Methadone Maintenance Treatment (MMT): A Review of Historical and Clinical Issues

Herman Joseph, Ph.D.¹, Sharon Stancliff, M.D.², and John Langrod, Ph.D.³

Abstract

Methadone maintenance has been evaluated since its development in 1964 as a medical response to the post-World War II heroin epidemic in New York City. The findings of major early studies have been consistent. Methadone maintenance reduces and/or eliminates the use of heroin, reduces the death rates and criminality associated with heroin use, and allows patients to improve their health and social productivity. In addition, enrollment in methadone maintenance has the potential to reduce the transmission of infectious diseases associated with heroin injection, such as hepatitis and HIV. The principal effects of methadone maintenance are to relieve narcotic craving, suppress the abstinence syndrome, and block the euphoric effects associated with heroin. A majority of patients require 80–120 mg/d of methadone, or more, to achieve these effects and require treatment for an indefinite period of time, since methadone maintenance is a corrective but not a curative treatment for heroin addiction. Lower doses may not be as effective or provide the blockade effect. Methadone maintenance has been found to be medically safe and nonsedating. It is also indicated for pregnant women addicted to heroin.

Reviews issued by the Institute of Medicine and the National Institutes of Health have defined narcotic addiction as a chronic medical disorder and have claimed that methadone maintenance coupled with social services is the most effective treatment for this condition. These agencies recommend reducing governmental regulation to facilitate patients’ access to treatment. In addition, they recommend that the number of programs be expanded, and that new models of treatment be implemented, if the nationwide problem of addiction is to be brought under control. The National Institutes of Health also recommend that methadone maintenance be available to persons under legal supervision, such as probationers, parolees and the incarcerated.

However, stigma and bias directed at the programs and the patients have hindered expansion and the effective delivery of services. Professional community leadership is necessary to educate the general public if these impediments are to be overcome.

Key Words: Methadone maintenance, heroin addiction, history, pregnancy, evaluation, HIV, hepatitis C.

Introduction

The purpose of this paper is to review historical and clinical issues, basic studies, evaluations, and procedures that led to the development and expansion of methadone maintenance treatment for heroin addiction. This review concentrates on the early development of the program and factors leading to its success and acceptance. From its inception, methadone maintenance treatment has been studied for medical safety and efficacy. The studies investigated not only medical and clinical issues but also the social factors (such as employment and criminality) that affect patient adjustment to the program.

Historical Background of Methadone Maintenance Treatment

Intravenous abuse of heroin intensified in New York City after World War II and, by the 1950s and 1960s, reached epidemic proportions (1, 2). From 1964 to 1970, the names of more than 151,000 addicted persons were reported to the Narcotics Register of the New York City Department of Health (2). Between 1950 and 1961, the death rate associated with the injection of heroin increased from 7.2 per 10,000 deaths to 35.8 per 10,000 deaths, with 75% of the deaths in the 15–35-year-old age group. During this interval, death related to heroin injection became the leading cause of death in New York City for young adults. The average age of death from heroin-related use was 29 years for both sexes (3).

Methadone, a long-acting agonist with a half-life of about 24 to 36 hours, was synthesized for analgesia prior to World War II in Germany. In 1949, Isbell and Vogel, working at the U.S. Public Health Hospital in Lexington, Kentucky, showed methadone to be the most effective medication for withdrawing addicts from heroin (4). The proce-
The principal effects of daily methadone dosing in maintenance treatment were determined...
from the team’s initial research (11–13, 16–18). For most patients, the amount of methadone prescribed orally, usually between 80–120 mg/d, should be sufficient to:

- relieve narcotic craving
- suppress the opioid abstinence syndrome for 24–36 hours
- block the effects of administered heroin
- develop tolerance to the euphoria, sedation or other narcotic effects of methadone which would impair emotional responses, functioning or perception
- develop tolerance to the analgesic properties of methadone

However, some patients might need higher doses to achieve these effects. Others would be able to function normally on lower doses of 60 to 80 mg/d. In 1990, the Government Accounting Office (GAO) in a review of methadone programs nationwide reported that the lowest effective dose for maintenance treatment was 60 mg/d.(19). Once an adequate dose of methadone has been achieved, there should be no narcotic effects noticeable to either the patient or observers of the patient in interactions of everyday life. Properly stabilized methadone patients who are not abusing drugs and alcohol experience normal emotions and acute and chronic pain. It should be noted that a blocking dose of methadone is dependent on the strength and amount of heroin that is used. Thus, during certain periods when street heroin is especially pure and/or inexpensive, higher doses may be needed to achieve blockade.

In 1965, Dr. Ray Trussell, then the New York City Commissioner of Hospitals, transferred the research pilot project from The Rockefeller University to the Morris J. Bernstein Institute of the Beth Israel Medical Center, for expansion and further evaluation. At the Bernstein Institute, an outpatient clinic model was opened; it was staffed by a physician, nurses and counselors to assist patients with their addiction and their medical, personal and social problems. In 1965, all patients in the Beth Israel program were treated with methadone for six weeks as inpatients before being discharged to the outpatient clinic. In 1966, initiation of treatment with methadone was transferred to the outpatient clinic. Evaluation of both methods showed no significant differences in outcomes (21). In 1966, the clinic model was adopted for expanding methadone maintenance treatment throughout the United States.

By 1998, the number of methadone patients in the United States had increased from the original six research patients (16) in 1964 to about 44,000 patients in New York State and179,000 patients nationwide (22). The IOM report (18) estimated that there are between 500 thousand and one million or more heroin users in this country. If this is the case, only 18 – 36 % of these heroin users are enrolled in methadone treatment. Methadone maintenance is now recognized as the most effective treatment for heroin addiction, as validated in reviews by the Institute of Medicine (IOM) (18) and the National Institutes of Health (23).

### Criteria for Admission

Admission criteria are now much more liberal than they were under the original research protocols, which limited applicants for admission to those between the ages of 21 and 40 with a minimum of four years of narcotic addiction. Excluded were those who had problems of alcoholism, mental illness or polydrug abuse. Patients originally had to have had episodes of prior treatment (e.g., detoxification from heroin or treatment in residential therapeutic communities) to qualify for admission. These original criteria were constructed to include hard-core addicts who were unable to abstain from using heroin, and to test the efficacy of methadone in a relatively “pure heroin addict.” The upper age limit was based on a theory that addicts “mature out” of addiction over the age of 40. During the ensuing years, as groups of patients were successfully treated, admission criteria were relaxed to include younger and older addicts. Heroin addicts with mental health and polydrug abuse problems, including alcoholism, also became eligible for acceptance. The current criteria have been established by the federal and state governments. State regulations (24) may not be more liberal than the federal mandates. In New York State, the regulations are as follows:

- Applicants age 18 and over must document at least one year of opioid addiction, mainly to heroin. This can be documented: by history provided by the patient and/or the statements of family members or friends; records of prior substance abuse treatment including detoxification and entry into different types of programs; signs of withdrawal or over-sedation; results of a urinalysis test taken at the time.
the applicant applies for entry; and needle marks or tracks on various parts of the body and/or erosion or severe irritation of the nasal septum, indicating that the patient has inhaled heroin over a long period of time.

