooth
- 3 piloerection of skin can be felt or hairs standing up on arms
- 4 prominent piloerection

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

Score:

- 5-12 = mild
- 13-24 = moderate
- 25-36 = moderately severe
- more than 36 = severe withdrawal

Initials of persons doing the assessment _____.

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ANNEXURE-4

Methadone Treatment Appropriateness Checklist

1. Is the person dependent on opioids?
2. Is the person in opioid withdrawal?
3. Does he/she exhibit signs of opioid intoxication?
4. Are there signs of other drug/alcohol intoxication?
5. Is the patient willing to undergo treatment with methadone?
6. Has the patient been told about the risks and benefits of methadone treatment?
7. Can the patient be expected to attend the MMT centre regularly?
8. Is the patient willing to go in for long-term treatment?
9. Is the patient having a psychiatric disorder? Is he/she under treatment? Is he/she mentally stable?
10. Does he/she exhibit active suicidal behaviour?
11. Is the patient currently dependent on or abusing alcohol?
12. Is the patient currently dependent on benzodiazepines or other sedative-hypnotics?
13. Is the patient using other drugs? If yes, list them.
14. Has the patient had prior adverse reactions to methadone?
15. Does he/she have family support?
16. If the patient is a woman, is she pregnant?

Adapted from Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction, DHSS, 2004

ANNEXURE-5

Treatment Contract

As a participant in the methadone for opioid dependence treatment protocol, I freely and voluntarily agree to accept this treatment contract, as follows:

1. I agree to keep, and be on time for, all my scheduled appointments with the doctor and his/her assistant at the clinic/treatment centre.
2. I agree to conduct myself in a courteous manner in the clinic/treatment centre.
3. I agree not to arrive at the clinic/treatment centre intoxicated or under the influence of drugs. If I do, the doctor will not see me and I will not be given any medication until my next scheduled appointment.
4. I agree not to sell, share or give any of my medication to another person. I understand that such mishandling of my medication is a serious violation of this agreement and would result in my treatment being terminated without recourse for appeal.
5. I agree not to deal, steal or conduct any other illegal or disruptive activities in the clinic/treatment centre.
6. I agree that my medication (or prescriptions) can only be given to me at my regular clinic/treatment centre visits. Any missed clinic/treatment centre visits will result in my not being able to get medication until the next scheduled visit.
7. I agree that the medication I receive is my responsibility and that I will keep it in a safe, secure place. I agree that lost medication will not be replaced regardless of the reasons for such loss.
8. I agree not to obtain medications from any physicians, pharmacies, or other sources without informing my treating physician. I understand that mixing methadone with other medications, especially benzodiazepines, such as Calmpose or Valium, and other drugs of abuse, can be dangerous. I also understand that a number of deaths have been reported among persons mixing methadone with benzodiazepines.
9. I agree to take my medication as the doctor has instructed and not to alter the way I take my medication without first consulting the doctor.
10. I understand that medication alone is not sufficient treatment for my disease and I agree to participate in the patient education and relapse prevention program, as provided, to assist me in my treatment.

Patient Signature

Witness Signature

Date

ANNEXURE-6

Signs and Symptoms of Methadone Intoxication and Toxicity

A triad of symptoms is typical of opioid overdose

**Pinpoint Pupils
Respiratory Depression
CNS Depression**

Methadone intoxication

Constriction of pupils
Itching/scratching
Sedation
Lowered blood pressure
Slow pulse
Hypoventilation

Methadone toxicity

Loss of consciousness
Respiratory depression
Pinpoint pupils
Hypotension
Bradycardia
Pulmonary Oedema

Patients who are thought to have taken a methadone overdose require prolonged observation.

Naloxone, which promptly reverses opioid induced coma, should be given as a prolonged infusion when treating methadone overdose. A single dose of naloxone will wear off within one hour.

ANNEXURE-7

Frequently Asked Questions related to Methadone Maintenance Treatment (MMT)

Q: What is detoxification?

A: Detoxification refers to the withdrawal over a short period from an opioid or sedative/hypnotic by the use of the same drug or a similar drug in decreasing doses. The objective of detoxification is to assist the patient's transition to a 'drug free' state.

Q: What are the limitations of detoxification?

A: Dependence on heroin and other opioids is a persisting condition and the 'quit' rates following detoxification are alarmingly low. The high relapse rates are nothing to do with being bad or having no will power. A long-term use of illicit opioids such as heroin changes the brain in such a way that the brain continues to need an opioid to function properly. For such people, short-term treatment does not work, and so long-term treatment with OST is necessary.

Q: What is opioid substitution treatment (OST)?

A: Opioid substitution is replacing the illicit drugs the drug user is taking with another drug or a similar drug (e.g., replacing heroin with sublingual buprenorphine). It may also mean using the same drug but taking it in a different way.

Q: What drugs are used in OST?

A: The two commonly used drugs worldwide for OST are: methadone and buprenorphine.

Q: What is methadone?

A: Methadone is an opioid medication belonging to the same family as opium and morphine.

Q: How is methadone administered?

A: Methadone is the only long-acting opioid that comes in both liquid and tablet form. The tablet can be divided or crushed. Methadone can be used when swallowing pills is difficult. Methadone syrup usually contains 5 mg/ml methadone hydrochloride.

Q: What should one know about methadone?

A: Methadone should NEVER be used by someone other than the person for whom it is prescribed. If used incorrectly, methadone can cause sedation, slowed breathing and even death. Never stop, start, or adjust methadone dose without clinician approval. As with many medications, response varies among individuals. It is important to monitor and report the response and any possible side effects to the MMT team.

Q: Why can't the doctor increase the methadone dose more quickly?

