Primary care prescribing for patients receiving methadone maintenance treatment

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Research question

What evidence is there to support the transfer of stable methadone patients to primary care prescribing?

Key points

- Ten distinct studies were identified for inclusion in the review; four were conducted in the United States (US), three in the United Kingdom (UK), two in Ireland and one in Australia.
- Three randomized controlled trials (RCTs), six cohort studies and one cross-sectional survey were included in the review.
- The three RCTs compared treatment outcomes of stable patients who were transferred from specialist care to primary care with those of stable patients who remained in specialist care. The remaining seven studies compared treatment outcomes for individuals treated in specialist care compared with individuals treated in primary care.
- Individuals treated in primary care had similar treatment outcomes to those treated in specialist care.
- General practitioners (GPs) participating in the included studies were often those with an interest in treating problem drug users (PDUs) or those treating large numbers of PDUs; therefore, they may not be representative of GPs in general.
- The evidence suggests that transferring stable methadone patients from specialist care to primary care does not result in adverse treatment outcomes.

Background

Methadone maintenance treatment (MMT) is effective at keeping individuals in treatment, reducing heroin use, and reducing drug-related behaviours with a high risk of HIV transmission (Mattick et al. 2009, Gowing et al. 2011). British policy seeks to encourage and expand the role of GPs and there is an increasing interest in the use of MMT in primary care (Gossop et al. 2003).

This brief topic review initially sought to identify the published literature in which i) stable MMT patients were transferred from specialist care to primary care, and ii) treatment outcomes of those who transferred to primary were compared with those who remained in specialist care. No UK-based research was identified which met these criteria; therefore, this review also included studies which focussed on treatment outcomes for individuals treated in specialist care compared with individuals treated in primary care.
Methods
An electronic database search was carried out using MEDLINE, EMBASE and Scopus. All databases were searched from inception to February 2013. Titles, abstracts and keywords/subject headings were searched using the concepts of primary care/general practice and methadone maintenance.

Results
The search retrieved 781 titles and abstracts: 358 were unique. Twenty-five were excluded because they were not in English. Further titles and abstracts were excluded due to irrelevant topic or focus (n=229), no empirical data (n=54) and no comparator (n=26). This left 24 reports remaining for full-text review. A further 13 reports were excluded from the review, these were:

- Two studies in which individuals receiving MMT were transferred from primary care to specialist care due to legislative changes (Buhl, Saelan and Sorensen 2004, Cahill et al. 2003).
- One cross-sectional survey of drug treatment services in inner London (n=4) including specialist clinics and shared care in primary care; treatment outcomes were not compared between the two settings (Dunn et al. 2007).
- Three secondary reports of three studies already included in the review (Fiellin et al. 2004, King et al. 2002, Tuchman and Drucker 2008).
- A ‘current opinion’ of office-based maintenance treatment, including methadone and buprenorphine maintenance. This was excluded due to a lack of empirical data (Gunderson and Fiellin 2008).

The remaining eleven reports pertaining to ten distinct studies were identified for inclusion in this review. These comprised three RCTs, three prospective cohort studies, three retrospective cohort studies, and one cross-sectional study. The studies are briefly discussed below (grouped according to study design).

Randomized controlled trials (n=3)
Fiellin et al. 2001
This open RCT was conducted in the US. Participants were patients who had been receiving methadone in a narcotic treatment program (NTP) without evidence of illicit drug use for 12 months and with no significant untreated psychiatric condition. Forty-six patients were randomized to receive office-based MMT from one of six primary care physicians who had received specialised training in the care of opioid-dependent patients or usual care in an NTP.

Outcomes were measured at six months. There were no significant between-group differences in illicit drug use, retention in the study protocol, SF-36 score or use of health, legal and social services as measured by the Addiction Severity Index (ASI). There were significant between-group differences in the percentage of patients reporting satisfaction with treatment; those receiving office-based treatment were more likely to be satisfied.
with the care received and rate the quality of care as excellent. There were no significant between-group differences regarding clinician satisfaction. The authors note that the power of the study to detect significant differences was limited by the small sample size.

King et al. 2006

This RCT reported the 12-month outcomes of 92 highly stable methadone maintenance patients. Participants were from one of two community-based MMT programmes in the US. Individuals had to meet the following criteria, amongst others, for the previous 12 months: an uninterrupted treatment episode, negative urinalysis for illicit drugs and verified full-time employment. Participants were randomly assigned to one of three conditions: i) office-based methadone medical maintenance (MMM), ii) clinic-based MMM or iii) routine care in a clinic setting. MMM patients consumed one observed dose of medication at the office or clinic and received 27 days of take-home medication. The routine care group consumed 1-2 doses of medication per week at a dispensing window at their clinic and received 5-6 days of take-home medication. Participants who failed medication recall or tested positive for illicit drugs were subject to adaptive stepped-care treatment intensification.