- Applicants between the ages of 16 and 18 require a two-year documented history of addiction, parental consent, and two previous unsuccessful treatment experiences.

- Pregnant, heroin-using applicants need to document current addiction and can be admitted to treatment with less than one year of heroin use if evaluated and approved for admission by the physician of the clinic. Upon giving birth, they will be reevaluated for continued treatment.

- Serious psychiatric co-morbidity and/or a history of abuse and addiction to substances other than opioid (e.g., cocaine and alcohol) may not exclude applicants from entering treatment. Once admitted, patients in this category would be treated for these conditions in the clinic, if appropriate, or referred to other agencies for psychiatric therapy and/or detoxification from other drugs. Methadone maintenance treatment (MMT) would be continued in the clinic while they were being treated for their co-morbid conditions.

- Applicants terminated from prior treatment for noncompliance with program regulations must be reevaluated before readmission and, if found not acceptable, may be referred elsewhere for treatment.

Proof of current addiction is not required of individuals who have prior histories of heroin addiction and treatment, and feel they are in danger of relapsing to heroin. This category includes applicants who were discharged from institutions, and former patients who successfully left methadone treatment within a two-year period and feel they are in danger of drug relapse.

**Intake Procedure**

Once the applicant meets the criteria for admission, he or she is provided with an orientation to MMT, as well as a handout of the regulations and services of the program, and is asked to sign various consent forms agreeing to program policies and allowing for the administration of methadone. The patient also receives a physical examination, which includes complete blood chemistries and testing for hepatitis, venereal diseases, tuberculosis, and pregnancy. A tetanus shot is provided to all patients. Urine tests are taken to verify the presence of opioids and other drugs. HIV testing is offered subsequent to admission, with the patient’s consent, following an orientation about the test and the disease of AIDS. The patient begins treatment upon completion of the admission procedure. A psychosocial assessment and treatment plan are completed within 30 days of admission.

Once accepted, patients report daily to the clinics and drink their prescribed doses of methadone, observed by a nurse. Reporting schedules are liberalized for patients who are compliant and show improvements in functioning. Eventually, patients can report once per week and receive six liquid doses in vials to take home for daily consumption. Patients submit a minimum of eight urine specimens a year, which are tested for the presence of methadone and illicit drugs, including heroin.

**The Methadone Induction Process**

At the beginning of treatment, patients present different levels of heroin dependency to the clinic staff. Therefore, the physician and staff must evaluate patients in order to determine the proper initial dose of methadone that will begin to relieve the abstinence syndrome of heroin and narcotic craving without inducing sedation. The patient may be prescribed a starting dose of up to 30 mg, which can be supplemented by an additional 5–10 mg after a two-hour observation period if abstinence symptoms persist. Also, the observation period is required by federal regulations to ensure that the patient is not sedated. By government regulation, the first dose of methadone cannot exceed 40 mg.

Based on observation of the patient for the presence of sedation or the persistence of the abstinence syndrome, doses can be increased by 5–10 mg every day or every other day, up to a dose of 60 mg. After this level is reached, dosing takes place on an individual basis until the patient reaches a level — usually 80–120 mg/d or above — where the three principal effects of methadone are achieved: relief of craving, blocking of narcotic effects of heroin, and relief of abstinence syndrome. If the dose increase is too rapid, the patient may experience transient episodes of urinary retention, edema and abdominal distention. Therefore, the build-up process to an adequate maintenance dose must be carefully calibrated to the needs of the individual patient (16, 25).
Major Evaluations

In 1965, an impartial committee was organized, headed by Dr. Henry Brill of the New York State Department of Mental Hygiene, to evaluate the methadone maintenance program. The evaluation itself, which began in August of 1965, was conducted over a period of six years by Dr. Frances Rowe Gearing of the Columbia University School of Public Health. Dr. Gearing reported semiannually to Dr. Brill’s committee (21).

A final report was issued in 1974 (21), by which time some 17,500 patients had been admitted to methadone treatment in the five counties of New York City, plus Nassau, Suffolk and Westchester counties, during the period from January 1964 to December 1971. The following are highlights of the report:

- As of December 1973, there was an overall 77% retention rate of patients in treatment.
- For the first 1,230 patients admitted to the program, there was a 35% improvement in productive behavior — employment, education and homemaker status for women — compared to the patient’s status at the beginning of treatment. Increases in social productivity at the end 1973 were recorded for all cohorts of patients admitted annually from 1964 through 1971.
- Arrest rates dropped from 201 arrests per 100 person-years prior to entering treatment to 1.24 arrests per 100 person-years after entering methadone treatment. About 75% of the patients were not arrested. In the three years prior to entering treatment, all patents had records of criminal arrests.
- The follow-up status of the first 356 patients who left treatment showed that few if any were free of problems related to addiction and criminality: 38% were arrested, 26% had records of detoxification after relapse to heroin, 15% were in other types of drug treatment programs that did not offer methadone, 6% had died, 7% returned to methadone treatment.
- About 25% of the patients presented with alcoholism and non-opioid drug abuse (e.g., barbiturates, amphetamines, and cocaine problems). These problems were the major causes of discharge from the program. Alcoholism was a major problem for patients over age 30 and also among black patients, while non-opioid drug abuse was a major problem among white patients under age 30.
- In the early 1970s, an increasing proportion of patients entered methadone treatment with serious life-threatening illnesses, including heart disease, cancer, and neurological and other conditions. This trend highlighted the need for methadone programs to be affiliated with hospital and medical backup facilities.
- The death rate of patients in treatment was slightly higher than the death rate of the New York City population aged 20–54 between 1969 and 1970 (7.6 vs. 5.6 deaths per 1,000 population). However, the death rate of patients who left treatment was more than three times the rate of patients in treatment (28.2 deaths per 1,000 population). And 64% of the ex-patient deaths after leaving treatment were probably drug related as opposed to 30% of the deaths of patients in treatment.

