Outcomes after methadone maintenance and methadone reduction treatments: two-year follow-up results from the National Treatment Outcome Research Study

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Abstract

This paper provides a detailed analysis of the 2-year outcomes for 351 drug misusers allocated on an intention-to-treat basis to methadone maintenance or methadone reduction treatments. Both groups showed substantial reductions in their use of illicit drugs and in other outcome areas. However, whereas most methadone maintenance patients received maintenance, only about one third of those allocated to methadone reduction received methadone reduction, and many actually received a form of methadone maintenance. Reduction patients were more likely to receive low doses of methadone, and were less likely to remain in treatment. For maintenance patients, higher doses and retention in treatment were both associated with improvements in illicit heroin use at 2 years. For the reduction patients, the more rapidly the methadone was reduced, the worse the heroin use outcomes. For patients in both treatment conditions, reductions in heroin use were associated with improvements in other outcome areas. The more severely dependent patients showed better outcomes in methadone maintenance. Methadone reduction treatment processes were associated with poor outcomes, and many patients who were allocated to methadone reduction treatment did not receive reduction treatment as intended. This calls into question the appropriateness of either the initial treatment planning process or the treatment delivery process, or both. A clearer distinction should be made between methadone maintenance and methadone reduction. Treatment goals should be made explicit both to the patient and to the clinical staff at the start of treatment. We suggest the need for a reappraisal of the goals and procedures of methadone reduction treatment. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Methadone maintenance treatment; Methadone reduction treatment

A huge amount of research has been carried out on methadone treatments. Most studies have shown reductions in illicit drug use, and many have shown improvements in other outcomes (Farrell et al., 1994; Marsch, 1998; Marsden et al., 1998a; Ward et al., 1998). There is increasing awareness of the considerable variation both between and within programmes in the ways in which treatment is actually provided to patients (Ball and Ross, 1991; Gossop and Grant, 1991). The provision of methadone treatments to opiate addicts in the UK has a different history to that in other countries. The prescribing of methadone became established as an important part of the national treatment response during the early 1970s (Mitcheson, 1994). But unlike the United States where methadone treatments were introduced with specific protocols and often with stringent controls, in the UK they have been subject to only the most general controls. As a consequence, methadone has been provided in a variety of forms. It has been given as tablets, in several forms of syrup or liquid, and in ampoules. It has been prescribed for periods of time varying from a few weeks to unlimited duration. For many years, methadone has been routinely provided in the form of prescriptions which are taken to a retail pharmacist where the drug is given to the patient and is taken away to be used in unknown ways under uncontrolled conditions. Methadone maintenance programmes, as they are understood in the United States and in most other countries, (providing oral-only forms
of methadone to be taken under supervision at the clinic) have been relatively slow to establish themselves in the UK, and it is only in recent years that these have begun to play a major role within the national system of treatment services, though forms of methadone maintenance treatment (MMT) have been provided to individual patients for many years.

Methadone reduction treatment (MRT) has been widely used in the UK for many years. Seivewright (2000) commented that “it would be impossible to overstate the importance of this form of methadone prescribing in the UK”. Typically, this has involved the prescription of unsupervised methadone over relatively long periods of time, with the expectation that the dose of methadone would gradually be reduced and that the patient would eventually be withdrawn from the drug and would become abstinent from opiates. The policy of ‘reduction’ was formulated soon after the establishment of the British clinic system. The prescription of opiates was 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’ (Connell, 1969). Edwards (1969) also noted that clinic attendance was ‘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’. From the 1970s clinic policy moved towards ‘an attempt to replace indefinite prescribing and a limited stabilisation period was followed by reducing prescriptions’ (Mitcheson, 1994).

It is misleading to regard methadone reduction simply as a detoxification procedure. It is a less well-defined, and, in practice, a more complicated procedure. However, although not directly comparable, MRT, as delivered in the UK, has certain similarities to methadone programmes in other countries. There are some similarities, for example, with the gradual methadone detoxification programmes (Senay et al., 1977), and with the 90-day, and 180-day detoxification programmes that have been implemented in the United States (Iguchi and Stitzer, 1991; Institute of Medicine, 1995; Reilly et al., 1995; Sees et al., 2000). The 180-day methadone programmes were made available after Federal Guidelines were revised in 1989 to provide this modality as an ‘intermediate’ form of treatment between short-term 21-day detoxification and long-term maintenance.

In contrast to methadone maintenance treatments, which have been extensively researched and about which a great deal is known, little research has been done with methadone reduction treatments. Strang et al. (1997) compared outcomes of patients randomly allocated to methadone maintenance or methadone re-duction treatments, and found improvements in a range of substance use and other problem behaviours during the first month of treatment, but with no differences between the two methadone conditions. Other studies of shorter-term outpatient reduction programmes have found generally poor outcomes with high drop-out rates, and few patients achieving abstinence (Gossop et al., 1986; Dawe et al., 1991; Unnithan et al., 1992).