Outcomes were measured using the ASI, Client Satisfaction Questionnaire (CSQ), Helping Alliance Questionnaire II Patient version and a behavioural assessment. There were no significant between-group differences in the percentage of patients retained in treatment, positive urinalysis or failed medication recalls. No significant between-group differences were found in the rating of the quality of the therapeutic alliance between patients and therapists from the patients’ perspectives. No between- or within-group difference was found for ASI composite scores. Patients assigned to either MMM condition were significantly more satisfied with treatment and demonstrated significantly larger reductions of time spent in clinic-related activities than those receiving routine care. A greater proportion of individuals in the MMM conditions initiated new vocational or social activities than those in routine care (p<.001).

Participants were required to have been in full-time employment for the 12 months prior to entry and therefore the generalizability of this study is limited. Furthermore, one of the two physicians providing office-based MMM was an addiction physician.

Tuchman et al. 2006

In this RCT a primary care model of methadone prescribing in conjunction with community pharmacy dispensing and social work treatment was compared with routine care in an MMT programme. Twenty-six stable female patients were recruited from two MMT programmes in New Mexico. Participants were required to have a minimum of six months in MMT, six months of relatively stable methadone doses, privileges to have at least two take-home doses per week and no significant psychiatric illness.

Participants were randomly allocated to one of the two treatment conditions and followed-up for 12 months. Retention in methadone treatment was 100% in the primary care condition compared with 89% in the routine care condition. However, two primary care participants were returned to usual care due to clinical instability i.e. illicit drug use and mental illness early in the study period.

A greater proportion of those in routine care tested positive for illicit opiate use (78% vs. 23%), cocaine use (44% vs. 23%) and benzodiazepines (44% vs. 8%). The between group differences were not statistically
significant. This authors note that the lack of statistical significance was most likely due to the small sample size and thus reduced power.

**Prospective cohort studies (n=3)**

**Comiskey and Cox 2010**

The Research Outcome Study in Ireland Evaluating Drug Treatment Effectiveness (ROSIE) was a prospective cohort study which followed individuals commencing a new treatment episode. Individuals entering methadone maintenance/reduction, structured detoxification and abstinence-based treatment were recruited. This article provides the one-year treatment outcomes for 78% (n=167) of individuals in the methadone modality. This modality comprised individuals in three treatment settings: community-based clinics (n=35), primary care (n=45) and health board clinics (n=82).

There was a significant increase in heroin abstinence rates and a significant decrease in the number of days of heroin use in all three settings. The quantity of heroin used significantly decreased for those treated in primary care and health board settings, but not for those treated in community-based settings. The majority (88%) of those treated in primary care were in some form of treatment at one year, which was similar to the 93% and 90% of those treated in community-based settings and health board settings respectively.

There were no significant changes in the proportion of individuals experiencing physical health symptoms over the previous 90 days between baseline and follow-up, or in the frequency of physical health complaints, for those treated in primary care. For those in community-based settings, there was a significant increase in the proportion experiencing ‘numbness/tingling’, and in the mean number of days participants reported experiencing ‘stomach pains’ and ‘numbness/tingling’. Results for those treated in health board settings were mixed; there was a significant increase in the proportion experiencing ‘stomach pains’, but a significant decrease in the mean number of days that participants reported having a ‘poor appetite’. There were no significant changes in mental health outcomes for those treated in community-based or health board settings at one-year follow-up; however, there were significant increases in the mean number of days that participants treated in primary care reported ‘feeling tense’ and ‘nervous/shaking inside’.

The findings demonstrate that methadone is effective at reducing heroin use regardless of treatment setting; however, it is not particularly effective at addressing physical and mental health symptoms.

**Gossop et al. 2003, Gossop et al. 1999**

The National Treatment Outcome Research Study (NTORS) was a prospective cohort study in the UK which followed individuals commencing a new treatment episode. Individuals were recruited into one of four treatment modalities: specialist inpatient treatment, rehabilitation programmes, methadone maintenance programmes and methadone reduction programmes. This article reports the two-year treatment outcomes of individuals receiving methadone treatment from a specialist clinic (n=161) or primary care (n=79). The primary care sample was drawn from seven programmes, five of which were co-ordinating shared care services in which methadone treatment is provided by the GP whilst the clinic provides counselling services.

