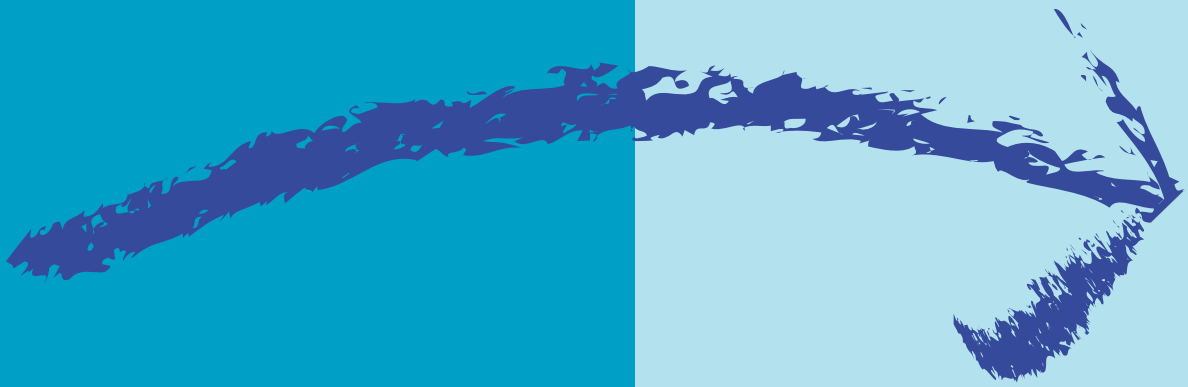
Methadone *Guidelines*



Annete Verster, Ernst Buning

English

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Annette Verster, Ernst Buning

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For more information:

Euro-Methwork
Q4Q- room 350
Nieuwe Achtergracht 100
1018 WT Amsterdam, The Netherlands

tel. : + 31 20 3303 449
fax : + 31 20 3303 450
email : methwork@q4q.nl
website : http://www.q4q.nl/methwork

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Summary

Opioid dependence is a common phenomenon all European countries are confronted with. In most European countries, some form of methadone treatment is offered. Depending on the size and history of the problem, a small or large percentage of the opioid dependent population will actually be in treatment. The manner in which methadone is prescribed and dispensed, varies considerably from one place to another. The criteria for entering treatment also differ and partly depends on the availability of resources and on ideological beliefs.

A large body of scientific evidence suggests that methadone treatment, when delivered to an appropriate standard of care, is a safe substitution medication for opioid dependence. Methadone has proved to be an effective means in retaining people in treatment and hence, averts heroin use when in treatment. Methadone reduces the risk of HIV infection, and improves both physical and mental health as well as the quality of life of the patients and their families. Methadone also reduces criminal activities.

Methadone treatment has also proved to be cost effective. The British NTORS study found that for every £1 spent on treatment there is a return of more than £3 in terms of savings associated with victim costs due to crime. Moreover, methadone treatment reduced demands upon the criminal justice system.

Methadone is mostly orally administered once daily for therapeutic purposes of preventing or substantially reducing the consumption of illicit opioids such as heroin. Its primary function is to improve the health status and psychological well-being of the opioid-dependent person.

Assessment of addiction and the degree of dependence is essential before prescribing methadone. Induction, treatment plan and initial dosage should all be determined with care. Patients need to be informed not only about the actual pharmacological effects of methadone and the dangers of using other substances when on methadone, but also about the potential risk of overdose.

Methadone is prescribed in many ways: as a short- and long-term maintenance and as a short- and long-term detoxification treatment. Evidence suggests that the severer the dependence, the higher the dosage should be and the longer the treatment should last.

New entrants into treatment should be kept under supervision for the first few hours. The initial doses should be low. Patients who are kept under supervision, can be given an additional dose if withdrawal signs reappear.

It is highly recommended that new entrants start receiving methadone in the morning and preferably early in the week, so that the peak blood methadone concentrations occur when the clinic is still open and staff are available for consultation and intervention. In general, the initial dose will be between 10 - 30mg. In cases where tolerance to opioids is high, the normal dose will be between 25 - 40mg. When tolerance is low or uncertain, a dose between 10-20mg is more appropriate. If a starting dose is low, it is vital that the patient is kept under observation for a few hours. Additional small amounts can be administered if withdrawal symptoms occur. While too much methadone can be fatal, insufficient methadone is unlikely to be effective.

During the first week in an outpatient detoxification scheme, patients should be seen daily so that a stabilisation dose can be established. Where doses need to be increased during this first week, the daily increase should be a maximum of 5 to 10mg and not exceeding 20mg within a week of the initial dose.

For a longer period of detoxification and for maintenance treatment, it is recommended that doses are not increased by more than 20mg per week up to a maximum daily dose of 60-120mg. It can take up to six weeks or more to be properly stabilised on methadone treatment. Compliance will only be maintained if both patient and doctor agree that a reduction scheme is desirable.

The majority of individuals in maintenance treatment will require 60-120mg per day. Although some individuals can be successfully maintained on lower doses, an average heroin dependent person will use less heroin and stays longer in treatment, if maintained on higher rather than lower doses of methadone.

Some groups, such as pregnant women, people with HIV/AIDS, patients with young children, etc., could be given priority to enter methadone treatment. They may also need special attention. Liaison should be co-ordinated with specific services as antenatal, infectious diseases, so that their immediate problems can be addressed.

Methadone treatment should not be seen as an isolated intervention but as part of a comprehensive

programme of care. It is important to identify and address other problems such as medical, social, mental health or legal problems. This can be done either by the staff within the methadone programme or through liaison with other services and institutions. A multidisciplinary approach to methadone treatment is essential.

Prescribing is the sole responsibility of the doctor who signs the prescription. This responsibility cannot be delegated.

Apart from methadone, a range of other substitution medication is prescribed in different countries with success, such as buprenorphine, LAAM, long acting morphine and heroin.

People working in methadone treatment will require specific training which addresses the pharmacological, toxicological, medical and psycho-social aspects of the treatment of opioid dependence. The attitude of the staff needs to be non-judgemental. Supervision and regular team meetings are important elements of good practice. To ensure high quality of the services delivered, continuous training is highly recommended.

Summary

Keeping records of prescribing and of any activity surrounding a patient is necessary as in any medical practice. A central list of patients in methadone treatment may prevent double prescribing. The information contained on this list should be confidential and access to the list should be restricted to doctors who provide the treatment.

A methadone treatment programme should be a safe place. It should be easily accessible (centrally located and flexible opening hours) and clean. At all times, patients should be assured of the confidentiality of their information and that it will not be used for non-medical purposes. A good rapport between the staff and the patient is vital for the success of the treatment.

When planning and designing a new treatment service, it is important to involve users of this service in the process as well.

Monitoring activities and evaluation of outcomes should be undertaken on a regular basis.

Introduction

Most European countries have been confronted with a drug problem. Since 1970, methadone maintenance treatment has been the dominant form of substitution treatment for opioid dependence. It is estimated that half a million people are maintained on methadone world-wide. Most European countries have some form of methadone treatment for opioid dependence.

The European Commission, Directorate General V, has funded Euro-Methwork to develop methadone guidelines as part of the project "Euro-Methwork in 1999: Methadone Assistance Point (M.A.P.), Methadone Guidelines and Training" (project 99CVF2-215).

Because methadone treatment was controversial in the early stages, and remains so in some places today, it has been more rigorously evaluated than any other treatment for opioid dependence. These guidelines are based on reviews of the scientific evidence and long- term experience in different parts of the world. Further, existing guidelines from individual countries as well as crucial discussions with experts in the field, facilitated us in presenting a summary of findings of how methadone treatment could best be organised and delivered to opiate addicted people.

During a workshop held in Amsterdam in May 2000, where experts from the UK, the Netherlands, Italy and Slovenia were invited to participate, a draft version of this paper was discussed in order to reach an overall agreement on the contents of this final paper. Appendix 1 contains a list of people who attended the workshop in Amsterdam and others who have been consulted during the process of writing this paper.

Limitations

Given the diversity in the current availability, stage and state of methadone treatment in Europe, the differences between Western- and Central-Eastern Europe and even within individual countries, a careful approach is needed. Differences in historical, cultural, social, economic and political background as well as differences in how health-care is organised within Europe could question the feasibility of introducing guidelines to which all European countries would be able to apply. These guidelines therefore do not intend to dictate, but rather provide guidance and recommendations for good clinical practice of methadone treatment. In the end, every community needs to reach its own consensus and these guidelines can be instrumental in this process.

Another point in question was the potential contradiction of overall regulations or guidelines for good clinical practice, in the sense of the danger that guidelines can obstruct clinical practice. Of critical importance is the recognition that, as in every other area of medicine, treatment must be tailored to the needs of the individual patient. Regulations can limit the flexibility and responsiveness of the programmes. It is feared that in the absence of evidence, clearly applicable to the case at hand, a clinician might be forced by guidelines to make use of evidence which is only doubtfully relevant, generated perhaps in a different grouping of patients in another country and some other time and using a similar but not identical treatment (Hurwitz, *1999*).

