

# POSITION PAPER

## WHO/UNODC/UNAIDS position paper Substitution maintenance therapy in the management of opioid dependence and HIV/AIDS prevention



World Health  
Organization



UNITED NATIONS  
*Office on Drugs and Crime*



Joint United Nations Programme on HIV/AIDS  
**UNAIDS**  
UNICEF • WFP • UNDP • UNEPA • UNODC  
ILO • UNESCO • WHO • WORLD BANK

WHO Library Cataloguing-in-Publication Data

Substitution maintenance therapy in the management of opioid dependence and HIV/AIDS prevention : position paper / World Health Organization, United Nations Office on Drugs and Crime, UNAIDS.

1.Opioid-related disorders - rehabilitation 2.Analgesics, Opioid - therapeutic use  
3.HIV infections - prevention and control 4.Substance abuse, Intravenous - complications 5.Treatment outcome 6.Guidelines I.World Health Organization II.United Nations. Office on Drugs and Crime III.UNAIDS.

ISBN 92 4 159115 3 (NLM classification:WM 284)

**© World Health Organization, United Nations Office on Drugs and Crime,  
Joint United Nations Programme on HIV/AIDS, 2004**

Published by WHO on behalf of the copyright holders. All rights reserved. Publications of the World Health Organization can be obtained from Marketing and Dissemination, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel: +41 22 791 2476; fax: +41 22 791 4857; email: [bookorders@who.int](mailto:bookorders@who.int)). Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – should be addressed to Publications, at the above address (fax: +41 22 791 4806; email: [permissions@who.int](mailto:permissions@who.int)).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization, United Nations Office on Drugs and Crime and the Joint United Nations Programme on HIV/AIDS concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization, United Nations Office on Drugs and Crime and Joint United Nations Programme on HIV/AIDS in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

The World Health Organization, United Nations Office on Drugs and Crime and the Joint United Nations Programme on HIV/AIDS do not warrant that the information contained in this publication is complete and correct and shall not be liable for any damages incurred as a result of its use.

Designed by Tushita Bosonet and Valérie Rossier, Graphic Vision Sàrl, Geneva, Switzerland

Printed in France

# Content

Joint WHO/UNODC/UNAIDS statement on substitution maintenance therapy.....	2
<b>Introduction .....</b>	<b>3</b>
Epidemiology and burden of opioid use and dependence .....	4
Nature of opioid dependence .....	7
Treatment of opioid dependence: objectives and principles.....	8
<b>Substitution therapy of opioid dependence .....</b>	<b>11</b>
Definition of substitution therapy and the rationale for substitution maintenance therapy in the management of opioid dependence .....	12
Pharmacological agents used for opioid substitution maintenance therapy .....	14
Methadone .....	14
Buprenorphine .....	15
Other pharmacological agents .....	16
Impact of opioid substitution maintenance therapy .....	18
Benefits .....	18
Risks.....	19
Factors influencing treatment outcome.....	20
Cost–effectiveness .....	21
Opioid substitution maintenance therapy as part of a health care system .....	22
Provision of opioid substitution maintenance therapy to people with opioid dependence and HIV/AIDS.....	24
Special considerations in provision of opioid substitution maintenance treatment.....	26
Regulation of opioid substitution therapy and training .....	28
<b>Conclusions .....</b>	<b>31</b>

## Joint WHO/UNODC/UNAIDS statement on substitution maintenance therapy<sup>1</sup>

---

Opioid dependence, a complex health condition that often requires long-term treatment and care, is associated with a high risk of HIV infection when opioids are injected using contaminated injection equipment. Drug dependence treatment is an important strategy to improve well-being and social functioning of people with opioid dependence and to reduce its health and social consequences, including HIV infection. As no single treatment is effective for all individuals with opioid dependence, sufficiently diverse treatment options should be available. Substitution maintenance therapy is one of the most effective treatment options for opioid dependence. It can decrease the high cost of opioid dependence to individuals, their families and society at large by reducing heroin use, associated deaths, HIV risk behaviours and criminal activity. Substitution maintenance therapy is a critical component of community-based approaches in the management of opioid dependence and the prevention of HIV infection among injecting drug users (IDUs). Provision of substitution maintenance therapy – guided by research evidence and supported by adequate evaluation, training and accreditation – should be considered as an important treatment option in communities with a high prevalence of opioid dependence, particularly those in which opioid injection places IDUs at risk of transmission of HIV and other bloodborne viruses.