The National Treatment Outcome Research Study (NTORS) is a prospective, multisite outcome study of a cohort of more than 1000 clients treated for substance use problems in four types of treatment modalities across England, and it is the first study of its kind to be conducted in the United Kingdom. Previous papers have reported the characteristics and problems of the clients admitted to the four NTORS modalities (Gossop et al., 1998b), the 6 month outcomes for clients from the four modalities (Gossop et al., 1997), and the 1-year outcomes for the clients who were admitted to the residential setting programmes (Gossop et al., 1999). In a previous paper, we found that patients who sought treatment in the methadone maintenance and the methadone reduction programmes achieved substantial improvements at 1-year follow-up (Gossop et al., 2000). We noted that it was surprising that patients recruited to two such different treatment modalities apparently achieved such similar outcomes. However, there were variations in treatment delivery within each modality. There were also similarities between the modalities in the treatments received by patients (e.g. in methadone doses and in treatment retention rates). For these reasons, we suggested that it was unsafe to interpret the previous findings as showing that methadone maintenance and reduction treatments led to similar outcomes. Instead, the outcomes were provisionally regarded as reflective of exposure to some general methadone substitution treatment (probably including de facto forms of methadone maintenance), and we suggested that more detailed investigation of the outcomes for the two types of methadone treatment should be conducted with closer attention paid to the impact of specific treatment components.

The present investigation builds upon the study of Gossop et al. (2000) and provides a further analysis of the two forms of methadone treatment and their outcomes. This is done using data from intake through to 2-year follow-up. The use of a longer follow-up period provides a more secure basis for analysis of changes in problem behaviours after entry to treatment. In particular, this paper seeks to test the null hypothesis that the type of methadone treatment continues to be unrelated to outcome when treatment type is classified (not at the modality level but) according to the nature of the treatments as they are actually provided to patients. The paper has three specific aims: (i) in order to obtain a more precise classification of patients according to
treatment type, the 2-year outcomes are reported for the two methadone treatments for patients classified on an intention-to-treat basis; (ii) the paper provides data on the treatments actually provided to patients; and (iii) it relates treatment factors to observed outcomes. The paper presents data on a range of outcomes, including the use of illicit drugs, the use of alcohol, injecting behaviours, psychological and physical health problems, and crime behaviours.

1. Method

NTORS uses a longitudinal, prospective cohort design. The methodology and procedure for the study has been fully described elsewhere (see Gossop et al., 1998a,b), and only a brief description is presented in this paper. This report presents follow-up data on the 2-year outcomes for patients from 31 outpatient/community methadone treatment programmes. Treatment programmes were purposely selected for inclusion in NTORS and, in this paper, comprised 16 methadone maintenance programmes and 15 methadone reduction (maintenance-to-abstinence) programmes.

1.1. Measures

Data were collected using a structured interview. The interview contained items and scales developed specifically for this project as well as measures adapted from published instruments (Marsden et al., 1998b). The outcome measures presented in this paper are: illicit drug use, other substance use behaviours (including route of administration, sharing injecting equipment, and alcohol use), health, and criminal behaviour. Measures were taken for the 90-day periods prior to each interview. The six target drugs included in the analyses were heroin, non-prescribed methadone, non-prescribed benzodiazepines, crack cocaine, powder cocaine, and amphetamines. Regular use of illicit drugs is defined as weekly or more frequent use. Urine screening for illicit drug use was conducted on clients from programmes randomly selected on a one-in-two basis, at intake and at 1-year follow-up. The results of urine screening provided evidence of the validity of self-reported drug use and these results have been presented elsewhere (Gossop et al., 1997, 2000). Physical health symptoms were recorded in the interview using a 49 item checklist from the Opiate Treatment Index (Darke et al., 1991). Psychological health problems were assessed using anxiety and depression sub-scales derived from the Brief Symptom Inventory (BSI) of Derogatis (1993). Crime data is presented separately in the paper for acquisitive crimes (shoplifting, robbery, burglary and fraud), and for drug selling offences.

1.2. Treatment modalities

1.2.1. Methadone maintenance treatment (MMT)

Since the establishment of the British drug clinics in the late 1960s, outpatient/community methadone maintenance treatment has usually been delivered by specialist drug dependence clinics. More recently, MMT has also been delivered by general practitioners either independently or in association with a specialist drugs agency as a form of ‘shared-care’ (Wilson et al., 1994). A basic feature of methadone maintenance is that the drug is prescribed on a stable-dose, non-reducing basis, and following stabilization at a suitable dose level, the patient may be maintained for either a fixed or for an indefinite period.

