PREVENTION OF TRANSMISSION OF HIV AMONG DRUG USERS IN SAARC COUNTRIES

TD/RAS/03/H13

METHADONE SUBSTITUTION

INTERVENTION TOOL-KIT
UNDER TESTING
**Module 5**
'Methadone Substitution'

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Intervention Tool-kit

Module-5
Methadone Substitution
EXTRACT FROM THE OPENING STATEMENT OF ANTONIO MARIA COSTA, UNODC EXECUTIVE DIRECTOR AT THE 48th SESSION OF THE COMMISSION ON NARCOTIC DRUGS, VIENNA, MARCH 7–14, 2005

"In many countries, the current dramatic spread of blood-borne infections, from HIV/AIDS to Hepatitis C, is aggravating the suffering that comes from the chronic abuse of drugs. As a result, people at risk of HIV, or already infected by AIDS need tangible, targeted and immediate help before this pandemic evolves into the biggest killer in history ... My office is mandated, via the UN Drugs Conventions, not just to reduce the prevalence of drug abuse, but also to reduce the harm caused by drugs.

The best form of dealing with the problem is, of course, abstinence and at UNODC, we've invested substantial resources in prevention and treatment. We are increasing the assistance to populations at high HIV/AIDS risk, and we work with governments so that they can reach people before they join the ranks of the HIV-positive. This is where we can make a significant difference. This is where resources are well spent, as it is always easier to attack a problem before it materialises, or spins out of control.

My office believes that greater attention and more resources should be invested in drug control programmes aimed at checking the spread of blood-borne diseases. These initiatives must not stand alone, but be part of comprehensive efforts aimed at reducing drug use. We unequivocally reject any initiative, well intended as it may be, that could lead to a perpetuation of drug abuse...

Governments can, and must ensure both drug control and HIV prevention.

As stated by the INCB in its 2003 report: ‘... governments need to adopt measures to reduce the demand for illicit drugs taking into account... the drug-related spread of HIV infection. At the same time... prophylactic measures should not promote and/or facilitate drug abuse’.

UNODC'S COMPREHENSIVE PACKAGE APPROACH

HIV/AIDS prevention and care programmes for injecting drug users typically include a wide variety of measures (the 'package' approach), ranging from drug dependence treatment, including drug substitution treatment, outreach providing injecting drug users with information on risk reduction and referral to services, clean needles and syringes, and condoms, voluntary counselling and testing, treatment of sexually transmitted infections, antiretroviral therapy, and interventions for especially at-risk populations such as prisoners and sex workers who inject drugs. Such a comprehensive package of measures also usually includes treatment instead of punishment for persons convicted of minor offences, since drug treatment not only constitutes a humane, cost effective alternative, but also incarceration usually increases the risk of HIV transmission.
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1. AIMS

The current module on 'Methadone Substitution' is the fifth in the series of the six modules of the intervention tool-kit developed under the UNODC-ROSA project entitled 'Prevention of transmission of HIV among Drug Users in SAARC[^1] Countries' (Project code- AD/RAS/03/H13). The aims of the current module are:

- 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.

[^1]: SAARC is the South Asian Association for Regional Co-operation.
Opioid use, and in particular heroin use, is on the increase in South Asia. The diffusion of injecting drug use is causing concern in the region (UNODC-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. 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 effective, 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. A recent Cochrane review recommended that the provision of substitution treatment for opioid dependence in countries with emerging HIV and injecting drug use problems as well as in countries with established populations of IDUs should be supported (Gowing et al, 2004). The provision of substitution maintenance therapy 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 & UNAIDS, 2004).

Methadone is the most employed agent in substitution treatment around the world. Methadone treatment for heroin addicts was first used in a small trial in New York City in 1964. The first scientific report suggesting the benefits of methadone in heroin dependence was by Dole and Nyswander in the Journal of the American Medical Association, where they stressed that while taking the medication, addicts lost their cravings, they focussed on normal life events and largely ceased their compulsive drug use with all its risks and disadvantages (Dole and Nyswander, 1965). Following the American experience, a few other

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2 The Cochrane reviews are based on the best available information about healthcare interventions. They explore the evidence for and against the effectiveness and appropriateness of treatments (medications, surgery, education, etc) in specific circumstances. The Cochrane Database of Systematic Reviews is a product of the Cochrane Collaboration, an international non-profit and independent organisation, dedicated to making up-to-date, accurate information about the effects of healthcare readily available worldwide. More details on how to access the Cochrane Library are available at www.cochrane.org
countries introduced methadone to various degrees and in a variety of manners over the years. Hong Kong, Holland, Germany, France and Queensland in Australia currently operate large-scale methadone programmes. In Asia, apart from Hong Kong, Thailand and Nepal offer methadone substitution treatment to opioid dependents. A scaled-up programme with methadone is under consideration in the Republic of China and pilots have been initiated in some provinces.