---

1 In this document the term “substitution maintenance therapy” refers to treatment fulfilling the following criteria: agents used for substitution therapy have been thoroughly evaluated; treatment is administered by accredited professionals in the framework of recognized medical practice; and there is appropriate clinical monitoring.

# Introduction

## Introduction

## Epidemiology and burden of opioid use<sup>2</sup> and dependence

- **1** Opiates are a group of psychoactive substances derived from the poppy plant, that includes opium, morphine, codeine and some others. The term “opiate” is also used for the semisynthetic drug heroin that is produced from poppy compounds. The term “opioids” refers to opiates and other semisynthetic and synthetic compounds with similar properties. Opioids are dependence producing substances, which elicit their effects by activating opioid receptors in the brain. Opioids are generally consumed by injection, oral ingestion or inhalation of the fumes produced by heating. Regular use of opioids can lead to opioid dependence.
  - **2** Opioid users constitute only a very small proportion of the world population (less than 1% of those aged 15 years and above). Parts of the world where opioid use and related problems are predominant include North America, Western, South and South-East Asia, Europe, and the Middle East. Injection opioid use has rapidly increased in Central Asia and in Central and Eastern Europe. Recent information also indicates that pockets of opioid injection have emerged in some urban centres in Africa, and the levels of opioid use are higher than was previously thought in Africa.
  - **3** The cost of opioid use to individual users and to society as a whole, is high. Studies indicate that opioid dependence results in significant costs to society through unemployment, homelessness, family disruption, loss of economic productivity, social instability and criminal activities. Major health consequences of opioid use include higher risk of premature death and, when opioids are injected, increased risk of bloodborne infections such as HIV and hepatitis B and C.
- 
- 2** In this document the term “opioid use/user” is utilized to refer to any form, level and pattern of non-medical use of opioids, including occasional and prolonged consumption.

---

**4** Individuals with opioid dependence – who often inject drugs of unknown potency and quality and in conjunction with other substances – frequently experience overdose, with a high risk of death. Longitudinal studies suggest that approximately 2–3% of them die each year. The mortality rate for dependent heroin users is between 6 and 20 times that expected for those in the general population of the same age and gender.

---

**5** Globally, between 5 and 10% of HIV infections result from injection drug use; however, in some countries in Asia and Europe, over 70% of HIV infections are attributed to injection drug use, with opioids being the most commonly injected drugs in these regions.

---

**6** Injecting drug users (IDUs) are vulnerable to infection with HIV and other bloodborne viruses as a result of sharing/reusing injecting equipment and drug solution, sexual contact with other IDUs, and high-risk sexual activity. Although most IDUs are males, female drug users may be more vulnerable to HIV than their male counterparts, as they are more likely to use their partner's injecting equipment and it is often difficult for them to negotiate low-risk sexual practices and condom use. IDUs are relatively more likely to be involved in the sex industry.

---

**7** Injection drug use is now the dominant mode of transmission of hepatitis C virus. Infection with hepatitis C virus results in chronic infection in at least 50–85% of cases. Approximately 7–15% of chronically infected persons progress to liver cirrhosis within 20 years and of these, a proportion will subsequently develop liver cancer.



---

**8** There are strong links between opioid use and dependence, and criminal behaviour: people with opioid dependence often commit crimes to obtain money to purchase drugs; crimes are committed under the influence of drugs; and there is an overlap between the factors associated with the development of criminal behaviour and those associated with the initiation of illicit drug use. The criminal offences involved are generally acquisitive crime, drug trafficking or sex trade.