Methadone in the UK is often provided to the patient by means of a prescription form which is taken to a retail chemist. The pharmacist gives the drug to the patient, and the drug is taken away and consumed without supervision. More recently, some services have begun to deliver methadone in a manner more similar to the system used in US clinics whereby the drug is both dispensed and consumed under supervision on the clinic premises. This has sometimes been referred to in the UK as ‘structured’ methadone maintenance. Eight such structured methadone maintenance programs were established by the Department of Health at the beginning of 1995 and these programs and their patients are included in NTORS.

1.2.2. Methadone reduction treatment (MRT)

Outpatient/community methadone reduction programmes have been widely used in the UK for many years. In principle, they provide a form of medium-term, abstinence-oriented substitution treatment. However, in practice, 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 few weeks to many months (possibly even years). Reduction schedules may be ‘fixed,’ (i.e. set by the prescribing agency without the patient having any involvement in the duration of the treatment, or the timing or rate of reduction), or they may be ‘negotiable’ with the patient having some involvement in decisions about how dose reductions are being made. Even where reduction schedules are fixed, alterations may be made to the timing of dose reductions or the duration of the treatment because of changed circumstances or crises presented by the patient. In reduction programmes, methadone is usually provided by means of prescriptions which are filled by retail pharmacists with the drug being taken away and consumed without supervision. One of the purposes of this study is to provide further information about the ways in which reduction programmes are provided.
1.3. Subjects and procedure

The study sample comprised 351 patients. This sample was constructed in the following ways. An initial sample of 667 patients was recruited to the NTORS methadone treatment programmes during a 5-month period between March and July 1995. For the 2-year follow-up, a random stratified sample was selected (by SPSS random selection procedures) from the full NTORS cohort to include approximately the same percentages within the treatment modalities as at intake. At 2 years, 370 patients from the methadone treatment modalities (94% of the 395 patients in the eligible sample) were successfully interviewed. Intake interviews were carried out by agency staff. All 2-year follow-up interviews were carried out by independent professional researchers from the Office for National Statistics (ONS). Detailed information was also collected on the methadone doses provided to each patient throughout a monitoring period of 12 months after intake to treatment. Data were collected at monthly intervals throughout the 1st year of treatment. Although it would have been desirable to collect methadone dose data throughout the full treatment episode for every patient, the administrative burden of this task was such that it was decided during the planning stages of the project that a fixed period of 12 months from intake would be established. During the 12-month monitoring period, data on methadone doses were missing for 19 patients, and these were excluded from the analyses.

Data regarding the type of methadone treatment was collected for all patients on an intention-to-treat basis. This was recorded by clinical staff on the intake interview schedule. Staff recorded planned treatment as maintenance (n = 240; 68%), or reduction (n = 111; 32%). The maintenance group comprised short-term maintenance of 6 months or less (n = 51, 15%) and long-term maintenance of more than 6 months (n = 189, 54%). The reduction group comprised short-term reduction of 1 month or less (n = 5, 1%) and long-term reduction of more than 1 month (n = 106, 30%).

2. Results

The mean time to follow-up was 2.2 years (790 days; S.D. = 87). A logistic regression analysis was carried out to compare the intake characteristics of the study sample with those of the methadone clients recruited to NTORS but not interviewed at 2-year follow-up. There was little difference between the two groups. Variables included in the analysis were: age, sex, ethnicity, relationship status, use of heroin, cocaine, amphetamines, and benzodiazepines, injecting, sharing needles or syringes, alcohol consumption, acquisitive crime and selling drugs. The model showed a significant difference between contacted and non-contacted patients (χ² = 33.39, P < 0.01). This difference was largely due to the difference between the two groups for frequency of heroin use during the 3 months prior to intake. This was the only variable to show a statistically significant association with follow-up status (Wald = 17.76; P < 0.001). Patients interviewed at 2 years had used heroin less frequently prior to intake (60 days) compared to those that were not followed-up (73 days). The mean age of the study sample at intake was 30 years; 72% were men; 90% described their ethnicity as ‘white/UK’; and 65% were either married or living with a partner.

2.1. Intention-to-treat

Comparisons were made between the methadone maintenance and methadone reduction treatments for patients classified on an intention-to-treat basis (see Table 1). At intake, there were no statistically significant differences between the two groups in frequency of substance use, physical and psychological health, or criminal behaviour. The 2-year outcomes for illicit drug use were compared with drug use at intake using analyses of variance with covariate adjustment for intake levels of drug use. Statistically significant reductions in the frequency of use of all illicit target drugs were found at 2-year follow-up. These reductions are shown as main effects in Table 1. Data were collected separately for crack cocaine and powder cocaine. Frequency of use for both forms of cocaine was significantly reduced at follow-up. The results also show statistically significant reductions from intake to 2 years in frequency of alcohol use, in anxiety and depression, physical health symptoms, and for both acquisitive crime and drug selling offences.

