Chapter 8 – Medical management of drug dependence: the doctor's role in managing heroin addiction

8.1 Introduction

This chapter examines management of drug dependence by medical practitioners. It then presents a detailed description of opioid substitution therapy (OST), the evidence for its effectiveness, and an analysis of the ingredients of effective treatment. This analysis provides a model for the components of effective medical management of drug dependence.

OST has been extensively researched, and evidence that it can reduce the adverse effects of heroin addiction has led to its widespread use internationally.[1] OST has always generated disquiet, as it challenges the intuitive notion that the best way to overcome addiction is to stop using drugs, and become drug free.[2] This chapter provides a brief overview of the extensive research evidence indicating that OST is as effective, or more effective, than short-term treatments aimed at 'cure' of heroin addiction, and describes the factors that have been identified as improving the outcomes of treatment.

In **Chapter 9**, medical responses to the use of other illicit drugs and drug-related harms are considered, while **Chapter 10** examines medical management of illicit drug use within the criminal justice system.

8.2 Managing drug dependence as a medical issue

Among people seeking treatment, heroin addiction tends to be a chronic, relapsing and remitting disorder, with few people achieving stable, sustained abstinence after an episode of care. The notion of medical management of chronic disease seems more useful than episodes of care.[3] The medical management of dependence is usually more difficult and challenging than for other chronic disorders. By the time they come for treatment, many dependent drug users are socially marginalised, or in prison, lacking access to the rewards arising from employment, personal relationships and family participation. As a result, there is little in their lives motivating them towards recovery. Treating heroin addiction frequently involves the social reintegration of marginalised individuals lacking in skills and having few and often tenuous social connections.

As outlined in **Section 4.4**, there is a positive correlation between the prevalence of problematic drug users aged 15 to 64 years and deprivation. Hospital admission rates for drug-specific conditions have also shown a strong positive association with deprivation. Deprivation appears to be a strong predictor of drug-related harm.

8.2.1 Tackling stigma and the 'addict identity'

The stigma surrounding drug use further complicates management. Drugs, especially illicit drugs, are viewed with fear and disapproval (see **Sections 2.5 and 6.4**). The stigma associated with addiction is a significant barrier in providing healthcare to people misusing drugs, as negative attitudes – on the part of both practitioners and patients – can compromise effective care (see **Sections 2.5 and 6.4**).

Stigma may have a public health benefit, in making certain risky or harmful behaviours less attractive, and the stigma associated with illicit drugs probably discourages many people from using them. Stigma can also attract troubled young people; which probably explains why many drug prevention programmes paradoxically lead to more, rather than less, drug use.[4] Breaking rules, and experiencing the disapproval of family and peers, confirms their sense of badness, while providing a self-defeating sense of autonomy and independence (see **Section 6.3.1**).[5] Drug use is reinforcing, producing wellbeing and relaxation and relieving negative mood states such as pervasive guilt and shame, or alleviating painful conditions. Repeated use can lead to the development of dependence syndrome (see **Section 1.1.2** and **Glossary**), with physical and psychological symptoms that include characteristic narrowing of the individual's range of interests and activities, as drug use comes to displace other activities. This can progress to increasing isolation, disrupted relationships with family, and loss of social supports. All these factors contribute to the development of the 'addict identity' – someone who has become conditioned to see himself existing outside of normal society, isolated and defiant.

For people with an 'addict identity', seeking treatment can seem like a defeat. Once in treatment, and able to stop compulsive drug use, it is not rare for the patient to sabotage his own treatment, for example by dropping out, or missing scheduled appointments, taking refuge in the familiar experience of failure, disapproval and conflict.[6] This desire for the familiarity of experience, and the associated learned behaviour, can be understood as a form of conditioning (see **Section 4.3.2**). There is a major element of behavioural treatment in how doctors, nurses and pharmacists respond to the challenge of disaffected, impulsive behaviour. Clinics delivering the same 'treatment' often achieve dramatically different outcomes, and the quality of the therapeutic relationship is one factor contributing to the greater effectiveness observed in some settings.[7]

8.2.2 Staff attitudes

Managing a chronic disease is based on a partnership between doctor and patient, and the patients' self-efficacy and responsibility for their own wellbeing are critical determinants of outcome. Managing addiction involves long-term support, educating patients about their condition, promoting engagement in and compliance with treatment, monitoring symptoms and dealing with complications.

Practitioners treating drug-dependent patients require not just skills and knowledge, but also a positive attitude towards treatment and recovery. Negative attitudes on the part of drug-dependent patients may sabotage treatment, but so too can negative attitudes on the part of practitioners. Four decades ago, Dole and Nyswander, pioneers of methadone treatment (MT) for opiate addiction, recognised the critical importance of changing the addict identity,[8] a change encapsulated in Marie Nyswander's phrase '*from drug addict to patient*'. Their theme was that, freed from the cycle of addiction and treated with respect and dignity, heroin users can develop a different image of themselves, and behave with self-respect and dignity. They emphasised that negative assumptions about drug users need to be balanced by a belief in their capacity to change, and a sense of the practitioner's role in fostering that change.[8]

8.2.3 Shifting opinion: is drug dependence 'sickness' or 'badness'?

A shift in viewing dependence, from 'sickness' to 'badness', has been documented in the USA, and labelled the '*demedicalisation*' of treatment.[9] The result was widespread delivery of treatment out of line with research evidence,[10] and a proliferation of programmes oriented to abstinence rather than medical maintenance treatment of opioid addiction (see **Section 8.4**). In response to the weight of evidence that OST can reduce the harms of heroin addiction, there has been a 'remedicalisation' of treatment of addiction in the USA over the last 15 years. From the mid 1990s, neuroscience research has been promoted as showing that addiction is a '*chronic relapsing brain disease*' (see **Section 1.1**).[11] In 2000, the passage by Congress of the Drug Abuse Treatment Act liberalised regulations surrounding treatment, permitting the use of office-based treatment of addiction for the first time in the USA.[12]

8.3 Example of managing drug dependence as a medical issue: OST

The following case study illustrates an example of heroin addiction.