There were no significant pre-treatment differences between the two groups in terms of age; gender; length of heroin career; frequency of use of heroin, illicit methadone or stimulants; rates of injecting or sharing needles; involvement in acquisitive crime; previous methadone treatment, or levels of anxiety or depression.
Some pre-treatment characteristics differed significantly between the groups. The primary care sample were more frequent users of non-prescribed benzodiazepines and were more likely to have received prior treatment from a GP. Those treated in specialist clinics were more likely to have received prior treatment from a clinic. The clinic sample had significantly more physical health problems than the primary care sample. There was no significant difference between the samples in methadone dose at the start of treatment.

Both groups experienced significant reductions in the frequency of use of illicit opiates, non-prescribed benzodiazepines and stimulants. The reduction in the use of non-prescribed benzodiazepines was significantly greater for those treated in primary care. Rates of injecting, sharing needles, frequency of acquisitive crime and physical health problems significantly decreased in both groups, with no significant differences between the two. Psychological health problems significantly reduced in both groups, with a greater reduction among those treated in primary care.

There are limitations to this study. Firstly, the study was a ‘natural’ cohort design and therefore there was no randomization; however, both samples had similar characteristics at intake with the exception of those noted above and there was no indication that the primary care sample was less problematic with regard to drug use. The authors note that the GPs in this study may not be representative of GPs in general due to their willingness to actively involve themselves with PDUs. Furthermore, a substantial proportion of the GP sample was drawn from primary care services which were involved with relatively large numbers of drug users.

MacGowan et al. 1996

This cohort study involved 674 clients entering seven MMT clinics in the US. Eligibility for MMT required documented proof of opioid dependence and being aged 18 or above. Clinics were categorised based on drug treatment philosophy and the availability and integration of HIV services into the drug treatment program. Two were categorised as a primary care programme model, two as a case management model, and three followed a 12-Step approach to treatment.

Logistic regression analyses found three variables significantly predicted retention in treatment at six months; increased age and enrolment in the primary care model increased the likelihood of treatment retention whilst patients injecting three months after enrolment were half as likely to remain in treatment. These three variables were also found to significantly predict treatment retention at twelve months.

Those in the primary care model received more substance abuse counselling and higher methadone doses compared to the other two. Entry criteria were unrestrictive but clients self-selected into each clinic.

Retrospective cohort studies (n=3)

Mullen et al. 2012

Opiate users commencing methadone treatment in Ireland in 1999, 2001 and 2003 (n=1269) were randomly selected from the central methadone treatment list. The aim of the study was to determine the retention in MMT at one year and to indicate factors that increase the likelihood of retention.

61% (n=770) remained in treatment for more than 12 months. Retention in treatment at 12 months was independently and positively associated with older age, being female, treatment by a primary care physician and a methadone dose of 60 mg/day or higher. Age was not an independent factor in retention once it was adjusted for. Individuals attending a specialist treatment were twice as likely to leave MMT within 12 months.
compared to those treated by a GP. The most important predictor of retention was methadone dose; those receiving less than 60 mg/day were three times more likely to leave treatment within 12 months.

The authors note that specialist clinics in Ireland often have more ‘chaotic’ patients i.e. those unsuitable for treatment in primary care. Patients receiving MMT are often transferred from specialist care to primary care when stable.

**Lewis and Bellis 2001**

This was a retrospective review of patient records which looked at differences in treatment outcomes between general practice and specialist care in Liverpool. All patients prescribed MMT in one general practice (operating a shared-care policy) during a two-year period (n=36) were compared with one third of patients treated at a specialist clinic during the same period (n=89). The specialist clinic kept a chronological list of all new patients seen and every third patient from this list was included, with the exception of those who were not prescribed methadone. Patients were followed-up for a minimum of nine months.

The groups did not differ significantly in terms of age, sex, opiate use, injecting history, previous prison sentences, or previous courses of methadone treatment. Women treated in the specialist clinic were more likely to be pregnant at intake and more likely to be commercial sex workers but this difference was not significant. Pregnancy and commercial sex work were criteria for priority treatment at the specialist clinic.

The likelihood of a ‘good’, ‘OK’ or ‘bad’ outcome did not differ significantly between the two groups. Remaining in treatment or becoming drug-free were considered to be good outcomes; moving away or being transferred elsewhere were considered to be ‘OK’; and using illicit opiates, being in prison or having an unknown outcome were considered to be ‘bad’ outcomes. When split into smaller categories, those in the GP setting were significantly more likely to be in prison, whereas those treated in specialist care were significantly more likely to have an unknown outcome. There was no significant difference between the groups in the number of patients attending accident and emergency.

