

Methadone: Is It Enough?

Michael Gossop

Summary

This paper looks at the applications of methadone in day-to-day clinical practice. It reviews the evidence of effectiveness, including those areas in which the outcomes of methadone treatment are less satisfactory. Although the majority of patients respond well to methadone maintenance, about one in four tends not to respond well to treatment. An important question is how to achieve a better understanding of the reasons why patients respond or fail to respond to methadone treatment. The paper considers some ways in which methadone treatments could be strengthened.

Key Words: Methadone Maintenance - Treatment goals
- Outcomes - Non-responding patients

What is the purpose of methadone treatment?

One issue which is of considerable importance to our understanding of methadone treatment programmes concerns the choice of treatment goal. Methadone is used both as a medium- or long-term replacement treatment that is intended to meet a goal of harm reduction (elimination or reduction of illegal drug use, injecting, needle sharing, criminal behaviour, etc), and also as a treatment in which abstinence from drugs is the goal.

Address for reprints: Professor Michael Gossop, Head of Research, National Addiction Centre Maudsley Hospital/Institute of Psychiatry, 4 Windsor Walk, London, SE5 8AF

E-mail: m.gossop@iop.kcl.ac.uk

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Detoxification with methadone treatment

For dependent opiate users, an intermediate treatment goal, and a preliminary phase of treatments which are aimed at abstinence, involves withdrawal from drugs or “detoxification”. Within US federally funded treatment programmes, more than 40 percent of those who were treated for heroin dependence during the early 1980s received treatment in a detoxification programme ⁽⁹⁾. This compared with about a quarter who were admitted to methadone maintenance programmes and about a third who were admitted to drug-free treatment during the same period. A more recent estimate suggested that 50%, or about 116,000 admissions per year in the United States were for detoxification as a primary form of treatment ⁽²²⁾.

The reasons why detoxification is popular with some users and treatment providers are easy to understand. Detoxification attracts drug misusers who believe (generally incorrectly) that this is all they need to get off drugs and remain drug-free, as well as those who want only short-term relief from their habit. Detoxification can also be a first step in a longer treatment process. Some residential programmes require drug users to be drug-free before they enter treatment, and some methadone maintenance programmes require patients to have made at least one detoxification attempt before they are eligible to receive maintenance. For service providers, detoxification alone also offers the tempting prospect of a comparatively inexpensive treatment.

Attempts to treat opiate addiction by means of detoxification alone have repeatedly been shown to have high rates of relapse to addictive drug use, and most patients achieve little benefit from detoxification alone. Usually, detoxification needs to be supplemented with some sort of relapse prevention or rehabilitative programmes. Outcomes for detoxification patients are consistently worse than for those who receive methadone maintenance, therapeutic community, or outpatient drug-free treatment ⁽²⁶⁾. Outpatient detoxification offers no more therapeutic benefit than formal intake-only procedures (i.e. without treatment).

The specific goals of detoxification are limited. Detoxification is a clearly delineated phase of treatment designed to eliminate or to reduce the severity of withdrawal symptoms when the physically dependent user stops taking drugs. The criteria by which the effectiveness of detoxification should be judged are: symptom severity (is the treatment effective in the specific sense of reducing or eliminating the discomfort and distress of withdrawal?), duration of withdrawal (does the treatment reduce the overall duration of the withdrawal syndrome?), and completion rate (do a sufficient number of patients complete the programme and achieve a drug-free state at the end of the detoxification treatment?). Other relevant criteria could include: acceptability (is the user willing to seek and undergo the intervention?), and side-effects (the treatment should have no side-effects, or less severe effects than the untreated withdrawal symptoms).

One of the most widely used methods to manage withdrawal from opiates involves gradually reducing doses of methadone. Typically, methadone is substituted for heroin prior to withdrawal, and detoxification is implemented with gradually reducing doses of methadone over periods of 10-28 days ^(10,11,29).

One drawback of gradual methadone withdrawal is that it leads to a protracted residual withdrawal response, with withdrawal symptoms persisting well beyond the last methadone dose^(11,13). Residual withdrawal symptoms may continue for as long as the original detoxification procedure. When given over a 21 day period, patients are not fully recovered until 40 days after the beginning of withdrawal⁽¹¹⁾. The same residual withdrawal effect can be seen for 10-day reductions with symptoms persisting for about 20 days⁽¹⁶⁾. The period around the end of the methadone reduction schedule is generally associated with the greatest levels of discomfort. This can cause clinical management problems since many patients expect the last methadone dose to coincide with the last day of withdrawal discomfort, and the continued presence and relatively high severity of the residual withdrawal symptoms may be unsettling. It is likely that the place of methadone as the first choice for detoxification medication may be challenged by newer, and possibly more effective medications such as lofexidine and buprenorphine.

