

# Methadone dose and methadone maintenance treatment

## Methadone series

There is now substantial evidence on the effectiveness of methadone maintenance treatment. Research has also identified the factors likely to be necessary to achieve optimal methadone treatment. Three briefings for drug treatment providers and commissioners have been produced on these factors:

- Methadone dose and methadone maintenance treatment
- Enhancing outcomes of methadone maintenance treatment with counselling and other psychosocial interventions and provision of 'ancillary' services
- Engaging and retaining clients in drug treatment

Decisions about the dose of methadone to be used for methadone maintenance treatment, and how practitioners and services make these decisions for individual service users, are crucial questions for effective management of care.

Adequately high methadone doses for individual need, as well as responsive and flexible individualised decisions on dosing, may be key factors that may assist practitioners in achieving improved outcomes. This briefing looks at the evidence relating to these issues.

## Key findings

- Methadone doses used for maintenance treatment that are adequate for individual need can lead to higher retention rates and improved outcomes.
- There is a consistent finding of greater benefit from maintaining individuals on a daily dose between 60mg and 120mg (and higher doses in exceptional cases). Lower doses may also be appropriate for some.
- In British methadone treatment, doses are on average less than 50mg daily and only just over a quarter of service users receive over 60mg.
- Higher doses have been consistently shown to encourage treatment retention and reductions in illicit drug use in methadone maintenance regimes.
- Lower dose levels may be undermining the provision of optimal services and compromising the therapeutic relationship between service user and key worker.
- Recent research shows that responsive and flexible individualised dosing can help foster the therapeutic relationship and may lead to improved outcomes and reductions in illicit drug use.

Safe flexible systems of assessment and supervision of appropriate dose must be in place for the provision of methadone maintenance treatment, taking into account the risk of overdose and needs of the service user. The key findings can only be considered to apply in such circumstances

## Research into practice briefings

These briefings commissioned by the NTA are summaries of the research evidence on a particular topic to help inform providers and commissioners of services. They are not NTA guidance but are aimed at helping providers and commissioners reflect on local service provision. It is important to note that UK-based research on the issues covered by this series of briefings is currently limited and many of the studies reported here have been conducted in the USA. How such research evidence, relating to methadone maintenance treatment, is applied appropriately to clinical practice in the case of individual service users is a decision for prescribing clinicians and team members. This should be applied in discussion with the service user taking all the relevant issues in to account. Clinical teams should work within clinical governance including clear protocols and regular clinical audit to ensure good practice.

# 1. Introduction

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This briefing looks at the evidence for the importance of dose level of methadone in promoting optimal maintenance treatment and the importance of flexibility in determining dose on outcomes.

Factors other than methadone dose level that contribute to improved outcomes include the use of counselling and other psychosocial interventions and provision of 'ancillary' services. In addition, approaches that engage and retain service users in treatment enhance positive treatment outcomes. These issues are addressed in the other briefings in this series.

Evidence on the effectiveness of methadone maintenance is well established<sup>1</sup>. National US studies have shown that in methadone programmes a good therapeutic relationship between service users and clinicians, marked by arriving at appropriate dose levels and by discussion of health and drug-related issues during counselling sessions, can contribute to improved treatment retention and good outcomes<sup>2</sup>. Retention is an important goal in treatment, with unplanned exits from methadone services risking relapse to injecting drug use, HIV and other high-risk behaviour. A study in New York showed that service users stayed much longer at methadone clinics that responded constructively to their problems, such as by adjusting their methadone doses to meet their needs<sup>3</sup>.

In Britain what little we know about the preferences of the users of methadone treatment services suggests that they consider a flexible response to individual need to be most important. In one study, the majority of users identified mutual consent as their preferred option for deciding methadone dose levels and imposition by treatment staff as their least<sup>4</sup>. The service user/key worker therapeutic relationship can be threatened by disagreement over methadone dosage levels, which may undermine treatment effectiveness<sup>5 6</sup>.

Setting appropriate dosing levels is a critical factor in improving maintenance treatment outcomes. Based on the national and international evidence, the Department of Health's *Drug misuse and dependence - guidelines on clinical management* states that 'there is a consistent finding of greater benefit from maintaining individuals on a daily dose between 60mg and 120mg (and higher in exceptional cases)'<sup>7</sup>.