Case study: Treatment of heroin addiction with injectable diamorphine

Mr HT is a 42-year-old man who has been receiving injectable diamorphine treatment since March 2010.

Mr HT was adopted at the age of six months. He found school challenging, and truanted from mid primary school. The secondary school he attended recognised that he had learning difficulties and he was sent to a boarding school for children with special needs. His behavioural problems worsened there. At the age of 14 he began using drugs, and he was expelled at the age of 15. He had not learned to read and write.

Instead of returning to his home, Mr HT went to live in a 'hippy compound', supporting himself with occasional manual work, busking and some begging. Aged 22 he came to London, sleeping on the streets and squatting. He was to live on the streets for most of the next two decades. Within two years he was addicted to heroin, spending £150 to £200 daily on the drug, gaining the money by begging, thieving and raiding phone boxes and parking meters. He acquired an extensive criminal history, including five periods of imprisonment. The first thing he would do on release from prison was 'score' heroin.

In 2004, a community drug project found Mr HT sleeping on the streets and offered him a bed in a hostel. He began an MT programme, but continued to inject heroin and crack cocaine. He lost his place in this hostel during one of his spells in prison. In 2007, again homeless, he was picked up by another community drug project and placed in a hostel. He restarted an MT programme, but continued to inject street heroin, and to smoke crack cocaine and cannabis. His health and personal hygiene were poor. When his peripheral veins were scarred and difficult to inject, he began injecting street heroin into his neck, and his hostel referred him to an NHS injectable opioid clinic in 2010. Here, diamorphine (pharmaceutical heroin) is prescribed for patients not responding to oral methadone. Administration of diamorphine is all supervised by trained staff, and the service users attend twice daily and engage in frequent reviews and keyworking (see **Glossary**) sessions.

When first assessed for diamorphine treatment, Mr HT expressed doubt that he would be able to attend the clinic twice daily seven days per week. For the first several months he remained chaotic and disorganised, often missing doses and continuing to use street drugs. His dose was progressively increased, until he was stabilised on 200mg

diamorphine intramuscularly twice daily and 70mg of methadone once a day. In August 2011, although continuing to smoke crack about twice per month, he had ceased illicit heroin use, and his personal hygiene, mood and outlook had improved dramatically. He acquired a publicly funded flat, and began occupational therapy sessions to improve his literacy.

Mr HT presented as someone who, having lived on the streets for most of his adult life, lived 'for the moment', with little capacity for planning, and little motivation or hope that his life might be different. His primary reaction is surprise that he has made such a vast improvement in his life.

Case study details provided by Dr James Bell, Consultant in Addictions Medicine.

The case history starts with a story that is not rare. Mr HT was a vulnerable adolescent with limited education and a disadvantaged background, and went on a downward spiral as a result of dependence on drugs. Criminal sanctions were no deterrent to his drug-using career, and he did not respond to methadone. At present, his downward spiral has been interrupted and reversed by diamorphine treatment. The continuing challenge is to build a sustainable recovery, based on self-care in stable housing and gaining employment. That would provide a basis for progressively reducing his frequency of injecting, and eventually returning to oral medication.

Prescribing diamorphine for heroin addicts is a poorly understood, often controversial, modality of treatment. Diamorphine has been shown to reduce heroin use and improve self-reported quality of life in those who are not responding to MT,[13-15] but there has been little reflection on why injectable treatment has advantages over oral medication. This case history is presented to illustrate some of the reasons why prescribing diamorphine can have advantages over other treatment approaches. This is discussed further in **Section 8.4**.

Opioid substitution therapy is the prescribing and administration of a pharmaceutical opioid as a 'substitute' for illicit opioids, to patients who have become dependent. The most common form of OST is MT, but there is a rapidly increasing experience with buprenorphine, and a small experience with prescribed diamorphine (pharmaceutical heroin) in the management of heroin addiction.

In the 1980s, recognition that injecting drug use represented an important mode of transmission of HIV and other blood-borne viruses led to increasing provision of OST internationally.[16] Methadone is the most commonly used OST medication, and has the most extensive literature surrounding it. There has been increasing delivery of MT in primary care worldwide, placing medical practitioners in the frontline in delivering treatment.

Although it is thought of primarily as a pharmacological treatment, OST has important behavioural and interpersonal elements that contribute to outcome.[7] Opioid substitution requires ritualised, daily attendance for administration in a predictable, safe, non-punitive and non-judgemental treatment space, and establishment of a long-term therapeutic relationship with a keyworker (see **Glossary**) or doctor (see **Section 8.4.3**).[7] For a small proportion of people, the respite from withdrawal offered by MT is not sufficient to allow them to move away from repetitive heroin use.[7,17] For many marginalised individuals with little sense of purpose or planning beyond short-term survival, prescribed diamorphine is sufficiently reinforcing to motivate them to attend and comply with the requirements of treatment. Daily attendance provides a structure and routine in a previously chaotic life. Clear rules and expectations of behaviour, enforced consistently, offer a new (and sometimes challenging) experience for previously asocial or antisocial individuals.

The cornerstone of treatment is an adequate dose of opioid – in the words used by patients on prescriptions, the dose that 'holds' them. Psychodynamic psychotherapy involves 'holding' clients with the experience of empathy, while allowing them to come to terms with their own unacceptable thoughts and impulses. Prescribing opioids 'holds' patients with medication, while allowing them to explore the challenging possibility that they are acceptable, and capable of social reintegration.

8.3.1 The effectiveness of OST

Traditionally, treatment of dependence on alcohol and drugs has been based on two premises – that recovery from addiction requires abstinence from drugs, and that it requires a change of attitude and identity. The principle of OST – that people can recover while still dependent on an opioid – has challenged the assumption that the objective of treatment should be abstinence from all drugs (including methadone).This is currently re-emerging as an issue in the UK, as there are proposals in the *Drug strategy 2010* that the funding of drug treatment services should reward abstinence from all drugs.[18]

A comprehensive Health Technology Assessment undertaken in the UK in 2007 reviewed the evidence for the effectiveness of methadone and buprenorphine, and concluded that both drugs were effective in treating opioid dependence.[17] This finding was based on a synthesis of randomised trials, observational evidence

and expert opinion. This section seeks to go beyond the finding that OST is effective, and investigate how well it achieves the many different objectives of treatment of drug dependence.