---

**9** It has been estimated that in some countries around three-quarters of people in prison have alcohol or other drug-related problems, and more than one-third may be opioid dependent. Around one-third will have been imprisoned for drug-related offences. Some level of continued drug use often occurs in prison and is usually associated with high risk of HIV transmission due to sharing/reusing injecting equipment and drug solution. On release, prisoners with opioid dependence are at high risk of relapse and overdose. Consequently, substitution therapy is provided to inmates of correctional facilities in some countries. The costs of law enforcement, court time and imprisonment together contribute substantially to the social costs associated with opioid dependence. In general, studies indicate that pure criminal justice interventions, without associated opioid dependence treatment, have very limited impact on drug-using behaviour and re-offending among individuals with drug dependence.



## Nature of opioid dependence

- 
- 10** Opioid dependence develops after a period of regular use of opioids, with the time required varying according to the quantity, frequency and route of administration, as well as factors of individual vulnerability and the context in which drug use occurs. Opioid dependence is not just a heavy use of opioids, but a complex health condition that has social, psychological and biological determinants and consequences, including changes in the brain. It is not a weakness of character or will.
- 
- 11** The key elements of opioid dependence are: a strong desire or sense of compulsion to take opioids; difficulties in controlling opioid-taking behaviour; a withdrawal state when opioid use has ceased or been reduced; evidence of tolerance, such that increased doses are required to achieve effects originally produced by lower doses; progressive neglect of alternative pleasures or interests; and persistence with opioid use despite clear evidence of overtly harmful consequences. It is these aspects that make opioid dependence particularly damaging to the individual, family and community.

## Treatment of opioid dependence: objectives and principle

- 
- 12** Treatment of opioid dependence is an important strategy to address the health and social consequences associated with drug dependence at individual and societal levels. Failure to provide adequate treatment for opioid dependence is generally costly to health services and to the community.
- 
- 13** As with other health conditions such as hypertension, diabetes and heart disease, people with opioid dependence can stabilize their condition by developing and incorporating behavioural changes and by appropriate use of medications.
- 
- 14** Relapse following detoxification alone is extremely common, and therefore detoxification rarely constitutes an adequate treatment of substance dependence on its own. Simple detoxification or stopping opioid use is often insufficient: a therapeutic process is required. Detoxification, however, is a first step for many forms of longer-term abstinence-based treatment. Both detoxification with subsequent abstinence-oriented treatment and substitution maintenance treatment are essential components of an effective treatment system for people with opioid dependence.
- 
- 15** The main objectives of treating and rehabilitating persons with opioid dependence are as follows: to reduce dependence on illicit drugs; to reduce the morbidity and mortality caused by the use of illicit opioids, or associated with their use, such as infectious diseases; to improve physical and psychological health; to reduce criminal behaviour; to facilitate reintegration into the workforce and education system and to improve social functioning. The ultimate achievement of a drug free state is the ideal and long-term objective but this is unfortunately not feasible for all individuals with opioid dependence, especially in the short term. An exclusive focus on achieving a drug free state as an immediate goal for all patients may jeopardize the achievement of other important objectives such as HIV prevention.

---

**16** No single treatment is effective for all individuals. Individuals seeking treatment for opioid dependence will have different patterns of risk and protective factors, and different psychological and social problems. Therefore services should be sufficiently varied and flexible to respond to the needs of clients, their severity of dependence, personal circumstances, motivation and response to interventions. The rational management of opioid dependence calls for the balanced combination of pharmacotherapy, psychotherapy, psychosocial rehabilitation and risk reduction interventions.

---

**17** Treatment should be readily available. Most people with opioid dependence express a strong desire to be abstinent but remain ambivalent about treatment. Frequently a crisis (financial, legal, physical health, partner or family) triggers a treatment episode. Consequently, it is important that treatment is readily available to take advantage of the motivation created by these crises.

---

**18** Remaining in treatment for an adequate period of time is critical for treatment effectiveness. The appropriate duration of treatment for an individual depends on their problems and needs, but research indicates that for most people with drug dependence, the threshold of significant improvement is reached after about three months in treatment, with further gains as treatment is continued. Because people often leave treatment prematurely, and premature departure is associated with high rates of relapse to drug use, programmes should include strategies to engage and keep patients in treatment. Many patients need several years in treatment.

---

**19** For those individuals who are currently unable or unwilling to stop using drugs, treatment interventions should be directed at reduction of morbidity, disability and death caused by, or associated with, substance use. Reduction in risk behaviours associated with drug dependence is an achievable goal.



