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A Risk-Benefit Analysis of Methadone Maintenance Treatment

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Abstract

Methadone maintenance treatment for heroin (diamorphine) addiction has been extensively researched. There is consistent evidence that while in treatment, heroin addicts are at a lower risk of death, are less involved in crime, and feel and function better than while using heroin. Despite the research evidence supporting methadone treatment, there remains widespread public scepticism about this form of treatment. This scepticism is frequently expressed in terms of the perceived risks of methadone treatment. The perceived risk that methadone treatment may maintain people in an addicted lifestyle is not supported by research literature. The risks of treatment include an increased risk of death during induction into treatment, and risks of diversion of drugs to the black market. For some patients, adverse effects of methadone pose a problem and the availability of new pharmacotherapies may provide useful options for these patients. Risks can be reduced and benefits increased by directing greater attention to the quality of treatment.

The synthetic opioid methadone has been used in the treatment of heroin (diamorphine) addiction for more than 30 years. Diverse approaches to treatment have evolved and are collectively referred to as methadone maintenance treatment. However, it is a little misleading to speak of the risks and benefits of methadone maintenance treatment as though it were a standardised form of treatment. Although approaches to methadone maintenance treatment all have the drug methadone in common, methadone maintenance treatment involves much more than merely a pharmacological treatment. There are many approaches and there is strong evidence that both the risks and benefits of

treatment, as it is actually delivered, vary widely between different treatment approaches.[1]

This review aims to provide health professionals with information that will enable them to address the concerns of prospective patients. It therefore addresses the key issues of concern to potential consumers of methadone, namely individuals with heroin addiction and their families. A guide to the concerns patients have about treatment comes from a UK survey of patients taking methadone, who identified 3 major concerns about treatment.[2] First, they were concerned at the addictiveness of methadone and that taking it would increase or prolong their dependency on drugs. Secondly, they were concerned about the impact of methadone on their quality of life. Finally, and most interestingly, many patients expressed concern at what they perceived to be the poor quality of treatment delivered in some methadone clinics. An unpublished Australian survey has identified identical concerns expressed by users of heroin not in treatment. Accordingly, this review addresses the first 2 perceived risks of methadone maintenance treatment by a review of the literature. The issue of quality of programmes is beyond the scope of this review, but will be seen to be a recurring theme in all aspects of treatment.

While patients receiving methadone maintenance treatment readily acknowledge the benefits of being in treatment (reduced drug use, reduced crime, improved lifestyle),[2] many health professionals have serious concerns about methadone treatment and actually discourage individuals from participation in this treatment. A degree of professional negativity towards methadone maintenance treatment has been a feature of its history.[3] To the extent that objections focus on empirical issues, these can be addressed by a review of the literature. There is a small published literature questioning both the safety of methadone treatment[4,5] and its effectiveness in rehabilitation.[6] Accordingly, this review addresses the issues of safety and effectiveness of methadone maintenance treatment.

There is an enormous literature on methadone treatment, much of it focusing on specific approaches and interventions. Preparatory to this review, a literature search was performed which identified over 9000 articles on methadone published since 1966. The method adopted was to perform detailed literature reviews on 3 specific topics – the impact of methadone maintenance treatment on survival, the quality of life of patients taking methadone, and the impact of methadone maintenance treatment on eventual recovery from addiction. Only a few landmark studies on the overall effectiveness of treatment are reviewed.

It is beyond the scope of this review to address complex issues such as use of methadone in pregnancy, methadone in prison settings, and the management of individuals with opioid addiction with coexisting mental disorders.

1. Mortality

Methadone maintenance treatment protects against death by heroin overdose, the most common cause of mortality among individuals using heroin. The positive impact of methadone maintenance treatment on the mortality rate of individuals using heroin has been confirmed in many studies. An early North American study followed 17 500 patients admitted for methadone maintenance treatment in New York City between 1964 and 1971.[7] The authors found that the all-cause mortality rate for patients receiving methadone maintenance treatment was similar to the mortality rate for the general population whereas the mortality rate of untreated individuals using heroin was more than 15 times higher. These observations have been reinforced by several studies confirming the protective effect of methadone treatment, and recent studies reporting 3- to 4-fold increases in likelihood of drug-related fatalities among individuals who discontinue treatment compared with those still undergoing treatment.[8-10]