Textbook or guidelines?
It should be made clear that this report will not address all issues of methadone treatment. We have made an effort to discuss the most relevant aspects and the nature of this report is to give guidance and recommendations for good clinical practice of methadone treatment.

There is an expanding range of treatment options and new medications for opioid dependence and increasing evidence of their effectiveness. This report will contain recommendations on the best practice of one type of treatment for one type of addiction, i.e. methadone treatment for opioid dependence. At the end of chapter 3, one paragraph will be dedicated to other types of substitution treatment presently used in different parts of the world, such as buprenorphine, LAAM, long acting morphine and heroin itself.

Target group and outline paper

These guidelines address anybody working in the drug field and might be particularly useful for those who discuss new treatment options.

The first part is of a general nature starting with a brief history of methadone treatment and the state of the art of methadone treatment in Europe. Chapter two gives a general and brief introduction on methadone and its pharmacology and reviews the available scientific evidence. Those involved in policy making and planning might be particularly interested in the section on why methadone treatment is effective both from the clinical and cost-benefit perspective.

The central part is more focussed on people directly involved in drug treatment. Chapter three discusses

the clinical practice of methadone treatment followed by the more organisational aspects of good practice in chapter four.

Chapter five discusses recommendations for monitoring of activities and evaluation strategies.

In the Bibliography the consulted literature (the references) is listed alphabetically. Appendix 1 lists the people who have worked on the preparation of these guidelines.

Introduction

Chapter 1 : State of the Art of Methadone in Europe

Opiate addiction in Europe

Practical all European countries today have been confronted with a drug problem. In the late sixties and early seventies, heroin addiction reached an epidemic proportion among young people in North Western Europe, followed by Spain, Portugal and Greece in the late seventies and early eighties. Central and Eastern European countries followed in the nineties. Some of the Northern European countries such as Sweden and Finland appear to have comparatively lower levels of heroin dependence and higher rates of amphetamine use and dependence (Farrell *et al.*,1999).

Despite efforts on the European level to co-ordinate monitoring systems per country regarding drug use, such as projects by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) with their REITOX project and yearly country reports, it is nonetheless not easy to give estimates for the opiate dependent populations per country. Monitoring systems still differ considerably in the way data are gathered which make comparisons difficult. One project carried out in 1999 to review current practice in drug substitution treatment in European Union Member States provided some interesting general estimates of the number of problematic opiate users per country (Farrell *et al.*,1999).
Belgium, Portugal, Italy, Ireland, Spain and France scored highest with an estimate of over 400 per 100.000 population (aged 16-60). The UK, Greece and Denmark was estimated to have between 300 and 400. Austria, Germany and the Netherlands between 200 and 300 and Finland, Luxembourg and Sweden, under 200 per 100.000 population (aged 16-60).
Other European countries have not been included in this review. However, there are several indications which point to a substantial heroin problem in the Central and Eastern European countries. Here, it is a relatively new phenomenon and most countries are presently in the process of developing treatment programmes.

History of Methadone Substitution Treatment

Methadone as a substitution treatment for opiate addiction was first used in North America, by Halliday in the late fifties in Canada and by Dole and Nyswander in the sixties in the USA (Fischer, 1999). Dole and Nyswander introduced orally administered maintenance doses of this synthetic opioid medication as a drug-substitution treatment for opioid dependence. Dole and Nyswander demonstrated that opioid dependence was ‘a physiological disease characterised by a permanent metabolic deficiency’ which was

best managed by administering to the opioid dependent person 'a sufficient amount of medication to stabilise the metabolic deficiency' (Dole and Nyswander, 1965; Ward *et al*., 1998). It was claimed that high or 'blockade' daily doses of oral methadone removed the craving for heroin and blocked its euphoric effects, thereby providing an opportunity for the individual to improve social functioning by taking advantage of the psycho-therapeutic and rehabilitative services that were an integral part of the programme (Dole and Nyswander, 1965; Ward *et al*., 1998).

Once it had been shown to reduce heroin use and criminal activity, methadone maintenance treatment quickly became the most common form of substitution therapy for opioid dependence. Since the sixties, the form of methadone treatment has undergone several important changes, both in goal, dosages and the extent of ancillary services. Within a period of a few years, the treatment goal shifted from long-term maintenance to abstinence of all opiate medications, including methadone. The average dose changed from the high 'blockade' dose favoured by Dole and Nyswander to much lower doses that were more politically acceptable. Clinicians, who had to adhere to certain bureaucratic limitations and to prescribe dosages that averted withdrawal symptoms, sometimes failed in their attempts to do this. What's more, because of the cuts in funding, part of the ancillary services no longer existed. The reverse of this trend was introduced by the HIV/AIDS epidemic in the eighties which led to a review of the evidence on the effectiveness of methadone maintenance treatment. Dosages lower than 60mg are considered ineffective. In this age of AIDS, a low dose policy can be fatal to the opioid dependent person in treatment as well as for his/her sexual partners and children (Newman, 1998; Schuster, 1989). Nowadays, it is a strongly held view that some patients need long-term maintenance treatment and that this is done without serious side effects.

Methadone Substitution Treatment in Europe

In Europe, methadone substitution treatments have a long and varied history across the continent where changes in medical opinion and legislation have led to developments and changes in prescribing practices. As previously stated, several Central and Eastern European countries are in the process of establishing their first methadone programmes. In Western Europe, introduction of the first methadone programmes varied from the late sixties in Sweden, the UK, the Netherlands and Denmark to the seventies in Finland, Portugal, Italy and Luxembourg to the eighties in Austria and Spain and to the nineties in Ireland, Germany, Greece and France.

The type of methadone programmes varies from low threshold programmes in some countries to high threshold ones in others.

Low threshold programmes:

- Are easy to enter
- Harm reduction oriented
- Have as primary goal to relieve withdrawal symptoms and craving and improve the quality of life of patients
- Offer a range of treatment options

High threshold programmes:

- Are more difficult to enter / may have selective intake criteria
- Abstinence oriented (including methadone abstinence)
- Have no flexible treatment options
- Adopt regular (urine) controls
- Inflexible discharge policy (illegal opioid use not consented)
- Compulsory counselling and psychotherapy

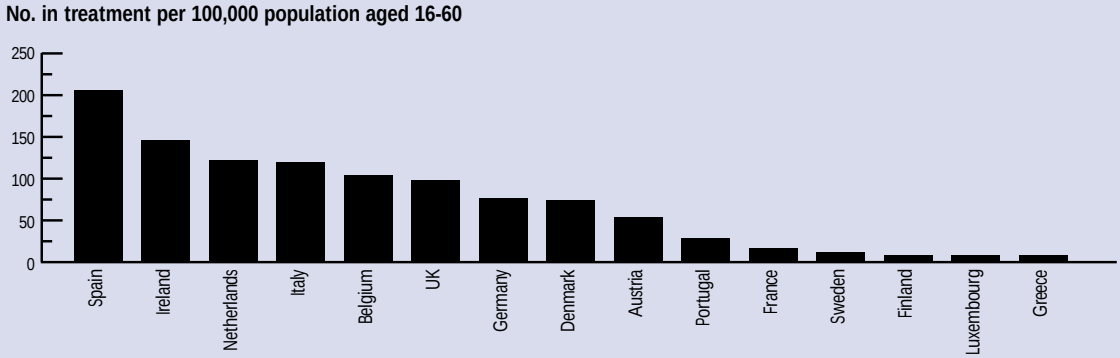
Most countries have seen a rapid expansion in the provision of substitution services, especially in Spain, France, Greece and in some Central and Eastern European countries. A rapid expansion is even more evident in countries like Luxembourg, Finland and Greece, which had lower baseline levels of provision. The impetus for the expansion has largely been a response to the HIV/AIDS epidemic among drug users. Whilst most countries have experienced few problems during this growth period, concern has been expressed in some member states. It concerned the lack of training and skills of some practitioners who are now involved in substitute prescribing. This is particularly notable among specialist services, including general practitioners and pharmacists (Dpt. Of Health UK guidelines, 1999; Farrell *et al*.,1999). There is also concern about controls on prescribing and the risk of possible diversion of methadone onto the black market (Farrell *et al*.,1999).

In 1997, 9742 kilograms of methadone were manufactured world-wide and 8321 kg were consumed, according to data of the International Narcotics Control Board of the United Nations (INCB/UN, 1999).

It is estimated that approximately 300,000 people are on methadone in Europe, 180,000 in the United States and 20,000 in Australia. There are many countries in the world where different forms of drug substitution take place. However, the bulk of methadone treatment to date is still carried out in Europe, North America and Australia. These overall estimates would suggest that there are nearly half a million people on this type of drug substitution globally (Farrell *et al*.,1999; Parrino, 1999).

The estimated number of addicts in methadone substitution treatment per 100.000 population aged 16-60 was reported for 1997 in the afore-mentioned report of EMCDDA for the European member states. The numbers ranged between 6 (per 100.000 population aged 16-60) in Finland, Luxembourg and Greece, to 12 and 16 in Sweden and France, 33 in Portugal, 75 in Denmark and Germany, to between 96 and 145 for respectively the UK, Belgium, Italy, the Netherlands and Ireland, and finally up to 206 in Spain (Figure 1, copied from the Farrell *et al*.,1999).