There were no statistically significant interaction effects, indicating that there were no differences between the patients in the two treatments in terms of the changes from intake to follow-up.

The mean methadone dose for all patients was 48.2 mg. The majority (n = 234, 67%) were receiving mean treatment doses in the range 30–60 mg, with 70 (20%) receiving mean doses greater than 60 mg and 47 (13%) receiving mean doses lower than 30 mg. For the purposes of this study, and to compare the intention-to-treat classifications with methadone doses received, two operational definitions of methadone maintenance and methadone reduction were used. Methadone maintenance was defined as receiving 70% or more of consecutive methadone prescriptions at the same dose (i.e. dose on occasion x + 1 = dose on occasion x): methadone reduction was operationally defined as receiving 50% or more of consecutive doses of methadone at a reduced dose.
2.2. Treatment received

Patients allocated to MMT on an intention-to-treat basis were significantly more likely to receive maintenance than patients allocated to MRT were to receive a reduction programme ($\chi^2 [1] = 37.24, P < 0.0001$). Of the patients allocated to maintenance, 169/240 (70%) received maintenance according to our operational definition. In contrast, only a minority of the patients allocated to MRT received reduction (40/111, 36%). The patients whose treatment failed to meet our operational definition of methadone reduction appear to have received some form of maintenance with mean doses remaining at around 45–50 mg throughout the 12-month monitoring period.

Other differences were found between MMT and MRT in terms of doses prescribed and in terms of treatment retention (see Table 2). Although there was no statistically significant difference between the two groups in mean starting dose, more of the methadone reduction than the maintenance patients received low starting doses (less than 30 mg). This difference became more pronounced during the course of treatment with the methadone reduction patients being more likely to receive low mean treatment doses, and less likely to receive either medium dose (30–60 mg) or higher doses (more than 60 mg). The rate of reduction among the patients who remained in the reduction programmes was slow. The mean dose for methadone reduction patients at intake was 45 mg. At 1 year, it was 25 mg. (i.e. an average reduction of only about 1.5 mg per month). Treatment retention was superior for patients receiving maintenance treatment. The MMT patients were more likely still to be in their index treatment at 6 months, at 1 year, and at 2 years.

2.3. Factors associated with outcome

Further analyses were conducted to identify factors associated with regular use of illicit heroin at follow-up. Logistic regression analyses were conducted separately for patients allocated to MMT and for patients allocated to MRT. Analyses were conducted to measure the influence of treatment variables on outcome. Co-variates included in the analysis were: age, sex, pre-treatment levels of each dependent variable, pretreatment polydrug use, severity of dependence (as measured by the SDS; Gossop et al., 1995), mean methadone dose, percentage of reducing doses, percentage of maintenance doses, duration of treatment (less than 3 months, 3–6 months, more than 6 months, still in index treatment at follow-up), and contact with other (non-index) treatment agencies prior to, and subsequent to intake.

For the maintenance patients, two treatment factors were predictive of favourable heroin use outcomes. For MMT patients who remained in index treatment to 2 years, the odds of being a regular heroin user were approximately halved compared to those who left treatment earlier. Higher maintenance doses were also predictive of reduced heroin use, with each milligram of prescribed methadone producing a 2% reduction in the likelihood of using heroin regularly. Two substance use variables predicted heroin use at 2-year follow-up. Patients who were regular users of illicit heroin prior to intake were almost 3 times more likely to be regular users at follow-up, and patients with higher severity of dependence (SDS) scores achieved improved heroin use outcomes (Table 3).

For the methadone reduction patients, two factors were predictive of outcomes. As for the maintenance