Despite clear evidence of reduced mortality during treatment, several studies have identified the period of induction into methadone maintenance treatment as a time of increased risk of death.[11,12] Deaths during induction into treatment are usually due to drug toxicity and appear to be the result of prescription of doses of methadone that exceed the

individual's level of tolerance.[13,14] Inadequate assessment of prospective applicants and rapid increases in prescribed doses[12] have been identified as factors that increase risk. The most consistent finding in relation to deaths during induction into methadone maintenance treatment is that multiple drugs are usually involved.[12,15,16]

The risks associated with induction into methadone maintenance treatment should be minimised by detailed pretreatment assessment of opioid dependence and polydrug use, and by closer monitoring of newly inducted patients.[17]

1.1 Risks to People Not Receiving Treatment

The contribution of methadone maintenance treatment to mortality is not confined to those in treatment. Up to two-thirds of deaths associated with methadone maintenance treatment occur as a consequence of diversion of methadone to persons not in treatment.[18] The presumed source is 'takeaway' methadone, where the drug is dispensed to be taken at home rather than taken under supervision at the dispensing point. A study in Sydney found that black market methadone was almost entirely (88%) made up of diverted takeaway doses.[19]

The extent to which methadone is diverted, and hence the likelihood of overdose deaths, depends on the way in which treatment is delivered. In Australia, where methadone is usually dispensed for daily consumption under supervision at a clinic, heroin deaths constitute the overwhelming majority (80%) of opioid deaths.[20] In the UK, although the overall opioid-related death rate is lower, methadone deaths account for about half of opioid fatalities.[21] In the UK, most treatment is delivered by prescription – the patient receives a prescription for methadone, has it made up at a pharmacy, and takes the medication home to use without supervision. Diversion of methadone, or its use other than as directed, may account for the substantially greater proportion of methadone deaths in the UK.[22] Diversion of methadone is probably an indication of an unmet demand for treatment, and of styles of treatment which deter addicts from participation.[23]

It is commonly feared that diversion of methadone into the black market places previously opioid-naive persons at risk of death and developing opioid dependence. This concern is not substantiated by the very limited research into recipients or purchasers of illicit methadone. What scant data are available indicate that consumers of diverted methadone are mostly established heroin users.[18,23] However, there is 1 group of opioid naive persons at risk of death from takeaway doses of methadone. Children, especially those of parents taking part in a methadone programme, have occasionally died as a result of ingesting methadone. An Australian study[18] found that methadone was detected postmortem in 8 children who died between July 1990 and December 1995 in New South Wales. In 5 of these children, methadone was presumed to have contributed to death. In 3 children, the child had ingested the mother's takeaway dose.

A recent study attempted to calculate the impact on mortality of methadone maintenance treatment, taking into account not only death in treatment but also deaths of people not in treatment who succumbed to an overdose (including those who took diverted methadone).[24] The authors concluded that, on balance, methadone maintenance treatment had a substantial net benefit in terms of mortality. They appropriately argue that deaths of people not in treatment need to be minimised by ensuring that doctors comply with clinical guidelines. Indeed, the recurrent theme in all areas of methadone maintenance treatment is that risks and benefits depend greatly on the quality of treatment delivered.

2. Rehabilitation

The treatment of heroin addiction is best conceptualised as a form of rehabilitation, as a means of reintegration into society of individuals marginalised by disability. In the context of heroin addiction, rehabilitation is usually measured in terms of changes towards less involvement in crime and prostitution, and more involvement in activities such as work, education and child rearing.

The most convincing studies of treatment efficacy come from randomised, controlled trials. In the first such trial of methadone treatment,[25] 32 prisoners awaiting release were randomised to receive either methadone or no treatment. Both groups were followed for 12 months from release. Four patients randomised to methadone maintenance treatment did not enter treatment, leaving a treatment group of 12. At 12 months, none of the methadone maintenance treatment patients had returned to daily heroin use, whereas all 16 in the no treatment group had done so. Only 3 of the methadone maintenance treatment patients had returned to jail; all 16 in the control group had done so. Even on an intention-to-treat analysis (that is, including the 4 who did not enter treatment), the dramatic reduction in heroin use and crime witnessed in the treatment group was statistically significantly better than the outcomes observed in the no treatment group.