Individuals treated in general practice were significantly more likely to have been tested for Hepatitis B and C, and to have been fully immunised against Hepatitis B or to have natural immunity against it than those in specialist care. Of those tested for Hepatitis B, the proportion testing positive was significantly higher in those treated in specialist care.

Doctors involved in this study had an interest in drug dependence and therefore they may not be reflective of all GPs. In addition, the GPs worked closely with community psychiatric nurses (CPNs) from the clinic and had easy access to advice from CPNs or a consultant psychiatrist at the clinic. Thus findings have limited generalizability.

**Ernst et al. 2002**

This was a retrospective data analysis of methadone-related deaths in Western Australia from 1993-1999. Cases were identified by methadone detected from toxicological analysis of post-mortem samples. A methadone-related death does not imply that methadone was the cause of death; death may also have occurred due to a medical condition or traumatic event.
In 1997 a Community Based Methadone Programme (CBMP) was introduced which allowed accredited GPs and community pharmacies to provide MMT. Previously, this was provided solely by the government sector by specialist drug and alcohol services and clinic pharmacies.

Less than half (43%, n=36) of decedents were registered in a methadone maintenance programme at the time of death, with 61% (n=22) of these in specialist care and 39% (n=14) in CBMP. In 1998, the risk of death was 3.4 times higher for those in CBMT than for those in specialist care, although this was not statistically significant. The proportion of deaths occurring within the first week of treatment was significantly higher for those in CBMT compared with those in specialist care, with 57% of CBMT deaths and 9% of specialist care deaths occurring within the first week of treatment. With one exception, all methadone doses for decedents who died in the first week of MMT complied with the recommendations of the National Methadone Policy at the time. The coroner’s verdict for the exception was suicide.

The authors concluded that there were very few methadone-related deaths occurred in MMT during the seven year period, and that death was generally not associated with methadone alone or excessive amounts of methadone. An increase in mortality followed the expansion of MMT into general practice. Authors noted that these findings are similar to those from other Australian States in that the induction period is of particular high risk for patients treated by GPs.

**Cross-sectional survey (n=1)**

**Speed and Janilklewicz 2000**

The aim of this study was to compare the satisfaction levels of patients treated in primary care with those treated in specialist clinics using a questionnaire. Individuals receiving MMT were recruited from eight GP surgeries (n=73) and two specialist clinics (n=97) from the North-West of England.

There were significant differences between the groups in reported happiness with treatment, self-reported emotional happiness, and satisfaction with prescribed medication, GP contact, relationship with prescriber, help available for ‘general problems’, and help available for prescription-related problems. Those in the GP sample were significantly more satisfied in each of these areas.

There were no significant differences between the groups in relation to satisfaction with contact with key workers or in reported health status in the previous 30 days.

The study demonstrates that those treated by their GP indicated a greater level of satisfaction than those treated in specialist clinics. The study did not examine whether greater satisfaction was associated with improved treatment outcomes.

**Methodological points**

The length of follow-up varied between studies but was generally quite good, with NTORS reporting a two-year follow-up (Gossop et al. 2003).

The generalizability of the included RCTs is limited. All three were conducted in the US. One included female participants only (Tuchman et al. 2006) whilst another required that participants were in verified full-time employment for 12 months prior to enrolment (King et al. 2006). Two of the three RCTs had sample sizes
fewer than 50 and therefore the power to detect significant changes was limited (Fiellin et al. 2001, Tuchman et al. 2006).

With regard to the cohort studies, individuals treated in specialist clinics may have more severe problems than those treated in primary care, although Gossop and colleagues noted that there were few significant pre-treatment differences between the groups in their study (Gossop et al. 2003).

The GPs who participated in these studies were often those who had an interest in treating PDUs or those treating greater numbers than the average GP; therefore, they may not be representative of GPs in general.

**Conclusion**

There is evidence to support the transfer of stable methadone patients to primary care prescribing, particularly if the primary care physicians are interested in this group. However there is insufficient evidence for transfer to a more ‘representative’ GP population. Whilst there were methodological issues with many of the included studies, patients treated in primary care were found to have similar outcomes to those treated in specialist clinics regardless of whether they were randomized into these treatments or self-selected them. Studies which measured and compared patient satisfaction found that patients treated in primary care reported significantly higher levels of satisfaction than those in specialist clinics (King et al. 2006, Speed and Janiklewicz 2000).
References