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Methadone maintenance</th>
<th>Methadone reduction</th>
<th>Intake</th>
<th>2 years</th>
<th>Intake</th>
<th>2 years</th>
<th>Main affect</th>
<th>Group difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroina</td>
<td>58.5</td>
<td>23.9</td>
<td>59.4</td>
<td>23.1</td>
<td>266.42***</td>
<td>0.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-pres. methadone</td>
<td>15.2</td>
<td>6.8</td>
<td>14.0</td>
<td>4.7</td>
<td>127.04***</td>
<td>0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-pres. benzodiazepines</td>
<td>23.6</td>
<td>3.3</td>
<td>21.8</td>
<td>3.2</td>
<td>667.21***</td>
<td>0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crack cocaine</td>
<td>5.5</td>
<td>2.0</td>
<td>4.8</td>
<td>2.3</td>
<td>30.09***</td>
<td>0.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cocaine powder</td>
<td>2.1</td>
<td>0.9</td>
<td>1.7</td>
<td>0.7</td>
<td>62.50***</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amphetamines</td>
<td>2.4</td>
<td>2.0</td>
<td>3.5</td>
<td>2.3</td>
<td>2.78</td>
<td>0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>19.4</td>
<td>19.4</td>
<td>21.4</td>
<td>20.6</td>
<td>0.03</td>
<td>0.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety and depressionb</td>
<td>3.4</td>
<td>2.6</td>
<td>3.4</td>
<td>2.8</td>
<td>60.26***</td>
<td>0.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical health symptomsbc</td>
<td>16.1</td>
<td>11.1</td>
<td>16.0</td>
<td>12.0</td>
<td>131.45***</td>
<td>1.44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquisitive crimec</td>
<td>21.2</td>
<td>4.2</td>
<td>27.0</td>
<td>5.7</td>
<td>100.51***</td>
<td>0.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug selling</td>
<td>24.0</td>
<td>2.4</td>
<td>23.0</td>
<td>3.8</td>
<td>93.44***</td>
<td>2.09</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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a Substance use variables refer to mean frequency of use during the previous 90 days.

b Sub-scales from BSI (range 0–8).

c OTI health scale (range 0–49).

d Crime variables refer to number of offences committed during the previous 90 days.*** P < 0.001.
patients, those who were regular users of illicit heroin prior to intake were much more likely to be regular users at follow-up. The only treatment factor to predict heroin use at follow-up was percent of reducing doses. This was related to poor outcome. The more reductions in methadone that were given during treatment, the more likely the patient was to be a regular heroin user at follow-up.

To investigate improvements for outcomes other than heroin use, a composite variable was constructed by coding outcome scores as regular use of stimulants (cocaine and amphetamines), benzodiazepines, injecting, drinking above recommended limits (RCP, 1986), involvement in acquisitive crime, and scores above or below the median for psychological health and physical health. The composite score was the sum of scores for each of these seven variables. Higher scores represent better outcomes for a wider range of domains. The same composite measure was constructed for pre-intake behaviour. There was no difference in the performance of the MMT and MRT patients at intake on this composite outcome score ($\bar{x} = 2.8$ and 2.9, respectively; $t = 0.46$, $P = 0.64$, ns). Multiple regression analyses were conducted for both MMT and MRT patients including as covariates, age, sex, changes in regular heroin use from intake to follow-up, SDS scores, percentage of maintenance dose, percentage of reducing doses, average dose, and treatment status at follow-up. The intake composite score was also entered in the analysis as a covariate.

For the MMT patients, 22% of the variance in scores on the final model ($F = 34.02$ [2237], $P < 0.0001$) was predicted by the two remaining covariates. Improvements in heroin use (giving up regular use) was predictive of better outcomes for the range of domains as measured by the composite score ($\beta = 0.26$, $P < 0.0001$). Better pre-intake performance as measured by the composite measure was also predictive of better overall outcomes as measured by the composite score at 2-year follow-up ($\beta = 0.41$, $P < 0.0001$). For the MRT patients, 22% of the variance in scores on the final model ($F = 10.15$ [3107], $P < 0.0001$) was predicted by the three remaining covariates. As with the maintenance patients, improvements in regular heroin use, and pre-intake performance as measured by the intake composite score, were both predictive of better overall outcomes at 2-year follow-up ($\beta = 0.29$, $P < 0.001$, and $\beta = 0.26$, $P < 0.01$, respectively). In addition, MRT patients with higher severity of dependence (SDS) scores

Table 2
Methadone doses and treatment retention for patients classified by intention to treat

<table>
<thead>
<tr>
<th>Variable</th>
<th>Methadone maintenance ($n = 240$)</th>
<th>Methadone reduction ($n = 111$)</th>
<th>$t/\chi^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean starting dose (mg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% &lt;30</td>
<td>6</td>
<td>15</td>
<td>8.47**</td>
</tr>
<tr>
<td>% 30–60</td>
<td>73</td>
<td>65</td>
<td>2.36</td>
</tr>
<tr>
<td>% &gt;60</td>
<td>21</td>
<td>20</td>
<td>0.05</td>
</tr>
<tr>
<td>Mean treatment dose (mg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% &lt;30</td>
<td>6</td>
<td>29</td>
<td>33.36***</td>
</tr>
<tr>
<td>% 30–60</td>
<td>71</td>
<td>58</td>
<td>5.93*</td>
</tr>
<tr>
<td>% &gt;60</td>
<td>23</td>
<td>14</td>
<td>4.20*</td>
</tr>
<tr>
<td>Mean percentage of reducing doses</td>
<td>14</td>
<td>36</td>
<td>6.95***</td>
</tr>
<tr>
<td>Mean percentage of maintaining doses</td>
<td>79</td>
<td>55</td>
<td>6.76***</td>
</tr>
<tr>
<td>Mean percentage of increasing doses</td>
<td>8</td>
<td>9</td>
<td>0.55</td>
</tr>
<tr>
<td>Mean days of treatment$^b$</td>
<td>466</td>
<td>408</td>
<td>1.59</td>
</tr>
<tr>
<td>% in index treatment at 1 month</td>
<td>88</td>
<td>86</td>
<td>0.37</td>
</tr>
<tr>
<td>% in index treatment at 6 months</td>
<td>71</td>
<td>58</td>
<td>5.93*</td>
</tr>
<tr>
<td>% in index treatment at 1 year</td>
<td>62</td>
<td>50</td>
<td>4.62*</td>
</tr>
<tr>
<td>% in index treatment at 2 years</td>
<td>42</td>
<td>30</td>
<td>4.6*</td>
</tr>
</tbody>
</table>