A placebo-controlled trial of methadone maintenance treatment in Hong Kong recruited 100 consecutive patients eligible for methadone maintenance treatment.[26] All participants were stabilised on methadone 60 mg/day for 2 weeks, then randomised to either receive placebo or continued methadone. Both groups were followed for 3 years. Over this period, 4 times as many people were discharged from treatment for persisting heroin use in the placebo group. At 3 years, 56% of methadone maintenance treatment patients were retained in treatment, compared with 2% in the placebo group. Thus, this study confirms greater treatment retention and reduced heroin use in people treated with methadone.

The third controlled trial of methadone maintenance treatment was conducted in Sweden and involved patients randomised to methadone maintenance treatment or drug-free treatment (in effect, the control group received no treatment, as none accepted drug-free treatment).[27] Methadone maintenance treatment patients received intensive psychosocial support as well as methadone and could remain in residential treatment for up to 6 months. Sequential patients were randomised to the 2 groups until significant differences in outcomes became detectable. This occurred after randomisation of the 36th patient, 17 of whom received methadone maintenance treatment. Thereafter, those who had entered the trial were followed for 2 years. The differences between treated and control groups were dramatic. At the end of that time, 12 of 17 methadone maintenance treatment patients were not using heroin regularly and were employed or undertaking education. The remaining 5 patients had been discharged from the programme for continuing drug abuse. Two patients were excluded from the control group because they had commenced methadone maintenance treatment in another programme. Of the remaining 17 control patients, 1 was drug-free, 12 were abusing opioids, 2 were in jail and 2 were dead. This small but important trial indicates not only reduced heroin use in a majority of people receiving methadone, but also improved social reintegration. It is reasonable to deduce that improved retention in this programme of intensive psychosocial support is associated with a range of better outcomes.

The consistent finding in these 3 landmark trials of methadone treatment is that patients receiving methadone are more likely to remain in treatment and use less heroin than those not receiving methadone. Significant reductions in crime[25] and improvements in social functioning[27] were also noted in specific trials.

These studies are now dated and took place in settings rather different to those of the 1990s. However, more recent studies continue to replicate these results. A randomised trial of 'interim' methadone demonstrated significantly lower heroin use in the group receiving methadone, compared with a control group randomised to being placed on a waiting list for treatment – effectively, a no-treatment group.[28] A randomised trial that compared methadone with buprenorphine in terms of a range of outcome variables concluded that patients in both groups showed 'significant and substantial improvements' in psychosocial functioning, and in opioid and cocaine use.[29]

In addition to these randomised trials, there have been multiple observational studies evaluating methadone maintenance treatment. The results of large scale observational studies are valuable in that they give an indication of the effectiveness of treatment as it is actually delivered outside the context of a controlled trial. However, they are less reliable indicators of treatment effectiveness because issues of patient selection and differential attrition from treatment make it more difficult to attribute the outcomes observed to the intervention provided.

In the case of methadone maintenance treatment, observational studies are consistent with the results of randomised trials. Analysis of 1 large study is sufficient. The Treatment Outcome Prospective Study (TOPS) prospectively followed more than 11 000 people using illicit drugs who commenced treatment between 1979 and 1981.[30] The 3 major modalities of treatment for heroin addiction – methadone maintenance treatment, residential therapeutic communities, and drug-free outpatient counselling – were studied. During the in-treatment phase of the study, new entrants to treatment were interviewed, then re-interviewed every 3 months while they remained in treatment. Subsequently, a subset of patients who had left treatment was followed up for 3 to 5 years (depending on the year of their enrolment).

Methadone maintenance treatment was associated with the best retention in treatment of all treatment modalities. The key findings from this massive study were that patients in all modalities reduced their drug use and involvement in acquisitive crime during treatment. Outcomes were expressed relative to the group of patients who left treatment after less than 1 week – essentially, a no treatment reference group. At follow-up interviews, patients remaining in long term methadone maintenance treatment had about one-quarter the prevalence of regular heroin use, and about one-third the prevalence of acquisitive crime, compared with this reference group. Both differences were statistically significant.