8.3.2 Is OST effective in promoting abstinence from all drugs, including OST medications?

International studies suggest that for opioid-dependent persons in the criminal justice system, and those seeking treatment, addiction is a chronic, relapsing and remitting condition. People cycle through differing episodes, and differing modalities of treatment. In 2001, Hser et al reported on a group of heroin addicts in the USA, followed up 33 years after entering treatment.[19] Forty per cent were dead; many remained addicted. Among those who achieved prolonged abstinence, one-quarter had eventually relapsed in subsequent observations. Relapse was observed even among patients abstinent for as long as 15 years. Long-term follow-up studies documenting the natural history of heroin addiction estimate that among subjects who seek treatment, 2 to 5 per cent per year achieve stable abstinence from opioids.[20,21]

It has been argued that this view is overly pessimistic, and many more people can and do recover from dependence on drugs. The phenomenon of spontaneous recovery from addiction has been well documented.[22] Community surveys (notably, the Epidemiological Catchment Area (ECA) study from the USA), have identified a number of respondents who report previous dependent use of drugs, but are no longer dependent, confirming that many people do 'recover' from dependence. The prognosis for people who seek treatment for drug dependence is consistently worse than in non-treatment samples. Among people seeking treatment for addictive disorders, whether alcohol dependence[23] or heroin addiction,[22] the course of dependence tends to be chronic and relapsing, and recovery is less likely in this group than among people who never seek treatment. The reason for this disparity is most likely that people who present seeking treatment have more severe problems – '*problems that will not be resolved just by getting them off drugs*'.[22]

This is not to suggest that individuals cannot leave MT and remain abstinent. People leaving MT are less likely to relapse if they have ceased injecting heroin, and have achieved a degree of social reintegration – employment, a stable relationship, or community connections – before they attempt to withdraw from methadone.[24]

To optimise the effectiveness of OST, the NTA's Recovery Orientated Drug Treatment Expert Group has drawn attention to the importance of delivering OST in line with National Institute for Health and Clinical Excellence (NICE) clinical guidance. In their 2012 report, the group advised doctors and health professionals working with heroin addicts to:

- review all existing patients to ensure they are working to achieve abstinence from problem drugs
- ensure treatment programmes are dynamic and support recovery, with the exit visible to patients from the moment they walk through the door
- integrate treatment services with other recovery support such as mutual aid groups, employment services and housing agencies.[25]

A recent study from Scotland confirmed the protective effect of methadone treatment on mortality, but also found that longer duration of methadone treatment was associated with less likelihood of achieving abstinence from heroin.[26] This has been interpreted as showing that treatment with methadone may actually impede recovery from dependence, but a simpler explanation is that people with more severe problems tend to remain in treatment longer, and have a poorer prognosis.[26]

The implication of the chronic, relapsing nature of heroin addiction is that responding to an individual seeking help for heroin addiction is best conceptualised as management of a chronic disease, characterised by exacerbations and remissions (see **Glossary**), variable levels of disability, and risk of complications. The objectives of long-term management are reduced risk of death and disease, suppression of drug use, improvement in mental health and outlook, and restoration of impaired social roles. These are the key elements of 'recovery', and each element – cessation of heroin use, reduction in other drug use, improvements in health and social functioning – supports each other element in a holistic, biopsychosocial approach to chronic disease management.

8.3.3 How effective is OST in suppressing the use of illicit drugs?

Three major large-scale observational studies from different countries provide a reasonably clear indication of the effectiveness of OST in suppressing use of heroin, use of illicit drugs such as cannabis and cocaine, and misuse of alcohol and benzodiazepines.[27-29] These studies compared the effectiveness of OST with that of residential rehabilitation (RR), a drug-free approach to treatment involving prolonged residential treatment in a highly structured environment based on self-help and mutual support (see **Glossary**). Some observational studies have also compared OST to short-term detoxification (see **Glossary**).

The Treatment Outcome Prospective Study (TOPS) followed a large sample of US patients treated in RR and on MT.[27] The National Treatment Outcome Research Study (NTORS) was undertaken in the UK, using a similar methodology to TOPS,[28] and the Australian Treatment Outcome Study (ATOS) followed samples of heroin users entering RR, MT, detoxification or no treatment.[29]

These studies provide surprisingly consistent results. Over time, heroin use was reduced, with 25 to 35 per cent of heroin users reporting continuing heroin use 3-5 years after beginning their index treatment. Many were still in treatment at follow-up, and the majority of subjects had been though several episodes of treatment, making it difficult to attribute outcomes to any particular treatment modality – and emphasising that treating heroin addiction is best conceptualised as chronic disease management.

Three-quarters of subjects were using other drugs, mainly cannabis and alcohol. This is important, as there are few 'pure' heroin users, and most people entering MT have used, or are using, multiple drugs.[22] Results of large-scale, observational studies suggest both OST and residential, drug-free programmes seldom result in long-term abstinence from all drugs, and that alcohol misuse and cannabis use are common.[27,29]

The NTORS demonstrated that for every pound spent on treatment in the UK, a reduction of £3 in public costs was observed.[30] Economic benefits were largely accounted for by reduced costs of crime. Among clients recruited to NTORS (549 in total, recruited from 54 residential and community treatment programmes), criminal behaviour costs were estimated to fall by £16.1 million during the first year of treatment, and by £11.3 million during the second year.[31] The findings demonstrate that there are clear economic benefits to directly funding treatment of drug users, which far outweigh the costs.