In 1978, Dole and Joseph reported their study of 846 randomly selected patients who were discharged for a variety of reasons from methadone clinics in New York City (26). The following was noted at the time of the interviews and examination of community agency records at an average of approximately two years after the patients had left MMT.

- Only 8% of the discharged patients appeared to be doing well, had not relapsed to the use of heroin, were free of alcohol or non-opiate drug problems, and had not been rearrested.
- 64% had relapsed to the use of heroin and were re-addicted; 6% were using heroin once or twice per week; 22% had other serious problems related to alcohol, non-opioid drugs and crime.
- About 66% of the patients who had left “in good standing” were either re-addicted to heroin, were using heroin once or twice per week or were involved with serious alcohol, non-opiate drug problems and crime, while 98% of the patients who had left for cause were involved with these problems after leaving treatment. Conversely, 34% of the patients who had left in good standing and 2% who had left for cause were apparently well, with no problems related to addiction or criminality.
• Duration of heroin addiction, length of time in methadone treatment and type of termination from methadone treatment (e.g., in good standing vs. for cause) appeared to be major predictors of a patient's post-treatment adjustment and relapse to heroin. Gender, ethnicity and level of education were not predictors of post-treatment use of heroin. Patients who had been addicted for less than five years, had remained in treatment three or more years, and had left the methadone treatment program in good standing appeared to have a better chance of doing well (e.g., no relapse to heroin) after leaving treatment compared to patients with longer histories of using heroin, treatment duration of less than three years, and exit from treatment for cause, without proper social supports (e.g., no employment, continued substance abuse and criminal activity).

• Death rates of patients after leaving treatment were more than twice the death rates of patients who remained in treatment. Alcohol-related illnesses were the major causes of death for patients in treatment. Narcotism or heroin overdose was the major cause of death, followed by alcohol-related illnesses, for patients who left treatment, with the highest rate of death occurring during the first month after leaving treatment.

• Alcoholism was a major factor in 26% of the terminations from MMT. It should be noted that more than 80% of the patients who had alcohol problems prior to admission to methadone treatment continued drinking excessively while in methadone treatment.

• Pretreatment arrest rates were higher for patients who had left during the first year of MMT, as compared to patients who remained in treatment for more than one year (1.5 vs. 0.8 arrests per person-year).

• The major predictors of post-treatment heroin use were type of discharge from treatment (favorable vs. for cause), duration of heroin addiction prior to treatment, and employment status at discharge.

In the mid-1980s, an evaluation of the effectiveness of MMT was undertaken by Ball and Ross (27), who investigated the adjustments of 617 male patients in six programs located in three major metropolitan areas with large populations of heroin addicts — New York City, Philadelphia and Baltimore. Factors examined in this study of methadone treatment included criminality, use of heroin and other drugs, and a follow-up of patients who left treatment during the course of the project. The administration of the six programs and the services that were offered were also investigated.

• 77% of the patients stopped their intravenous use of heroin over a period of six months. After 4.5 years of treatment, 92% had stopped heroin use. 96% reported no use of barbiturates and amphetamines, and 83% were not using cocaine. Dosage of methadone was an important factor in reducing heroin use, irrespective of the program in which patients were enrolled. For a 30-day period prior to patient interviews and medical record checks within the first months of the study, 28% of the patients receiving doses of methadone of less than 45 mg/d were using heroin as opposed to 5.4% who were on doses of at least 46 mg/d. However, there was no heroin use in the subgroup of patients receiving 71 mg/d or more of methadone.

• For patients enrolled in methadone treatment for six months or more in this study, there was a 79% reduction in all types of crime from pre-treatment levels. Reduction of crime was related to time in treatment, with patients in treatment three or more years committing fewer crimes than patients in treatment less than three years.

• 82% of 105 patients who had left methadone treatment relapsed to heroin addiction within 12 months. Of the 23 patients in this group who had left in good standing (e.g., socially rehabilitated, not abusing drugs, responded to counseling and completed withdrawal from methadone), 16 (69.5%) relapsed within the course of the year following treatment. Seven (30.4%) had not relapsed.

Ball and Ross noted that the administration and policies of programs influenced patient outcomes. Those programs with developed services and committed staff achieved better results. Favorable outcomes were better correlated with the extent and quality of the services offered by the programs than with patient characteristics at admission. These researchers expressed the view that additional quality services were needed in the programs.
**Length of Treatment and Methadone Dose: Implications for Treatment**

The studies by Gearing and Schweitzer (21), Dole and Joseph (26), and Ball and Ross (27) demonstrate that methadone maintenance is a corrective therapy, not a curative therapy. That is, the vast majority of those who withdraw from methadone will relapse to heroin use (28). While shorter use of heroin and longer treatment with methadone and social stability are correlated with abstinence in a small number of patients, there are no clear predictors of success (26). However, D’Aunno’s 1995 study of selected clinics in the U.S. found that a majority of clinics encourage withdrawing after only one year of treatment (29). Patients may also be withdrawn for noncompliance with treatment— including continued use of illicit drugs or even failure to become employed (30).

Methadone dose has been shown to be an important factor in retaining patients in treatment. Watters and Price reviewed 44 methadone programs in the United States and found that dose level was the single most important factor affecting retention in treatment. The higher the dose of methadone, the longer patients remained in treatment (31). Caplehorn and Bell reported the same phenomenon in Australia (32). Patients stabilized at 80 mg/d or more had higher retention rates in treatment than patients who were on lower doses and had used less heroin. Factors associated with good patient outcomes, such as employment, level of education and reduction in criminality, appeared to have less of an effect on retention than did the level of dose. Leavitt et al. report that doses in excess of 100 mg/d, even as high as 780 mg/d, are safe and necessary to eliminate opiate abuse and, in some cases, reduce abuse of alcohol and other drugs (20). Hartel et al. have shown that methadone doses of more than 80 mg/d help protect patients from acquiring HIV, as compared to lower doses (33).

Despite this evidence, many programs do not adhere to medically sound dosing protocols. D’Aunno also found the average daily dose in the majority of clinics surveyed to be 59 mg, which is less than the lower end of the therapeutic range of doses. Additionally, 66% of the clinics had an upper dose limit of 80 or 100 mg (29), despite the fact that many patients need doses of 100–120 mg, and a smaller number need much higher doses. Furthermore, research protocols are still being carried out which randomize patients to ineffectual doses as low as 20 mg, 30 mg and 50 mg. (34, 35). In contrast, the Office of Alcoholism and Substance Abuse Services (OASAS) of New York State has obtained a waiver allowing physicians in methadone programs to prescribe up to 150 mg/d of methadone for those patients who continue to use heroin. Doses above that level require state notification, with justification.