Figure 1: Estimated number of drug users in methadone substitution treatment in 1997



Source: Annual report on the state of the drugs problem in the EU (EMCDDA 1998)

In some countries, there are more people in substitution treatment, but not with methadone. For example, in France in 1997 there were only 5000 people receiving methadone against an estimated group of 25.000 receiving buprenorphine. Methadone was being prescribed only in specialised centres, while every doctor could prescribe buprenorphine. This means that the framework for buprenorphine is much more flexible than for methadone (Lebeau, 1997).

Throughout Europe, there is considerable variation as to who can prescribe methadone treatment for opioid dependence. Some countries like Denmark, Finland, France, Greece, Italy, Portugal, Spain and Sweden have centralised methadone treatment in specialised programmes with little involvement of General Practitioners. Others, such as Austria, Belgium, Germany, Luxembourg, the Netherlands and the UK, have a less centralised structure with GPs and specialised centres. Most Eastern European countries have implemented some type of methadone treatment programmes (Lithuania, Slovenia) and most of them operate on a pilot basis or as a single treatment service (Bulgaria, Croatia, Czech Republic, Estonia, Latvia, Poland, Romania and Slovakia). In Hungary, psychiatrists and GPs prescribe methadone on an individual basis, although new guidelines are being prepared for treatment services.

Chapter 2: The evidence for the effectiveness of methadone

Pharmacology

Methadone (*methadone hydrochloride*, or 6-dimethylamino-4, 4-diphenyl-3-hepatone hydrochloride) is a synthetic opioid agonist that has effect on humans similar to those observed with morphine. Methadone is well absorbed from the gastro-intestinal tract, irrespective of formulation type (e.g. syrup vs. tablet). It has very good bioavailability of 80 to 95% The elimination half-life of methadone has been estimated to be 24 to 36 hours, with considerable variation across individuals (10 to 80 hours). The main site in the body for the biotransformation of methadone is the liver. Methadone is eliminated from the body in the form of metabolites resulting from biotransformation and by excretion of the drug itself in urine and faeces (Ward *et al*., 1998; Humeniuk, 2000). This pharmacological profile makes methadone useful as a substitute opioid medication, because it allows oral administration, single daily dosage and achievement of steady-state plasma levels after repeated administration with no opioid withdrawal during usual one-day dosing interval.

The rate of metabolism of methadone by the CYP3A4 enzyme effects the clearance of methadone from the body. The expression of the CYP enzyme is influenced by genetic and environmental factors and by certain medications. It is highly variable which can result in methadone toxicity and at the other extreme, in opioid withdrawal. Certain medications interact with the blood level concentration of methadone and special attention has to be given to people using other medications such as HIV medications, antibiotics, some anti-epileptics and medications that treat tuberculosis. For more information on the interaction of methadone and other medications we refer to appendix 14 of the UK Guidelines and to the Methadone Briefing by Andrew Preston, 1996. The UK Guidelines can be consulted on the internet: http://www.doh.gov.uk/drugdep.htm Drug Misuse and Dependence-Guidelines on Clinical Management.

Side effects of methadone occur in the neuro-vegetative and psychological area. The most common side effects include: increased transpiration, constipation, disturbances of sleep, sex drive and concentration. Such undesirable side effects may persist over longer periods of treatment, but mostly remain without medical consequences. In total, these side effects affect less than 20% of methadone clients (Swiss Methadone Report, 1996).

Methadone treatment with full tolerance and stable doses does not usually impair the ability to drive. However, before issuing or reissuing a driver's license, careful checking is advisable to determine whether the client's situation is stable; whether there are any chances of relapse, and whether there is consumption or misuse of other substances. Especially the simultaneous use of alcohol and/or medications (e.g. benzodiazepines) should be taken into consideration (Swiss Methadone Report,1996).

Historically, methadone *maintenance* therapy (MMT) was the earliest form and continues to be the most widely used form of opioid substitution (or replacement) therapy in the United States, Australia and Europe. However, over the years methadone has increasingly been prescribed as part of a *detoxification* treatment.

Detoxification programmes provide supervised withdrawal from opioid dependence with methadone (and often combined with other medications) in order to minimise the severity of withdrawal symptoms. After the peak of the withdrawal syndrome, the substitute medication (i.e. methadone) is gradually reduced.

Research

Today, there is extensive evidence that methadone maintenance is an effective treatment for heroin addiction. It has proved to significantly reduce illicit opioid use and opioid overdose deaths, and to decrease the frequency of injecting, needle sharing and HIV transmission. Methadone maintenance programmes significantly reduce the risk of sudden death from all causes including heroin abuse, compared to people outside of programmes. Methadone maintenance treatment has also proved to significantly decrease criminal activity, and to improve the quality of life of patients, including positive changes to health, employment potential, and social and physical functioning. Finally, oral methadone maintenance programmes have proved to be effective for the individual patient, for public health and in terms of cost-effectiveness.

Some of the benefits of methadone treatment are not directly due to the drug itself. Methadone programmes attract patients per se., and keep them in contact with services that offer a range of other facilities such as syringe exchange, counselling, social services, etc. (Dole & Nyswander, 1965; Ball & Ross, 1991; Farrell *et al*., 1994; Ward *et al*., 1998; UK Guidelines, 1999; Humeniuk *et al*. 1999).

Opiate addiction is a complicated condition that has both metabolic and psychological components. It is important to deal with both aspects of this condition. Since it is a condition where a patient is prone to relapse, careful risk assessment of this possibility should preclude any decision to stop methadone prescribing.

Some researchers conclude that the process of neuro-adaptation that takes place in the brain during prolonged periods of opiate use may be very hard to reverse in all cases. Subtle changes in the body's own endorphin system may be a factor that contributes to the relapsing nature of opiate dependency (Newman, 1998).

One of the criticisms sometimes made about methadone treatment, is the view that patients are not seen to be 'drug-free' and no real change occurs in the patient's situation.
People with such a view, however, misunderstand the purpose of methadone treatment. The value of methadone treatment is in the acute phase of opiate dependency – at the time when a person is not able to stop the use of opiates. Methadone can enable a dependent drug-user to stop, or greatly reduce, the use of illicit opioid drugs. It can also assist in reducing, and sometimes eliminating injecting drug behaviour. Achieving this goal alone has considerable value in terms of harm reduction to the individual.

Methadone maintenance treatment is probably the most evaluated form of treatment in the field of drug abuse treatment and continues to arouse professional and political controversy. We will limit ourselves here to discussing the major findings from reviews of the many studies done by others in different parts of the world.

Most research on methadone has been done in the USA. The National Institute on Drug Addiction (NIDA) has funded and co-ordinated several studies which have examined various treatment outcomes of methadone maintenance treatment in the United States. Some of these research projects were: The Drug Abuse Reporting Programme (DARP) studies with a 12 year follow-up; The Treatment Outcome Perspective Study (TOPS) gathered data before, during and after treatment on a nation-wide scale and The Methadone Research Project (The Ball and Ross Studies) looked at the effectiveness and status of MMT in six programmes in three cities (International Forum, 1994).

Anther important study is the British follow-up study of the National Treatment Outcome Research Study (NTORS), which monitored the progress of 1075 clients in residential and/or community treatment services over five years (Gossop *et al*., 1998).

Farrell *et al*. carried out a review of the scientific evidence of MMT in 1994. Major conclusions included:

- Possible benefits of oral methadone treatment range from impact on illicit opiate use and injection related risk taking behaviour to reductions in the level of criminal activity and other positive social changes
- The most important active ingredient of treatment has been debated: is it simply the provision of a strong opioid in a controlled manner or is it the counselling and programme structures that are the key ingredients promoting change?
- There is clear evidence that programmes may vary substantially in their efficacy
- Programme factors include dosage of prescribed methadone, maintenance versus abstinence, and support services
- Operational issues include monitoring the use of non-prescribed drugs, diversion of methadone, use of other psychoactive drugs, and oral versus injectable methadone

The Drugs and Alcohol Review Group of the *Cochrane Collaboration* has been co-ordinating several ongoing systematic reviews on the effectiveness of methadone treatment for opioid dependence. The *Cochrane Collaboration* bases its systematic reviews on the meta-analysis of Randomised Controlled Trails (RCTs) and Clinical Controlled Trials (CCTs) on a global scale. To date, their Trials Register contains 547 RCTs and CCTs on the use of methadone as treatment for opioid addiction. So far, no reviews have been completed and published on the *Cochrane Library* (the Cochrane Library, 2000).

Most studies have focussed their attention on the effectiveness of methadone as a maintenance treatment and to a lesser extent to methadone detoxification programmes. However, there is some evidence that opioid detoxification programmes with methadone have become more successful over the years, with decreased withdrawal symptoms and increased rates of completion of detoxification (Mattick, 1996).

Taken together over two decades, the randomised-controlled studies of methadone maintenance demonstrate consistent, positive results over different cultural contexts (US, Hong Kong, Sweden, Thailand). Furthermore, the numerous observational studies demonstrate that treatment delivered in different settings confers substantial positive change (WHO, 1998).