8.3.4 How effective is OST in improving physical and mental health?

Opioid substitution reduces the risk of death by overdose, the commonest cause of death among active heroin users. There is a long-recognised risk of death during induction into MT, and an increased risk of death by overdose after leaving any form of treatment. Clausen and colleagues had the opportunity to follow risk of death in subjects entering MT, and in subjects placed on a waiting list for MT.[32] This study demonstrated the protective effect of entry to treatment; despite risks during induction and an increase in mortality after leaving treatment, subjects entering MT had a lower risk of death than those placed on a waiting list for treatment. There is some indirect evidence that the reduction in risk for those entering treatment translates into a public health benefit. In France, in 1994, there were only 52 people

in treatment with methadone, and an estimated 160,000 people injecting illicit opioids. Five years later, there had been an expansion in MT to 7,000 people, and 60,000 people were being prescribed buprenorphine. Deaths from heroin overdose in France fell from 505 in 1994 to 92 in 1999.[33] A similar observation was made in Sweden following liberalisation of access to OST, particularly buprenorphine.[34] The number of patients in treatment increased more than threefold from 2000 to 2006, with the greatest increase for buprenorphine, which was introduced in 2000. There was a significant 20 to 30 per cent reduction in opioid-related mortality and inpatient care between 2000-2002 and 2004-2006 but not of other drug-related mortality and inpatient care. A small but significant increase in buprenorphine- and methadone-related mortality occurred. The authors concluded that liberalisation of Sweden's drug policy, and expanded access to OST, contributed to a decrease in overall opioid-related mortality and inpatient care.

Opioid substitution also reduces the risk of transmission of blood-borne viruses (HCV and HIV), particularly in conjunction with availability of clean needles and syringes.[35,36] There is considerably less data on which to assess mental health outcomes. Residential rehabilitation programmes usually place emphasis on attitude change and growth of a new consciousness. In TOPS, at five years post treatment, improvements in depression were identical in the MT and RR cohorts.[27] The ATOS study reported substantial self-reported reductions in risk taking and injection-related health problems, and improvements in general physical and mental health.[29] Positive outcomes were associated with more time in maintenance therapies and RR and fewer treatment episodes.

A 2010 review of studies of quality of life among opioid-dependent individuals identified 38 articles addressing the topic.[37] The results were quite mixed, but a few conclusions emerged. The subjective quality of life (QoL) and health-related quality of life (HRQoL) of opioid-dependent individuals is relatively low compared to the general population, and is most comparable with the QoL of individuals with psychiatric problems. Users of opioid drugs reported lower scores on mental health in particular, while their physical wellbeing was less affected. Entry to substitution treatment generally had a prompt beneficial effect on QoL, although this may reflect the fact that people enter treatment in very poor condition.[38]

The influence of drug use on HRQoL was inconsistent, although a negative impact of excessive alcohol use on the HRQoL of opioid users was shown in various studies.[37]

8.3.5 How effective is OST in improving social reintegration of marginalised heroin users?

One of the primary reasons for public support of treatment for heroin addiction is that treatment is associated with reduced acquisitive crime. To the extent that people in treatment reduce their use of illicit drugs (and reduce expenditure on illicit drugs), the level of acquisitive crime diminishes in individuals in treatment.[39] An Australian analysis of community rates of offending has demonstrated a statistically significant link between increased numbers in MT and falling levels of acquisitive crime in the community.[40]

There are very few quantitative data available on which to assess the extent to which people in MT are able to achieve social reintegration. One early randomised trial comparing MT to drug-free treatment included intensive psychosocial input, comprising vocational retraining and limit setting in relation to continued drug use. It is one of few studies demonstrating that MT can dramatically improve social reintegration.[41] The control group received no treatment, as none accepted drug-free treatment. At two years, 12-17 MT subjects were not using heroin regularly, and were employed or undertaking education. The remaining five subjects had been discharged from the programme for continuing drug use. These impressive results were dramatically better than the outcomes observed in subjects randomised to drug-free treatment, and, although the sample size was small, the study provides clear evidence that, with appropriate resources and policies, MT can contribute to social reintegration.

8.4 What are the components of effective OST?

There has been a proliferation of models of MT, with clear evidence that some treatment programmes are more effective than others.[7,42,43]

Ball and Ross investigated what actually occurred in treatment in six clinics in the USA, and compared the outcomes of patients treated in these clinics.[7] They reported that clinics achieving better outcomes had an '*orientation to maintenance*' (as opposed to an orientation to abstinence; see **Section 8.4.4**), had on-site medical services, and were better managed, with stable clinic leadership. They reported that patients who did better had received higher methadone doses, and reported a good relationship with at least one clinic staff member.

8.4.1 Drug and dose – the pharmacology of OST

Drug use starts out primarily as pursuit of the euphoric effects of drugs, but dependent drug use comes to be primarily driven by the compulsion to avoid withdrawal. The appeal of OST for dependent heroin users is that a daily dose of methadone (or buprenorphine) will abolish withdrawal symptoms (see **Section 8.3**). A dose of methadone means opioid-dependent individuals are no longer sick when

they are not using heroin, and this increases their control over their heroin use.[44] Methadone doses of 30-50mg/day are sufficient to block withdrawal for 24 hours in the majority of dependent heroin users. For around 10 per cent of heroin users seeking treatment, respite from withdrawal is sufficient to enable them to cease drug seeking and drug use.[25]

Heroin use is a powerfully reinforcing and motivating factor shaping the behaviour and consciousness of people who have been addicted. Dependence and the additional conditioning (see **Section 4.3.2**) associated with injecting drug use mean that in the first months of treatment, people maintained on low doses of methadone tend to continue injecting. By increasing the daily methadone dose, patients' tolerance to opioids is progressively increased, and high tolerance attenuates the individual's response to injected heroin. Heroin becomes less reinforcing, helping to extinguish the habit. This explains why high-dose methadone is far more effective in suppressing heroin use than low doses. A reasonable approach to dose setting is that after entry to treatment, the methadone dose should be progressively raised until patients cease heroin use, or reach a dose of 100mg/day. Once patients have ceased use of heroin for a period, it may be reasonable to lower the dose of methadone if side-effects are problematic, but there is a significant likelihood that, as doses are lowered, patients will return to heroin use.[45]

Not everyone responds to adequate doses of methadone. Up to one-third of heroin users metabolise methadone sufficiently rapidly that they experience low-grade withdrawal symptoms in the latter half of the dosing interval, when their blood concentration of methadone is falling. These patients experience withdrawal dysphoria, low mood and craving, and are more likely to persist in heroin use and to use other drugs.[46,47] Increasing the methadone dose in these subjects is unlikely to be effective, as the problem is not the absolute blood concentration of methadone, but the rate at which the concentration is falling.[46] In patients who have continued to use heroin despite receiving doses of methadone of 100mg/day, it may be that buprenorphine, or slow-release oral morphine, would be more effective in suppressing withdrawal symptoms and heroin use.