Although detoxification offers various opportunities for benefit, the achievement of a drug-free state is not a risk-neutral event. Among patients who have been detoxified in inpatient or residential services, an initial lapse to opiate use often occurs very soon after leaving the programme. The first few weeks after discharge represent a critical period in terms of the individual's chances of staying off drugs. Within one week of leaving an inpatient treatment programme many patients will have used opiates on at least one occasion, and within six weeks of discharge, as many as three quarters could be expected to have used opiates^(2,11). Although this initial lapse to opiate use does not necessarily herald a full-blown relapse to addiction, the reduction or loss of tolerance that occurs during and subsequent to detoxification puts the individual at risk of a drug overdose if opiate use is resumed. Drug overdose continues to be one of the most frequent causes of death among drug misusers, and increased rates of fatal overdose have been reported among recently detoxified opiate addicts⁽²⁸⁾. Detoxification programmes need to be aware of the potential risks of overdose among patients who have been successfully withdrawn from opiates and who have lost their tolerance to the effects of opiates.

Despite the limited impact of detoxification programmes on the long-term addiction career of drug users, it seems likely that these will continue to be extensively used. Detoxification services have high utilization rates because they are desirable to addicts and acceptable to treatment funders. They have become an established part of treatment services. For this reason, it is necessary to consider how further supportive procedures or services can be used to improve programme completion rates and patient outcomes. Of importance here would be better integration of services, and especially closer ties between detoxification and aftercare services. Thus, while detoxification is often used as a stand-alone treatment or as a crisis management response, this service should be viewed as one component within the broader context of long-term treatment and intervention strategies.

Methadone reduction treatment (MRT)

Outpatient detoxification is often implemented over prolonged periods of time, as with methadone reduction treatment (MRT), for example, which has been widely used in the UK for many years. Typically, MRT involves prescribing methadone over relatively long periods of time, with the expectation that the dose will gradually be reduced, and that the patient will eventually be withdrawn from the drug and become abstinent from opiates.

MRT programmes are implemented in the UK and in many other countries. Such programmes share some similarities with the gradual methadone detoxification programmes⁽²⁵⁾, and with the 90-day, and 180-day detoxification programmes that have been implemented in the United States^(18,20,23). The 180-day methadone programmes were made available as an “intermediate” form of treatment between short-term 21-day detoxification and long-term maintenance. In the United States, methadone reduction is sometimes provided in what are referred to as “maintenance-to-abstinence” programmes.

Such programmes are widely used. It has been suggested that “it would be impossible to overstate the importance of this form of methadone prescribing in the UK”⁽²⁴⁾. Typically, MRT involves prescribing methadone over relatively long periods of time, with the expectation that the dose will gradually be reduced, and that the patient will eventually be withdrawn from the drug and become abstinent from opiates. Although the objectives of methadone reduction treatment are seldom stated, its practice generally involves providing the lowest dose at which the discomfort of withdrawal can be prevented.

In this type of treatment, the prescription of opiates is often seen as a “lure” to attract drug misusers into the treatment services so that “regular contact between the addict and the doctor ... gives the opportunity for a relationship to be built up which may eventually lead to the addict requesting to be taken off the drug”⁽³⁾. The role of the clinic is “not for the continuing handouts of drugs, but for treatment: the patient may not initially be motivated to accept withdrawal but motivation will gradually be built [and] dosage gradually reduced”⁽⁸⁾.

Methadone reduction is not simply a detoxification procedure. It is a less well-defined, and, in practice, a more complicated intervention. In principle, outpatient methadone reduction programmes provide a form of medium-term, abstinence-oriented substitution treatment, but the parameters of methadone reduction programmes are frequently not clearly stated, and such programmes are implemented in a variety of ways. Reduction programmes may vary in duration from a several weeks to many months, and possibly even years.

In contrast to methadone maintenance, relatively little research has been done with methadone reduction treatments. Studies of shorter-term outpatient reduction programmes have found generally poor outcomes with high drop-out rates, and few patients achieving even short-term abstinence at the end of the treatment regime^(6,13,30).

In a detailed study of methadone treatment, it was found that MRT was frequently

not delivered as intended⁽¹⁴⁾. Whereas the majority of patients allocated to methadone maintenance received maintenance doses, only about a third of patients allocated to MRT received reducing doses. The more reducing doses that patients actually received, the worse their outcomes. Where MRT patients achieved improved outcomes, this may have occurred because of some generic treatment effect conferred by receiving a medically prescribed supply of methadone, or, alternatively, because many of them actually received some form of maintenance. Where MRT was delivered as intended, it was associated with poor outcomes.