$^a$ Levels of statistical significance are shown as: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.
$^b$ Means as at 2-year follow-up.

Table 3
Factors predicting regular heroin use at 2 years for patients classified by intention to treat

<table>
<thead>
<tr>
<th>Variable</th>
<th>Methadone maintenance ($n = 240$)</th>
<th>Methadone reduction ($n = 111$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin $^a$</td>
<td>2.73 (1.26, 5.92)**</td>
<td>7.21 (4.38, 11.86)***</td>
</tr>
<tr>
<td>Dependence</td>
<td>0.87 (0.79, 0.96)**</td>
<td>–</td>
</tr>
<tr>
<td>In index treatment at 2 years</td>
<td>0.52 (0.44, 0.61)**</td>
<td>–</td>
</tr>
<tr>
<td>Percent reducing doses</td>
<td>–</td>
<td>1.02 (1.01, 1.02)$^*$</td>
</tr>
<tr>
<td>Average dose</td>
<td>0.98 (0.97, 0.98)**</td>
<td>–</td>
</tr>
</tbody>
</table>

$^a$ Regular (weekly or more frequent) use of heroin at intake to treatment.$^* P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. 

To investigate improvements for outcomes other than heroin use, a composite variable was constructed by coding outcome scores as regular use of stimulants (cocaine and amphetamines), benzodiazepines, injecting, drinking above recommended limits (RCP, 1986), involvement in acquisitive crime, and scores above or below the median for psychological health and physical health. The composite score was the sum of scores for each of these seven variables. Higher scores represent better outcomes for a wider range of domains. The same composite measure was constructed for pre-intake behaviour. There was no difference in the performance of the MMT and MRT patients at intake on this composite outcome score ($\bar{x} = 2.8$ and 2.9, respectively; $t = 0.46$, $P = 0.64$, ns). Multiple regression analyses were conducted for both MMT and MRT patients including as covariates, age, sex, changes in regular heroin use from intake to follow-up, SDS scores, percentage of maintenance dose, percentage of reducing doses, average dose, and treatment status at follow-up. The intake composite score was also entered in the analysis as a covariate.

For the MMT patients, 22% of the variance in scores on the final model ($F = 34.02$ [2237], $P < 0.0001$) was predicted by the two remaining covariates. Improvements in heroin use (giving up regular use) was predictive of better outcomes for the range of domains as measured by the composite score ($\beta = 0.26$, $P < 0.0001$). Better pre-intake performance as measured by the composite measure was also predictive of better overall outcomes as measured by the composite score at 2-year follow-up ($\beta = 0.41$, $P < 0.0001$). For the MRT patients, 22% of the variance in scores on the final model ($F = 10.15$ [3107], $P < 0.0001$) was predicted by the three remaining covariates. As with the maintenance patients, improvements in regular heroin use, and pre-intake performance as measured by the intake composite score, were both predictive of better overall outcomes at 2-year follow-up ($\beta = 0.29$, $P < 0.001$, and $\beta = 0.26$, $P < 0.01$, respectively). In addition, MRT patients with higher severity of dependence (SDS) scores
had poorer outcomes at follow-up ($\beta = -0.18$, $P < 0.05$).

3. Discussion

Patients in both the methadone maintenance and methadone reduction treatments showed substantial reductions in their use of illicit drugs at 2-year follow-up. There were also marked reductions in psychological and physical health problems, and in acquisitive and drug selling crime. This finding is similar to the results obtained at both 6 months (Gossop et al., 1997), and at 1 year (Gossop et al., 2000). In a different study, Strang et al. (1997) reported similar outcomes for methadone maintenance and reduction in the immediate post-intake period. The improvements after MMT which we report for the NTORS sample are broadly consistent with the findings from a large number of studies from many countries (Farrell et al., 1994; Marsden et al., 1998a; Ward et al., 1998). Perhaps the only respect in which they are remarkable is in the broad range of improvements observed at follow-up (i.e. drug use, psychological and physical health, and criminal behaviour). The reductions in problem behaviours that were found at 2 years reflect changes which were found at earlier follow-up points, and this stability in outcomes was found both at the group level and at the individual level (Gossop et al., in press).