Qualitative interviews with a group of patients maintained on methadone provide an idea of the role of medication in enhancing social reintegration.[44] Gaining control over one's life and daily functioning and no longer being sick when no heroin is available, were only some of the frequently mentioned benefits of following a MT programme. The respondents emphasised that methadone did not cause changes in their lives, but allowed change to occur in important areas such as relationships. Methadone treatment can create the necessary preconditions to deal with a number of issues (eg developing one's skills to practise a job) that can enhance individuals' quality of life. Opiate-dependent individuals valued methadone's ability to help them

function normally, overcome their psychological problems and dependence on illicit opioid drugs, and support them in achieving certain life goals.[44] Stigmatisation, discrimination, dependence on methadone and the drug's paralysing effects on their emotions were mentioned as common negative consequences. A number of consequences (difficulty and unpleasantness of withdrawing from methadone, and stigmatisation) were mentioned as having a negative impact on important aspects of being in treatment.[44]

Buprenorphine

Buprenorphine is a partial opioid agonist, with different pharmacological properties to methadone. It has high mu-receptor affinity, remaining bound to opioid receptors for longer periods than drugs such as morphine or methadone. While receptors are occupied, they can no longer be activated. At low doses, buprenorphine is a potent opioid agonist, but as doses are increased, opioid receptors remain occupied and blocked, meaning that the effects of buprenorphine are self-limiting. Above quite low dosage levels, increasing doses prolong opioid actions, but do not produce increased sedation or respiratory depression. Buprenorphine has greater safety than other opioids in overdose.

Buprenorphine has a prolonged half-life, and a single daily dose produces sufficient opioid activity to block withdrawal for 24 hours or longer. Through prolonged receptor occupancy, buprenorphine also attenuates the response to heroin. It is thus a useful drug in treatment of addiction, and it has been used in OST for many years. A Cochrane review examined trials comparing buprenorphine and placebo, and reported that buprenorphine was statistically significantly superior to placebo in retaining patients in treatment and suppressing heroin use (although low doses of buprenorphine were not effective in suppressing heroin use).[47] Comparisons with methadone were reported as showing that methadone was more effective than buprenorphine in retaining patients in treatment.[48]

Buprenorphine is an important treatment option, for two reasons. Firstly, some patients tolerate methadone poorly, and the availability of buprenorphine provides a valuable alternative. More importantly, buprenorphine treatment is associated with a lower risk of death by overdose than that associated with MT.[49]

Diamorphine

For a small proportion of patients, relief from withdrawal is not sufficient to motivate them to comply with treatment. In this group of '*poorly motivated or treatment-resistant*' patients, who persist in heroin use despite other forms of treatment, injectable diamorphine has been shown to be effective in reducing street heroin use and improving self-reported quality of life.[13,15]

The rationale for this treatment is that, as illustrated by the case study at the start of the chapter, and discussed in **Section 8.3**, diamorphine is a more reinforcing drug than methadone, and provides a greater incentive to comply with treatment than methadone. Most of these participants have lost family support, and are so entrenched in a daily cycle of drug seeking and drug use that they have little other reward in life, and little capacity to hope or imagine that things might ever be different. Injectable diamorphine treatment is highly structured, requiring twice-daily (or more frequent) attendance to administer diamorphine under medical supervision. These onerous requirements deter many individuals who are addicted to heroin from participating in this treatment, but for others, access to diamorphine provides sufficient motivation to comply with the requirements of treatment. For many demoralised trial participants, the transition (not always smooth) from addict to patient begins a process of social reintegration that is made possible because sufficient incentive is offered to participate in structured treatment.

8.4.2 Supervised administration

The randomised trials establishing the effectiveness of methadone, buprenorphine and diamorphine treatment have all involved supervised administration.[13-15,48,50] There has been a substantial deviation from the model of care supported by evidence, namely a reduction in the requirement for supervision of administration. Although the benefits of supervised administration of OST are recognised and understood by patients,[51] they have received relatively little study. There is only one randomised controlled trial (RCT) comparing supervised and unsupervised treatment, and it showed no difference in effectiveness.[52] Entry criteria for the study were restrictive, and only 22 per cent of new entrants to treatment were eligible for randomisation. The main reason for excluding potential subjects was homelessness. For people in chaotic circumstances, it is plausible that structured treatment is more likely to be effective (see **Section 8.2**), while for those who are reasonably high functioning, the requirement to attend daily for treatment may well be a deterrent to participating. By only randomising relatively stable patients, this study would have missed the main potential benefit of supervised treatment, which is to treat marginalised individuals living in chaotic circumstances. At present, all that can be concluded is that for patients who have stable housing and no active mental health problems, treatment without direct observation of administration was as effective as supervised treatment.