Studies of methadone reduction treatments have raised serious questions about their effectiveness. Patients who receive MRT have poorer outcomes than those who receive stable dosing and faster dose reduction is associated with poorer outcomes than slower reduction^(14,23,25). A major problem for MRT is that it represents an uneasy compromise between maintenance and detoxification: in many cases, it fails to achieve the benefits of either form of treatment.

Methadone maintenance treatment (MMT)

First – the good news

The pragmatic rationale for methadone maintenance is that it enables opiate addicts to be assessed and supported in tackling a range of behavioural, social and health problems, and that the evidence from many studies suggests that it can be effective in this respect^(20,31).

Marked and statistically significant reductions in frequency of use of illicit opiates and benzodiazepines were found among methadone patients after admission to treatment in the National Treatment Outcome Research Study (NTORS)^a. Frequency of heroin use was more than halved after one year and remained at this level throughout the full follow-up period. Illicit methadone use was reduced after one year and remained low at 5 year follow-up (where it was at 20% of intake levels). Improvements were also found in the use of non-prescribed benzodiazepines. The greatest reduction in use occurred during the first year. At 5 year follow-up, benzodiazepine use had dropped to less than a quarter of levels of use at intake.

With regard to the risks associated with injecting drugs, the results are also encouraging. The percentage of methadone patients who were injecting drugs fell from 61% at intake to 37% after 5 years. The rate for sharing injecting equipment fell from 15% at intake to 5% at 5 years. Both for injecting and for sharing, the greatest reductions were found after 1 year.

The reductions in crime are among the more striking findings from NTORS. One year after starting treatment, there were substantial reductions in the numbers of crimes, and these reductions were maintained through to 5 years. Reductions were found both

^a The National Treatment Outcome Research Study (NTORS) was commissioned by a UK Government Task Force to investigate the outcomes over a 5 year period of people treated for drug dependence problems in national treatment agencies. Much of the data presented in this paper is taken from NTORS.

for acquisitive crimes and for drug selling crimes. The number of acquisitive crimes at 1 year fell to less than a third (28%) of intake levels, and this type of crime remained low throughout the follow-up period. At 5 years, levels of acquisitive crime were at 23% of intake levels, significantly lower than at intake. Drug selling crimes were also lower during the full follow-up period than at intake. For drug selling, at 1 year the number of offences fell to 13% of intake levels and at 5 year follow-up, drug selling was at 17% of intake levels.

The high levels of criminality that are associated with opiate addiction represent a formidable social and economic problem. The NTORS results point to the role that treatment interventions can play in helping to tackle crime among drug misusers. The reductions in crime among patients treated with methadone maintenance represent improvements which are of practical importance. They provide substantial and immediate benefits to society through the reduced economic costs of crime, and they provide equally important if less tangible benefits through the reduced levels of distress caused to victims.

Now – the not so good news

Alcohol is an important if often neglected component within the multiple substance use problems of drug misusers in treatment services. Heavy drinking and alcohol problems are often reported among patients in drug treatment services, and some drug misuse treatment programmes pay insufficient attention to the drinking problems of their patients. Heavy drinking can be a serious threat to the health of drug misusers because of the increased risk of overdose when alcohol and sedative drugs are used together ⁽¹⁵⁾. Heavy drinking can also increase the risk of health problems because of the high rates of chronic infection with hepatitis B and C among drug injectors. Indeed, heavy drinking among patients with liver disease leads to a greatly increased risk of mortality.

In contrast to the generally satisfactory outcomes that were achieved in terms of reduced illicit drug use at follow-up, the results with regard to alcohol use were poor. There was no reduction in the numbers of patients who were drinking heavily. At one year, about a quarter of the sample were drinking above recommended limits. Almost one in five of the drinkers was drinking more than 15 units (equivalent to about half a bottle of spirits) on a typical drinking day. Even among the patients who reduced or ceased to use illicit drugs, there was often no reduction in rates of heavy drinking. The findings suggest that the drinking behaviour of the methadone patients in our sample was largely independent of illicit drug use outcomes.

Where reductions in drinking were found within the NTORS cohort, this was often a reduction from extremely heavy drinking to heavy drinking rather than to non-problematic levels ⁽¹²⁾. The heavy drinking of many patients in the methadone treatment services is a problem area that has not received the attention it deserves, and the poor drinking outcomes of many patients represents an area of weakness which deserves to be given priority as an issue to be addressed by the existing methadone treatment services.