Methadone is an opioid falling under the same category as other synthetic and naturally-occurring opioids such as pethidine, heroin, morphine, codeine, etc. All these substances on repeated administration produce tolerance and dependence. But, 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).

Major observational studies have indicated that methadone maintenance treatment reduces illicit drug use and criminal activities (Ball and Ross, 1991; Hall et al, 1998). Scientific evidence suggests that substitution treatment with methadone can help reduce criminality, infectious diseases and drug-related deaths; and improve the physical, psychological and social well-being of dependent users (Gibson et al, 1999). Patients stabilised 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 the injection drug use and drug-related high-risk sexual behaviour (NIDA/NIH, 1999). The beneficial role of methadone maintenance in HIV prevention among injecting drug users has good scientific evidence to support it (Metzger et al, 1993; Ward et al, 1998; Gibson et al, 1999). The cost effectiveness of methadone has been examined and the treatment with methadone is found to be efficient (Zaric et al, 2000). There is also evidence on the safety of methadone maintenance treatment (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).

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3 Tolerance is a state of adaptation in which exposure to a drug induces changes that result in reduction of one or more of the drug's effects over time.

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Scientific evidence for methadone treatment

- Effective in retaining people in treatment
- Reduces the risk of HIV infection
- Improves physical, mental health and the quality of life of patients and their families
- Reduces criminal activities
3. WHAT NEEDS TO BE IN PLACE BEFORE INITIATING METHADONE SUBSTITUTION?

Box 1: What needs to be done in methadone clinics prior to initiating opioid dependence treatment

- Establish policies and procedures for methadone maintenance treatment (outpatient delivery in supervised settings)
- Plans for staff education and training
- Backup coverage for the absence or leave of the medical doctor / core team
- Assurance of the privacy and confidentiality of addiction treatment information
- Linkages with other drug treatment services, who will accept referrals for other forms of treatment (e.g., abstinence-oriented approaches; psycho-social interventions)
- A referral network of medical specialists
- Timely physical examinations
- Linkages with medical treatment facilities including HIV treatment and care
- Linkages with addiction and psychiatric treatment programmes (e.g., detoxification centres, psychiatric clinics)
- Listing of community referral resources, including specific self-help groups who would welcome patients on methadone substitution

Regulatory rules

As methadone is a controlled narcotic drug, the central authority in each country will be responsible for procuring methadone for the substitution programme. 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 Programme should be undertaken under the guidance of the central authority of any given country.

Assessment of the capacity of the agencies

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 recognised services offering drug treatment. Box 1 lists procedures that need to be established in methadone clinics at the outset.

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4 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
The implementation of methadone substitution is organised into five subsections. The first subsection on 'clinical pharmacology' provides information on the effectiveness of methadone. The second 'assessing patients for substitution treatment with methadone' deals with the assessment of opioid dependent individuals and considers candidates for methadone treatment. Subsection III describes the guidelines and procedures for methadone maintenance treatment. Subsection IV discusses the issues relating to the administration of methadone and the rollout plan for delivering methadone to the patients. The final subsection focuses on training needs and ongoing support.

I. Clinical Pharmacology
In this subsection, the following will be discussed: i) About methadone pharmacology; ii) adverse effects and toxicity; and, iii) drug interactions.

i) About methadone pharmacology
Methadone is an opioid agonist\(^5\) 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. Familiarity with the following characteristics of methadone is important for the safe and effective use of methadone.

- Peak plasma concentration occurs one to five hours after oral dosing
- Long half-life\(^6\)
- Low therapeutic index\(^7\) (the risk of overdose is high during the first few days of treatment)
- Repeated dosing leading to accumulation

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5 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.

6 Half-life: time taken for half of the drug to be metabolised 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 hrs and after first few days of methadone, the half-life is 25 hrs.