The TOPS study was also able to demonstrate that some benefits of treatment persisted after individuals had left treatment. However, post-treatment outcomes were heavily influenced by the duration that individuals had remained in treatment – the longer people remained in treatment, the lower their likelihood of regular heroin use or involvement in acquisitive crime after discharge. Relative to those who left treatment within 1 week, regular heroin use post-discharge was significantly lower only in patients who had remained in treatment for at least 12 months. After leaving methadone maintenance treatment, involvement in acquisitive crime was also lower for patients who had longer periods in treatment, but the difference did not reach statistical significance.

One other study is important to mention. The work of Ball and Ross[31] was the first large-scale study to investigate what actually occurs in methadone treatment. Although in all 6 clinics they studied there was evidence that methadone treatment was associated with reduced heroin use and crime, there were significant differences in outcomes across the clinics. This important observation confirms repeated findings from experimental studies that how treatment is delivered can make considerable difference. In particular, adequate methadone dose[32] and extent of counselling interventions[33] have been demonstrated to influence methadone treatment outcomes.

2.1 HIV Risk Reduction

Given that patients in methadone maintenance treatment programmes use and share needles less, it is reasonable to expect that they would be at proportionately lower risk of acquiring HIV infection. Two prospective cohort studies from the US have confirmed this expected protective effect. The first study followed 255 individuals who injected heroin over 3 years.[34] The HIV seropositivity in the sample receiving methadone treatment changed from 13 to 18% in that time. Among the sample not receiving treatment, seropositivity increased more substantially, from 21 to 39% over the same period. In the second study, 685 patients were followed.

The first group comprised people receiving methadone maintenance treatment; the second group came from a detoxification programme. Adjusting for other HIV risk factors, individuals who spent less than 1 year receiving methadone treatment were nearly 3 times more likely to test positive for HIV than those who underwent detoxification only.[35]

However, a series of studies from The Netherlands have documented the failure of 'low-threshold' methadone programmes to reduce HIV risk taking behaviour and HIV transmission.[36] This finding emphasises the importance of quality assurance in methadone maintenance treatment, as the risks and benefits depend on how treatment is delivered. The current literature suggests that methadone programmes can protect individuals by reducing their risk of HIV, but simply providing a dose of methadone – particularly a suboptimal dose – is not sufficient to achieve this objective.

2.2 An Overview of Methadone in Rehabilitation

Although outcomes vary depending on the quality of treatment delivered, there is consistent evidence that on entry to methadone treatment, most individuals who use heroin promptly and substantially reduce their use of heroin. However, methadone treatment does not abolish heroin use. Around 50% of people in treatment persist in occasional heroin use, and up to 10% of patients who enter methadone maintenance treatment continue to use heroin regularly.[37,38] Most people who leave treatment relapse to heroin use.[39]

Parallel to the reduction in heroin use is a reduction in participation in acquisitive crime and risk of contracting HIV. These reductions can be substantial.[31,40]

3. Quality of Life

A review of the literature on the medical safety of methadone maintenance treatment concluded that long term administration of methadone does not result in any adverse biochemical or tissue changes.[41]

A small number of studies have reported improvements in well-being following entry to methadone maintenance treatment. Reno and Aiken[42] studied life activities in heroin users at the time of entry to methadone maintenance treatment and over the ensuing 8 months. Patients reported a prompt and substantial improvement in life activities (such as 'spending more time with family') in the 2 months following entry to treatment. There was little discernible change in the following 6 month interval. Similarly, Torrens et al.[43] reported an 'early and substantial improvement' in health-related quality of life. Both these studies used large samples and provide convincing evidence to support the observation that entry to methadone maintenance treatment is associated with positive changes.

Nevertheless, there have also been reports of negative effects of methadone which might be expected to contribute to reduced quality of life. For example, Martin et al.[44] observed 6 patients who were administered methadone in a closed ward over a 15 week period (7 weeks of ascending methadone dose up to 100 mg/day, followed by 8 weeks on a stable dose of 100 mg/day). They reported that long term administration of methadone produced sedation, lethargy and decreased motivation. Reduced sense of well-being and efficiency, and reduced sexual interest and activity, were also observed. Patients also slept more during the day. In addition, once stabilised on methadone 100 mg/day, patients reported an increase in symptoms of opioid abstinence. Although the numbers in the study were small, and many of the trends reported by the authors did not reach statistical significance, these effects resemble symptom complaints made by patients in treatment.