Reports from France have shown that less clinical monitoring was associated with more heroin use and more injecting or prescribed buprenorphine,[53] and that less supervision of administration was associated with worse retention and more heroin use.[54]

There have been a variety of studies confirming that clear policies and expectations of behaviour produce better treatment outcomes. The most recent (2010) came from the USA, demonstrating that structured treatment (delivered according to protocol), is more effective than treatment that does not follow protocol.[55]

8.4.3 Counselling

There have been two randomised trials, both from the USA, comparing the effectiveness of differing levels of counselling in MT. The first reported that the provision of counselling and support improved outcomes – several counselling sessions were more effective than few, and few were more effective than none.[a,56] The second showed no difference in outcome between new entrants to MT offered no counselling, monthly counselling or weekly counselling.[57]

Interpretation of these trials is compromised by the fact that neither could be conducted double blind. Treatment is more likely to be effective when staff believe in the treatment they are delivering. In a trial to demonstrate the potential value of interim methadone (without counselling), it is probable that staff believed this approach would be effective – and it was.[58] In the McLellan trial,[56] staff probably believed that those who were randomised to minimal counselling were receiving suboptimal care – and found they were. The most plausible interpretation is that when staff believe in the treatment they are providing, it works better.[58]

The McLellan study,[56] finding benefit from formal counselling, is also at odds with the experience of Dole and Nyswander, who reported that although counselling was offered to their patients, very few availed themselves of it.[8]

Consistent with these observations, a recent Cochrane review analysed the results of trials of psychosocial interventions in conjunction with OST, and found no significant benefit of psychosocial services in terms of retention, non-prescribed opioid use, psychiatric symptoms, compliance or depression.[59]

This finding does not negate the possibility that some individuals can benefit from psychological interventions, but in randomised trials no benefit was shown overall. While there is little evidence for formal counselling, there is substantial evidence that the quality of interaction between a patient and staff is an important ingredient of treatment (see **Section 8.2.2**).[7]

a One treatment group received no counselling; the second group received counselling on a weekly or biweekly basis; and the third group received the same as the second but could also access additional sessions with a psychiatrist, an employment counsellor and a family therapist.

It is worth reiterating that daily interaction with health professionals, in a non-judgemental, non-punitive environment in which there are clear rules and expectations of behaviour, enforced consistently, offers safety and structure to previously marginalised and chaotic individuals.

8.4.4 Orientation to maintenance

Longer periods in MT (and in RR)[b] are associated with better treatment outcomes – the duration of treatment is a linear, non-threshold predictor of outcome, with better outcomes from longer treatment.[61] After leaving treatment, relapse is usual.[26] Time-limited MT is not effective.[62,63] For these reasons, there are risks associated with encouraging or pressuring patients to withdraw from treatment, and OST is best regarded as a maintenance intervention.

The majority of patients aspire to an opioid-free life without methadone,[44] and an orientation to maintenance does not mean that people should be discouraged from seeking to withdraw from treatment if they are doing well, and have sufficient 'recovery capital' (social supports such as a relationship, job, family support, affiliation with mutual support groups – see **Glossary**) to sustain long-term abstinence. People who achieve good social reintegration, particularly employment, are more likely to be able to leave treatment without relapse.[24]

While, in general, individuals should be encouraged to remain in treatment, patients who are deriving no observable benefit from treatment, or who are compromising the safety of the treatment space, may need to be discharged. An unstructured environment without enforced expectations is unlikely to be a therapeutic environment.

8.4.5 Patient education and relapse prevention

The controlled withdrawal from an opioid is termed detoxification (see **Glossary**). Patients should be given detailed information about detoxification and the associated risks, including the loss of opioid tolerance following detoxification; the ensuing increased risk of overdose and death from illicit drug use; and the importance of continued support to maintain abstinence and reduce the risk of adverse outcomes.[64] Following detoxification, rehabilitation, or other periods of abstinence from opioid use, relapse is common.[65,66] Relapse prevention is discussed in more detail in **Section 9.5** and is likely to require continued community support in addition to the teaching of relapse prevention skills.

b The therapeutic community (TC) (see **Glossary**) for the treatment of drug abuse and addiction has existed for about 40 years. In general, TCs are drug-free residential settings (residential rehabilitation) that use a hierarchical model with treatment stages that reflect increased levels of personal and social responsibility. Peer influence, mediated through a variety of group processes, is used to help individuals learn and assimilate social norms and develop more effective social skills.[60]

Long-term favourable outcomes are more likely in those who remain in some kind of treatment, whether this includes OST with community support, or abstinence with community support, for example participation in Alcoholics Anonymous (AA), Narcotics Anonymous (NA) or other mutual-help programmes (see **Glossary** for further information on AA, NA and mutual-help groups).[67]

8.4.6 The role of naltrexone in relapse prevention

The opioid antagonist naltrexone is licensed in its oral form for use as an adjunct in relapse prevention for people who have undergone opioid detoxification, to help them remain abstinent. An essential safety precaution for the medical professional to be aware of and educate patients about is the risk of a fatal overdose if they return to heroin use after naltrexone treatment, because of loss of tolerance to heroin.[68]

While pharmacologically it is consistent that naltrexone would be an effective preventive strategy, the use of oral naltrexone requires significant motivation to remain compliant, and thus for it to be an effective therapeutic strategy. The results of studies have not been favourable, except in cases where there are added significant external motivating factors, such as might be the case for an opioid-dependent health professional.[69] Long-acting naltrexone preparations, in the form of an implant or depot, are not currently licensed in the UK. In a series of small trials, and one large study from Russia, implants were demonstrated to be superior to oral naltrexone and to placebo in reducing the risk of relapse.[68]

8.5 The limitations of treatment for heroin addiction

Like all forms of treatment for drug dependence (and like management of most chronic diseases), OST relies on patient motivation – willingness to accept treatment and, more importantly, the willingness, personal resources and social opportunities to take advantage of the respite from dependence to take steps towards sustained recovery.

8.5.1 Patient choice and motivation

The importance of patient choice and motivation was illustrated in an early randomised trial reported by Bale et al in 1980, in which 457 patients completing inpatient detoxification for heroin addiction were randomised to either MT or RR.[70]

Based on a retained-in-treatment analysis, both methadone and a long-term TC were more effective than no treatment or short-term treatment, but – as in other comparisons between these modalities – did not differ significantly in terms of heroin use, other drug use, crime or employment.[70]

The important aspect of this study was the failure of most subjects to accept any ongoing treatment, and especially failure to accept allocation to a treatment that they did not want.[70] It is an important illustration about the treatment of heroin addiction. The assumption underlying most clinical trials in medicine, that people will accept allocation if there is a reasonable expectation that the alternative treatments will be safe and effective, does not apply to people seeking treatment for addiction. Individuals who are addicted to heroin only enter treatment if it is perceived to offer some advantage over their drug-using state.[71] Often this means entering treatment during crisis, and only remaining in treatment until the crisis is past.