**Substitution  
therapy of opioid  
dependence**

## Definition of substitution therapy and the rationale for substitution maintenance therapy in the management of opioid dependence

- 
- 20** Substitution therapy (“agonist pharmacotherapy”; “agonist replacement therapy”; “agonist-assisted therapy”) is defined as the administration under medical supervision of a prescribed psychoactive substance, pharmacologically related to the one producing dependence, to people with substance dependence, for achieving defined treatment aims. Substitution therapy is widely used in the management of nicotine (“nicotine replacement therapy”) and opioid dependence.
- 
- 21** Agents suitable for substitution therapy of opioid dependence are those with some opioid properties so that they have the capacity to prevent the emergence of withdrawal symptoms and reduce craving. At the same time, they diminish the effects of heroin or other opioid drugs because they bind to opioid receptors in the brain. In general, it is desirable for opioid substitution medicines to have a longer duration of action than the drug they are replacing so as to delay the emergence of withdrawal and reduce the frequency of administration, thereby resulting in less disruption of normal life activities by the need to obtain and administer medicines. Whereas illicitly used opioids are usually injected or inhaled by drug users, these prescribed medicines are usually administered orally in the form of a tablet or a solution, thereby reducing the risk of infections associated with injections.
- 
- 22** Medicines used in substitution therapy can be prescribed either in decreasing doses over short periods of time (usually less than one month) for treatment of withdrawal or for detoxification, or in relatively stable doses over a long period of time (usually more than six months) for substitution maintenance therapy, which allows stabilization of brain functions and prevention of craving and withdrawal. The term “substitution therapy” is often utilized as an equivalent to “substitution maintenance therapy”.

---

**23** Substitution maintenance therapy is one of the most effective types of pharmacological therapy of opioid dependence. There is consistent evidence from numerous controlled trials, large longitudinal studies and programme evaluations, that substitution maintenance treatment for opioid dependence is associated with generally substantial reductions in illicit opioid use, criminal activity, deaths due to overdose, and behaviours with a high risk of HIV transmission.

---

**24** Substitution maintenance therapy of opioid dependence is an important component of community-based approaches in that the treatment can be provided on an out-patient basis, achieving high rates of retention in treatment and increasing the time and opportunity for individuals to tackle major health, psychological, family, housing, employment, financial and legal issues while in contact with treatment services.

---

**25** The prescription for substitution therapy and administration of opioid agonists to persons with opioid dependence – in the framework of recognized medical practice approved by competent authorities – is in line with the 1961 and 1971 Conventions on narcotic drugs and psychotropic substances.



## Pharmacological agents used for opioid substitution maintenance therapy

### Methadone

---

**26** Methadone is a synthetic opioid that is typically administered orally as a liquid. Methadone is the medication that is most commonly used for substitution therapy of opioid dependence. Methadone maintenance treatment is also an extensively researched treatment modality. There is strong evidence, from research and monitoring of service delivery, that substitution maintenance therapy with methadone (methadone maintenance treatment) is effective in reducing illicit drug use, reducing mortality, reducing the risk of spread of HIV, improving physical and mental health, improving social functioning and reducing criminality. Higher doses of methadone are generally associated with greater reductions in heroin use than either moderate or low doses.

---

**27** Methadone maintenance treatment is associated with a low incidence of side-effects and with substantial health improvements. Around three-quarters of people who commence substitution maintenance therapy with methadone respond well. However, for various reasons, methadone does not suit all people with opioid dependence. For this group it is important that alternative approaches are available to encourage their retention in treatment. Some require several episodes of treatment before major progress is achieved.

## Buprenorphine

---

**28** Buprenorphine is a prescribed medication with weaker opioid agonist activity than methadone. Buprenorphine is not well absorbed if taken orally, therefore the usual route of administration in treatment of opioid dependence is sublingual. With increasing doses of buprenorphine, effects reach a plateau. Consequently, buprenorphine is less likely than either methadone or heroin to cause an opioid overdose condition, even when taken with other opioids at the same time. The effectiveness of buprenorphine is similar to that of methadone at adequate doses, in terms of reduction of illicit opioid use and improvements in psychosocial functioning, but buprenorphine may be associated with lower rates of retention in treatment. Buprenorphine is currently more expensive than methadone.