Methadone treatment may also not lead to improved crack cocaine outcomes.

Results from NTORS appear to show no change in rates of use for crack cocaine at 5 years. However, these overall figures disguise different patterns of crack use among those who were using crack and those who were not using crack during the period prior to intake. Among those who were using crack at intake, levels of use were more than halved at all follow-up points. In contrast, among those who were not using crack at intake, there was a gradual increase in the use of this drug. For this reason, the results regarding use of crack cocaine should be interpreted not as indicating a tendency to relapse to pre-admission patterns among those who were already using this drug at intake, but as being largely driven by the initiation of crack use among those who were not using crack at intake.

Non-responding patients

Although overall improvements in many problem areas have been found among patients receiving methadone treatment, most studies report overall or aggregated results. It is known that some patients demonstrate greater benefit than others. The US Institute of Medicine report⁽⁹⁾ noted that a significant proportion of patients treated in methadone programmes will not respond well to treatment, and estimated this proportion at about one in four. An important research question, therefore, is how to achieve a more precise differentiation of the ways in which patients respond to methadone treatment.

The patterns of drug use among the NTORS patients, as among most problem drug takers typically involve a range of different substances. Whilst looking at improvement in drug use one drug at a time is a useful exercise, a deeper examination of outcomes must consider changes within the broader drug-use profile. The NTORS results, which are based upon changes in the frequency of use of illicit opiates, stimulants and benzodiazepines, show considerable variation in treatment outcome based upon a broader picture of problems prior to intake and the extent of change at follow-up.

More than half of the methadone patients (59%) showed reductions in illicit drug use after treatment. This result is consistent with, and adds to previous findings which have reported aggregated improvement scores^(1,17). The patients who showed improvements in illicit drug problems after treatment also showed reductions both in their use of drugs by injection and in their sharing of injecting equipment. Such findings confirm that many patients achieve substantial and wide-ranging improvements in their illicit drug use behaviours.

However, there were also those patients (almost a quarter of the sample) who failed to show improvement at follow-up on virtually all outcome measures. In some respects, it is encouraging that only a minority of patients showed achieved such poor outcomes. On the other hand the failure of these patients to improve on a range of different outcome measures despite their access to, and often extensive input from the methadone treatment services, is a matter for concern. The finding that these patients were least likely to have remained in their index treatment at one year may be reflected in their poor outcomes.

There were improvements in areas other than those involving substance use behaviours. There was an overall improvement in the physical and psychological health

problems of the sample at follow-up. Again this improvement was not found for all patients. Physical and psychological health symptoms were reduced among patients in the Improved Response groups. The patients in the Poor Response group showed no improvement in psychological health symptoms.

Patient responses may be related to the variation in treatment procedures. An important clinical question, therefore, is how to achieve a more precise understanding of the ways in which patients respond to different procedures and interventions provided in methadone treatment.

Strengthening methadone treatment

No single, uniform treatment response can be expected to be appropriate to the needs of all drug dependent patients. This is not a viable objective. Different patients are likely to require different treatment packages. Patients with serious psychological or psychiatric problems will require different treatment input to those without such problems. The need for vocational and rehabilitative counselling will be different in a programme where most of the patients are already employed at admission to that in a programme where few patients are employed. Similarly, programmes in which the patient group includes a large proportion of mothers with young children or pregnant women should provide different treatment components to meet the special needs of these individuals.

After decades of clinical experience and research with methadone as a treatment for opiate dependence, the question of appropriate dosing remains controversial. Clinics vary greatly in the average dose of methadone prescribed, with some clinics prescribing low-doses and others using high doses.

Comprehensive reviews of the research literature have been conducted on the relationship between methadone dose and treatment outcome^(4, 31). These reviews concluded that treatment outcomes are improved when doses of 50 mg or more are used, when compared to lower doses. They also concluded that there was no evidence to suggest that routine dosing at levels in excess of 100 mg per day resulted in any benefit for the majority of patients, though relatively few studies of high dose treatment have been carried out. Ward et al.⁽³¹⁾ suggested that the evidence from both randomised controlled trials and from observational studies showed better outcomes for patients in programmes where the majority of patients are maintained in the range of 50-100 mg per day. However, it is possible that some patients may be successfully maintained on lower doses, especially if they are more highly motivated to change and more psychologically stable.