7 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.
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 CNS depressants like alcohol
- Occasional reports of hypotension (low blood pressure), collapse and oedema
- Spasm of biliary and renal tracts
- Change in menstruation
- Dependence

**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.

<table>
<thead>
<tr>
<th>Abused drug</th>
<th>Pharmacokinetic interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Increased sedation</td>
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<tr>
<td></td>
<td>Increased respiratory depression</td>
</tr>
<tr>
<td>Opioids</td>
<td>Used with methadone increases respiratory depression</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Increase the risk of respiratory depression</td>
</tr>
</tbody>
</table>

There is potential for pharmacokinetic interaction between methadone and drugs that inhibit or induce methadone metabolism by hepatic enzymes.8

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Opioid poisoning triad

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

8 Methadone is metabolised by the hepatic enzyme system (cytochrome P450 3A4).
II. Assessing patients for substitution 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 methadone maintenance treatment.

i) How to assess and diagnose opiate dependence?

A) History:

Reason for presentation

- In crisis (health or economic or legal crisis).
- Brought in by a concerned parent, relative, spouse, employer, friend or outreach worker.
- Want help for their drug use and motivated to change their behavior.
- Usual source of drugs not available.
- Referred from another medical practitioner.
- Pregnant.

<table>
<thead>
<tr>
<th>Drugs that inhibit the hepatic enzymes⁹</th>
<th>Drugs that induce the hepatic enzymes¹⁰</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV drugs (zidovudine, ritonavir, etc.)</td>
<td>Some anti-epileptics (phenobarbitone, phenytoin, carbemazepine)</td>
</tr>
<tr>
<td>Broad-spectrum antifungals, antibacterials (ketaconazole, clotrimazole, etc.)</td>
<td>Anti-tuberculosis drugs (rifampin)</td>
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<tr>
<td>Antibiotics (erythromycin, etc.)</td>
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<tr>
<td>Anti-depressants (sertraline, etc.)</td>
<td></td>
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<tr>
<td>Anti-hypertensives - Calcium channel antagonists (nifedipine, diltiazem)</td>
<td></td>
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</table>

⁹ Medications that inhibit this enzyme system will potentially increase blood levels of methadone.
¹⁰ 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 of the possibility of drug interaction.
Past and current drug use (last 4 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?
- Symptoms experienced when unable to obtain their drugs.

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 injection 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/works?
- Has the patient thought 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 any relapses.

B) Examination
Assessing motivation
Is the patient motivated to stop or change their pattern of drug use or to make other changes in their life?

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 – Assessing the medical syndromes associated with opioid use (see Annex)
  - Side effects (constipation, hallucinations)
  - Overdose (e.g., respiratory depression)
  - Withdrawal (e.g., irritability, restlessness and pain) - (see Annex)

Assessment of mental health – co-existing psychiatric problems

Assessment of social and family situation

C) Special investigations with full informed consent
Hematological investigations
- Hemoglobin
- Liver function tests
- Hepatitis B and C

Urine assessment: Opiates persist in the urine up to 24 hours
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
- 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

**ii) Criteria to determine suitability for treatment with methadone**

**Patient Selection Criteria**

- Age above 18 years
- Regular opioid users (non-injecting) who have failed conventional treatment at least twice earlier or injecting opioids (injecting heroin and/or other synthetic opioids) users
- Persons willing for 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 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 psycho-social aspects of the patients. These aspects include, but are not limited to:
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 s/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

Intake Process
Opiate-dependent individuals – diagnosed by qualified and/or trained physician/psychiatrist

Informed consent for treatment with methadone

Treatment contract signed (see Annex)

Involvement of family member (desirable)

Decision about maintenance with methadone jointly made by the physician and patient

Treatment protocols explained clearly

III. Guidelines and procedures for methadone maintenance treatment

Physicians who use methadone to treat opioid dependence must consider the entire process of treatment, from induction, through stabilisation, and then maintenance. At each stage of the process, 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 stabilisation; iii) maintenance dosing; iv) missed doses; v) frequency of visits; and, vi) take-home dose; vii) withdrawal from methadone; and viii) information that needs to be provided to the patients

i) Induction
Having established that the patient is suitable for methadone treatment, determine 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. Only use initial doses higher than 30 mg 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 milligrams) and adjust the dose after reviewing the patient soon after commencing treatment. At review before the third or fourth dose, titrate the dose according to the patient's symptoms (suggesting either opioid withdrawal or methadone toxicity) and their 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.