For example, Angle et al.[45] reported a significant rise in somatic distress in 93 patients after 12 months in methadone treatment. Another study of methadone adverse effects in 102 male patients found that the most common complaints were sweating, constipation, drowsiness, sexual problems and aches in bones and joints.[46] While there were no statistically significant differences be-

tween patients who have recently started treatment and patients who have received long term therapy, the latter appeared more likely to be bothered by sweating than the former, whereas constipation occurred most frequently during the initial stages of treatment. However, the authors stated that complaints were found, in general, to be minor and did not constitute a barrier to patient retention in treatment.

Importantly, many of the symptoms reported in the study by Langrod et al.[46] resembled chronic, low-grade symptoms similar to opioid withdrawal. It has been reported that about one-third of patients taking methadone maintenance treatment reported symptoms of opioid abstinence.[47]

One notable adverse effect of methadone appears to be the accelerated development of dental caries. There are many factors contributing to poor dental hygiene among individuals addicted to heroin. Methadone contributes to reduced salivary flow, which is a factor that promotes caries.[48]

From the limited data on well-being, a reasonable summary would appear to be that people receiving methadone feel and function better than when they were using heroin. However, there are persisting adverse effects during treatment which may detract from quality of life of some patients, and drug-free ex-addicts feel and function better than those taking methadone.[49]

A final, important issue concerns the effects of methadone on skills such as driving. Although there have been studies suggesting a slight slowing in reactions among individuals taking opioid drugs,[50] most research on people receiving a daily dose of methadone has shown little if any psychomotor or cognitive impairment.[51] Based on studies to date, it seems reasonable to conclude that people receiving a stable dose of methadone can safely drive motor vehicles.

It is likely that more attention will be paid to the adverse effects of methadone in the future as new alternative maintenance agents become available. Current data suggests that both buprenorphine and levacetylmethadol (levomethadyl acetate) are approximately equivalent in efficacy to methadone as maintenance drugs for heroin addiction.[52] In the future, it is likely that patients who experience adverse effects and/or lack of efficacy on methadone maintenance treatment will be able to switch to an alternate drug.

4. Does Methadone Maintenance Treatment Perpetuate Addiction?

Consumers and potential consumers are often the most stringent critics of methadone treatment. A survey of attitudes to methadone found that although frequently used by individuals who are addicts of heroin and who are not in treatment, methadone is not highly valued as a euphoriant drug.[53] When used by people not in treatment, such use was mainly for the purpose of treating withdrawal. Potential consumers perceived the patient receiving methadone as being locked into a drug-using, static lifestyle. This negative perception of methadone maintenance treatment is expressed in an interesting quote from an individual with heroin addiction, not in treatment, who said of patients taking methadone '. . . [They] are just lazy individuals who don't want to do anything. They come and pick up their juice, then sell it. They go crack a few scripts, sell that. They get high, they stumble around the streets'.[53]

The central issue in these comments is the image of patients receiving methadone as having settled into a drug-dependent lifestyle with little motivation to change. This is the essence of criticism of methadone maintenance treatment; while taking methadone, patients are 'still addicted', both in the sense that they are still taking a drug and, more broadly, in the sense that they are still living a lifestyle revolving around drug use. The patients have become methadone addicts instead of heroin addicts.[6]

This is a difficult claim to respond to since, in part, it is challenging the validity of methadone treatment on *a priori* grounds – that because people on methadone are still taking an opioid, they are 'still addicted'. Patients taking methadone maintenance treatment are clearly dependent on methadone, but the implication of the label 'addiction'

is that of a lifestyle based around drug seeking, drug use and crime. There are 2 important questions which need to be asked about methadone maintenance treatment and which are relevant to concerns that methadone maintenance treatment may prolong addiction. First, does methadone maintenance treatment impede patients from achieving a drug-free state? Secondly, does methadone maintenance treatment reduce the long term likelihood of meaningful social rehabilitation?

These questions were investigated by collecting long term follow-up data on a cohort of individuals with heroin addiction who had entered treatment more than a decade previously.[54] The first group comprised 77 individuals with heroin addiction who over a 10-year period had spent less than 12 months receiving methadone treatment (designated the nonmethadone maintenance treatment group), and the second group 95 patients, each of whom had a minimum of 12 months' methadone maintenance treatment (mean 54 months). Both groups were followed in terms of serial interviews and collection of data (including arrests, treatment episodes and deaths) from a variety of official records.