**Polydrug Abuse**

Among heroin addicts, the frequent use of non-narcotic substances has been documented as far back as 1967 by Langrod et al. (36). They reported that 91% of 413 heroin addicts committed to the New York State Civil Commitment Program admitted to having used other drugs, with 55% using four or more illicit drugs. Among patients receiving MMT, examination of the latest available data indicates that about 40% of methadone patients use cocaine or crack upon admission to the program. Kreek et al. indicated that in the 1970s about 20% of the methadone patients had serious alcohol problems upon admission to the program (37). Joseph and Appel found that alcohol-related diseases were major causes of death of patients in methadone treatment, and that approximately 23% of the terminations from treatment were related to alcohol (38). Since polydrug and alcohol abuse exist prior to admission to the methadone program, the extent of the problem needs to be assessed and appropriate treatment methods applied when patients enter treatment. Also, patients with serious problems of anxiety or depression may turn to the abuse of illegal substances if they are not properly diagnosed and treated. Treatment should include psychiatric care and medication as well as detoxification from non-prescription substances and behavioral interventions as needed. In New York State, methadone patients who are alcoholics can now be admitted to inpatient programs of Addiction Treatment Centers. However, there are no effective long-term medical interventions for cocaine addiction. Nevertheless, sharp and significant reductions in cocaine use have been reported in a cohort of 133 methadone patients who remained in treatment for 18 months and received adequate doses of methadone (39). Cocaine-using methadone patients may also reduce their use of cocaine by participating in individual counseling, a Cocaine Anonymous group or cognitive therapies (40).

**Impact of MMT on the Community**

While it is important for the practitioner to be aware of how the patients fare on the program, the impact on public health and safety within a
community can only be inferred. In New York City, from 1971 through 1973, there was a 142% increase of patients, from 14,000 patients up to about 34,000, as a result of a rapid expansion of methadone clinics under the direction of Dr. Robert Newman of the former Health Services Administration. In the 1970s, estimates of the number of heroin addicts in New York City varied from about 164,000 to 203,000. Therefore, in 1973, only an estimated 15–18% of the heroin users in New York City were enrolled in MMT. However, the following decreases in social and medical problems associated with heroin addiction, for every 1,000 admissions to methadone programs in the City, were noted from 1971 through 1973:

- Addiction-related property crime (reduced by 3,869 per 1,000 admissions)
- Drug arrests (reduced by 1,251 per 1,000 admissions)
- Hepatitis (reduced by 75 cases per 1,000 admissions)
- Deaths related to drug dependence (reduced by 16 deaths per 1,000 admissions) (40)

A similar phenomenon was noted in Hong Kong, where reductions in addiction-related property crimes and incarcerations were found after methadone treatment was introduced in 1976 (41).

**Diversion**

Diversion of methadone has always been a source of concern in the community. The fear of diversion has been a factor in the opposition to the expansion of MMT and the opening of new clinics. However, the Institute of Medicine’s (IOM’s) report (18) regarding the regulation of methadone treatment suggests that diversion of methadone, while of concern, does not appear to be serious enough to take precedence over accessibility to treatment for untreated addicts. This conclusion is based on data collected from many sources throughout the United States, such as health departments, medical examiners, etc. The IOM report (18) and reports from the street studies unit of the New York State Office of Alcoholism and Substance Abuse Services note the following reasons related to sales or purchases of methadone:

- Patients sell methadone to supplement their incomes.
- Patients may buy methadone to supplement their program doses if they are inadequate.
- Individuals may buy or sell methadone to assist relatives or friends who are in withdrawal and require it.
- Addicted persons who cannot enter treatment because of waiting lists, who do not have Medicaid, and who are unable to afford to pay for their treatment, buy street methadone to stave off withdrawal symptoms from heroin.
- Addicted people buy diverted methadone to maintain themselves outside of a program if heroin is not available. Some addicts buy street methadone to obtain a “high” in combination with other drugs. Other addicted persons may buy methadone because they find program regulations and rules too onerous, or to preserve confidentiality about their addictions by not being identified when entering a neighborhood methadone program.

Thus, diverted methadone is purchased primarily to withdraw and maintain an untreated heroin-addicted population. Primary addiction to methadone is rare, since methadone does not produce the sharp euphoria of heroin. Therefore, regulations based solely on fears of diversion can be counterproductive (18). Availability of MMT should be increased and made more affordable, and doses in treatment should be adequate for the patients’ needs.

Two options exist for patients who are not compliant with their methadone treatment regimens. One option is to require that they attend the clinic six or seven days per week with little or no privileges to take out methadone doses. The second option is the use of levomethadyl acetate (LAAM), which can be administered orally in the clinic two or three times per week (42).

**Pregnancy**

Methadone is the only approved medication for treating narcotic addiction during pregnancy. The use of narcotic antagonists such as naltrexone is contraindicated, since these medications precipitate the opioid abstinence syndrome and can result in spontaneous abortion, fetal distress, premature labor, and stillbirth. The use of LAAM in pregnancy has not been studied. Therefore, women who become pregnant are not eligible to receive LAAM or are transferred to methadone if they become pregnant while receiving LAAM.
The use of heroin during pregnancy subjects the fetus to daily fluctuations of the abstinence syndrome, which can result in stillbirth, premature delivery, low birth weight, and sudden infant death syndrome. The lifestyle associated with heroin addiction during pregnancy can lead to poor nutrition, transmission of infectious diseases, including HIV and hepatitis, and complications such as endocarditis and abscesses from use of contaminated needles. In addition to the fluctuation of opiate levels, destructive lifestyles and the use of other drugs, tobacco and alcohol may result in spontaneous abortion, premature rupture of membranes, intrauterine growth retardation, pre-term labor, breech presentation, and toxemia (43–47).

Methadone in pregnancy has been studied since the late 1960s. The following outcomes have been noted from various studies (43–47):

- Methadone maintenance during pregnancy has the potential to eliminate the use of heroin by injection, smoking or inhalation, as well as help reduce the use of other legal and illegal drugs.

- MMT by itself is insufficient to deal with all the issues that confront a pregnant heroin addict. The patient must be referred to a comprehensive program that includes prenatal and medical care, nutritional counseling, and attention to resolving the many medical, personal and social problems that the patient presents.

- Methadone, because it is a long-acting medication, provides the fetus with an environment for development that is not subject to the fluctuations associated with the abstinence syndrome.

