

4. IMPLEMENTATION

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

- I. Clinical pharmacology
- II. Assessing patients for treatment with buprenorphine
- III. Guidelines and procedures for maintenance treatment
- IV. Roll-out plan for buprenorphine administration
- V. Training and support

I. Clinical Pharmacology

In this subsection, the following will be discussed: i) about buprenorphine; ii) onset and duration of response to buprenorphine; iii) buprenorphine withdrawal syndrome; iv) side effects; v) safety; vi) drug interactions; vii) properties and the clinical implications; and, viii) a comparison between buprenorphine and methadone.

i) About buprenorphine

Buprenorphine is a synthetic opioid derived from the morphine alkaloid thebaine. It has low intrinsic activity² and high affinity at the opioid receptors responsible for some properties of opioids like analgesia and euphoria.³

Buprenorphine suppresses the craving for heroin as well as blocks the effect of additional heroin and other opioid use.

² Buprenorphine is a partial agonist and has both agonist (opiate like) and antagonist (blocking the action of opiates) activity at the opiate receptors.

³ Several opioid receptor subtypes have been described and characterised. Receptors: Classic opioids like morphine bind here preferentially. They are believed to be responsible for most analgesic properties of opiates, as well as for euphoria, sedation, constipation, respiratory depression and dependence.

ii) Onset and duration of response to buprenorphine

Buprenorphine has poor gastrointestinal bioavailability but has a fair sublingual bioavailability. It is easily absorbed within 5-10 minutes.

Onset of effects	30 - 60 minutes
Peak clinical effects	1 - 4 hours
Duration of effects	8 - 12 hours at low dose (e.g. < 4 mg) 24 - 72 hours at high dose (e.g. >16 mg)

Higher doses have prolonged duration of response

The reasons for the extended action of buprenorphine are:

- ♦ Tight binding at opioid μ receptors and slow dissociation
- ♦ Release of low levels of buprenorphine from the fat stores very slowly

Extended duration of action helps a daily dose or thrice a week dose

iii) Buprenorphine withdrawal syndrome

Withdrawal effects from full agonists like heroin, morphine or methadone are marked but only a low level of withdrawal effects are observed when buprenorphine is abruptly withdrawn. The low level of withdrawal symptoms also appears delayed and for 72 hours, there may be no significant withdrawal symptoms following cessation of the drug. Its partial agonist properties, along with its slow dissociation from opioid receptors, are thought to explain why opioid withdrawal syndrome is milder.⁴

iv) Side effects

The medical effects of acute buprenorphine administration are similar to those of opioid agonists. Opioid dependent individuals show tolerance to many of these effects. Since buprenorphine tablets dissolve readily in water, these can be injected. The use of combination tablets of buprenorphine and naloxone⁵ (in doses of 2 mg of buprenorphine and 0.5 mg naloxone) will help mitigate potential diversion and abuse. This combination will also permit sublingual use without precipitating withdrawals.

Side effects

Constipation
Disturbed sleep
Drowsiness
Sweating
Headaches
Nausea

v) Safety

Buprenorphine exerts a "ceiling effect" and as the dose of buprenorphine increases, the agonist effect reaches a peak and then reduces in magnitude. In contrast to full opioid agonists, overdose of buprenorphine (by itself) does not appear to cause lethal respiratory depression in non-compromised individuals.

Overdose of buprenorphine (by itself) does not appear to be fatal.

⁴ Treatment with opioid antagonists (e.g., Naltrexone) can be commenced within days of the cessation of low-dose buprenorphine treatment without precipitating severe opioid withdrawal. This enables patients to transfer promptly to naltrexone treatment, and avoid relapse and treatment dropout.