There is evidence that many drug treatment services in Britain are not providing even the minimum of the dose range identified by the reviews of more effective average doses. Consequently, they may not be providing the optimal methadone maintenance treatment. Findings from the National Treatment Outcome Research Study (NTORS) show that the average methadone maintenance dose in specialist services in the mid-1990s was approximately 50mg. Only a quarter of service users receive over 60mg<sup>8</sup>. Recent surveys have also shown that many GPs are prescribing at levels less than the evidence suggests is likely to be most effective<sup>9</sup>. Substantial regional variations in the mean doses prescribed for the treatment of opiate dependence have also been documented<sup>10</sup>.

But while the evidence supports the use of methadone maintenance at doses higher than currently prescribed in Britain, individualisation of the dose is important. Daily doses higher or lower than the recommended range may need to be prescribed. This is partly because individuals vary widely in blood levels reached after the same dose of methadone, and also because of a range of other factors including clients' subjective experiences, how responsive they are to the dose, the side effects they may experience with methadone and their medical or psychological condition<sup>11 12</sup>. Other issues to be considered are the use of illegal drugs and alcohol, and interaction with other therapeutic drugs prescribed to the client, for example anticonvulsants, anti-tuberculosis and some anti-retroviral medications. Titration of the dose in response to service user's requirement rather than the absolute levels of dose is essential. Other mechanisms to ensure safety must also be in place to avert the dangers of abuse and diversion (e.g. supervised consumption schemes, where appropriate).

It is also important to note that research also shows that the benefit of methadone maintenance treatment is enhanced by, and should be complemented with, a range of psychosocial services. Other factors required to provide optimum treatment have also been identified. These are discussed in other briefings in this series.

## 2. Retention in treatment

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Findings from national drug outcome studies in the UK and the USA have identified significant improvements in treatment outcomes amongst clients who stay in methadone maintenance treatment for at least a year (i.e. reduction in injecting and illicit heroin use). Research shows, however, that services do not always retain clients. In NTORS, 38 per cent of maintenance clients had left by one year and 58 per cent by two years. At both points the treatment leavers had worse outcomes. The American Drug Abuse Treatment Outcome Study (DATOS) also found wide variability in the ability of US methadone clinics to retain clients. In DATOS' 'worst' performing programmes, six out of seven service users left within 12 months; in the 'best', three-quarters stayed for at least this period.

## 3. Benefits of higher doses

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The majority of studies of clinical populations have demonstrated the benefits of higher doses of methadone in bringing a decrease in illicit opioid use and improvements in retention<sup>13</sup>. Studies show that higher doses of methadone are associated with a greater likelihood of cessation of injecting. For example, findings from an Australian series of studies showed that the risk of unplanned exit from treatment was almost halved for those whose daily dose was between 60 and 79mg of methadone and almost halved again when doses reached 80mg or more daily<sup>14</sup>. Data from these same studies also show that clients' likelihood of using illicit heroin while in treatment were reduced by two per cent for every 1mg increase in the maintenance dose. A similar finding was made by NTORS amongst clients still in maintenance treatment at two-year follow up in comparison to those who left treatment: each 2mg increase a day was associated with a two per cent reduction in the risk of regular illicit heroin use<sup>15</sup>. Similarly, a one-time increase of 20mg on top of a treatment dose of 50mg (the average dose found in methadone treatment in Britain) at a clinic in Baltimore led to substantial reductions in self-reported heroin use<sup>16</sup>.

However, research findings on the value of higher maintenance doses on retention have not been universal. For example, a US study comparing service users with 100mg regimes with those on a moderate dose of 40-50 mg found that the high dose group had lower levels of illicit drug use, but there was no evidence of higher rates of retention in treatment<sup>17</sup>.

## 4. Is there an upper limit?

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There is a smaller evidence base that determining the upper range of dosage of methadone maintenance, titrating against clinical indices, may bring benefits. A recent study demonstrated that high maintenance doses of methadone of 120mg blocked the effects of heroin for longer than 30mg and 60mg doses<sup>18</sup>. In another US study, methadone doses for service users already receiving 100mg a day, but unable to control their heroin use, were increased until each individual no longer felt discomfort or the need to supplement their<sup>3</sup> dose with heroin. Doses rose to an average of 211mg a day until heroin use was eliminated<sup>19</sup>. A study in an Italian clinic specialising in service users who had not responded to treatment elsewhere also increased methadone doses so that supplementary heroin use was very infrequent. For service users without psychiatric complications, this averaged 99mg but for those with diagnosed mental illness it averaged 154mg<sup>20</sup>. Both these studies showed significant improvements in levels of illicit heroin use when higher methadone maintenance doses were prescribed.