Cost-effectiveness

What is significant from the perspective of policy making in health-care and criminal justice, is the fact that methadone treatment has also proved to be cost-effective. The Department of Substance Abuse Services and the National Institute for Drug Addiction have estimated the yearly cost to maintain an opioid addict in New York in 1991: untreated on the street ($43.000), in prison ($43.000), in a residential drug-free programme ($11.000), and in MMT ($2.400) (International Forum, 1994).

The British NTORS programme calculated that for every extra £1 spent on drug misuse treatment, there is a return of more than £3 in terms of cost savings associated with victim costs of crime, and reduced demands upon the criminal justice system. The increased expenditure of £1.6 million for treatment interventions yielded an immediate cost saving of £4.2 million in terms of the reduced victim costs of crime, as well as cost savings within the criminal justice system of about £1 million. The true cost savings to society may be even greater than this (Gossop *et al*., 1998).

In conclusion, research supports the conclusion that methadone maintenance is more effective than no treatment or placebo in retaining people in treatment, reducing use of heroin and other illicit drugs, preventing HIV infection, improving the health- related quality of life, and reducing involvement in criminal activity and imprisonment rates. Detoxification alone is seldom effective in producing long-term change. The benefits of methadone maintenance programmes can be maximised by retaining clients in treatment, prescribing higher rather than lower dosages of methadone, orientating programmes towards maintenance rather than abstinence, offer counselling, assessment and treatment of psychiatric co-morbidity, and social treatments and the use of contracts and counselling to reduce the use of additional drugs (Preston, 1996; Farrell, 1994; Mattick, 1996; Ward, 1998).

Chapter 3: Outline of Best Clinical Practice

Criteria for treatment

There are two internationally accepted diagnostic criteria that cover drug dependence: the tenth revision of the *International Classification of Diseases* (ICD 10) published by the World Health Organisation (WHO) in 1992, and the fourth edition of the *Diagnostic Manual of Mental Disorders* (DSM-IV) published by the American Psychiatric Association in 1994. Because of the European nature of these guidelines, we refer to the first criteria of ICD 10 which defines Dependency syndrome as: *"A cluster of physiological, behavioural, and cognitive phenomena in which the use of a substance or a class of substances takes on a much higher priority for a given individual than other behaviours that once had a greater value …….. "* (WHO Expert Committee on Drug Dependence, 1998).

Substance dependency is diagnosed if at least three of the following criteria had been present in the previous year:

Psychological:
- Strong desire or compulsion to take the substance;
- Difficulty in controlling behaviour regarding the onset, termination or levels of use;

Physiological;
- Characteristic withdrawing syndrome for the substance if not taken;
- Evidence of tolerance and need of increased dose to achieve effect;

Social:
- Progressive neglect of alternative interests/pleasures and increased time necessary to obtain, take or recover from substance;
- Persisting with substance use despite the negative harmful consequences.

The criteria for entering methadone treatment differ widely between programmes.
High threshold programmes adopt strict criteria, such as:
- a minimum of 5 years of opioid addiction

- a minimum age of 18
- history of failed treatment attempts
- strong motivation to enter treatment
- one of the international diagnostic criteria for opioid dependence

Some methadone programmes only accept heroin addicts for treatment if they suffer from illnesses, such as HIV/AIDS or tuberculosis.

At the other end of the scale there are low-threshold programmes which would welcome anybody with a proven addiction to opioids who wishes to enter a treatment programme.

The criteria differ according to the type of treatment (maintenance or detoxification) because of the length of time a patient is expected to be in treatment. Other factors, such as the availability of places, may influence inclusion criteria. In areas where there are no waiting lists, programmes can adopt looser criteria than in places where there is a larger demand than supply of treatment possibilities.

In general, the best situation is where everyone who is opioid dependent and in need of treatment can enter methadone treatment after appropriate assessment and treatment induction. It is recommended that the availability of treatment places is taken into account when adopting admission criteria. A minimum age, length of opioid addiction, physical and mental health and personal motivation of the patient, could all be taken into consideration. Some groups, such as pregnant women or patients with HIV/AIDS or other illnesses, should be given priority over the general opioid addicted population. This, however, should not entail compulsory HIV-antibody testing of patients.

Assessment

Before starting any type of methadone treatment it is necessary to determine whether the patient is taking opioids and to establish the presence and severity of opiate dependence. The clinician will have to conduct a personal interview with the patient and carry out a physical and mental state examination and do an urinalysis. The final decision for the type of treatment should be taken on the basis of the needs of the individual patient and the options open to the clinician. To ensure a successful treatment programme, the clinician or assessor is required to give the patient information on the full range of treatment options. It should be ensured that the patient is matched to the most appropriate treatment for their current

needs. Further, when starting methadone or psychoactive substances, the clinician should give detailed information on the treatment, on the possible side effects of the medication and the potential social consequences (such as long-term dependency and increased tolerance).

Urinalysis can be helpful in confirming opioid use, however, this should be considered with care. It may encourage the use of opioids prior to an assessment. Furthermore, it can only confirm opioid use, but it does not provide any information about the extent of use or dependence. Its main usefulness may be in determining the use of other substances presently being used by the applicant (Ward *et al*., 1998).

Treatment plan and treatment goal (duration and dosage)

Although these guidelines cannot modify potential local restrictions in therapeutic options, it can be stressed that the international literature, as well as the experience over time in different parts of the world, underline the importance of the availability of room for individual treatment assessment and design. Restrictions in availability of places, in dosage and duration or type of treatment are counter-productive in the effective treatment of opioid dependent patients. Making decisions about the treatment of individual clients has to be based as much as possible on a thorough assessment of what will work for that person and on reliable information about what works (Preston, 1996). The decision about what treatment to offer is based on what treatment is available locally, on the client's previous history, current situation, social support network and expressed wishes. The decision is also based on the clinician's judgement of the required degree of structure, monitoring and support.

In 1990, the World Health Organisation suggested a standard terminology for methadone treatment divided into four categories:

- Short-term detoxification: decreasing doses over one month or less;
- Long-term detoxification: decreasing doses over more than one month;
- Short-term maintenance: stable prescribing over six months or less;
- Long-term maintenance: stable prescribing over more than six months.

(See Preston, 1996, pp. 94-97 for an extensive description of the indications and contra-indications for these four categories of methadone treatment).

Opioid use and dependence is associated with a range of medical, legal and psychosocial problems. A person is suitable for substitution treatment with methadone if the individual and social harms associated with the opioid use are likely to be reduced by entry into treatment. Additional problems should be addressed from the very beginning, either by the methadone programme itself or through referral to an appropriate service.

Induction

There are several forms and formulas of methadone. The most widely used form is the liquid 1mg/1ml solution, which will be adopted here as prototype.

The calculation of the right starting dose should take the following factors into account:

- That the right dose varies according to the treatment aim;
- That illicit heroin varies in purity from area to area and from time to time;
- That methadone is a long acting opiate;
- That too much methadone can be fatal but insufficient methadone is unlikely to be effective.

Starting patients on a dose of methadone that is too high may result in toxicity and death. However, there is some danger inherent in the administration of a dose of methadone that is too low, in that withdrawal may occur. The experience of withdrawal symptoms may prompt patients to seek relief from other sources, such as illicit opiates and benzodiazepines. The combination of methadone with other substances may result in toxicity and death. Furthermore, some patients may metabolise methadone quite rapidly and may also be in danger of withdrawal and self-medication (Humeniuk *et al.*, 2000). There is evidence that people entering treatment have a higher risk of dying during the first month than before they entered treatment (Caplehorn, 1999).

Once opioid dependence has been confirmed in a patient, tolerance and methadone dose need to be assessed. The usual way to determining tolerance is by clinical assessment of the patient's medical and drug use history upon presentation. Accuracy of clinical assessment may be improved by using corroborating evidence such as examining veins for evidence of injecting opioid use or urine tests. A good

rapport with the patient is vital in obtaining the necessary information. It is important that enough time is allocated for the clinical interview as well as communication with other practitioners whom patients may have seen.

The absolute condition for an effective start of methadone treatment is to provide the patient with relevant information which should include the following:

- The delay of 2 to 4 hours before methadone has a peak effect;
- The accumulation of methadone over time resulting in a greater effect over 3 to 5 days or more, even on a fixed dose;
- The risks of poly-drug use while on methadone, particularly other opiates, cocaine, benzodiazepines and alcohol;
- The effect of medications that induce or inhibit activity on subsequent methadone concentrations. (for more information we refer to appendix 2).

One or more of the following criteria can identify patients with a higher risk of methadone toxicity:

- It is their first presentation to that practitioner and their medical and drug use history is unclear;
- They are at high risk of poly-drug use or dependence;
- Their degree of neuro-adaptation is uncertain;
- There is a risk of overdose on methadone or any other drug;
- They have a clinically significant respiratory disease;
- They have a clinically significant liver disease;
- They are currently being administered drugs that inhibit the CYP3A4 enzyme (*).

These patients should be re-assessed two to four hours following the first three to five doses of methadone in order to identify signs and symptoms of methadone toxicity and they should not have their doses increased in the first 2 to 4 days (Humeniuk et al, 2000).