- However, during the course of the pregnancy, there are marked differences in methadone blood plasma levels that have to be closely monitored. A variety of maternal, placental and fetal factors, including an increase in fluid space, a large tissue reservoir, and metabolism by the placenta and fetus may lead to the need for higher doses, particularly in the third trimester. This increase may be required to prevent the manifestation of the opiate abstinence syndrome, which would be stressful to the developing fetus. Kaltenbach et al. (45) stress the need for understanding the metabolic changes and the increase in blood volume during pregnancy, since pregnant methadone patients frequently develop withdrawal symptoms that must be treated with increases in methadone dose.

- Methadone maintenance reduces obstetrical complications that are found in pregnant heroin addicts. Higher maternal methadone doses in the first trimester may result in higher neonatal birth weights (43–46).

Neonates born to methadone-maintained women may or may not experience some form of the opioid abstinence syndrome, usually within 24 to 72 hours or longer after birth. Prolonged observation is essential.

A variety of studies (43–45) have shown conflicting data regarding the correlation between methadone dose and manifestation of the abstinence syndrome. These data range from no correlations with any dose level to a correlation at all dose levels. While this syndrome is not usually fatal in adults, neonates are more sensitive and must be treated if symptoms appear. The neonatal abstinence syndrome can be pharmacologically controlled with medication such as paregoric or phenobarbital. Paregoric is preferred to phenobarbital since few seizures, if any, are observed with the use of paregoric as compared to the greater number associated with the use of phenobarbital. The neonatal abstinence syndrome is brought under better therapeutic control in a shorter period of time with paregoric, and there is a more rapid normalization of the sucking reflexes in paregoric-treated infants (44, 45).

A study of infants who experienced seizures related to the abstinence syndrome following birth, showed early abnormal neurological examinations. However, within the first year, abnormalities disappeared and EEG tracings became normal. Furthermore, infants with seizures during the first year of life did not differ otherwise from those who did not have seizures. This favorable outcome suggests that the long-term prognosis for abstinence-related seizures is better than that for seizures related to other pathologies (46).

Breast feeding of infants is encouraged during the first six months of pregnancy. However, breast feeding is contraindicated if the mother is HIV positive, and/or abusing drugs such as alcohol, amphetamines and heroin, all of which can reach significant levels in breast milk. The rates of the concentration of methadone in milk and plasma, in contrast, have been shown to be low (43–45, 48). Accordingly, monitoring of methadone levels in the breast milk and infant plasma is not necessary. Weaning should not nor-
mally represent a problem with respect to withdrawal symptoms (45, 48).

A follow-up study of 25 four-year-olds whose mothers were maintained on methadone during their pregnancies and who had received prenatal care showed normal development as compared to controls. Neurological examinations, Wechsler Pre-School and Primary Scale of Intelligence, language development and motor-free visual perception tests were administered. The results of all neurological examinations were within normal parameters, and there was no relationship between IQ scores and the severity of the abstinence syndrome at time of birth. There were no statistical differences between the infants exposed to methadone in utero and non-exposed controls: average IQ scores were 106.5 for methadone-exposed infants and 106 for controls. To date, no chronic conditions or abnormalities attributable to methadone have been identified in those children exposed to methadone in utero when their mothers also received prenatal care. However, follow-up studies are needed on older groups of children exposed to methadone in utero compared to normal controls (43, 44, 45).

To summarize, the use of methadone fosters both a healthy infant and a healthy mother. However, methadone can cause some complications in the first weeks of life, but these are medically manageable and preferable to the fluctuations in opiate levels found in heroin addiction and the dangers of the associated lifestyle.

Medical Safety and Side Effects

Medical safety issues regarding methadone maintenance have been monitored since 1964 (18). Long-term methadone maintenance is a medically safe, nontoxic treatment with minor, mostly transitory side effects, found mainly during the induction phase of treatment. In general, the overall health status of patients improves after spending time in treatment (18). The chief complaints are increased perspiration and constipation. While methadone is metabolized by the liver, it is not hepatotoxic; patients entering MMT with normal liver function maintain normal liver function (12, 18). However hepatitis B and C (and in some parts of the country hepatitis delta) are common infections with prevalence rates of up to 80% among heroin injectors (47). Therefore, abnormalities of liver function among methadone patients are usually caused by infections acquired prior to entering treatment and/or as a consequence of alcoholism. There are no toxic effects on the kidneys, though again, patients may enter treatment with chronic renal disease, which is a common problem among heroin addicts (18).

Methadone, when properly prescribed at adequate doses in long-term maintenance treatment, normalizes the physiological functions that are deranged by heroin addiction (12, 18). These include:

- stress responses of the central nervous system and down-regulation of the hypothalamic-pituitary-adrenal axis
- reproductive hormones of the hypothalamic-pituitary-gonadal axis resulting in abnormal functioning
- indices of immune functioning linked to neuroendocrine functioning (18)

The impaired functioning of these systems may be related to the drug-seeking behavior of heroin addicts. Addiction to heroin may cause irregularities in menstrual functioning among women and loss of libido and potency among males. Patients may relate concerns about sexual function. However, the IOM report (18) on methadone indicated that more than 80% of the men and women who reported sexual irregularities while addicted to heroin revert to normal functioning within one to three years: women experience normal menstruation; and libido and potency are restored to the males, although some may report delayed ejaculation (12, 18).

Several researchers investigated sexual problems that MMT patients attributed to the medication. Of the 101 patients reported by Langrod, Lowinson, and Joseph (51), 17% reported problems related to delayed ejaculation and potency at the time of the interview. The patients (with a mean age of 35 years) compared their current sexual functioning to the period prior to heroin use, which was during their teenage years. Other studies note, however, that methadone patients report an increase in libido upon entering methadone treatment, as compared to the period when they were using heroin (12, 18).

Functional Potential of Methadone-Maintained Patients, Employment, and Driving

Methadone patients have been employed in a wide variety of jobs that encompass the range of skills found in the job market. Patients in the
Methadone Medical Maintenance Program are owners of businesses, managers, salespersons, professionals, computer technicians, and blue-collar workers in the building trades (52). An analysis of the jobs held in 1972 by 951 patients known to the New York City Health Services Administration Methadone Program shows that patients were employed across the spectrum of the job market: building trades (14%), municipal government (0.7%), federal government (0.6%), clerical work (4.5%), professional (2.6%), skilled work (17.1%), semiskilled work (5.5%), services and management (3.7%), sales (9.0%), social services (2.7%), and unskilled work (39.4%) (53).

Gordon and Appel found that methadone patients were within the normal range on tests of intellectual functioning, reaction-time studies, tests of sustained attention and perceptual-motor skills (54). In reviews of driving records and interviews with patients not impaired by use of alcohol or depressants, it was found that methadone patients do not differ significantly in the number of accidents or traffic violations compared to age-matched, non-drug-users or former heroin addicts who were not enrolled in MMT and were abstinent.