In a previous report on the 1-year outcomes for patients receiving methadone treatments within NTORS (Gossop et al., 2000), we cautioned against interpreting these findings as showing that methadone maintenance and methadone reduction treatments lead to similar outcomes. The study design did not include random allocation of clients to modalities, and there were differences in problem type and problem severity between the clients entering different modalities (Gossop et al., 1998b). More importantly, Gossop et al. (2000) found marked similarities in the type of treatments received by the two groups of patients, and suggested that the similar outcomes might be regarded as reflective of exposure to some general form of methadone substitution treatment. This suggestion is supported by the findings of the present investigation. When analysed on an intention-to-treat basis, the majority of patients allocated to MMT were found to receive maintenance, whereas only about one third of those allocated to MRT received methadone reduction. Many of the MRT patients actually received a form of methadone maintenance (i.e. stable doses over a prolonged period). For this reason, the apparent lack of differences in outcomes between the two treatment conditions is not surprising. In the study of Strang et al. (1997), no data were available about the treatment interventions actually provided, and it is possible that their failure to demonstrate any differences between methadone maintenance and reduction may reflect a treatment ‘crossover’ effect such as that shown in the present study, with many reduction patients actually receiving some de facto form of maintenance. This ‘drift into maintenance’ has also been noted by Seivewright (2000).

There were differences between the MMT and MRT conditions in relation to methadone doses and in treatment retention. The patients allocated to MRT were more likely than the maintenance patients to receive low starting doses. Eighty percent of those allocated to MRT were prescribed a starting dose of 60 mg or less, and 15% received a starting dose of less than 30 mg. During the course of treatment, the MRT patients were more likely to receive low doses of methadone. It has been suggested that methadone dose is an important treatment factor, and that patients on higher doses achieve significantly better outcomes than those on lower levels. In a randomised, double blind trial, Strain et al. (1999) found the high-dose methadone group showed greater reductions in illicit opiate use than a low dose group. The comprehensive review of Ward et al. (1998) suggested that doses of 60 mg or more were associated with longer stays in treatment and reduced heroin use. Overall, the methadone doses prescribed to the NTORS patients are similar to those reported elsewhere for patients receiving methadone treatment in Britain (Strang and Sheridan, 1998). Compared to many international studies, the methadone doses prescribed to the NTORS patients were relatively low, with only one fifth of the patients receiving doses of 60 mg or more.

The patients allocated to methadone maintenance were more likely to remain in treatment at all follow-up points except for the one conducted immediately after treatment intake (at 1-month follow-up). To some extent, this is to be expected since some of the patients receiving reduction treatments may have completed their programmes. However, if this is the case, it is certainly not reflected in any improved outcomes among these patients. Nor is it consistent with the finding that many intended reduction programmes were extended over periods of time well beyond what might be regarded as reasonable. Half of the MRT patients were still in treatment after 1 year, and almost a third of them were still in treatment after 2 years. The finding of lower retention rates among the MRT patients is consistent with the results of the randomised controlled trial conducted by Sees et al. (2000) which found that patients receiving 180 day detoxification were less likely to remain in treatment than patients receiving maintenance.

The lower retention rates among the methadone reduction patients in our study may be associated with the lower doses which they received, with the reductions
made to their doses, or they may be associated with the pressure to accept a reduced dose even when the reducing doses were not implemented. In practice, the issue of implementing a reducing dose programme is a frequent (and sometimes acrimonious) topic of discussion within the clinical sessions, with clinic staff pressing for dose reductions and the patient resisting them. This may lead to stressful and difficult sessions for both staff and patients, which may in turn contribute to poor programme implementation and to problems of treatment retention. Mitcheson (1994) noted that “an inordinate and wearisome amount of time was spent in (usually polite) mutual manipulation between staff and patients regarding type of drug and dose.”

But whatever the reasons for the higher drop-out rate among the reduction patients, the differences in doses received and in retention rates are important to understanding the outcomes. For the MMT patients, higher doses and retention in treatment were both associated with favourable heroin use outcomes at 2 years. Research has tended to show that the effects of methadone are most evident for the primary treatment goals (e.g. reduced illicit heroin use), and that its effects are less marked for other outcomes (e.g. use of other illicit drugs or social functioning) (Ward et al., 1998). In the present study, we found improvements in a range of outcome domains, and also that reduced heroin use was related to improvements in other outcome areas. Patients in both MMT and MRT who had been able to stop regular use of heroin at follow-up showed improvements across a range of other outcome areas.