It is highly recommended that methadone is commenced in the morning and preferably early in the week, so that the peak blood methadone concentrations occur when the clinic is open and able to intervene.

The aim of induction is to eliminate withdrawal. In general, the initial dose is between 10 - 30mg. If tolerance to opioids is high the usual dose is between 25 - 40mg. In cases where tolerance is low or uncertain, a dose between 10-20mg is more appropriate. Where a starting dose is low, it is important to keep the patient under observation for a few hours and if withdrawal symptoms occur, to administer additional small doses.

In the first week of an outpatient detoxification scheme, patients should be seen daily in order to establish a stabilisation dose. Where doses need to be increased during this first week, this should be done with a maximum daily increase of 5 to 10mg and not more than 20mg within a week from the initial dose.

For a longer period of detoxification and for maintenance treatment, it is recommended that increased doses do not exceed 20mg per week up to a total of between 60 - 120mg. The time needed to properly stabilise someone on methadone treatment can take up to six weeks or more

Detox regime suggestion

After a thorough review of the available research and clinical experience, Ward and colleagues state: *"..... it is important to remember that abstinence is only one option available to the patient and that an otherwise fulfilling life while attending for methadone maitenance is another"* (Ward *et al,* 1998, p.353).

In the period of stabilisation, reduction regimes should only be initiated if the patient continues to abstain from heroin use. After a patient has become stabilised on the prescription, and has made other changes in lifestyle, a formal drug reduction regimen can be set up. Compliance will only be maintained if both patient and doctor agree that a reduction scheme is desirable. If a reduction scheme is carried out against the wishes of the patient, compliance is expected to be low. Hence, if the patient is not going to be fully compliant, it is best to continue with the existing, stable regimen.

After a period of stabilisation, the daily dose can be reduced, for example, by 5mg per fortnight. Some clinicians suggest that if the stabilisation dose is over 120 mg, the dose can be reduced by 20 mg per month. The dose should be reduced on the first day of the first week and then kept stable for the following three weeks. If the dosage ranges between 60 and 120 mg, the dose can be reduced according to the above mentioned procedure by 10mg per month. For patients who have a daily dose of 30-40mg, it can be reduced by 5mg monthly.

The UK Guidelines suggest considering the following:
" Stability on a substitute prescription offers the opportunity to discover and address those issues that have led to drug misuse. It may take months, or even years, for a drug misuser to reach a stage where a reduction in their prescribed drugs can be considered.
Many patients, despite requesting detoxification, are more suitable for maintenance treatment. The treatment options should be sensitively explored with the patient, and the overall goal should be to maximise the patient's potential health gain. Undertaking a regular clinical review, on at least a three-monthly basis, of all long-term patients, will ensure that the potential goal of abstinence can always be re-considered. Better co-ordination of local services might enable substitute drug-maintained patients to become drug-free" (UK Guidelines, 1999: p47).

Maintenance programme suggestions

Research suggests that the majority of individuals require 60-120mg per day. Although some individuals can be successfully maintained on lower doses, an average heroin dependent person will use less heroin and stay in treatment longer, if maintained on higher rather than lower doses of methadone. In situations where high daily doses fail to prevent withdrawal during the full 24 dosing cycle, it should be determined if the individual is taking enzyme-inducing drugs concurrently, or if the individual metabolises methadone at a faster rate than average and higher methadone doses will be needed. (Humeniuk *et al*, 2000; Preston, 1996; Ward *et al*, 1998).

Although the majority of patients can be adequately treated with a daily dosage of between 60-120mg, there are no objective data (including methadone plasma concentrations) to stabilise the adequate daily dose for an individual patient. Asking the patient's opinion about methadone dosage can have a positive effect on the treatment.

It should be noted that people with a high level of emotional distress or cluster A personality disorders or schizophrenia-like personality disorders, should be maintained on higher rather than lower daily doses of methadone. Caution needs to be observed about high doses if there is associated alcohol or benzodiazepine dependence. Yet, one should keep in mind that alcohol and/or benzodiazepine dependence could be the result of an under-medication with methadone. In this case the stabilisation dosage needs to be reconsidered (Maremmani & Shinderman, 2000).

It has been demonstrated that patients can responsibly manage their own methadone dose levels and that this may have positive effects on their treatment outcome.

Initially, patients may need to be seen by the doctor at least fortnightly and then, if stable, at least monthly. A more thorough review may be useful every three months to consider what has been achieved and to set new goals. Random urine checks may be helpful, e.g. at least twice a year. Co-existing physical, social, psychiatric and legal problems should be addressed as much as possible.

If, for whatever reason, patients miss methadone doses, they need to be re-assessed for intoxication and withdrawal before methadone administration is recommenced. If the patient hasn't had methadone for three days, it may be appropriate to reduce the dose as their tolerance may be reduced. In cases where patients have abstained for five days or more, a full assessment is required before methadone is recommenced.

Detoxification from Methadone Maintenance Treatment

Detoxification from methadone maintenance will induce withdrawal syndrome. Because of the relatively long elimination half-life of methadone and the fact that it accumulates in body tissue during maintenance treatment, its withdrawal syndrome is more protracted than that of shorter acting opioids such as heroin and morphine. However, it is also said that withdrawing from methadone is less intense. In order to prevent or reduce the anxiety of the client it is vital to give clear and accurate information about what is going to happen.

The available research suggests that the slower the course of diminishing doses, the better. However, like all other decisions regarding the treatment plan, this can best be set individually in consultation with the patient. One option is to reduce the dose blindly, as some people may prefer not to know the reduction details in order to prevent anxiety or expectancy effects. Supportive counselling is also considered an

important part of withdrawing from methadone maintenance and this should be continued after patients have finished the reduction regimen because of the post-methadone syndrome. This syndrome is associated with mild symptoms of the protracted withdrawal phase as well as with issues related to leading an opioid-free life. The development of aftercare services in some places is an answer to these problems and involve a mix of education, skills training and features derived from self-help groups like Narcotics Anonymous (Ward *et al*., 1998).

The process of detoxification has not received the ample attention it needs in developing methods and there is a clear need for more research in this specific part of treatment.

Special groups and settings

World-wide, the majority of people who are prescribed methadone are men between 25 and 40 years old. While they do not form a homogenous group with the same needs, there are groups with specific needs. In this section, the following groups are discussed:

- pregnant women
- neonates
- opioid users with small children
- young people
- people with HIV/AIDS
- people with hepatitis
- people with mental health problems
- poly-drug users
- minority ethnic groups

Also, the situation of people in specific settings is briefly discussed, such as people in hospital, in prison and people who travel. Because we can only summarise some of the topics, we recommend that further guidance is sought when confronted with special groups and situations.

Pregnant women

Attracting and maintaining pregnant women in treatment services and preferably with their partner, is vital. It is advisable to give pregnant women priority to enter methadone treatment because of the health risks for both the mother and the foetus associated with substance abuse, such as premature labour,

multiple drug-use that can damage the foetus as well as poor nutrition, infection through unsafe injecting, etc. The long-term outcome of women who enter methadone treatment programmes during pregnancy is better in terms of their pregnancy, childbirth and infant development, irrespective of continuing illicit drug use. Women attending treatment services usually have better antenatal care and better general health than drug-using women not in treatment, even if they are still using illicit drugs (Finnegan, 2000).

Once a stable treatment programme has been established, liaison with other medical services, particularly for antenatal care, can be stimulated. It is recommended that a case-manager be identified to co-ordinate the care of the mother and child.
Although many women would wish to detox, long-term methadone maintenance treatment is considered the best option for opioid dependent pregnant women. In the third trimester, many women will need higher doses because of weight gain and other physiological changes. In some cases, dividing the daily dose and administering it twice daily could be considered.

If a woman wants to detoxify, it is recommended not to do this in the period prior to week 12 or after week 32 of pregnancy (Council of Europe, 2000). Withdrawal symptoms should be avoided during the first three months of pregnancy because of the risk of premature labour in this period. The normal maximum reduction in the daily dose is between 2.5-10 mg weekly, fortnightly or monthly, depending on the woman's response. The final, slower part of a detoxification is often carried out (under close medical supervision) in the final three months of pregnancy without risk to the baby.

If detoxification is unsuccessful and the patient's drug use becomes uncontrolled, methadone dosage should be re-assessed until stability is regained, so that detoxification and maintenance can be interchanged.

Neonates of opioid dependent women
Over 60% of neonates born to opioid dependent mothers have symptoms of neonatal abstinence syndrome (NAS) that tend to occur 24-74 hours after delivery and include the following: high-pitched cry, rapid breathing, hungry but ineffective sucking and excessive wakefulness. Hypertonicity and convulsions could also occur. The intensity of the NAS does not correlate with the dose of the methadone or other opiods used by pregnant women.

They can usually be cared for in a normal maternity environment on condition that in case of emergency, they could be transferred to special care units. Withdrawal symptoms can be prolonged and also include respiratory problems and depression if the mother takes methadone together with benzodiazepines.