The finding of the study was that over the 10-year follow-up period, the methadone group had significantly better outcomes in terms of employment, and significantly lower mean months of imprisonment than the nonmethadone group. The percentage of people identified as problem drinkers was similar in the 2 cohorts (64 and 72% in the methadone and nonmethadone groups, respectively) confirming the high incidence of alcohol (ethanol) abuse in treated opioid addicts. Similarly, the mean duration of daily heroin use in the 2 groups was similar (14 and 12 months, respectively). The methadone group reported much longer periods of 'occasional' heroin use (usually during methadone treatment) than the nonmethadone maintenance treatment group (mean of 18 *vs* 7 months, respectively), a finding consistent with previous studies that had indicated that episodic use of heroin during methadone maintenance treatment is common. However, at 10 years' follow-up, very similar proportions of individuals reported either regular heroin use (9.5 *vs* 9.1% in the methadone and nonmethadone groups, respectively) or occasional heroin use (4.2 *vs* 2.6% in the methadone and nonmethadone groups, respectively). 27% of the methadone maintenance treatment group was still receiving methadone.

Importantly, 27% of the nonmethadone group were institutionalised (mostly in jail) at 10 years' follow-up, compared with only 12% of the methadone group. Another important finding was that 17% of the methadone maintenance treatment group and 10% of the nonmethadone maintenance treatment group were dead 10 years after entry to treatment (although this difference was not statistically significant). The study also found that 10 years after first entry to treatment, 26% of the nonmethadone maintenance treatment group *vs* 7% of the methadone maintenance treatment group were classified as having at least 3 years' continuous voluntary abstinence from opioids. This difference was significant, and supports the hypothesis that methadone maintenance treatment may reduce the likelihood of eventual abstinence from opioids.

These results provide a useful perspective on the risks and benefits of methadone maintenance treatment. Over 10 years, the methadone maintenance treatment group experienced significantly less imprisonment and significantly more employment than the nonmethadone maintenance treatment group. However, the price of this improvement is the likelihood of remaining on methadone for prolonged periods. In the narrow sense that one-quarter of patients are still taking methadone, opioid dependence has been prolonged with methadone maintenance treatment. However, the compensatory improvements in social functioning and cessation of heroin use mean it is inappropriate to speak of methadone maintenance treatment as 'prolonging addiction'.

The high incidence of alcohol abuse in this cohort of aging former opioid addicts is of serious concern, particularly as the combination of alcohol abuse and chronic hepatitis C can produce accelerated liver disease. However, there are indications

that this pattern of drug abuse may be changing. In more recent cohorts of individuals who are addicted to opioids, use of marijuana is much more common than alcohol abuse, both in treatment[30,31,38] and post-treatment.[30] The important issue is that abuse of drugs other than opioids is not rare and may be an important obstacle to rehabilitation among patients in methadone maintenance treatment.[40]

In addition to following a cohort of their own patients, Maddux and Desmond[55] have reviewed several long term follow-up studies to assess whether methadone maintenance treatment impedes eventual attainment of abstinence from opioids. Contrary to the finding in their own cohort, they found little evidence to support the observation that fewer methadone maintenance treatment patients achieved abstinence from opioids than did opioid users who had entered other modalities of treatment. In 5 follow-up studies of patients entering methadone maintenance treatment, they found that the percentage of patients voluntarily abstinent from opioids ranged from 9 to 21%. In 6 follow-up studies of patients receiving drug-free treatment, the percentage voluntarily abstinent ranged from 10 to 19%. Although there are serious limitations in comparing studies with different methodologies and ways of defining abstinence, these figures are remarkably similar and provide little evidence for the hypothesis that methadone maintenance treatment reduces the likelihood of eventual abstinence from opioids. They also emphasise the low proportion of treated individuals who are addicted to heroin who achieve abstinence.

Thus, on the available evidence, the perception that methadone maintenance treatment contributes to stasis and the perpetuation of a drug-centred lifestyle is not well founded. Rather, what follow-up studies repeatedly demonstrate is the chronicity of heroin dependence and the multiple associated problems which people with heroin addiction experience.