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

Factors Determining the Initial Dose
- The 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 drugs or illicit drugs
- Body weight

In single-dose overdose cases, death has been reported with methadone doses as low as 50 mg in non-tolerant individuals. Methadone blood levels continue 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 stabilisation

<table>
<thead>
<tr>
<th>Typical reasons for dose increase</th>
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<tbody>
<tr>
<td>1) Signs and symptoms of withdrawal</td>
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<tr>
<td>2) Amount and/or frequency of opioid use not decreasing</td>
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<tr>
<td>3) Persistent cravings for opioids</td>
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<tr>
<td>4) Failure to achieve a dose that blocks the euphoria of short acting opioids</td>
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Dose adjustments during the period of stabilisation are in the range of 5-15 mg.
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 minimise 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 maintenance dose should be individualised to the patient's needs.
- Evidence indicates that a maintenance dose of at least 60 mg per day is more effective than lower doses in achieving treatment outcomes such as decreased illicit drug use.11

iv) Missed doses
A clinically significant loss of tolerance to opioids may occur with 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 that 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 that initial dose over three days, the dose may be safely increased relatively quickly toward the previous stable dose of methadone.

v) Frequency of visits
When a patient is initiated on methadone, he or 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.

vi) Take-home dose
The following three criteria should be assessed prior to initiating take-home doses. These criteria should be re-assessed regularly with regards to continuing carries ?? and/or increasing/decreasing the level of take-home doses.

Clinical stability – the patient demonstrates clinical stability when:
- The dose has reached a stable level.
- he/she demonstrates this stability by stable housing, support system and activities and regular attendance at clinic appointments.

11In Nepal, most of the patients were maintained with a daily dosage of methadone between 40-60 mg. In Hong Kong, the majority received a dose of 60 mg as maintenance dose.
The length of time in methadone treatment.
- Not recommended during the first two months of treatment.

Ability to safely store medication.
- Patients with unstable living arrangements, such as those living on the street or in places without storage facilities may not be appropriate to receive take-home doses.
- Ensure children don't have access to the medicine.

### 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

#### vii) 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 stabilise. The majority of patients tolerate the following rate of withdrawal:

**Methadone dose rate of withdrawal (per week)**

1. Over 50 mg  
2. 30-50 mg  
3. Less than 30 mg
   - 5 mg
   - 2.5 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 clinics
- Continued use of dangerous quantities of other CNS depressant drugs
- Trafficking of take-away doses
viii) Information to be provided to the patient

<table>
<thead>
<tr>
<th>Information to Give Patients</th>
</tr>
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<tbody>
<tr>
<td>✦ The dynamics of stabilisation (starting slow and going slow)</td>
</tr>
<tr>
<td>✦ The hazards of poly drug use, particularly in the first week of treatment</td>
</tr>
<tr>
<td>✦ The effects and side effects of methadone use</td>
</tr>
<tr>
<td>✦ Program guidelines and conditions</td>
</tr>
<tr>
<td>✦ Expected behaviour</td>
</tr>
<tr>
<td>✦ Risks and symptoms of an overdose</td>
</tr>
</tbody>
</table>

**IV. 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 to a rational, evidence-based approach to the treatment of drug users.\(^{12}\) 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) **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 stabilised the dose, a pharmacist or nurse or a community health nurse can administer the drug subsequently.

Prior to administering the medication, 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

ii) **Administering methadone**

To prevent possible diversion of the methadone, directly supervise the patient as they take the dose, and engage them in conversation to ensure they have

\(^{12}\)In Hong Kong, the government recognised the usefulness of methadone substitution programmes in the early 1970s and sustained the programme. The Government of Hong Kong supports additional ancillary services for drug users through significant involvement of the non-governmental sector.
consumed the dose. It is recommended that methadone doses are administered in disposable containers, or that the clinic has some appropriate means of sterilising glass 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.

### iii) Rollout plan for methadone substitution

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

- a medical doctor; 
- a documentation officer; 
- six nurses; 
- a counsellor; 
- security staff and 
- clinic maintenance staff. 