⁵ Naloxone is an opiate antagonist (preventing activation of opiate receptor by an opioid); it is short acting; used in the treatment of overdose; 10-20 times more potent by injection than by sublingual route.

vi) Drug interactions

Drugs

Sedatives
(benzodiazepines)

Opioid antagonists

Opioid agonists

Hepatic enzyme
inhibitors⁶

Hepatic enzyme
inducers⁷

Drug interactions

Additive sedative effects

Deaths reported with combinations

High doses of naloxone required for treating overdose
Naltrexone can precipitate a delayed withdrawal
syndrome

Difficult to achieve analgesia with short-term opiate
agonists in patients maintained on buprenorphine

HIV drugs like Ritonavir[®], Saquinavir[®];
Ketoconazole[®]

HIV drugs Nevirapine[®], Efaviren[®];

vii) Properties of buprenorphine and their clinical implications

Property	Clinical implication
Opioid effects	Reduces cravings for heroin
Partial agonist	Less sedating than full agonists (heroin, morphine or methadone)
Prevents or alleviates heroin withdrawal symptoms	Can be used for maintenance or withdrawal treatment of heroin dependence
Diminishes the effects of additional opioid use (e.g. heroin)	Diminishes psychological reinforcement of continued heroin use.
Long duration of action	Allows for once a day to three-times-a-week dosing schedules.
Ceiling on dose response effect	Higher doses prolong the duration of action but safer in overdose.
Preparation (sublingual)	Poorly absorbed orally. Accidental poisoning by children may not be fatal. More time required for directly observed therapy (DOT).
No severe withdrawal precipitated by opioid antagonists	Treatment with naltrexone can be commenced within days of buprenorphine.
Side effect profile similar to other opioids	Generally well tolerated, with most side effects transient.

Lintzeris et al, 2001

⁶ Buprenorphine is metabolised by the hepatic enzyme system (cytochrome P450 3A4). Medications that inhibit this enzyme system may potentially increase blood levels of buprenorphine. As yet, no controlled studies have examined the pharmacokinetic interactions.

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viii) Comparison between buprenorphine and methadone

Buprenorphine	Methadone
Partial agonist and produces only a low level of euphoria.	Full agonist and can produce significant intoxication.
Has low dependence potential compared with full opioid agonists.	Potential to produce significant dependence. As tolerance increases, dose increases over time are required.
Abstinence leads to mild withdrawal symptoms.	Abstinence leads to marked withdrawal symptoms.
At high doses, there is a ceiling effect. The risk of fatal respiratory depression by overdose of buprenorphine by itself is minimal. But when combined with benzodiazepines (diazepam), alcohol and other CNS depressants, respiratory depression has been reported.	Risk of fatal overdose by respiratory depression.
Sublingual tablets are effectively absorbed. It is not orally active. Sublingual tablets can be crushed, easily dissolved and injected.	Orally active.

II. Assessing patients for treatment with buprenorphine

To determine the appropriateness of buprenorphine substitution treatment, a comprehensive patient assessment is essential. A candidate for buprenorphine 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 buprenorphine maintenance treatment. Additional information on the appropriateness of buprenorphine treatment is found in the Annex.

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 / outreach worker.
- ◆ Want help for their drug use and motivated to change their behaviour.
- ◆ Usual source of drugs not available.
- ◆ Referred from another medical practitioner.
- ◆ Pregnant.

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 | - <i>(See Annex A for assessing medical syndromes associated with opioid use.)</i>
Side effects (e.g. constipation)
Overdose (e.g. respiratory depression)
Withdrawal (e.g. irritability, pain) - <i>(See Annex B for opiate withdrawal scale.)</i> |

Current medication - What drugs? If HIV status known, whether on HIV drugs?

Assessment of mental health - co-existing psychiatric problems

Assessment of social and family situation

C) Special investigations with full informed consent

Haematological investigations

- ✦ Haemoglobin
- ✦ 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

The physician then decides about the appropriateness of buprenorphine treatment for the patient. (*See Annex C for buprenorphine treatment appropriateness checklist.*)

Criteria to determine suitability for treatment with buprenorphine

Patient Selection Criteria

- ✦ Age above 18 years
- ✦ Regular opiate users (non-injecting) who have failed conventional treatment at least twice earlier or injecting opiate (injecting heroin and/or buprenorphine) users
- ✦ Persons willing for sublingual buprenorphine (provide informed consent for treatment)

Contraindications

- ✦ Patients with serious medical conditions like acute respiratory failure, acute hepatic disease, acute alcoholism, and delirium tremens.
- ✦ Patients under 15 years of age.
- ✦ Female patients who are pregnant or breastfeeding.
- ✦ Known hypersensitivity to buprenorphine.