A: When the patient first starts methadone, he/she wants to get on the right dose as soon as possible. However, the doctor has to increase the dose slowly over several weeks because the body takes time to adjust to methadone. Unlike other narcotics, methadone builds up slowly in the bloodstream over several days. A dose that may feel like too little on a Monday could land the patient in hospital by Thursday.

Q: What are the side-effects?

A: Constipation is common with any opiate and rarely resolves without treatment. Medications or measures to prevent constipation are recommended with start of methadone treatment.

Encourage patients to consume plenty of fruits and vegetables and non-alcoholic fluids each day. All opioids may cause drowsiness, mild confusion, nausea or itching. Any new symptoms should be reported. Some side-effects may go away over time with continued use of the medication. Excessive sweating is commonly reported among MMT clients and dose reduction may not help. Sweating can also be a prominent symptom in withdrawal and so careful history taking and observation of the patient prior to dosing may be necessary to assist in making the distinction. In rare cases, methadone may cause increased sleepiness or slowed breathing. The health-care team should be informed if these symptoms occur while taking methadone.

Q: Can a patient take any medicine while on methadone?

A: Some medications may interact with methadone. They include HIV drugs, anti-TB medication, anti-epileptic drugs, anti-fungal drugs and anti-depressants. It is important to review the medications taken by the patient while on methadone with the health care team and let them know about this.

Q: Does methadone produce teeth problems?

A: All opioids including methadone reduce the production of saliva, while illicit use is associated with poor nutrition and poor dental hygiene. Consequently dental problems are common at entry to MMT. It is common for patients to blame methadone for their dental problems. Salivary flow can be increased by chewing. Encourage patients to improve dental hygiene.

Q: How to address sleep disturbance in MMT patients?

A: Sleep problems can be addressed by sleep hygiene and simple relaxation techniques. The following are the measures used to improve sleep hygiene:

Arise at the same time each day.

Limit time in bed to a normal duration of 6–7 hours daily.

Discontinue the use of drugs that act on the CNS such as caffeine, tobacco, alcohol, opioids and stimulants.

Avoid daytime napping.

Exercise in the morning and remain active throughout the day.

Substitute watching television at night with light reading and listening to music.

Have a warm bath near bedtime.

Eat on schedule and avoid large meals at night.

Follow an evening relaxation routine.

Ensure comfortable sleeping conditions.

Spend no longer than 20 minutes awake in bed.

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

Q: How to address reduced libido and sexual dysfunction in MMT patients?

A: Reduced dose may help but needs to be balanced against the risk of return to heroin use. Psychological support will also be helpful.

Q: What are the signs of opioid overdose?

A: The signs and symptoms of methadone overdose are as follows:

Pinpoint pupils

Nausea

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

The symptoms may last for a day or more. Death generally occurs due to respiratory depression.

Q: How to prevent the risk of diversion of methadone?

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

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

Q: Can methadone be prescribed for pregnant opioid dependent woman?

A: Pregnant opioid dependent women have high priority for access to methadone maintenance programs in order to minimize the risk of complications. Pregnant women should be maintained on an adequate dose of methadone to achieve stability and prevent relapse or continued illicit opioid drug use.

Q: What are the signs of neonatal abstinence syndrome?

A: Babies born to mothers on MMT may experience a withdrawal syndrome. Available evidence gives little support to the existence of a relationship between the severity of the neonatal withdrawal syndrome and maternal methadone dose at delivery and its occurrence is unpredictable. The benefits of MMT for both the mother and the baby outweigh any risks from the neonatal withdrawal syndrome. Common signs include:

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

Q: Can mothers on methadone breastfeed their babies?

A: As breast milk contains only small amounts of methadone, mothers can be encouraged to breastfeed regardless of methadone dose provided they are not using other drugs. Breastfeeding may reduce the severity of the neonatal withdrawal syndrome.

Q: Can MMT patients use benzodiazepines?

A: Benzodiazepine injection is associated with vascular damage as well as mortality. Use of benzodiazepines can lead to dependence, memory disturbances and irritability. Benzodiazepine users exhibit patterns of increased risk and poorer psychological functioning. Patients must be advised about the interactions of benzodiazepines and methadone leading to increased potential for overdose and respiratory depression. In most overdose related deaths, benzodiazepine is found to be the cause.

Q: Can MMT be offered to HIV positive opioid user?

A: Certainly, as MMT improves adherence to ART. Methadone doses must be monitored due to the potential for interactions between methadone and HIV medications. Higher methadone doses may be necessary if HIV medications increase methadone metabolism.

Q: Can methadone be offered to opioid dependent users with Hepatitis C?

A: A high percentage of patients entering methadone programs will be Hepatitis C antibody positive. Patients with chronic liver disease on long term methadone maintenance generally do not need dose alterations, but abrupt changes in liver function might necessitate substantial dose adjustments.

Q: What is the influence of depression in MMT?

A: Depression has been found to predict poor psycho-social functioning and to increase the risk of relapse to heroin use in the event of life crises. Unless there is a particular indication for tricyclics, Selective serotonin re-uptake inhibitors SSRIs are preferred in the treatment of depression.

Q: What are the benefits of methadone substitution?

A: Maintains a majority of patients in treatment
Improves the patient's physical well being
Decline in the new infections of HIV, Hepatitis B and C
Reduces the criminality significantly
Improves the client's quality of life
Keeps clients in treatment for longer duration
Causes few side-effects
Has only mild withdrawal symptoms
It is not likely that people can overdose on it. Is safe
It is a long-acting drug so it does not have to be taken every day; thrice weekly dosing with methadone is possible
It is a good opioid substitution drug for people with mild to moderate opioid dependence
It is an attractive treatment for opioid users