If medication is required, a range of opioid and non-opioid drugs can be used. An oral morphine concentrate is the drug of choice and phenobarbiton may be used if the mother had been taking other substances, such as benzodiazepines.

Research from Austria has demonstrated that babies born to opioid dependent mothers and maintained on buprenorphine did experience less neonatal abstinence syndrome (Fischer *et al*., 1998).

Breast-feeding is encouraged not only because of its general advantages but also because some methadone may pass to the baby in very low doses and this in turn may help reduce any withdrawal symptoms of the baby. In case of HCV infection, the benefits of breast-feeding should be considered according to the mother's viral load (Council of Europe, 2000). Contra-indications for breast-feeding however are: if the mother has HIV/AIDS or if she uses high doses of benzodiazepines or if she continues illicit drug consumption.

Finally, because pregnant women and young mothers may suffer from severe guilt feelings, psychosocial care and counselling is highly recommended.

Parents of young children

Drug use alone is not a reason to introduce care proceedings. The needs of young children of drug dependent parents are, however, paramount. Workers in methadone programmes will need to include the care of the children in their treatment plan and have some means of supervision. In some countries, there are special programmes co-ordinating the care of the parents and young children. Case management of these clients is a key issue and the specific needs of the children should be considered explicitly.

Young People

Methadone is unlikely to be an appropriate treatment for people under 16 years of age as they are unlikely to fit the criteria of:

- Long-term opioid use
- Significant tolerance
- Level of problematic opioid use which would not be possible to treat with another form of treatment and help.

If methadone treatment were nevertheless considered, specialist assessment and management is advised. Most countries require parental consent.

People with HIV/AIDS

Drug users who have a positive HIV test have a variety of reactions and needs. The positive result may not change their drug using behaviour, but it could change dramatically both in a positive and negative way. In principle, methadone treatment options are the same, regardless of their HIV status.

Methadone treatment can reduce risk behaviours that could further damage the immune system. It can reduce stress and improve the general health of the patient by helping to live a regular life. Methadone maintenance treatment is an exceptionally good tool to improve retention in treatment which in turn can allow for early diagnosis and HIV treatment.

Liaison with specialist care, particularly with the HIV physician, is strongly recommended. Prescribing should be done in collaboration with the HIV specialist to avoid potential risk of interactions between methadone and HIV medications (Humeniuk et al, 2000). Attention should be paid to specific issues, such as the reduction of tolerance on account of periods of illness and the risk of overdose in case of memory (Preston, 1996).

People with Hepatitis

It is strongly recommended that all people in treatment should be tested for Hepatitis B and those without protective antibodies, should be vaccinated.

Hepatitis C is a serious health problem for injecting drug users, both in terms of prevalence and its clinical effects. There is a great need for improved methods of diagnosis and management of people with

hepatitis C. The dose of methadone will have to be reviewed and analysed, according to the liver function of the patient. Specialist referral should be managed for assessment and possible treatment of HCV. People who are stable on methadone can be very compliant with HCV treatment. Finally, as in the case of people with HIV, it is important to reiterate the importance of avoiding any sharing of injecting equipment.

People with mental health problems

A third or half of opioid users may suffer from mental health problems, including anxiety and depression. A quarter of opioid users presenting at services have suicidal and self-harm risk. Entry into treatment has a significant positive impact on their psychological well-being. A minority (circa 10%) have severe enduring mental health problems that require close collaboration with mental health services (Marsden, *et al*., 2000).

Dually diagnosed opioid dependent patients who survive early attrition, tend to stay in treatment longer than those without psychiatric co-morbidity do, when treated with higher methadone doses during the stabilisation phase (Maremmani *et al.*, 2000).

Multiple-drug users

In order to deal with additional substance drug use, including alcohol, first of all the worker must be aware of it. The best situation is if the therapeutic relationship is such that these issues can be discussed. The threat of removal from treatment on discovering additional drug use is not considered useful for a rapport based on trust and co-operation between prescriber and client.

Strategies to reduce risk behaviour include: increasing the methadone dose and possibly other medication, the frequency of collection, supervised consumption, setting realistic treatment goals and finally, in some programmes, the suspension of methadone prescribing.

Minority ethnic groups

In many areas, opioid dependence can be a problem among ethnic minorities. Often, services are developed for and run by people from the mainstream population and culture. In order to make services more attractive to ethnic minorities, it is important to offer culturally appropriate services. It can also be advantageous if the staff of the drug services mirrors the population constellation in the area.

People in prison

People in prison should have access to the same treatment options as in a community setting. In 1998, the Prison and Drugs Conference in Oldenburg, presented recommendations for drug services in a prison setting. They recommended that a wide range of drug services should be available to prisoners, including substitution treatment (both detoxification and maintenance). It was also recommended that prison staff needed to be trained on drugs and related (health) problems.

Individuals on maintenance in the community should have the option to continue to be maintained upon entry to prison. This option is important since the discontinuity of methadone maintenance treatment is likely to result in higher levels of risk behaviour (Swiss Methadone Report, 1996).
People receiving substitution treatment in prison must be able to continue with such treatment on release. There is a particularly high risk of overdose and death after release if patients have been abstinent from opioids (Darke *et al*., 1996). Decisions on continuity should be taken in consultation with the treatment programme in which the prisoner participates once outside prison (European Recommendations, 1998).

People in hospital

It is important that general hospitals recognise a patient with an opioid dependence. After proper assessment and communication with the drug treatment service, patients should be able to continue their methadone medication managed in such a way as to ensure the completion of the medical treatment for which the patient entered the hospital. It is worth noting that general hospitals should not be considered as detox centres. The conditions in the hospital should simply favour the recovery and treatment of the medical problem.

The emergency department of a hospital will mainly encounter two situations:

- The management of severe abstinence and or overdose;
- The management of other drug related problems.

Liason between drug services and emergency departments are essential and joint policies between the two departments should be developed at the local level.

People who travel

People should be able to travel and take their own supply of medication with them. Where continued daily supply is required, arrangements should be made with an appropriate local service. Several websites provide information on methadone programmes which are willing to prescribe methadone to people from other countries. See: the European Methadone Assistance Point (MAP) of Euro-Methwork: http://www.euromethwork.org and the International INDRO based in Germany: http://home.muenster.net/~indro/

Figure 2 : Steps in Methadone Treatment

Individual comes to the programme

↓

Welcome by one member of the staff
Administrative intake of personal details
Check if individual meets intake criteria (if applicable)

↓

Medical intake by doctor
Assessment of opioid dependence through:
personal interview
medical assessment
urinalysis

↓

Assessment of level of dependence

↓

Treatment plan (maintenance, detoxification)

↓

Induction and calculation of starting dose
Patient kept under supervision for a few hours to check if initial dose is correct
in case withdrawal symptoms reoccur, an additional dose will be given
Patient given detailed information on the treatment and on the risks of using other drugs

↓

Psycho-social intake by social worker/drug worker
Assessment of problems to be addressed
Liaison with relevant services

↓

In case of co-morbidity liaison with relevant medical services

↓

Stabilisation period to establish the right dose
(may take up to six weeks)

↓

Maintenance or detoxification regimen
Regular review to set new goals (depending on type of treatment)

Other substitution drugs

There is a range of other substitution drugs in the treatment of opioid dependence, mainly opioids that connect to the (-receptors in the brain, that have been tried on a formal and informal basis in different countries. In the context of these methadone guidelines we will briefly discuss three of them: LAAM, buprenorphine and heroin.

*Levo-alpha-acetylmethado*l (LAAM) is an agonist and is a synthetic opioid analgesic of the morphine type related to methadone. It was investigated extensively in the seventies as an alternative to methadone. Its major advantage over methadone is its longer half-life of 48 hours and the opportunity for longer dose intervals.

Research suggests that treatment with LAAM is safe, and at least as effective as methadone for the treatment of opioid dependence, although issues of accumulation need to be given consideration (Johnson *et al*, 1999).
For patients coming directly from methadone maintenance treatment, the LAAM dose should be 1,2 or 1,3 times the methadone dose (not exceding 120 mg). It is recommended to administer LAAM for example on Mondays and Wednesdays and increase the dosage on Fridays with 15% to 40% for three days treatment.

Buprenorphine is a partial μ agonist and κ antagonist which has been used in many countries for pain management. Buprenorphine has morphine-like subjective effects and produces cross-tolerance to other opioids. It may not always be appropriate to treat all patients with a full agonist as methadone. The partial μ agonist and (antagonist action appears to make it safer in overdose and possibly less likely to be diverted than pure opioids. It may also provide a potentially easier withdrawal phase. Successful experiences have been reported in different places. It is registered as treatment for opioid dependence in France and Portugal under the name of Subutex® and overall, it is likely to find a place as an alternative pharmacotherapy in the treatment of opioid dependence (Mattick *et al* in: Ward *et al*., 1998).