The first 155 patients to receive methadone doses of 79 mg/d to 100 mg/d tested within the normal range of intellectual functioning (54). There was an absence of patients in the lowest range of IQs. Follow-up testing of 30 patients a decade later showed the following results: 25 scored higher than their original tests, one scored the same, and four showed modest declines within the normal range of scores.

Therefore, the major conclusion of studies concerning the functional potential of methadone patients is that they can perform any job for which they are qualified. Alcohol and depressants are more likely to be a source of problems for persons who drive or work around machinery than is methadone when used as a maintenance medication.

**Methadone Maintenance and HIV/AIDS**

Studies worldwide have confirmed that methadone maintenance plays a crucial role in the prevention of the transmission of HIV infection among injectors of heroin, reducing the risk 4- to 6-fold (55).

- Abdul-Quader et al. showed that methadone treatment could reduce risk behavior related to injection (56). The frequency of heroin injection and visits to shooting galleries (places where groups of addicts inject drugs and possibly share injection equipment) were reduced over time after enrollment in MMT.
- A prospective study by Metzger et al. (57) compared HIV-negative patients on methadone to HIV-negative heroin users who were not in treatment but who were recruited from the patients’ social network. In the course of 18 months, 3.5% of those remaining in treatment seroconverted to HIV positive, while 22% of those remaining out of treatment seroconverted.
- Hartel and Schoenbaum examined HIV infection in a group of 622 methadone maintenance patients in the Bronx who were former injectors of heroin and, in some cases, of cocaine (33). The social and medical data in this study cover a 20-year period back to the beginning of the HIV epidemic in 1978. In this group, a methadone dose of 80 mg/d, or more, played a central role in preventing transmission of HIV. Patients receiving more than 80 mg/d had significantly less HIV infection than patients receiving lower doses. The protective value of adequate high-dose methadone was independent of year of last cocaine injection, needle sharing in shooting galleries, number of injecting drug users who were sex partners, low income, counseling, and minority ethnicity (e.g., Latino, African American). The study emphasized the need for methadone maintenance programs in preventing transmission of disease and helping patients with other social and medical problems.
- Blix and Grondbladh (58) showed that patients who entered methadone maintenance in Uppsala, Sweden prior to 1983 had lower rates of HIV infection and AIDS than those admitted after 1983. The researchers concluded that for patients who remained in treatment, methadone maintenance offered protection against acquiring HIV, since injection of heroin was either eliminated or significantly reduced. The researchers also recommended that untreated heroin addicts enter methadone treatment as a precaution against HIV infection (58).
- Weber et al. conducted a three-year prospective study of a group of HIV-infected methadone patients and a group of HIV-infected heroin addicts (59). The progression to AIDS was faster among the heroin users...
than among the methadone-maintained patients.

- A study of 58 rehabilitated patients in New York City (e.g., employed, socially stable, not using illicit drugs or injecting heroin) showed that they were seronegative for antibody to HIV (60). These patients had used heroin for an average of more than 10 years prior to entering MMT, before the major onset of the HIV/AIDS epidemic. They were in methadone treatment for approximately 17 years and had stopped injecting heroin. However, prior to entering methadone treatment, they had engaged in high-risk behavior such as sharing needles and, as a result, 91% had markers for hepatitis B. Successful participation in methadone maintenance was therefore associated with an absence of HIV antibody.

- Magura et al. report that cocaine use among methadone patients has been related to a higher prevalence of HIV-risk behaviors (e.g., shared needle use and multiple sexual partners) than among methadone patients who do not use cocaine (61). However, among the cocaine-using population in methadone treatment, needle-related sharing and sexual risk behaviors declined significantly over a two-year period after admission to methadone treatment. The authors recommend that cocaine-using patients be retained in treatment and that services such as access to needle exchange and free condoms be increased. From a harm-reduction perspective, methadone maintenance was effective, even for cocaine-using patients, since injection of heroin declined. Discharge from methadone treatment would have the potential effect of increasing HIV-risk behaviors to pre-treatment levels.

**Stigma**

From the beginning of MMT, the program has been stigmatized by the belief that methadone treatment merely substitutes one drug for another. This belief blurs the crucial differences between an active heroin addiction and the use of methadone in a maintenance program. Gordis cites methadone maintenance as an example of a soundly researched medical program about which misperceptions and biases have had an adverse impact on implementation (62). Cooper indicates that methadone maintenance has met with limited acceptance by doctors because addiction is not regarded as a legitimate medical condition (63). Misunderstandings about addiction, the role of MMT, and the stigma associated with both may generate counterproductive policies such as excessive regulations and the prescribing of suboptimal doses for patients. Gordon reported that employers were more sympathetic to active alcoholics than to stabilized methadone patients (64). Programs for alcoholics were available, and even though workers might have been impaired by alcohol, they were referred to treatment programs that were sometimes affiliated with their jobs. Gordon observed that alcoholism is accepted by society, whereas enrollment in methadone treatment leads to social ostracism. Methadone patients, accordingly, are fearful of being suspended, fired, or not hired if their status becomes known to current and potential employers, despite the fact that they are not impaired by methadone maintenance and can perform job tasks for which they are qualified. Joseph reported that stigma pervades the lives of methadone patients, arousing fears about discovery and a need to conceal enrollment in the program from members of their families, friends, employers, and health personnel who treat them (65). Patients have indicated that if they inform people about their enrollment, then routine fatigue might be misinterpreted as narcotization from methadone. Also, communities have refused to allow the construction of methadone treatment centers even though a need for the treatment has been established. Miller, Bayer and Joseph have analyzed news articles, documentaries and journal articles that present methadone maintenance with distortions and biases which add to the stigma and misinformation (65, 66, 67). To fight stigma, discrimination, and questionable regulations, methadone patients have formed advocacy groups, most notably the National Alliance of Methadone Advocates, with affiliations throughout the United States, Europe, and Australia.

**Current Problems**

In the early 1970s, Gearing noted that patients were being admitted to methadone treatment with a greater prevalence of problems than those admitted in previous years (21): antisocial behavior; increases in polydrug abuse, including cocaine addiction and alcoholism; and life-threatening illnesses such as cancer, neurological problems, heart and lung conditions. In the social realm, Gearing identified the disappearance of the types of jobs that patients were able to obtain in the 1960s, when the program began, and the
reluctance of employers to hire methadone patients. These observations were harbingers of the serious social and medical problems that still impact on the patients and the program.