One particularly interesting follow-up study provided important information about one of the perceived risks of methadone maintenance treatment, namely the reluctance of many patients to take high doses of methadone because of fears that this will make them 'more addicted' and less able to eventually withdraw from methadone. Since ample research has indicated that higher doses of methadone are associated with better retention and less drug use in treatment, reluctance to take adequate doses of methadone is a serious clinical problem.[32] One study has investigated the hypothesis that greater neuroadaptation to opioids would make it more difficult to achieve eventual abstinence from opioids. This was a follow-up study of patients treated at 3 methadone clinics with different policies.[56] Two were 'high dose' clinics (mean doses 95 and 82mg), and the third a low dose clinic (mean 43mg). Retention in treatment was significantly better in the high dose clinics. The researchers traced and interviewed 86% of a sample of 347 patients, 6 to 7 years after entry to treatment. At interview, 17 and 20% of the high dose patients, and 11% of the low dose patients, were abstinent from all opioids and not incarcerated. This important study demonstrates that higher doses are not associated with a reduced likelihood of eventual voluntary abstinence. If methadone does reduce the likelihood of people with heroin addiction eventually becoming free of opioids, the mechanism does not appear to be through establishing a greater degree of neuroadaptation.

4.1 Methadone is a Maintenance Intervention

One reason people fear that methadone prolongs addiction is that both heroin users and those treating them want to 'cure' the problem and are not happy with a maintenance intervention. Some use methadone as a short term treatment, or as a time-limited treatment. However, there is substantial evidence that the benefits of methadone maintenance treatment pertain only while people are still in treatment.

As documented in the TOPS study, the major benefits of treatment (reductions in drug use and crime) are noted while patients continue to receive

methadone. Furthermore, as noted above, the protective effect of methadone maintenance treatment on mortality among people who are addicted to heroin persists only while people remain in treatment; indeed, mortality is increased in the 12 months after leaving treatment.[10] This could explain the observation in the cohort of Maddux and Desmond[54] of a higher death rate in the methadone group. The explanation for the increased risk is that a large proportion of patients who leave methadone treatment relapse to opioid dependence. For example, in the large observational study from North America conducted by Ball and Ross,[31] 82% of patients who left treatment had relapsed by 12 months. A reasonable proportion of patients who leave treatment in a planned fashion, with the support of clinic staff (who judge the patient is appropriately leaving treatment), are able to remain abstinent from opioids after leaving treatment.[39] However, most patients who drop out of treatment relapse to heroin use.[39] The critical issue is not that methadone prolongs addiction but that the natural history of addiction is prolonged.

5. Conclusion

The most important observation to emerge from the extensive literature on methadone maintenance treatment is that an assessment of the risks and benefits can only be performed in the light of the 'natural history' of heroin addiction. Many members of the community, and many clinicians, believe that heroin addicts should be able to stop using drugs. Many people who are addicted to heroin believe the same thing, and some of them do successfully stop. However, available data suggests that for most people who are addicted to heroin who seek treatment, addiction is a chronic problem associated with frequent relapses, serious health risks and social dislocation. Methadone maintenance treatment offers substantial benefits over no treatment and, in terms of being able to attract and retain people in treatment, it offers moderate benefits over other treatment modalities. The specific benefits are a reduced risk of death and disease, reduced heroin use and involvement in crime, and an improvement in well-being.

The second major observation is that both the risks and benefits of methadone maintenance treatment depend to a considerable extent on the way in which treatment is delivered. The benefits are less with poor quality programmes.[31,40] While 'quality' of treatment is tangential to the focus of this review, it is worth noting some of the components of quality identified in recent studies. The quality of the staff-patient interaction and attitudes of staff,[31] good management of clinics and quality of record keeping[38] are factors which have been linked to outcomes of treatment. Perhaps surprisingly, the issue of improving the quality of treatment has received relatively little attention in the copious literature on methadone maintenance treatment. The reason for this probably relates to pervasive community unease with the idea of treating addiction by using an opioid. There is a serious stigma attached to methadone treatment, and this is something which is experienced most acutely by patients in treatment.[57] This stigma is also a barrier to professional support for treatment, and may contribute to poor quality programmes.[58] It has also presumably skewed research emphasis regarding methadone maintenance treatment, as researchers have concentrated on repeatedly demonstrating that methadone maintenance treatment is effective rather than on how to reduce the risks and maximise the benefits of such treatment.

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