Buprenorphine should not be administered within at least four hours after the last dose of heroin in order to prevent withdrawal symptoms. If the patient comes from a methadone maintenance program, the daily

dose of methadone needs to come down to 30 mg/day before inducing buprenorphine.
Research has shown that buprenorphine is as effective as methadone as a maintenance agent in reducing illicit opioid use, in retaining patients in treatment and in reducing heroin craving and use. Furthermore, buprenorphine seems to contain a smaller risk of overdose compared to methadone because it produces relatively limited respiratory depression and is well tolerated by non-dependent people. Finally, theoretically the partial (agonist and (antagonist action of buprenorphine might make withdrawal from this medication less severe than from pure agonists, such as methadone and heroin, but more research is needed.

Buprenorphine has also proved to have abuse potential. Especially, when injected subcutaneously (but also intravenously or sniffed) it has shown to produce euphoria and opioid-like effects. In several countries (including Australia, France, Finland, New Zealand, Scotland and Spain) buprenorphine abuse has been reported.

Some research has suggested that initial induction onto buprenorphine can be useful before deciding on the most appropriate maintenance agent (Uehlinger, 1998).

Heroin, or diacetylmorphine is an opioid analgesic which is an illegal drug in most countries. Its main disadvantage is that because of its considerable shorter half-life, patients would need several medications per day, and thus, making it an expensive and inconvenient alternative. Only limited research has been carried out on this treatment option. The first research comes from the UK where psychiatrists have been able for a long time to prescribe heroin. It has only recently been systematically investigated in the form of controlled trials in some places (Switzerland, the Netherlands) as an alternative therapeutic treatment maintenance option (Uchtenhagen *et al*., 1999; Johnson, *et al*., 1999).

Route of administration: oral, injectable

Although most methadone is prescribed in oral form, there are several initiatives throughout the world to prescribing injectable substitution treatments. Some patients have poor performance on oral maintenance. Studies have compared groups that receive oral methadone to groups that receive injectable heroin or other substitution drugs. There is yet insufficient evidence which proves that prescribing injectable methadone maintenance has better results on the long term, in promoting healthy behaviour and risk reduction than oral methadone maintenance. All that can be said is that there may be significant risks and possibly some benefits associated with injectable methadone prescribing (Ward *et al*., 1998).

Psychosocial interventions

In most programmes, psychosocial interventions are considered a central part of methadone treatment. Research from the USA has demonstrated that there are several programme characteristics associated with treatment success, such as comprehensive services and the integration of medical, psychosocial, counselling and administrative services (Ball and Ross, 1991). McLellan *et al*. (1993) described that patients who received counselling and other psychosocial services with their methadone had better outcomes than those who only received methadone.

The importance of counselling as an adjunct to methadone in the treatment of opioid dependence is widely accepted. However, some limitations to counselling need to be addressed here. As is the case with any other patient populations receiving any kind of treatment, individual methadone maintenance patients may vary in their needs and they may differ in their responses to components of treatment. The need for counselling should therefore be assessed for each patient individually. Some patients need more assistance than others to get their lives in order and here, counselling may be helpful. On the other hand, there is no reason why stable patients without major life problems would require counselling at all.

Furthermore, experience teaches us that not all counsellors are equally effective in bringing about positive change in their clients. Whether the success of counsellors depend on teachable techniques or on personal characteristics of the counsellors, remains to be seen. In any case, there is a need to develop protocols and standards for counselling, which is not the scope of these guidelines. We highly recommend that initiatives be taken to produce special guidelines for counselling in methadone programmes.

Patients with psychiatric disorders could benefit from psychotherapy. However, there is no reason to believe that psychotherapy is a treatment for all opioid dependents.

Chapter 4: Practical issues of programme organisation

Methadone treatment services are organised in a variety of ways throughout Europe. Sometimes, local legislation only allows specialised centres to prescribe methadone while in other places general practitioners and community pharmacies are involved. One argument at hand is whether methadone treatment is considered a specialised service or part of primary care. This depends on local legislation and on the way health care is organised in a given area. Another argument is whether methadone treatment is based on prescribing or dispensing.

When a treatment system is developed in any country, it should be planned as an integral part of the community's overall resources to deal with health and social problems. It should be 'population-based' (WHO Expert Committee on Drug Dependence, 1998).

This chapter focuses on the elements that are vital in organising best practice of methadone treatment. The elements discussed include staff requirements, the role of other services and the physical setting of programmes.

Staff requirements

There is considerable variation across countries as to who can prescribe methadone medication for the treatment of drug dependence. Nevertheless, it always involves a medical doctor, be it a specialist, general practitioner or psychiatrist.

Training

It goes without saying that a medical doctor needs to be knowledgeable about specific issues related to opioid dependence in order to be an effective clinician. Training programmes are essential so that the doctor is equipped to carry out good clinical practice. Whether these training programmes are organised as part of the general training of doctors or only given to those who start working in the drug field remains open and dependent on the local situation. Obviously, the best practice would be a combination of the two. Medical schools should include drug dependence and the different forms of treatment in their curriculum. A specialised training programme should also be available to doctors who are about to start working in the field of drug dependence and methadone treatment.

Training possibilities are equally important for all other staff involved in the treatment of opioid dependence. The content of these courses should include the pharmacological, toxicological, clinical as well as psycho-social aspects of opioid dependence. Regular seminars, supervision and communication with colleagues always form an essential part in keeping abreast of current developments in any field of medicine.

Team work

Medical practitioners should not prescribe methadone in isolation. A multi-disciplinary approach to drug treatment is essential. If treatment is delivered by a general practitioner, the staff involved in methadone treatment should include the administrator and possibly the community pharmacy. If treatment is delivered in a specialised service, the staff of any treatment programme will include nurses and administrative personnel. Most programmes will also have social workers, counsellors and probably a psycho-therapist as part of the permanent staff or through liaison with other services. A full assessment of the patient, together with other professionals involved, should always be undertaken and treatment goals set.

Good management includes factors which are relevant to any type of organisation where people work together and where clients are involved. A clear description of each position including an detailed list of tasks are vital, as well as regular supervision. Regular team meetings will facilitate collaboration and case management of clients who need to see more than one staff member. Clear procedures within a programme are not only important for the staff but will also have an impact on the expected treatment outcome for the clients.

Role of the medical doctor

A doctor prescribing controlled drugs including methadone for the management of drug dependence should have an understanding of the basic pharmacology, toxicology and clinical indications for the use of the drug, dose regime and therapeutic monitoring strategy if they are to prescribe responsibly.

Irrespective of the composition of the staff of a methadone treatment programme, prescribing is the sole responsibility of the doctor signing the prescription. The responsibility cannot be delegated.

It is the responsibility of all doctors to provide care for general health needs and drug-related problems, regardless of whether the patient is ready to withdraw from drugs. It is the clinician's responsibility to

make sure that the patient receives the correct dose and that efforts are taken to ensure that the drug is used appropriately and not diverted onto the illegal market. Particular care must be taken with induction, especially in case of self-reporting dosage.

Clinical reviews of patients should be undertaken regularly, at least every three months, particularly of patients whose drug use remains unstable.

Role of the nurse

Nurses work with drug users in different settings, such as hospitals and drug treatment centres. Their role can vary from country to country. Their skills and techniques range from assessment of drug users, counselling, health education and carrying out treatment procedures, such as dispensing medication. Some are involved in wound care and the cleaning of abscesses. In most programmes, nurses are responsible for checking medication compliance and they co-ordinate the case management. In some programmes nurses assume the final responsibility for the treatment (Loth, 1998).

When take-home medication is prescribed, it is important that the patient is told that methadone and other prescribed drugs should be kept out of reach of children.

Role of the drug worker/social worker/counsellor

Drug workers can come from a variety of professional backgrounds, such as nursing, teaching, social work and the criminal justice system. Their professional function can be considered as the major part of the full range of psycho-social services required for comprehensive treatment. Drug workers may provide support, give advice and basic counselling, and may act as a client's case manager or key worker. They are often involved in other types of drug services, namely outreach work, needle exchange schemes and residential services.

The main function of a drug worker is to provide counselling to drug users and address family and personal relationships, child-care, housing, income support and criminal justice issues. The professional competence and clinical effectiveness is closely related to training, competent supervision, formal accreditation and personal skills.

Role of the clinical psychologist

Psychological techniques have become a central part of good clinical practice of drug dependence in most countries and are important adjuncts to pharmacotherapy. Clinical psychology provides models for drug dependence, combining social and neurobiological theories. For example, motivational techniques can be important in the assessment procedure in engaging drug users into treatment as well as preventing relapse during detoxification regimen. Patients with co-existing mental health problems can benefit from specific therapies, such as cognitive behavioural therapy.

Role of the pharmacist

Hospital pharmacists play a vital role when a patient, who is maintained on methadone, is admitted to hospital. They can advise clinicians and nurses of possible interactions of medications with methadone and how methadone can be prescribed appropriately on admission or discharge.

In some areas methadone is dispensed directly by community pharmacists. In this case, the prescribing doctor and the dispensing pharmacist should liase regularly about the status of the patient and the prescribing regime. Some countries advocate the possibility of supervised consumption in the pharmacy. If pharmacists are willing to do this they will need specific training and guidance and it goes without saying that the privacy of the patient should always be respected.

Pharmacists play a crucial role in checking on prescribing practices by monitoring prescriptions for drug interactions and of patient records. They can also check the legal validity of prescriptions and screen for errors. Apart from other services that pharmacies can provide such as the exchange or sale of injecting equipment, they can give information and advice to patients and refer them to drug treatment programmes.