- The HIV/AIDS epidemic within the drug-injecting population had affected a significant proportion of the patients by 1985 (68). Estimates ranged from 5 – 57% of the clinic population, depending on the location of the clinic and the number of years the patients injected drugs with contaminated injection equipment. By the mid-1980s, AIDS-related illnesses were the major causes of death within the patient population. TB, which was associated with AIDS, became a major public health concern. Therefore, in response to the manifestations of infectious diseases, clinics became centers for detection and treatment of TB and HIV. Coordinators were placed in New York State methadone clinics to educate patients about infectious disease.

- The cocaine/crack epidemic emerged in the early 1980s, creating serious behavior and medical problems, including transmission of syphilis and HIV, in the exchange of sex for drugs (69), and the exposure of neonates to cocaine in utero. Programs responded by creating special therapy groups to reduce the use of cocaine. However, cocaine and crack are still major problems, since there is no proven medication to treat the compulsive user. About 40% of the approximate 41,000 methadone patients in treatment in New York State on 12/31/99 admitted at the time of their admissions to the methadone program that they abused cocaine and crack in addition to heroin (70). The combined injection of heroin and cocaine, known as speedballing, has emerged as a problem among new admissions. However, with extended counseling and treatment, and doses of methadone more than 80 mg/day, speedballing can be reduced (69).

- In the 1990s, hepatitis C was identified at high levels of prevalence within the population of methadone patients who were former drug injectors. Novick (71), Hagan and Des Jarlais (50), and Salsitz et al. (52), all in this issue, indicate that hepatitis C has now become a major health problem among methadone patients.

- In the 1970s, 80s, and 90s, there was erosion of affordable housing, including single occupancy hotels (75). This erosion was accompanied by a change in the job market from relatively unskilled manufacturing and factory jobs to a service economy that demanded education and technical skills. These two trends produced high unemployment rates and homelessness, both of which were reflected in the admission statistics to the program. Currently, about 10% of the patients report upon admission that they are homeless or living as transients; only 20% are employed. When methadone maintenance started in the mid-1960s and 1970s, homelessness was not an issue and a greater proportion, about 33%, of the patients were employed at time of admission.

- Community resistance has prevented the opening of new methadone programs and clinics, thereby limiting the expansion of methadone maintenance. Community resistance is based on complaints of loitering or drug sales by the patients, whether or not these complaints are valid, and the sale and diversion of methadone by unemployed patients around the clinics (65, 71, 72).

- Currently, between 15 and 20% of the admissions to methadone treatment statewide have histories of either past or present mental illness and mental retardation. In addition to methadone maintenance, these patients also need mental health services (70).

Federal Regulation of Methadone

In 1995, the IOM issued a report entitled, “Federal Regulation of Methadone Treatment” (18). The report identified the following three tiers of governmental regulation at the federal level:

- The Department of Health and Human Services (DHHS) is responsible for setting standards concerning the circumstances under which methadone may be used in the treatment of opiate addiction.

- The Food and Drug Administration (FDA), which implements the standards set forth by the DHHS in conjunction with the Substance Abuse and Mental Health Services Administration (SAMHSA).

- Since methadone is a highly controlled substance, it is subject to regulations of the Drug Enforcement Administration (DEA) to prevent diversion.
In addition, state agencies and local (e.g., county or municipal) governments may promulgate their own regulations based on the federal requirements.

Thus, potentially, five tiers of regulation can exist to oversee MMT. The IOM report (18) while acknowledging the benefits of MMT, indicates that federal regulations are hampering the expansion and accessibility of the program. This is summarized in the following statement: “Current policy, in the committee’s view, puts too much emphasis on protecting society from methadone, and not enough on protecting society from the epidemics of addiction, violence, and infectious diseases that methadone can help reduce.”

The IOM recommended that:

- Regulations be modified to permit greater access to treatment for all opiate-addicted persons.
- Clinical practice should not be arbitrarily restricted.
- Withdrawal from treatment should not be promoted without considering the probability of the patient’s relapse after leaving treatment, and patients should be accorded valid reasons and/or hearings, if necessary, in the decision to terminate treatment.
- Dose levels of patients should be determined based on individual patient need.

National Institutes of Health Consensus Statement on Effective Medical Treatment of Opiate Addiction

A consensus statement by the National Institutes of Health (NIH) on the treatment of opiate addiction was released in November of 1998 (23). Some of the conclusions are as follows:

- Opiate dependency is a brain-related medical disorder, which can be treated. (This statement is validated by NIH through an investigation of neurobiological and epidemiological research that has documented the consequences of heroin use and the chronic relapsing nature of opiate dependency irrespective of the ethnicity, cultural background or social class of the patient.)
- Methadone maintenance coupled with relevant social, medical and psychological services has the highest probability of being the most effective of all available treatments for opioid addiction.
- Opiate-dependent persons under legal supervision — probation, parole, in jails and prisons — should have access to MMT. The U.S. Office of National Drug Control Policy and the U.S. Department of Justice should take the necessary steps to implement this recommendation.
- Stigmas and misunderstandings about addiction and methadone treatment are barriers to expanding treatment. Therefore, leadership, both political and medical, is needed to educate the public.
- Current regulations were deemed overly intrusive by the consensus panel. Recommendations included eliminating current FDA regulations and replacing them with accreditation for improving methadone treatment.
- With training of health professionals and guidelines for accreditation replacing regulations, methadone could be prescribed and dispensed in a variety of medical settings outside of the current clinic system, including physicians’ offices, primary care centers, and pharmacies.
- Funding for MMT must be increased. Coverage for treatment of opiate addiction should be included in public and private insurance.

As a result of the IOM and NIH reports, it is anticipated that the FDA regulations will be eliminated and replaced by the same accreditation process that hospitals undergo. The authority over the accreditation process will be transferred to the Center for Substance Abuse Treatment (CSAT) of SAMHSA. A major emphasis in this process will be the transfer of selected groups of patients from the clinic system to MMT primary care facilities and the office-based practices of a physician.

Innovations Supported by the New York State Office of Alcoholism and Substance Abuse Services (OASAS)

The New York State OASAS has anticipated several recommendations from the IOM and NIH reports. The programs developed in New York State have served as models for development throughout the country:
• Since 1987, MMT has been available in the New York City jail system in the Key Extended Entry Program (KEEP) and patients are referred from the jail to community programs for continued treatment.

• New York City has had a highly successful program of physicians prescribing methadone maintenance in their office-based practices since 1983. The program is known as Methadone Medical Maintenance. As of this writing, three methadone medical maintenance programs are in operation and a fourth in Buffalo has been approved.