**29** Buprenorphine is acceptable to heroin users, has few side-effects, and is associated with a relatively mild withdrawal syndrome. When used in opioid substitution therapy for pregnant women with opioid dependence, it appears to be associated with a lower incidence of neonatal withdrawal syndrome.

## Other pharmacological agents

---

**30** Levo alpha acetyl methadol (LAAM), like methadone, is a synthetic opioid which is effective when ingested orally. LAAM and methadone are of approximately equivalent effectiveness in terms of capacity to reduce illicit drug use, but LAAM has a slower onset of action and a longer duration of action compared to methadone, and can be administered every three days, providing greater flexibility for clients, with less need for unsupervised doses and thus less opportunity for dose diversion. LAAM is used in the United States of America, but in the European Union it has been removed from the therapeutic arena because of concerns about a possible effect on cardiac function.

---

**31** Dihydrocodeine is used in some countries for detoxification and substitution maintenance therapy. Tincture of opium (laudanum) is used in some countries in Asia for the management of opioid withdrawal and, less commonly, for substitution maintenance therapy. The various oral preparations of morphine formulated to provide slow release (also called sustained release, controlled release and timed release preparations) are also of potential value in the treatment of opioid dependence. However, controlled studies of the effectiveness of these preparations for substitution treatment are yet to be undertaken.

---

**32** The approach of providing medically prescribed diacetylmorphine (heroin) as an opioid substitution maintenance treatment has been the subject of extensive public debate, but has received relatively little research. National projects in the Netherlands and in Switzerland have assessed the feasibility of using medically prescribed diacetylmorphine as a treatment for severely dependent individuals. In both countries patients who had previously failed in methadone treatment were successfully engaged in treatment with diacetylmorphine. The relative contribution of the provision of psychosocial support concomitant to diacetylmorphine prescription on treatment outcomes is a subject for further research. The approach of prescribing diacetylmorphine is complex and costly and has been evaluated only in countries with well-developed treatment systems. Results from such evaluations indicate that in comprehensive treatment systems it might be an alternative for a small proportion of severely dependent long-term patients for whom other treatment options have been ineffective.

# Impact of opioid substitution maintenance therapy

## Benefits

- 
- 33** Several longitudinal studies examining changes in HIV risk behaviours for patients currently in treatment have found that longer retention in treatment, as well as completion of treatment, are correlated with reduction in HIV risk behaviours related to drug-taking or an increase in protective behaviours. IDUs who do not enter treatment are up to six times more likely to become infected with HIV than injectors who enter and remain in treatment.
- 
- 34** Substitution maintenance therapy of opioid dependence has been found to be more effective than placebo and detoxification alone in retaining opioid-dependent people in treatment and reducing heroin use.
- 
- 35** The death rate for people with opioid dependence in methadone maintenance treatment is one-third to one-quarter the rate for those not in treatment.
- 
- 36** There are fewer complications for pregnant women and their unborn children who are in substitution maintenance treatment in comparison with those who are not in treatment.

---

**37** Substitution maintenance therapy has also been associated with higher legitimate annual earnings. Some studies have indicated improved levels of employment and other indicators of social functioning associated with methadone maintenance treatment, but data on these aspects are limited. Assessment of the impact of substitution maintenance therapy on social dimensions is made difficult by the influence of other factors, including the social climate in which studies occur, and the circumstances of patients prior to treatment.

---

**38** Several studies have recorded very high levels of criminal involvement by drug users before entering treatment, with these levels reduced by around one-half after a year of methadone maintenance treatment. Benefits are greatest during and immediately after treatment, but nonetheless, significant improvements remain for several years after treatment. Reductions are most marked in drug-related criminal behaviour.

## **Risks**

---

**39** The most significant risk of methadone and other opioid agonists is overdose, which can be fatal. Research evidence indicates that the highest risk of overdose is during commencement of methadone substitution treatment. Therefore, low doses are recommended at the beginning of treatment. However, once a stable dose is achieved (about two weeks) the risk of overdose death is then substantially reduced in comparison with the risk prior to treatment.