Record keeping

Each intervention should be properly recorded and thorough, clearly written or computer records of prescribing should be kept. A patient-held record, countersigned by those involved in care, can be a useful adjunct to treatment. Other medical staff members who may see the patient should be informed of current treatment.

There is enormous variation in regulations about confidentiality throughout Europe. A central register where people receiving methadone are notified exists in some areas. This register should not entail

notification to any non-medical service or institution or have repercussions for the patient, such as loss of civil liberties. Its main purpose should be to protect the service, the service users and the service providers as well as to prevent multiple prescribing and to facilitate research or funding decisions (Irish Guidelines, 1997).

In areas where there is no register, there should be some form of control and monitoring of the prescription and supply of methadone.

Dispensing

The person whose name is on the prescription should collect the methadone himself, unless there are compelling reasons. At the early stage of treatment, methadone should be dispensed on a daily basis. When the patient is clearly making progress, the regimen can be reduced in gradual stages: from three times a week to twice weekly and finally weekly. It is not recommended to dispense more than a week's total dose at any one time, except for special arrangements and travel. The goal is to work towards maximum autonomy and control of one's own medication, for example using dispensing at community pharmacists.

In some countries supervised consumption has been recommended for some patients, especially for new entries. The need for supervised consumption for a longer period than just the induction phase should take the patient's social factors into account, such as employment and child care responsibilities.

Other services

As previously stated, the success of methadone treatment is partly influenced by the availability of other services than only pharmacotherapy. The importance of counselling and psycho- therapy has been discussed above. Liaison with other medical and social services have also been discussed elsewhere in this report. In case of co-morbidity, contact with other services should be encouraged and possibly co-ordinated by the staff of the drug team (case management).

It is considered part of the treatment programme to try to resolve any social, legal or medical problem. Other drug dependence services, namely the availability of clean injecting equipment either for sale or exchange and information on health and other risk behaviour, can form a welcome addition to the treatment programme. Finally, the presence of an outreach project in the area can be helpful in contacting

people who do not come to the existing services as well as keeping abreast of what happens in the drug scene.

Physical setting

A first condition for a programme is that it is safe. Safe in the sense that people can trust the workers and that personal information is treated according to medical standards and is not given to third non-medical parties. It may seem obvious, but essential for a successful programme is that people are being treated with respect and that their privacy is ensured.

A non-judgemental attitude of treatment staff is important. Some research has shown that in a methadone maintenance programme where the staff can be identified as "abstinence oriented" patients will leave quicker than when a programme is maintenance oriented. This difference ensued after correcting for methadone dosage (Vosseberg, 1998).

Another obvious pre-requisite for any medical service is that premises are clean. It is recommended that all staff involved in the treatment of opioid dependence be immunised against hepatitis B and undergoes tuberculosis control.

The location of the programme should meet some important conditions. Because patients will have to attend the programme regularly, and in many cases daily, it is important that it should be centrally located. Easy access to public transport is an advantage.

Opening hours should be flexible to accommodate clients who work. Ideally, the programme should open early on mornings or at the end of the working day, allowing people to attend the programme without having to lose part of their productive day.

In order to avoid stigmatisation it may be important to have a neutral façade, that the sign outside says something neutral, e.g. ‘health service’ instead of ‘unit for the treatment of drug dependence’.

It is recommended to seek contact with the local police corps in order to explain the importance of attracting people with a drug dependency to the programme without fear of coming into contact with the police. Agreements should be made to avoid the presence of police posting outside the centre or in

the neighbourhood which may cause panic and fear by clients and chase them away.

On the other hand, many new programmes will encounter community resistance when a drug treatment centre is started in the neighbourhood. Generally, drug services are thought to attract undesirable elements into localities and are seen to be associated with loitering, intoxication drunkenness, and house thefts. However, community resistance is mostly encountered before a programme has been established. Once they become operational, neighbourhoods seem to accept them.

When starting a new service in a given area, it is recommended to seek contact with community groups and representatives. Clear information should be given on the rules and regulations within the centre. Potential benefits of service provision and in particular, of the likely impact of reducing neighbourhood crime through the provision of treatment should be discussed. It may be important to set out rules and regulations for the clients to keep to in order to minimise any potential nuisance for the environment. An important rule would be to prevent clients from hanging around outside the premises.

Mobile units have been used in some places (the Netherlands, Italy and in Boston, USA), where it was not possible to establish permanent clinic sites. Mobile units have the added advantage in that they can reach out to more areas in a given territory.

Funding

In chapter two, we described studies which calculated the costs of methadone treatment in the USA and in the UK. Both studies concluded that methadone treatment is cost effective and that it is much cheaper to treat people with an opioid dependence with methadone than to leave them untreated on the streets. The new European Union Drug Strategy (2000-2004) emphasises that successful implementation of activities in the area of drug dependence necessitate appropriate resources (Council of European Union, 1999).

Who finances the costs of methadone treatment varies from one country to another. Some countries have methadone available free of charge to everyone undergoing treatment for opioid dependence. A percentage may come from health insurance, another part may be paid directly by the state. In some cases, patients pay for the treatment themselves. Funding of methadone treatment depends on the general finance system of health care in a given area.

An interesting system of funding has been introduced in Liverpool, UK. This 'Outcome Funding framework' is a joint investment and integration plan, where several public service departments work together, such as the City Council, the Social Services, the Probation Service and the Police. These investors developed and tested a system-wide approach to integrated planning, social delivery and funding (Dowds, 2000).

Consumer involvement

It is recommended that methadone patients be involved in the development and running of treatment programmes. Service users should be given regular opportunities to assess the services that they receive. Today, many programmes in Europe have service-user groups who work closely with clinical staff, and such groups should have an important voice in matters of policy and practice. Organisations such as NAMA, (National Alliance of Methadone Advocates), in the USA and The Methadone Alliance in the UK have demonstrated their value in supporting patients and enabling them to participate in the wider debate about drug treatments.

Such initiatives enable closer communication between patients and professionals, as well as better mutual understanding and concern. Some programmes also involve patients in the development of treatment protocols and facilitate access to patient advocacy services.
In the United Kingdom, following the adoption of the 'Patient's Charter', it is now common practice to involve health service patients in developing and shaping clinical services (Nelles, 2000)

Chapter 5: Monitoring and Evaluation

A great deal of research has been carried out on the different aspects of methadone treatment. Monitoring and evaluating services and programmes are an essential part of good practice. Most programmes will have some system of monitoring their activities: how many people are seen, with what frequency, how much methadone is prescribed, etc. However, evaluation of the treatment outcome or a costs-benefit analysis of treatment are rarely carried out.

One can argue whether a treatment that has shown to be efficacious, needs to be evaluated over and over again. The goal of the afore-mentioned Cochrane Collaboration is precisely exactly to prevent having to 'reinvent the wheel' by providing the available evidence for any given treatment and by updating it when new evidence becomes available on the electronic library published quarterly (http://update-software.com).

However, we have seen that the way in which treatment is offered is important for its outcome. It is therefore important that any service offered to the public should have a mechanism to evaluate its own success. It is important to have checking mechanisms to see if the different professionals are doing their work appropriately, or whether individual patients who are admitted into treatment are suited for that particular type of treatment.

Monitoring of the different activities should be common practice in any programme. Keeping records of activities is therefore essential, but even more important is giving attention to analysing these data. A descriptive analysis on the basis of the monitoring of activities is always possible and when set off against the costs of a given intervention, a cost-benefit analysis can be made.

For any type of evaluation of a given intervention it is essential to formulate a clear question, to define the objectives a priori and to assess the need of such intervention. Furthermore, it is essential to verify whether you are measuring what you want to know.

In addition to the well known quantitative methods of evaluation, such as monitoring of activities and making a descriptive or cost-benefit analysis, one can consider other types of instruments. A survey could be carried out among clients based on a questionnaire in order to check if clients are happy with what is being offered and the way in which it is offered to them.

Assessment of the quality of the service could be measured with more qualitative instruments, such as through a 'focus group', or in-depth interviews with workers, clients, consumer groups, neighbours, community leaders, police, etc.
It is always useful to involve external experts for this type of evaluation. Market researchers, management consulting or consumer unions could provide welcome suggestions to improve service delivery.

Evaluation should be an integral part of programmes, possibly by independent experts, and the results of these evaluations should be taken into account when designing new programmes. In this field, the European Monitoring Centre for Drug and Drug Addiction has issued, and will continue to issue, guidelines for evaluation of activities and models for the assessment of policies (Council of European Union, 1999).

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Appendix 1: List of experts involved

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Appendix 2: Recommended literature and useful websites

All literature referred to in these guidelines and reported in detail in the bibliography is relevant to the issue of methadone treatment for opioid dependence. However, some works are particularly useful because they provide a clear and practical overview on the issue. These include:

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Useful websites to visit are:

http://www.euromethwork.org

http://home.muenster.net/~indro/

http://www.doh.gov.uk/drugdep.htm

WWW.Q4Q.NL/METHWORK

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