Precautions

- ✦ Co-morbid dependence on high doses of benzodiazepines or other central nervous system depressants (including alcohol)
- ✦ Significant untreated psychiatric co-morbidity
- ✦ Significant medical complications
- ✦ Transfer from methadone maintenance

Intake Process

Opiate dependant individuals - diagnosed by qualified and/or trained physician/ psychiatrist



Informed consent for treatment with buprenorphine



Treatment contract signed (see Annex D for an example of a treatment contract.)



Involvement of family member (desirable)



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



Treatment protocols explained clearly

III. Guidelines and procedures for maintenance treatment

Physicians who use buprenorphine 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) factors that need to be considered before selecting an opioid dependent person for buprenorphine substitution; ii) induction; iii) stabilisation; iv) maintenance dosing; v) frequency of dosing; and vi) withdrawal from buprenorphine.

i) Before selecting an opioid dependent person for buprenorphine substitution

Response to treatment: Treatment goals to be agreed upon by the patient and the provider. Additional psychosocial support is beneficial for majority of patients and improves adherence to maintenance treatment.

Individual variation in absorption, metabolism and clearance rates of the drug, buprenorphine should be considered.

Adverse effects: People complaining of sedation with methadone prefer buprenorphine.

Logistics of participating in treatments:

- ✦ ease of access for participants
- ✦ frequency of dispensing (alternate day or thrice weekly is attractive for working patients)
- ✦ convenient location of treatment services (located where drug users live; central location; public transportation)

- ✦ user-friendly services
- ✦ costs to patients (free or subsidised treatment is most attractive to users)

Ease of withdrawal from maintenance buprenorphine treatment: Though withdrawals are milder compared to methadone, the relapse to heroin following discontinuation of buprenorphine is the same for both drugs.

General expectations of the treatment: Some patients have unrealistic expectations about the treatment and all patients must be told clearly about the treatment benefits and limitations.

Capacity for transfer from methadone maintenance: Patients who cannot reduce methadone⁸ below 60 mg are not ideal for transfer to buprenorphine.

Additional psychosocial care with buprenorphine improves treatment adherence

ii) Induction

Initial buprenorphine dose: inducting heroin users

The first dose of buprenorphine should be administered at least 6 hours after the last heroin use to reduce the risk of a precipitated opioid withdrawal. The initial dose should be between 0.4 and 4 mg.⁹ Induction is usually done in the first one or two days. The following must be taken into consideration when considering the initial dose:

- ✦ the degree of tolerance to opioids:
 - low or uncertain tolerance to opioids: 0.4 to 4 mg.
 - high levels of tolerance: 6 to 8 mg..
- ✦ severity of opioid withdrawal experienced by patient at first buprenorphine dose:
 - moderate to severe opioid withdrawal: 6 to 8 mg.
 - little or no opioid withdrawal: 0.4 to 4 mg, or delay initial dose.
- ✦ alcohol, sedative drug (benzodiazepines), or illicit heroin use warrants low initial buprenorphine doses, with frequent reviews.
- ✦ medical conditions may warrant the use of lower initial doses

iii) Stabilisation

The key principles to stabilising patients are:

- ✦ review of the patient by the prescribing doctor / members of the treatment team

⁸ Applicable in countries where both drugs (methadone and buprenorphine) are legally available for substitution treatment.

⁹ Clinical experience in India has indicated this dosage recommendation; however rigorous studies may be required in the region to establish proper initial doses.

- ✦ titration of the buprenorphine dose by the reviewing doctor according to:
 - ▶ features of intoxication, withdrawal, cravings over preceding 24 hours
 - ▶ additional drug use (e.g., heroin, sedatives)
 - ▶ side-effects or other adverse events
 - ▶ adherence to dosing regime (attendance at the buprenorphine clinic)
 - ▶ adherence to dosing route (injecting the crushed medicines)
 - ▶ patient satisfaction with buprenorphine dose
- ✦ dose changes:
 - ▶ increases should be by increments of 0.4 - 2 mg at a time
 - ▶ allow at least 2 - 3 days between dose increases

Patients' experience with an administered dose is relevant to determining proper dosage

At each review, the buprenorphine dose should be titrated in the light of:

- ✦ Intoxication, or significant side effects indicate a need to reduce the dose
- ✦ Adverse events (such as overdoses) - an indication to reduce the dose
- ✦ Cravings for heroin use, use of illicit and other drugs, reported withdrawal symptoms - reasons for increasing the daily dose

The stabilisation phase takes 2-8 weeks in general and the goal of buprenorphine treatment is to treat with the optimal dose of medication needed to address target signs, symptoms and desired benefits.