- 
- 40** There is a risk of diversion into illicit channels of the medications used for substitution treatment, as with other narcotic and psychotropic substances under international control. Effective implementation of national and international drug control procedures, and other mechanisms such as supervised administration of medication, can work together to minimize such risks.

### **Factors influencing treatment outcome**

- 
- 41** It is clear from research evidence that the effectiveness of opioid substitution maintenance therapy is dependent on timely entry into treatment, adequate medication dosage, duration and continuity of treatment, and accompanying medical and psychosocial services. In programmes that use higher doses of methadone, a majority of patients are retained in treatment for at least 12 months. Research indicates that higher doses of buprenorphine and LAAM are also more effective than lower doses. In all cases it is important that the dose selected is based on an assessment of the individual patient. Constructive (non-punitive) clinic responses to client problems improve retention and treatment outcomes.

- 
- 42** Substitution treatment for opioid dependence on its own is associated with reductions in illicit opioid use. However, there is evidence that the addition of psychosocial therapy adds to the overall effectiveness of substitution treatment programmes. Research evidence indicates that counselling is important for those who need it, but can be counter-productive if mandated.



## Cost-effectiveness

---

**43** Opioid dependence treatment is effective in reducing illicit opioid use and its associated health and social costs. Treatment is considerably less expensive than alternatives, such as not treating people with opioid dependence, or imprisonment.

---

**44** According to several conservative estimates, every dollar invested in opioid dependence treatment programmes may yield a return of between \$4 and \$7 in reduced drug-related crime, criminal justice costs and theft alone. When savings related to health care are included, total savings can exceed costs by a ratio of 12:1.

---

**45** There is scientific evidence that substitution maintenance therapy is a cost-effective treatment modality with cost-effectiveness measures comparing favourably with other health care interventions, such as medical therapy for severe hypertension or for HIV/AIDS.

## Opioid substitution maintenance therapy as part of a health care system

---

**46** Drug demand reduction and HIV prevention programmes should be integrated into broader social welfare and health promotion policies and preventive education programmes. Specific interventions should be based on regular assessment of the nature and magnitude of drug dependence and related disorders, as well as trends and patterns of HIV infection. A structured national HIV prevention programme should include comprehensive treatment of drug dependence, including substitution maintenance therapy for opioid dependence, where opioid injection places IDUs at risk of transmission of HIV and other bloodborne viruses.

---

**47** Given the scale of problems in most societies and the limited resources available, a clear and coherent approach to service planning is required. Overall, there is a need to develop services that can reach the maximum number of individuals and have the greatest impact at lowest cost. This is most likely to be achieved with broad community-based services that can work with individuals in their own communities over longer periods of time.

---

**48** In countries with a significant prevalence of heroin or other opioid dependence, methadone and/or other substitution maintenance treatment programmes should be considered as one useful treatment option in an overall national drug treatment policy.

---

**49** Such programmes and interventions should build on knowledge and expertise acquired from research, including empirical knowledge about the social milieu around which drug taking revolves, as well as lessons learned from the implementation of previous projects and interventions. In countries with no experience of substitution maintenance therapy, pilot projects should be implemented for possible later application at national level.

---

**50** So far, with few exceptions, the provision of opioid substitution maintenance therapy around the world has largely been implemented in specialized drug dependence treatment programmes, separated from general health services. Treatment of large numbers of individuals with opioid dependence, however, demands the development of community-based health and social services, and the development of substitution maintenance treatment programmes that are incorporated within general primary health care and welfare services.

---

**51** Participation in substitution maintenance therapy provides opportunities for early diagnosis of other health problems, for counselling and testing, and referral for additional services. The best drug dependence treatment programmes provide counselling and testing for both HIV and viral hepatitis, as well as hepatitis immunization, with due attention also given to counselling on the reduction of sexual risk behaviour. In addition, drug treatment programmes need to be involved in provision of HIV/AIDS treatment, care and support, as necessary, to their clients.