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 can receive uninterrupted medication, it is important that the substitution programmes 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 programmes. Community-based clinics are more attractive to drug users and the government-sponsored methadone clinics should be community based. Both the government (supply of substitution medication, monitoring of regulatory procedures) and the non-governmental organisations (NGOs) involved in community-based services, psychosocial care and support services for drug users should become partners in the delivery of treatment. The substitution programme 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 injecting drug users. The proportion of problem opioid users to be covered by the substitution (coverage) can be reviewed periodically in different geographical locations.

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13 The clinics in Hong Kong are located in geographical places with a large number of drug users. A large methadone clinic in Hong Kong remains open from 7 am to 10 pm daily. Approximately 1,000 clients are registered at the clinic of which about 850 attend each day. Staffing consists of one full time doctor, two part time social workers and 13 auxiliary medical service staff to carry out the day-to-day dispensing work. Volunteers who receive only stipend to cover their expenses support the clinic.

14 Society for the Aid and Rehabilitation of Drug Abusers (SARDA), a non-governmental agency that is primarily funded by the government provides the methadone clinics in Hong Kong with 21 full time social workers serving a client population of over 6,000 attendees daily. The other partners in service delivery are: Hong Kong Council of Social Services; Auxiliary Medical Services (AMS); former drug users as volunteers; and, Red Ribbon Centre for HIV/AIDS prevention.

15 Hong Kong’s early adoption of methadone substitution is an important factor in the low HIV infection rates among drug users. Additionally, the clinics provide the opportunity to disseminate HIV prevention messages to the drug users.
V. Training and support

The staff members at the clinics need to be trained and the training should be organised 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) 1-3 days training workshops; and, c) clinical placement in an existing methadone clinic. Apart from the initial workshops, there should be provision for follow-up training. A comprehensive training module can be developed that can be field-tested and widely used in the region.

It is likely that pilot projects will be established in many places in South Asia before large-scale methadone programme supported by respective Governments become operational. The staff participating at the pilot projects can be brought together for a centralised workshop. For the medical doctors, the one-day workshop 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 three days training programme 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 pilot projects, there could be exchange visits. Attendance at Harm Reduction Conferences and Drug Treatment Workshops should be encouraged for the methadone clinic team members. Core team members, who have been trained in the State/Province level three-day training workshops can train new members of the team with help from local consultants periodically.

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

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction to the workshop</td>
<td>Assessment of a patient with opioid use and criteria for methadone substitution</td>
<td>Enhancing 'quality' in patient care</td>
</tr>
<tr>
<td>Opioid dependence – concept, course and consequences</td>
<td>Effectiveness of methadone substitution</td>
<td>Liaison services and linkages</td>
</tr>
<tr>
<td>Effective treatment approaches</td>
<td>Regulatory procedures Confidentiality</td>
<td>Visit to a methadone clinic</td>
</tr>
<tr>
<td>Substitution treatment – definition, benefits and risks</td>
<td>Documentation and record-keeping</td>
<td></td>
</tr>
</tbody>
</table>

The workshops should adopt participatory training methodology and should be done by trainers well versed with the methadone substitution. The workshop should address practical issues and enhance the skills of the participants.
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
To ensure the following:
- Rapid and client-centred assessment and induction
- Flexible but adequate dose of methadone after stabilisation is provided
- Adequate duration of treatment
- Psychosocial services to deal with other concerns
- Trained staff
- Engagement with clients rather than punishment of continuing illicit drug use

The project should take the following quality assurance indicators in to consideration

Accessibility- These programmes 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 and emergency 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.

<table>
<thead>
<tr>
<th>Safe methadone use</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risks</strong></td>
<td><strong>Preventive measures</strong></td>
</tr>
<tr>
<td>Overdose during induction</td>
<td>Initial doses in range 15-30 mg Supervised ingestion of doses</td>
</tr>
<tr>
<td>Accidental poisoning of children</td>
<td>Take-home doses in childproof containers</td>
</tr>
<tr>
<td>Diversion</td>
<td>Take-home doses require a good response to treatment by patients</td>
</tr>
</tbody>
</table>
Preventing diversion- There is a valid public health basis for 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 minimise the risks and maximise 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 (see Section 4: III).

Efficacy- 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 (3-4 sessions in a group setting) with minimal staff investment should be planned.