There is a very small body of evidence that lower doses may sometimes work. A US study comparing service users with an average methadone maintenance dose of 39mg to those who dropped out of treatment after 30 days demonstrated that those who remained in treatment showed reductions in illicit heroin use, as well as less involvement in crime and improved employment compared to those who left.<sup>21</sup> In another study, service users on doses under 50mg showed similar levels of illicit drug use to those who had doses over 50mg, with gender and ethnic background unrelated to illicit heroin use<sup>22</sup>

## **5. Flexible dosing and patient self-regulation**

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Whilst higher maintenance doses are associated with better outcomes, flexible dosing may also have a role to play in achieving optimal treatment. The impact of flexible dosage regimes was demonstrated in a major comparative survey of 113 US methadone clinics in the late 1980s. In the study, those offering flexible dosing were more successful in retaining clients than those offering fixed dose<sup>23</sup>. Similarly, the more recent American<sup>24</sup> and Italian<sup>25</sup> studies mentioned above underline the value of flexible dosing, as illicit heroin use was significantly reduced or ceased altogether where doses were increased until individuals no longer felt discomfort. Both the client groups may have been considered treatment failures in less flexible regimes.

There is now growing evidence that allowing service users to set their own methadone maintenance dose may bring improvements in treatment retention and reductions in illicit heroin use. The most compelling evidence comes from a recent US study where the service users were long-term stable methadone maintenance patients who were already on relatively high doses<sup>26</sup>. As in earlier similar studies, the service users' heroin use declined and the clients did not elect to push up their doses to excessive levels. Doses rose only slightly from an average of 77mg to 80mg, with 90 per cent of the clients receiving doses of 100mg or less.

Whilst these studies of flexible dosing and self-regulation of dose have demonstrated the potential benefits of this approach compared to treatment services with inflexible regimes or those that have a bias toward low doses, they have not demonstrated their benefit over treatment services, which have a flexible policy aiming to improve treatment outcomes and client functioning and comfort, rather than minimising doses. These studies have shown ways of avoiding potential sources of friction and fostering good relations between staff and service users did demand a high level of loose dose monitoring, but with doses increased in small steps and several days apart to ensure avoidance of overdose. Its benefits for 'less stable' patients have not been investigated.

## 6. Client-worker relationship

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Methadone maintenance dose is not the only factor to promote good treatment outcomes – the relationship with the key worker is also important. The importance of the relationship between key worker and client was demonstrated in a study of patients in New York methadone clinics. There, those counsellors who responded to service users' problems had greater impact on treatment outcome than service users' characteristics did. Counsellor responses included increased dosing and increased help with problems<sup>27</sup>. One study of a US methadone clinic showed that the counsellor had more impact on retention and illegal drug use than the methadone dose levels did<sup>28</sup>. The results of these studies suggest that the client/key worker relationship, how methadone programmes are managed and how responsive they are to service users' needs can have an important impact on retention and treatment outcome. This and other relevant issues are discussed in greater detail in the other briefings in this series.

## 7. Optimal components of methadone maintenance programmes

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The research findings in this series suggest that optimal methadone maintenance treatment programmes can be achieved by taking forward developments on a number of fronts. This briefing paper has identified that adequate dosing, flexible individualised dosing regimes and positive client-worker relationships appear to be important components of improving outcomes

## 8. Additional information

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All briefings, background papers and updates on the NTA's related work programmes are available online at [www.nta.nhs.uk](http://www.nta.nhs.uk) or from [nta.enquiries@nta-nhs.org.uk](mailto:nta.enquiries@nta-nhs.org.uk), tel 020 7972 2214.

*Models of care*, a framework for substance misuse treatment, and the *Commissioning standards in drug and alcohol treatment and care* are available from the NTA, email: [nta.enquiries@nta-nhs.org.uk](mailto:nta.enquiries@nta-nhs.org.uk), tel 020 7972 2214.

*Drug and Alcohol Findings* magazine provides updates on relevant research and is available from [findings@alcoholconcern.org.uk](mailto:findings@alcoholconcern.org.uk), tel 020 7928 7377.

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