## Provision of opioid substitution maintenance therapy to people with opioid dependence and HIV/AIDS

- 
- 52** Substitution maintenance therapy has proven effective in terms of retention in treatment, reduction of drug use, improvement of psychological and social functioning, and reduction of high risk injecting and sexual behaviours. As such, substitution maintenance therapy should be given serious consideration not only as an HIV prevention measure, but also for individuals with opioid dependence who are already infected with HIV, so as to minimize the risk of further transmission of the virus and to stabilize their underlying condition.
- 
- 53** Treatment for people with HIV infection who are drug dependent must address clinical and psychosocial issues related to both conditions. The combination of opioid dependence and HIV infection can result in specific clinical situations such as the occurrence of particular HIV-related opportunistic infections; the masking of HIV-AIDS related symptoms by substitution medication; and interactions between opioid substitute medications and medications used to manage HIV infection. Those treating opioid dependence in persons with HIV/AIDS need to be aware of these clinical situations. Conversely, those treating individuals with both HIV/AIDS and opioid dependence need to be familiar with common approaches to the treatment of opioid dependence and related problems.
- 
- 54** Drug use in individuals with opioid dependence may interfere with adherence to treatment regimens for HIV/AIDS, and it is therefore imperative that treatment for opioid dependence is initiated to support adherence to antiretroviral treatment and medical follow-up. It has been demonstrated that stopping drug injecting slows the progression of HIV disease in infected subjects.

---

**55** People with both opioid dependence and HIV/AIDS are often doubly stigmatized. In many countries they are excluded from the provision of antiretroviral treatment in spite of the evidence that individuals with opioid dependence benefit from appropriately administered HIV/AIDS drug treatment, as do individuals without opioid dependence. Programmes that integrate substitution maintenance therapy of opioid dependence with HIV/AIDS treatment and care should therefore be encouraged. Directly observed therapy for opioid dependence also provides an opportunity for the implementation of directly observed antiretroviral therapy as well as therapy for opportunistic infections such as tuberculosis.

## Special considerations in provision of opioid substitution maintenance treatment

---

**56** While there is evidence of effectiveness of substitution maintenance therapy across a variety of cultural and ethnic groups and social contexts, a number of factors are recognized, which influence treatment outcomes in some communities, including socioeconomic status, poverty, differences in educational opportunities, and cultural responsiveness of treatment programmes. It will therefore be necessary to respond to the diverse needs and characteristics of different target groups when designing opioid dependence treatment programmes, in order to ensure equally good treatment outcomes.

---

**57** Women tend to have a different experience with both drug dependence and treatment, from that of men. There are major issues related to the high levels of both physical and psychological comorbidity of women with opioid dependence, which need to be taken into account in the provision of treatment. Females with opioid dependence often face a variety of barriers to treatment, including lack of financial resources, absence of services and referral networks oriented to women, and conflicting childcare responsibilities. In many countries increasing proportions of women prisoners have polysubstance dependence, including opioid dependence. Organizing appropriate treatment in this environment continues to be a major challenge.

---

**58** Effective pharmacotherapy treatment of opioid dependence can substantially improve obstetric, perinatal and neonatal outcomes. Opioid substitution maintenance therapy also has an important role in attracting and retaining pregnant women in treatment and ensuring good contact with obstetric and community-based services including primary care. Addressing childcare and family support issues for women continues to be a major gap in the delivery of services for women in most countries.

---

**59** Compared to the general population, other psychiatric conditions are relatively more common amongst people with drug dependence. The presence of comorbid psychiatric conditions increases the risk of treatment failure. Services need to be aware of these issues and should provide additional services as needed to manage psychiatric conditions present in addition to opioid dependence.

---

**60** People with opioid dependence and IDUs frequently use a range of psychoactive substances in addition to opioids, including alcohol. Research has shown that the use of cocaine in combination with opioids is, in particular, a factor that is associated with treatment failure. In addition, where drugs such as cocaine are used by injection, the effectiveness of opioid substitution therapy in managing risk behaviours is reduced. At the same time, research evidence indicates that when individuals with opioid dependence are retained in treatment, levels of use of cocaine are reduced, along with levels of opioid use.