In the Bale study,[70] methadone attracted a significantly higher proportion of patients than RR. Methadone treatment is as effective as other modalities of treatment, and the public health rationale for supporting OST is that it attracts and retains in treatment a higher proportion of heroin users than other treatment modalities.[72] Participation in treatment is often patchy, with people cycling in and out of treatment, having periods of heavy drug use, periods of treatment, periods of abstinence or controlled drug use, relapse to dependent use, and return to treatment.[73] The ATOS study established that the best outcomes were associated with people remaining in continuous treatment for prolonged periods, rather than cycling through treatment episodes.[29]

8.5.2 The need for alternative rewards

A second limitation of OST is that people need alternative rewards in their lives if they are to recover from drug dependence. The rewards of everyday life – for most people, a stable, intimate relationship, employment, and family life – are less accessible for people who are marginalised by drug dependence, and lacking in interpersonal and vocational skills. Employment is a key step in social reintegration, and in settings in which unemployment is high, and social cohesion low, prospects for sustained recovery are compromised. There is some evidence that participation in training and employment can be fostered by treatment. In the Swedish trial described earlier,[41] two-thirds of patients receiving methadone were in employment or training two years after programme entry (compared to none in the group randomised to no treatment). Social reintegration in two-thirds of subjects receiving MT is an impressive outcome. This occurred in a programme providing 'intensive' psychosocial input, including vocational retraining. The programme also involved limit setting – subjects persisting in heroin use were discharged. It is not possible without further research to ascertain whether it was psychosocial support, limit setting, or both, that contributed to better outcomes. This is an issue for further investigation.

8.5.3 Subtherapeutic dosing

The greatest limitation on the effectiveness of MT is that subtherapeutic dosing remains common, even among patients who persist in daily heroin use. Evidence suggests subtherapeutic dosing is common in the UK, where the mean methadone dose is 56mg per day,[74] below the 60-120mg range recommended in national guidelines.[75] This low dosing is associated with high levels of persisting heroin use, with more than 60 per cent of patients in treatment reporting heroin use within the preceding month.[76] Indeed, it is common for people who prefer to use heroin to enter MT as a protection against the daily experience of withdrawal, but to remain on low doses in order to be able to use heroin and experience the reinforcing effect. The evaluation of '*low-threshhold*' methadone in Amsterdam showed that failure to suppress heroin use did not protect against blood-borne virus transmission.[77]

8.5.4 Opioid dependence as a chronic medical condition

Part of the problem is that methadone is not really seen as medical treatment – by patients, or by health professionals. Patients and practitioners reflect community assumptions that drug use is a matter of personal responsibility, rather than a disease, and many heroin users are reluctant to see themselves as ill. Adopting the role of 'patient' involves relinquishing their 'addict identity', and they may prefer to see participation in treatment as taking advantage of the supports available to them rather than seeking to recover.[78] Practitioners who prescribe methadone have been noted to have polarised assumptions about the nature of treatment.[79] Some see it as a way to control deviance and reduce crime, others as support and palliation for disadvantaged patients. It is uncommon for doctors to think of it as management of a chronic medical condition.

8.6 The safety of OST

Heroin addiction is associated with increased risk of death, predominantly by overdose. While in MT, heroin users are substantially protected against the risk of death by overdose. The overall protective effect is diminished by two factors.

The first is the risk of death of individuals not in treatment, as a result of diversion (see **Glossary**) of methadone. The primary mechanism for reducing diversion is supervised administration. In the UK, increased supervised administration has been associated with a reduced number of deaths relative to the total amount of methadone dispensed.[80] As discussed earlier, there is evidence that buprenorphine is associated with fewer overall deaths proportionate to the amount prescribed.[81]

The second is that there is an increased risk of death during the first two weeks of treatment, and in the month after leaving treatment.[75] Induction into MT involves inducing a high level of tolerance to opioids, such that usual doses of street heroin cease to be reinforcing. This must be undertaken gradually, starting with doses in the

range 20-30mg/day – doses that would be safe in non-tolerant individuals. There is consistent evidence that during induction into MT, there is an increased risk of death by overdose. This is the basis for clinical guidelines recommending slow induction and close monitoring during the first week of MT.[75]

Overall, as elegantly demonstrated by a Norwegian study, the risk of death for heroin users is diminished by entering treatment.[32] In the short term, the risk of death appears lower for people entering MT than for people entering abstinence-oriented treatment, particularly detoxification.[82]

Offsetting the protective effects on mortality among people who enter treatment is the risk of fatal overdoses resulting from diversion of medication prescribed in treatment programmes. Diversion is an inevitable accompaniment of OST, and around two-thirds of methadone-related deaths occur in people who were not in receipt of a prescription.[83] In the UK, guidelines on increasing supervision of dosing appear to have reduced the rate of fatal methadone overdoses.[80]

8.6.1 Reducing drug-related deaths at times of increased risk

In doses that exceed an individual's tolerance at any one time, opioid drugs can cause respiratory depression and death. Experiencing or witnessing an overdose is a common occurrence among users of illicit opioid drugs,[84] but prescribed opioid drugs also carry these risks. It is essential that the medical professional understands the process of careful and safe assessment and prescribing, as well as recognising the times when a patient is most at risk. While OST has a greater than 85 per cent chance of reducing overall mortality among users of opioid drugs if the average duration approaches or exceeds 12 months,[66] in the first two weeks of OST, the mortality rate has been found to be three times higher (after adjustment for sex, age group, calendar period, and comorbidity) than that during the rest of the time on treatment.[66] Overdose may occur if the initial dose is too high or if patients continue to use non-prescribed opioid drugs during this time.[66,85] Although further research is needed on which to base better and safer management of OST, closer supervision of induction of treatment is important.[66] This requires careful titration, but may also include repeated urinary drug screens, clear safety and educational advice to the patient, and frequent reviews. All patients starting an MT programme must be informed of the risks of toxicity and overdose, and the necessity for safe storage of any take-home medication;[64,86-88] and supervised daily consumption is recommended for new prescriptions, for a minimum of three months.[75]