Where patients were intended to receive MRT, the treatment was frequently not delivered in this form. Where it was delivered as intended, it was associated with poor outcomes. The finding that almost two thirds of the patients who were allocated to MRT did not receive reduction treatment as intended raises several questions for British treatment providers and policy makers. If the majority of patients for whom MRT is planned and started, subsequently have this treatment changed, this calls into question the appropriateness of either the initial treatment planning process or the treatment delivery process, or both. In addition, our results raise other serious doubts about the effectiveness of MRT. For the methadone maintenance patients, the primary treatment goal (reductions in illicit heroin use) was associated with higher methadone doses and retention in treatment. The associations between methadone dosage, treatment retention, and treatment outcome are still not fully understood. However, many studies from different treatment settings and in different countries have shown positive associations between higher doses, increased retention and improved outcomes (D’Ippoliti et al., 1998; Ward et al., 1998; Strain et al., 1999). Treatment retention has been found to be one of the most consistent predictors of favourable treatment outcomes (Hubbard et al., 1989; Simpson et al., 1997a,b; McLellan et al., 1997).

It is possible that the MRT patients may have received other forms of treatment (usually some form of maintenance) because of operational failures to provide treatment as intended or because of changes in treatment goals which led to changes in treatment deliberately implemented within the clinical service. Alternatively, it is possible that patients were initially admitted onto reduction programmes as an ‘entry-level’ form of methadone treatment because of the reluctance of staff to put patients directly onto maintenance programmes. This suggestion is consistent with our previous findings that the patients in the methadone reduction modality were younger, had used heroin for a shorter period, were less likely to have multiple drug use or alcohol problems (Gossop et al., 1998a). However, despite the different aims and procedures of the maintenance and the reduction programmes, comments made to the research team during the inception phase of NTORS suggest that many clinical staff in UK services do not distinguish between the two types of treatment and believe that the two can, in some way, be alternated and/or provided seamlessly within a single treatment episode. In this respect, it is possible that the ‘crossover’ between methadone reduction and methadone maintenance may reflect a conflation of the two treatments which was deliberately implemented within the programmes.

For the patients who received MRT, the only treatment factor which was found to be (negatively) associated with outcome was the percentage of reducing doses. This was linked to more frequent heroin use at 2-year follow-up. A high percentage of reducing doses is indicative of a more rapid reduction schedule. The more rapidly the methadone was reduced, the worse the heroin use outcomes. These results cannot be attributed to differences between the two treatment condition in patient characteristics or problem behaviours at intake. There were no differences between the groups at intake in terms of frequency of substance use, physical and psychological health, or criminal behaviour. In addition, the regression analyses controlled for the effect of these variables, as well as age and sex. The finding that the more reducing doses that were given, the worse the outcome, suggests that the methadone reduction patients may have achieved any improvement in their outcomes at 2-year follow-up despite the specific characteristics of their intended treatment programmes (i.e. reducing doses). The outcomes of the reduction patients may be more reflective of some generic treatment effect conferred by receiving a medically prescribed supply of methadone. Alternatively, the outcomes may be reflective of the finding
that many of them actually received some form of maintenance.

One differential treatment effect concerned severity of dependence. The more severely dependent patients achieved better heroin use outcomes when they received MMT. Methadone reduction patients who were more severely dependent upon their main problem drug at intake had poorer 2-year composite outcomes. Where differential allocation of patients to either maintenance or reduction programmes is possible, we recommend that more severely opiate dependent patients be offered methadone maintenance as an outpatient treatment of first choice.

This study provides valuable information about the impact of methadone treatment programmes in the UK. The results may have implications for similar treatments provided in other countries. We suggest that methadone reduction be differentiated from, and seen as a different type of treatment to methadone maintenance. In particular we recommend that a clearer distinction be made in clinical practice between the time-limited, abstinence-oriented methadone reduction treatments, and the long-term, stable-dose maintenance treatments which are designed to achieve harm-reduction goals. Some of the uncertainty about appropriate procedures within methadone reduction programmes could be removed if treatment goals were made explicit both to the patient and to the clinical staff at the start of treatment. These results have particular importance with regard to the findings for methadone reduction treatment about which so little is known. The results raise serious questions about the purposes, the delivery, and the effectiveness of this form of treatment and suggest the need for a critical reappraisal of the purposes and effectiveness of this widely used form of treatment.

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References

Derogatis, L.R., 1993. The brief symptom inventory: administration, scoring and procedures, National Computer Systems, Inc.
Gossop, M., Marsden, J., Stewart, D., Rolfe, A., 2000. Patterns of improvement after methadone treatment: one-year follow-up results from the National Treatment Outcome Research Study (NTORS), Drug and Alcohol Dependence.