## Regulation of opioid substitution therapy and training

---

**61** Substitution therapy for opioid dependence must be subject to principles of good medical practice. Evidence-based guidelines are in place in many countries, and need to be elaborated where they are not. Such guidelines should include criteria to define who are considered eligible for substitution therapy as well as contraindications, and should outline best practices in clinical management, as well as relevant government regulations. Efforts should be made to ensure that guidelines are widely disseminated and programmes for monitoring treatment quality and outcomes are put in place.

---

**62** Opioid substitution maintenance therapy should be restricted to people who meet the clinical criteria for opioid dependence. However, excessive restrictive regulations regarding criteria for placement in substitution maintenance therapy and its provision, that have no significant effect on quality of provided treatment, are counterproductive with regard to access to treatment and HIV/AIDS prevention. Issues such as the maximum dose or maximum length of treatment should be left to the practitioner's clinical judgement, based on the assessment of the individual patient.

---

**63** The registration/accreditation of treatment providers and registration of those receiving treatment, are useful approaches to ensure the quality of service and to minimize the risk of prescribed medications being diverted into illicit channels.

---

**64** The introduction and expansion of substitution maintenance treatment programmes comes with the need to train practitioners. The target groups for substitution opioid pharmacotherapy training include: medical practitioners involved in prescribing and delivering treatment to people with substance use disorders; pharmacists involved in dispensing medications; alcohol and drug counsellors working with clients of substitution maintenance treatment programmes; health practitioners associated with infectious disease programmes; and general health professionals who may come into contact with clients on these programmes (such as ambulance officers, accident and emergency staff, general practitioners).



Conclusions

**Conclusions**

---

**65** Opioid dependence is a complex condition that often requires long-term treatment and care. No single treatment modality is effective for all people with opioid dependence. Adequate access to a wide range of treatment options should be offered to respond to the varying needs of people with opioid dependence.

---

**66** Substitution maintenance treatment is an effective, safe and cost-effective modality for the management of opioid dependence. Repeated rigorous evaluation has demonstrated that such treatment is a valuable and critical component of the effective management of opioid dependence and the prevention of HIV among IDUs.

---

**67** There is mounting evidence that improved outcomes from opioid substitution maintenance therapy arise from timely entry into treatment, longer duration and continuity of treatment, and adequate doses of medication.

---

**68** Individuals with opioid dependence benefit from substitution maintenance therapy through increased stability and improved well-being and social functioning. People receiving substitution therapy can make significant progress in their physical and emotional life, as well as in their relationships with others and their ability to contribute meaningfully to their community and society at large.

---

**69** Society as a whole benefits from substitution maintenance therapy through reductions in the incidence of criminal behaviour, reduced health and criminal justice system costs, reduced risks of transmission of HIV and other bloodborne viruses, and increased productivity. There is a strong case for investing in opioid substitution maintenance therapy, as the savings resulting from treating an individual far exceed the costs.

---

**70** Provision of substitution maintenance therapy of opioid dependence is an effective HIV/AIDS prevention strategy that should be considered for implementation – as soon as possible – for IDUs with opioid dependence in communities at risk of HIV/AIDS epidemics. Once HIV has been introduced into a local community of IDUs, there is the possibility of extremely rapid spread. 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.

---

**71** The practice of substitution maintenance therapy must be guided by research evidence and supported by adequate training and evaluation. Possible adverse consequences need to be minimized by adhering to best clinical practices, monitoring treatment quality and outcomes, and instituting adequate control measures and regulations to avoid diversion of the medicines into illicit channels.

**The World Health Organization (WHO), the United Nations Office on Drugs and Crime (UNODC) and the Joint United Nations Programme on HIV/AIDS (UNAIDS), have developed a joint position on substitution maintenance therapy for opioid dependence. Based on a review of scientific evidence and oriented towards policymakers, the WHO/UNODC/UNAIDS position paper covers a wide range of issues, from the rationale for this treatment modality, to the specific considerations regarding its provision for people with HIV/AIDS.**

*This publication is available on-line at:*  
[http://www.who.int/substance\\_abuse/](http://www.who.int/substance_abuse/)  
<http://www.unodc.org/>  
<http://www.unaids.org/>

*To obtain a hard copy, please contact:*  
[publications@who.int](mailto:publications@who.int)

ISBN 92 4 159115 3