Adequate and optimal dosing helps to reduce additional illicit drug use and promote adherence to maintenance treatment

Initiating and maintaining treatment with sublingual buprenorphine - a tentative schedule drawn from the experience in Chennai, India

Day 1: The doctor gives medication under observation. It should be taken sublingually. After receipt of the buprenorphine tablet, the patient should remain in the office for at least one hour to observe for any reaction. The dosage should be slowly stepped up depending on the prevailing withdrawal symptoms. Dispense enough medication to last till the next visit. The patient may be seen every day for a period of a week and be given medication under the direct observation therapy (DOT).

The time of the first dose of sublingual buprenorphine is six hrs (range: 4 - 8 hrs) after the last dose of heroin. Initial dose is 0.4 mg to 4 mg of sub-lingual buprenorphine tablet.

Week 1: Review with the doctor regarding the patient's progress, relapse if any, symptoms or adverse effects of the medication.

Week 2-5: Mandatory to meet the doctor every week and, if necessary more often too.

Week 6: Meet with the doctor for review of your treatment. At this time the decision whether to continue buprenorphine and the benefits and limitations of treatment are discussed in detail with the counsellor. The patient has been stabilised by this time and the dose that is required for maintenance is determined. This maintenance dose will be delivered to the patient regularly under DOT by the clinic staff.

Week 7 and beyond: Since the treatment continues for a longer period, the patient meets the doctor only periodically to assess progress. Encourage participation of the patient in psychosocial intervention programmes and self-help groups. If the clinic staff members feel that the patient is experiencing any special difficulty, then the patient is shown to the doctor.

The first few days of treatment are a difficult phase. Insomnia and restlessness can be frequently encountered and it can be reduced to a great extent by reassurance and reducing the anxiety of the patient. Craving usually comes in waves and can be triggered by external cues like seeing people using drugs, frequenting places where drugs are used, paraphernalia used and internal cues like stress, anger, depression, depression, anxiety and boredom. In addition, specific strategies to reduce craving can be taught to patients.

(Buprenorphine treatment for injecting opiate users in Chennai, India, SAHAI Trust, 1999–2002- supported by European Commission)

iv) Maintenance dosing

Buprenorphine doses should be individually titrated according to the patients' response to treatment. Effective maintenance doses that result in reduced heroin use and improved treatment retention are achieved with high buprenorphine doses in the range of 8 to 24 mg buprenorphine per day in Western studies. Little is known regarding the nature of adverse events at maintenance daily doses greater than 32 mg, therefore, the maximum daily dose of buprenorphine routinely recommended is 32 mg. In India experience indicates that persons dependent on opioids require a comparatively smaller dose (4 - 8 mg/day).¹⁰ For injecting buprenorphine users, the maintenance dose is approximately 2 to 4 times the dose that they are regularly administering by intramuscular or intravenous route (given the 42 per cent and 29 per cent buprenorphine bioavailability in the sublingual route relative to intramuscular and intravenous routes, respectively).

In India, a majority of patients require a maintenance dose of about 4 - 8 mg every day

v)) Frequency of dosing

Daily dosing with buprenorphine is required during induction and stabilisation. Once the patients' daily medication dose has been stabilised (usually after 2-8 treatment weeks) either an alternate day or 3 times a week dosing may be instituted as follows:

1. A dose equal to 2 times the daily dose on alternate days, not to exceed a maximum of 32 mg.
2. A dose equal to 2 times the daily dose to be given on Mondays and Wednesdays with a dose equal to 3 times the daily dose on Fridays not to exceed a maximum of 32 mg.