• Methadone maintenance is usually barred from many facilities treating other substance abuse problems, but since 1997, methadone has been available in the OASAS-operated Addiction Treatment Centers, formerly known as Alcohol Treatment Centers.

• OASAS has approved a statewide waiver which allows physicians working in methadone maintenance to prescribe doses of methadone found to be necessary for an individual patient — up to 150 mg/d without state approval and more than 150 mg/d with approval.

• The Lower East Side Service Center, a Manhattan-based drug treatment program licensed by OASAS, developed a program in 1982 integrating MMT within a residential setting. This program is known as the Short Stay Methadone Residence.

• Insight House in Utica, NY, and Horizon Village in Niagara County, NY, are therapeutic communities which have been offering MMT to eligible residents since 1999.

• OASAS was also instrumental in helping skilled nursing facilities with DEA-licensed pharmacies, including those serving AIDS patients, to offer MMT on the premises.

Discussion

Medical studies have shown that methadone maintenance is medically safe and nontoxic, can be used effectively in pregnancy, and does not impair intellectual, cognitive or motor functioning. Methadone maintenance is a corrective, not a curative treatment for heroin addiction. It may be necessary for patients to remain in treatment for indefinite periods of time, possibly for the duration of their lives. However, patients can work in any capacity for which they are trained, live normal lives with their families and, if not infected with HIV or hepatitis C, or afflicted with other potentially fatal illnesses, show improvements in their health status. And if infected, methadone-maintained patients can more easily access medical help than can untreated addicts.

Equally important, large-scale expansion of methadone treatment has been shown to benefit the community, with reduced addiction-related crime, reduced transmission of infectious diseases and reduced addiction-related mortality. With regard to optimum dosage, early studies recommending effective doses in the range of 80–120 mg/d and over have been validated in subsequent studies: patients remained longer in treatment and either greatly reduced or eliminated the use of heroin and other drugs. Also, patients maintained at higher doses had significantly less HIV infection than patients maintained on lower doses.

Since the 1970s, methadone programs have been admitting patients with potentially fatal illness (e.g., cancer, drug-resistant TB, AIDS, hepatitis C), polydrug abuse (e.g., cocaine/crack addiction, alcoholism, dependency on other drugs) and mental illness. Furthermore, the homelessness and low rates of employment among the new admissions have created a significant subgroup of destitute patients with serious medical and psychiatric problems, making the delivery of services more challenging for clinics. To address these issues, methadone programs are in the process of developing primary care components and liaisons with social and medical institutions, to create treatment models that address both the addiction issues and co-morbid social and medical conditions.

Stigma and the resulting discrimination appear to be the most powerful social forces preventing the full acceptance of methadone treatment. With a few notable exceptions, media reports have in general distorted methadone treatment, adding to its stigmatization.

Conclusion

The IOM and the NIH have reviewed the issues surrounding MMT. The agencies have concluded that opiate addiction is a medical disorder and that methadone maintenance with relevant ancillary services is the most effective treatment for opiate addiction. Both agencies stressed the need to expand the program to treat the hundreds of thousands of untreated heroin users.
nationwide. To increase accessibility to treatment, both agencies recommend the expansion of methadone maintenance, the training of more health personnel, the easing of regulations on federal, state and local levels to permit the opening of new programs, and the development of new models of treatment. However, effective medical and political leadership is necessary to reduce the social stigma surrounding addiction and methadone treatment in order to effectively implement these changes.

References

10. Trussell RE. Follow-up study of adolescent narcotic users treated at Riverside Hospital. Unpublished report addressed to Dr. Herman E. Hilleboe, Commissioner of Health of New York State, May, 15, 1959. (Copy available through Dr. Herman Joseph, New York State OASAS, 501 7th Avenue, New York, NY 10018.)
24. State Methadone Treatment Guidelines. Treatment Improvement Protocol (TIP) Series #1. (Available free through Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment, Publications, Rockwall II Building, 10th floor, 5600 Fishers Lane, Rockville, MD 20852, 1993.)
47. Center for Substance Abuse Treatment. Pregnant Substance-Abusing Women. Treatment Improvement Protocol (TIP) Series #2. (Available free through Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment Publications, Rockwall II Bldg. 10th floor, 5600 Fishers Lane, Rockville, MD 20852, 1993.)


Recent papers in Methadone Maintenance Treatment (MMT). Papers. People. The Trouble with Morality: The Effects of Twelve-Step Discourse on Addicts’ Decision Making. Since its development in the 1960s, researchers have extensively scrutinized methadone maintenance treatment (MMT) as a medical response to heroin addiction. Studies consistently find that MMT is more successful than other treatment more. Since its development in the 1960s, researchers have extensively scrutinized methadone maintenance treatment (MMT) as a medical response to heroin addiction. Methadone maintenance treatment (MMT) is the most common pharmacological treatment for opioid use disorder (OUD), and despite its documented effectiveness, a large number of patients respond poorly and experience relapse to illicit opioids. Some studies implicate cannabis use as a risk factor for poor MMT response. Although it is well established that substance-use behaviors differ by sex, few of these studies have considered sex as a potential moderator. The current study aims to investigate sex differences in the association between cannabis use and illicit opioid use in a cohort of MMT pati
Methadone maintenance treatment (MMT) is one of the best evidence-based opioid substitution treatments (OSTs), but there is uncertainty about whether methadone treatment reduces the risk of mortality among convicted offenders over extended follow-up periods. The objective of this study was to investigate the association between adherence to MMT and overdose fatality as well as other causes of mortality. Methods and findings. We conducted a retrospective cohort study involving linked population-level administrative data among individuals in British Columbia (BC), Canada with a history of conviction. Methadone maintenance treatment (MMT) is widely considered as an effective therapy for opioid dependence. During therapy, patients often suffer from sleep disturbances such as insomnia, sleep-disordered breathing, and poor sleep quality. The sleep disturbance prevalence rate of patients under MMT was high. Methadone-maintained individuals had lower sleep efficiency, shorter total sleep time, more awakenings, decreased rapid eye movement sleep, and shorter slow wave sleep. The Pittsburgh Sleep Quality Index and Epworth Sleepiness Scale scores in these patients were significantly higher than in MMT maintenance thereby became a treatment option for opiate dependence. It involves the daily substitution of one opioid drug with a long half-life (methadone), for a short-acting and usually injected opioid drug (heroin). The aspects of methadone that have led to its use as a substitute drug for heroin include the following: At the basis of methadone maintenance treatment (MMT), and all opioid replacement therapy, is the observation that opioid analgesics can be substituted for one another. The cross-tolerance between methadone and heroin means that a person tolerant to heroin will als