In a randomised double-blind trial of moderate- versus high-dose methadone⁽²⁷⁾, it was found that patients receiving doses of between 80-100 mg showed greater reductions in illicit heroin use than the moderate-dose group who received doses of between 40-50 mg. Both groups showed substantial and significant reductions in illicit drug use compared to pre-treatment levels. There were no differences in treatment retention between the high-dose and moderate-dose groups.

Where clinical problems arise in establishing an effective dose level for methadone,

this may be due to individual differences in the metabolism of methadone⁽³²⁾. Therapeutic drug monitoring of methadone concentrations in the blood provides a better measure of the amount of methadone available to the opiate receptors than the ingested dose. Dole⁽⁷⁾ suggested that the correct dose of methadone for the patient is the amount that sustains the plasma concentration above a critical minimum needed for continuous opioid receptor occupancy for the complete dosing interval.

In practice, the provision of methadone treatments is rarely restricted merely to the provision of methadone pharmacotherapy. Dole and Nyswander's original treatment regimen provided comprehensive medical and rehabilitative services, and the label "methadone treatment" may be misleading because it gives undue emphasis to the pharmacological aspects of treatment. Methadone treatment is generally a combination of both pharmacological and nonpharmacological therapies. Optimal outcomes are obtained when both are provided. For the majority of patients, improved clinical outcomes are seldom achieved simply by ingesting a daily dose of methadone.

These non pharmacologic aspects of methadone treatment can include individual counselling, group therapy, couples counselling, urine testing, contingency contracting, HIV testing and counselling, primary medical care services, and psychiatric assessments and treatment of comorbid disorders. The methadone clinic may be best viewed as a site for the comprehensive treatment of patients.

Nonetheless, there is some evidence that even the provision of a methadone-only intervention may help some patients. In an "interim methadone clinic" the provision of methadone alone, without counselling or other services, was found to produce significant reductions in opiate use when compared to the patients' pretreatment levels of drug use, and also when compared to patients on a waiting list comparison group⁽³³⁾.

In an investigation of the additional effects of counselling, medical care, and psychosocial services with methadone treatment, patients were randomly assigned to one of three treatment groups⁽²¹⁾. The three conditions were: minimum methadone services (MMS) - methadone alone (a minimum of 60 mg/day) with no other services; standard methadone services (SMS) - the same dose of methadone plus counselling; and enhanced methadone services (EMS) - the same dose of methadone plus counselling and medical/psychiatric and family therapy.

The provision of additional counselling, medical, and psychosocial services produced improvements in the efficacy of treatment compared to methadone alone. The enhanced treatment produced improvement in employment status, decreases in alcohol and other drug use and illegal activity, improved family relations, and improved psychiatric status. The enhanced group showed better outcomes than the standard treatment condition on 14 of the 21 outcome measures, with significantly better outcomes among the EMS patients in the areas of employment, alcohol use, and legal status.

Some patients who received the minimum methadone services showed improvements, but their response to treatment was generally unsatisfactory. More than two thirds of the patients in the MMS condition had to be "protectively transferred" from the trial because of problems associated with their continued use of opiates or cocaine,

or because of medical/ psychiatric emergencies.

This need for additional psychosocial treatment was emphatically stated by Dole, “Some people became overly converted. They felt, without reading our reports carefully, that all they had to do was give methadone and then there was no more problem with the addict. ...I urged that physicians should see that the problem was one of rehabilitating people with a very complicated mixture of social problems on top of a specific medical problem, and that they ought to tailor their programs to the kinds of problems they were dealing with..... The stupidity of thinking that just giving methadone will solve a complicated social problem seems to me beyond comprehension.” (quoted in 5: p.338)

A concluding observation.

As a final point, it is worth stating that those involved with addiction treatment sometimes have an unfortunate tendency to be excessively partisan about their favourite treatment. The least attractive feature of this is that it is often manifested as a tendency to attack or denigrate other treatment options. This is no way to approach the serious business of providing and improving the delivery of treatment services to our patients.

Methadone maintenance has been extensively studied in different countries, with different treatment groups, and over a period of four decades. It is the most thoroughly evaluated form of treatment for drug dependence and has yielded positive results for most of those who seek it. Supporters of methadone maintenance bring discredit upon themselves and their treatment by mean-spirited attacks on other forms of treatment.

An important conclusion to be reached from a study of the treatment research literature is that no single type of treatment can be expected to be effective for everyone who has a drug addiction problem. Methadone treatment alone is not enough to meet the clinical needs of all patients. Drug users are a diverse and heterogeneous group, and these individual differences are relevant to the selection of an appropriate and effective treatment. Different individuals prefer and may benefit from different kinds of treatment. A range of promising alternatives are available, each of which may be optimal for drug misusers with different problems and needs.

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