Daily Buprenorphine dose (mg)	Alternate Day Buprenorphine (mg)	Three times a week Buprenorphine dose (mg)	
		Mon & Wed	Fri
2	4	4	8
4	8	8	12
8	16	16	24
16	32	32	32
20	32	32	32
24	32	32	32

¹⁰Lesser compared with the maintenance dose suggested in the Western countries. The suggested dose is based on the clinical experience from India and studies are required to determine proper maintenance dose for persons with opioid dependence in the region

Alternate day dosing and thrice weekly dosing is an option to lessen the number of visits and is usually attractive to working patients. However, some patients (up to 15 per cent) experience craving and return to heroin use if transferred to thrice weekly dosing.

vi) Withdrawal from buprenorphine

There is no reason to believe that abstinence following buprenorphine differs greatly from abstinence following methadone. Research evidence confirms that both severity of withdrawal, and relapse post-detoxification,¹¹ appear similar for methadone and buprenorphine. Withdrawal from buprenorphine should only be conducted with the consent of the patient. A graduated reduction over weeks results in better outcomes. For patients on 8 mg and below, the dose reduction is 2 mg per week or fortnight and for those receiving 8 - 16 mg, the reduction shall be 2 - 4 mg per week or fortnight.

IV. Rollout plan for buprenorphine administration

Buprenorphine 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. It is preferable to deliver the drug in substitution programmes through directly observed treatment (DOT). Buprenorphine treatment should be part of a comprehensive treatment and care service for opioid dependents and in order to achieve this, government run community based buprenorphine clinics should work in close collaboration with non-governmental agencies as well as hospitals.

i) Procedures prior to administering the dose of buprenorphine

A psychiatrist at the substitution clinic or a physician trained in buprenorphine treatment shall prescribe the substitution substance buprenorphine. 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 for current prescription
- ✦ Check that the current day is a dose day on the patient's regime
- ✦ Confirm the dose for the current day if it is an alternate-day or three-times-a-week regime
- ✦ Record the dose in the recording system

¹¹Some patients may prefer to be detoxified with buprenorphine and it is important to transfer them, following detoxification, to either naltrexone or intensive psychosocial care for relapse prevention. Drug users who have failed with buprenorphine detoxification may be considered for buprenorphine maintenance.

ii) Administering buprenorphine through Directly Observed Treatment (DOT)

After recording dose details in the necessary documentation system, the following procedures should be observed. The drug is preferably given by way of Directly Observed Treatment (DOT). This will ensure that the drug is not taken away, crushed and injected by the clinic patients. There is considerable experience for the provision of buprenorphine through DOT in many centres across India.¹²

- 1) Count and check the buprenorphine tablets into a dry dosing cup. Double-check the number and strength.
- 2) Crush the tablets into powder
- 3) Place the powder under the tongue of the patient
- 4) Give the following instructions:
 - a) do not swallow saliva until powdered tablets have dissolved (2 - 5 minutes on average)
 - b) do not swallow the powdered tablets
 - c) once the tablets are given to you, they are your responsibility and will not be replaced.
- 5) Observe the patient until you are satisfied the tablets are not divertible (usually > 2 minutes).
- 6) Ask to see "how the powdered tablets are dissolving" enough times for this to become an acceptable part of the patient's delivery routine.
- 7) Patients should sign / affix thumb impression that they have received their dose. Offer water to rinse taste out of mouth.

The doctor should be notified if the dosing administrator has concerns that patients may be attempting to divert their medication.