Overdose in heroin users is common,[84] with intravenous drug use, polydrug use, early heroin use, not being in MT, and the initiation of substitution treatment all being periods of increased risk, in addition to being early in a period of abstinence

following opioid use, whether the abstinence is voluntary (such as detoxification in the community) or involuntary (such as in the prison setting).[84,89] The mortality rate is increased by eight- to nine-fold in the first four weeks after MT has stopped.[66]

Strategies to reduce the mortality rates from opioid overdose at these high-risk times are essential. One important strategy is training users of opioid drugs themselves,[84] and also healthcare staff and carers,[90] in the recognition of opioid (and other drug) overdose in the community and prison setting, and how to respond, including administration of the opioid antagonist naloxone. The possibility of prescribing take-home naloxone to high-risk groups was first suggested in the literature in 1996,[91] and has been proposed by others in the USA.[92] A national programme of naloxone provision and training has recently been rolled out in Scotland to those deemed to be at risk of opioid overdose (and their family, friends, carers and partners), including prisoners who use opioid drugs on release from prison.[93] An ongoing trial in England of supplying naloxone to newly released prisoners with a history of heroin use is described in **Section 10.11**.[94]

8.7 Research, training and resources for effective delivery of OST

8.7.1 Research needs

The foundation of OST remains suppression of illicit heroin use; currently 63 per cent of people in MT in the UK report continuing heroin use.[74] The immediate challenge for researchers and service providers is to find more effective ways to reduce heroin use. Ensuring delivery of a supervised, adequate dose of OST medication is the key to suppressing heroin use. In the UK at present, there is a substantial group of people on low or moderate doses of methadone, who continue to use heroin regularly.[74] Such people have settled into a pattern of treatment and are very resistant to change, whereas if, from the outset, treatment is approached with the objective of suppressing heroin use, outcomes tend to be better. Alternative methods of treatment for people not responding to methadone, such as slow-release oral morphine, could enhance consumer choice. Little is known about the efficacy of such approaches and research is needed in this area.

8.7.2 Training needs

The implication of delivering OST in primary care is that medical practitioners who choose to engage in this practice need the skills, knowledge and attitudes to work with heroin addicts. In order to deliver such care, doctors report that they need not just initial training, but ongoing supervision, support and reflection.[73]

8.7.3 Resource needs

Drug-dependent people, in particular those who inject heroin, are among the most challenging and disadvantaged of patients. Treatment requires structure, support and monitoring, and has been operationalised into clinical guidelines.[89] Compliance with guidelines is more expensive. A recent US study demonstrated that effective implementation of guidelines results in better outcomes, but is also considerably more expensive.[51] The authors reported that, after 12 months, treatment of new clients of highly staffed, guideline-concordant sites cost $10,252, which is significantly more than the $6,476 cost for less-concordant programmes.

In a climate of fiscal austerity, re-tendering of drug treatment programmes has become common, with a view to reducing costs in an already squeezed system. Quite apart from the financial pressure to provide minimalist services, re-tendering in itself risks compromising the quality and continuity of treatment. As reported by Ball and Ross,[7] more effective programmes are characterised by stable management, and frequent restructuring of services may compromise effectiveness. Clinical leadership, with well-understood, protocol-driven treatment and support and supervision for staff, are important ingredients of treatment.

Summary

- Medical management of drug dependence is more difficult and challenging than for other chronic disorders. Many users who present for treatment are socially marginalised, lead chaotic lifestyles and have little to motivate them towards recovery.
- Stigma and staff attitudes may also complicate management.
- Traditional methods for treating opioid addiction were based on two approaches – encouraging abstinence and a change of attitude on the part of the user.
- Although some individuals do recover spontaneously from opioid dependence, it is usually a chronic relapsing–remitting condition.
- The principle of opioid substitution therapy (OST) is to prescribe and administer a pharmaceutical opioid as a substitute for heroin. This attenuates the symptoms of withdrawal from heroin and allows the user to gain control over other aspects of their life, thereby creating the necessary preconditions to cease drug seeking and use.
- Substitution therapy provides a structured routine through daily attendance for administration in a safe non-punitive and non-judgemental treatment space, which may benefit users in restructuring a chaotic lifestyle.
- The basis of effective OST is suppression of opioid withdrawal.
- High-dose methadone is more effective than a low dose, because it progressively increases the patient's tolerance to opioids, making heroin less reinforcing and cessation of use more likely.
- For some users, the respite from withdrawal offered by methadone is insufficient to allow them to move away from heroin use; treatment with diamorphine is more reinforcing and successful in these individuals.

- Long-term studies suggest OST may reduce use of opioid drugs (in a relapsing–remitting manner), but seldom results in long-term abstinence from all drugs. Continued alcohol misuse and cannabis use are common.
- Opioid substitution has been shown to reduce deaths from opioid overdose and the risk of blood-borne viruses.
- Evidence on the effects of OST on mental health and quality of life is limited and equivocal.
- The National Treatment Outcome Research Study (NTORS) demonstrated that for every pound spent on treatment in the UK, a reduction of £3 in public costs was observed. Economic benefits were largely accounted for by reduced costs of crime.
- Opioid substitution has been shown to reduce rates of acquisitive crime and there is some evidence that it contributes to social reintegration.
- There has been little research on the effectiveness of supervised administration of OST, but limited evidence suggests it is more effective at reducing heroin use than non-supervised treatment.
- Randomised trials have shown no benefit overall of additional psychological interventions in terms of retention, non-prescribed opioid use, psychiatric symptoms, compliance or depression. There is substantial evidence that good-quality staff interactions are of benefit for recovery.
- Opioid substitution is associated with a risk of diversion of methadone to other individuals, as well as an increased risk of death during the first two weeks of treatment and in the month after leaving treatment. Overall, the risk of death is reduced by entering OST.
- Subtherapeutic dosing is a serious limitation on the effectiveness of OST.