Intake criteria- Specific selection criteria should be laid down (see Section 4: II).

User participation- The programme should be flexible and should involve patient participation at the level of planning and implementation. It should incorporate changes based on the requirements of the patients.

Cost effectiveness- The programme can function with minimal staff (See Section 4: IV)

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 publicising the programme, adequate utilisation of services can be ensured. Various methods can be used for this purpose depending on the suitability in the 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.

Patient retention- This can be enhanced by using adequate doses, empathic staff, having a programme that is receptive to the patients' needs, flexibility in the programme, other adjunctive facilities for which a liaison with other local NGOs can be made. The retention of patients in a maintenance programme is related to its efficacy as well as its "user-friendly" attitude.

Training of staff- Training that provides basic information about opiates, concept of abuse and dependence, complications related to opioid use, history taking, psychosocial assessment, information about effective approaches and methadone maintenance should be given to the staff. 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 Methadone Maintenance Therapy can be measured through outcome indicators. An independent outcome evaluation will indicate the benefits of methadone substitution. These indicators include:

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

Reduction in illicit drug use, reduction in criminal involvement and reduction in high risk behaviour have been observed in several settings including Hong Kong, a high-income Asian country. Continuation in treatment, reduction in crime and improvement in health has been observed among methadone maintenance clinic attendees in Nepal, a developing country setting (see case study below).

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**Methadone Maintenance Treatment in Nepal - A Case Study**

Nepal was the first developing country to establish a "Harm Reduction" Programme for injecting drug users. Similarly, the methadone treatment programme in Nepal is considered as one of the firsts in South Asia. Methadone treatment was started in 1994 at the Mental Hospital. The number of new patients enrolled during 1994-95 was 69 and increased to 162 in 2002-03. More than half the patients (54 per cent) were in the age group of 26-35 years. About two-thirds of the patients (73 per cent) have used opioids for more than six years. The treatment was evaluated and found to be beneficial for the opioid dependents.

There were also savings due to the methadone maintenance treatment. Whereas the average cost of maintaining the illicit drug use for one person per year was estimated at NRs. 100,375 (approximately US$1,400), the average cost of methadone for one person per year was calculated at NRs. 7,330 (approximately US$105) resulting in savings of NRs. 93,075. Improvement in health, reduction in criminal activities and decline in quarrel with family members was observed among patients maintained on methadone.

*Source: Mental Hospital, Nepal*

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16The methadone maintenance treatment programme in Hong Kong as of October 2000, has registered 9,434 patients out of 12,904 known heroin users and 69 per cent of the registered patients attend the methadone clinics daily. For those attending the clinics, the use of illicit drugs has been reduced. While attending the programme, about 50 per cent patients reported committing less crime. Their employment improved slightly following treatment. The incidence of HIV infection among the clinic attendees remained low. Unlinked anonymous screening found 0.27 per cent prevalence rate for the year 2000.
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
  Take-home doses
Other services provided at the clinic
  HIV prevention education/Overdose prevention education
  Primary medical care
Other psychosocial support and care services
  Liaison with other agencies proving 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

A suggested sample of costing heads is given below:

**Training costs**
Initial training programme for all Medical Officers in the country
One-day workshop (centralised at the National level)

Initial training programme for core team members from a
State/Province: Three-day training workshop (Centralised at
the State/Province level)

**Manpower**
The following personnel are required in a clinic that provides for
methadone treatment:
Medical doctor' (One doctor per clinic - 300 regular patients)
Counsellor' (One)
Six nurses' (One nurse for 50 patients)
Documentation officer' (One person per clinic for documentation)
Security person' (three per clinic)
Staff for clinic maintenance' (one per clinic)
(' To be recruited and supervised by the Government.)

Social Workers*
Outreach Workers*
Peer educators*
(* The services of these will be supported by NGOs working with the
methadone clinics.)

Cost of methadone - based on Nepal's experience
Cost of average dose of methadone/year/person
Cost of average dose of methadone/year /300 patients
8. REFERENCES


UNAIDS, AHRN and UNODC. Preventing HIV/AIDS among Drug Users - Case studies from Asia. Regional Task Force on Drug Use and HIV Vulnerability (publication year not specified).