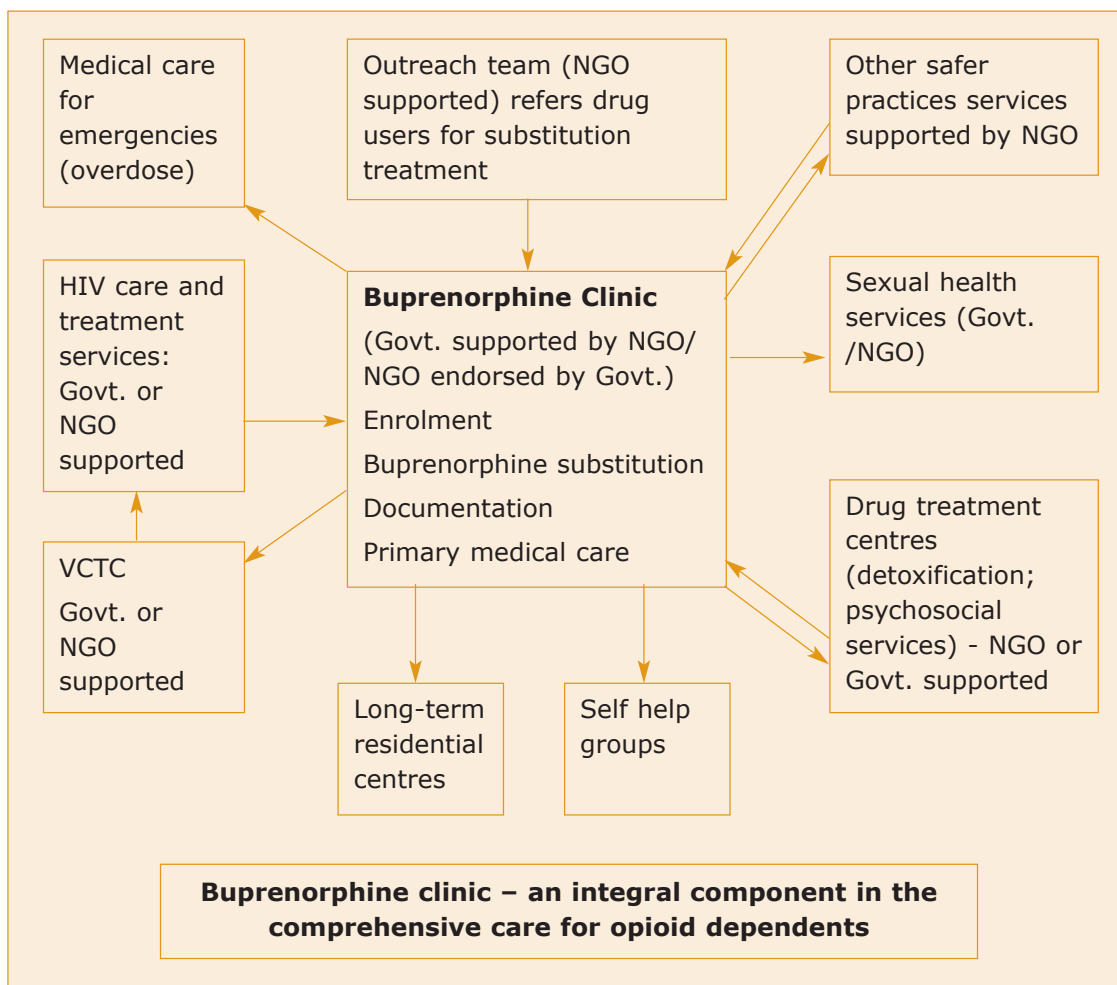
iii) Roll-out plan for buprenorphine substitution

The following personnel are required to operate a buprenorphine substitution clinic serving about 300 regular patients with opioid dependence: a medical doctor; a documentation officer; six nurses; one counsellor; security staff and clinic maintenance staff. Apart from 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 can receive the medication prescribed uninterrupted, 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.

¹²Through a European Commission supported programme, seven Indian NGOs (from the cities of New Delhi, Mumbai, Kolkata, Chennai and Imphal) provided sublingual buprenorphine substitution through DOT in community based clinics for more than 1,500 injecting opioid users / heroin users.

Community based clinics are more attractive to drug users and the government sponsored buprenorphine 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 the 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. A broad range of dosages (if possible, range of substitution substances – methadone and buprenorphine) should be offered in the clinics to match the profile of the patients. The proportion of problem opioid users to be covered by the substitution can be reviewed periodically in different geographical locations.



V. Training and support

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 buprenorphine will be the key to successful implementation of buprenorphine substitution. 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 buprenorphine clinic. Apart from the initial workshops, there should be provision for follow-up training and support. 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 buprenorphine 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 buprenorphine treatment, clinical pharmacology - dosing, drug interactions - and, buprenorphine in the context of dependence care and HIV services. For 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 buprenorphine clinic team members. The core team members, who have been trained in the State/Province level three days training workshops can train new members of the team with the help from local consultants periodically.

Topics for three days 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 buprenorphine substitution	Directly observed treatment of buprenorphine Enhancing 'quality' in patient care
Opioid dependence - concept, course and consequences	Effectiveness of buprenorphine substitution	Liaison services and linkages
Effective treatment approaches	Regulatory procedures Confidentiality	Visit to a buprenorphine clinic
Substitution treatment - definition, benefits and risks	Documentation and record keeping	

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