### Medical Syndromes Associated with Opioid Use

<table>
<thead>
<tr>
<th>Syndrome (Onset and Duration)</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opiate intoxication</td>
<td>Conscious, sedated, &quot;nodding&quot;; mood normal to euphoric; pinpoint pupils; history of recent opiate use</td>
</tr>
<tr>
<td>Acute overdose</td>
<td>Unconscious; pinpoint pupils; slow, shallow respiration</td>
</tr>
<tr>
<td>Opiate Withdrawal Anticipatory* (3-4 hours after last &quot;fix&quot;)</td>
<td>Fear of withdrawal; Anxiety; Drug seeking behaviour</td>
</tr>
<tr>
<td>Early (8-10 hours after last &quot;fix&quot;)</td>
<td>Anxiety; Restlessness; Yawning; Nausea; Sweating; Nasal stuffiness; Rhinorrhoea; Lacrimation; Dilated pupils; Stomach cramps; Drug-seeking behaviour</td>
</tr>
<tr>
<td>Fully Developed (1-3 days after last &quot;fix&quot;)</td>
<td>Severe anxiety; Tremor; Restlessness; Piloerection**; Vomiting, Diarrhoea; Muscle spasm***; Muscle pain; Increased blood pressure; Tachycardia; Fever, Chills; Impulse-driven drug-seeking behaviour</td>
</tr>
<tr>
<td>*Anticipatory symptoms occur as the acute effects of heroin begin to subside</td>
<td>**The piloerection has given rise to the term &quot;cold&quot; turkey&quot;. *** The sudden muscle spasms in the legs have given rise to the term &quot;kicking the habit&quot;.</td>
</tr>
</tbody>
</table>

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

**The 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".
**Clinical Opiate Withdrawal Scale**

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 & time: _____/_____/__

**Reason for assessment:**

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Resting Pulse Rate:</strong></td>
<td>0: pulse rate 80 or below 1: pulse rate 81 - 100 2: pulse rate 101 - 120 4: pulse rate greater than 120</td>
</tr>
<tr>
<td><strong>GI Upset:</strong></td>
<td>0: no GI symptoms 1: stomach cramps 2: nausea or loose stool 3: vomiting or diarrhoea 4: multiple episodes of diarrhoea or vomiting</td>
</tr>
<tr>
<td><strong>Sweating:</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>Tremor:</strong></td>
<td>0: no tremor 1: tremor can be felt, but not observed 2: slight tremor observable 4: gross tremor or muscle twitching</td>
</tr>
<tr>
<td><strong>Restlessness:</strong></td>
<td>0: able to sit still 1: reports difficulty 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</td>
</tr>
<tr>
<td><strong>Yawning:</strong></td>
<td>0: no yawning 1: yawning once or twice during assessment 2: yawning three or more time during assessment 4: yawning several times/minute</td>
</tr>
<tr>
<td><strong>Pupil size</strong></td>
<td>0: pupils pined 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</td>
</tr>
<tr>
<td><strong>Anxiety or Irritability</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>Bone or Joint Aches:</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>Gooseflesh skin</strong></td>
<td>0: skin is smooth 3: piloerection of skin can be felt or hairs standing up on arms 4: prominent piloerection</td>
</tr>
<tr>
<td><strong>Runny nose or tearing:</strong></td>
<td>0: not present 1: nasal stuffiness or unusually moist eyes 4: nose constantly running or tears streaming down cheeks</td>
</tr>
<tr>
<td><strong>Total score:</strong></td>
<td>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</td>
</tr>
</tbody>
</table>

Initials of persons completing Assessment
TREATMENT CONTRACT
As a participant in the methadone for opioid abuse and dependence treatment protocol, I freely and voluntarily agree to accept this treatment contract, as follows:

(1) I agree to keep, and be on time to, all my scheduled appointments with the doctor and his/her assistant.

(2) I agree to conduct myself in a courteous manner in the physician's office.

(3) I agree not to arrive at the office 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 doctor's office.

(6) I agree that my medication (or prescriptions) can only be given to me at my regular office visits. Any missed office 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 calmipose 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 programme, as provided, to assist me in my treatment.

Patient Signature /Witness Signature /Date
PREVENTION OF TRANSMISSION OF HIV AMONG DRUG USERS IN SAARC COUNTRIES

TD/RAS/03/H13

METHADONE SUBSTITUTION

INTERVENTION TOOL-KIT
UNDER TESTING