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## Chapter 2. History of Medication-Assisted Treatment for Opioid Addiction

### In This Chapter ...

#### Emergence of Opioid Addiction as a Significant Problem and the Roots of Controversy

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#### Regulatory History

This chapter describes the history of opioid use and addiction in the United States; changes in the population groups affected by opioid addiction disorders; and this country's social, political, legal, and medical responses. The chapter emphasizes factors affecting the development and course of medication-assisted treatment for opioid addiction (MAT) in opioid treatment programs (OTPs).

Opioid addiction has affected different population groups and socioeconomic classes in the United States at different times. Society's response has changed along with changes in the groups or classes most affected, shifts in social and political attitudes toward opioid addiction, and the accumulation of more and better information about its causes and treatments (Musto 1999). The consensus panel for this TIP believes that an appreciation for the roots of opioid addiction and treatment is important because attitudes and beliefs about opioid use and addiction that are rooted in U.S. history over the past 150 years continue to influence policies governing MAT.

### Emergence of Opioid Addiction as a Significant Problem and the Roots of Controversy

Many of today's substances of abuse including the opioids—primarily opium, morphine, heroin, and some prescription opioids—gained their early popularity as curatives provided by physicians, pharmacists, and others in the healing professions or as ingredients in commercial products ranging from pain elixirs and cough suppressants to beverages. These products usually delivered the benefits for which they were used, at least initially, such as pain relief, increased physical and mental energy (or “refreshment”), and reduced anxiety. For example, opioids were often the best available substances to relieve pain on Civil War battlefields. Unfortunately, the uncontrolled use of opioids either for prescribed and advertised benefits or for nonmedicinal effects leads to increased tolerance and addiction. Tolerance increases the need for larger quantities of opioids, more frequent use, or combination with other substances to sustain their effects; it also increases the severity of withdrawal when addiction is not satisfied. Recognition of this problem has spurred a long-running debate among patients and people who use opioids, their families, physicians, researchers, community leaders, patient advocates, and government officials. This debate centers on two different views: (1) opioid addiction is a generally incurable disease that requires long-term maintenance with medication; or (2) opioid addiction stems from weak will, lack of morals, other psychodynamic factors, or an environmentally determined predilection that is rectified by criminalization of uncontrolled use and distribution and measures promoting abstinence.

### The Changing Face of Opioid Addiction

Opioid addiction first emerged as a serious problem in this country during and after the Civil War, when opioids were prescribed widely to alleviate acute and chronic pain, other types of discomfort, and stress. Although a smaller pattern of nonmedical opioid use continued as well, mainly opium smoking among Chinese immigrants and members of the Caucasian “underground” (e.g., prostitutes, gamblers, petty criminals), iatrogenic addiction was much more common (White 1998). By the late 19th century, probably two-thirds of those addicted to opioids (including opium, morphine, and laudanum) were middle- and upper-class White women, a fact Brecher and the Editors of *Consumer Reports* (1972, p. 17) attribute to “the widespread medical custom of prescribing opiates for menstrual and menopausal discomfort, and the many proprietary opiates prescribed for ‘female troubles.’” Civil War veterans who were addicted by medical procedures composed another group, but their numbers were dwindling. By 1900, an estimated 300,000 persons were opioid addicted in the United States (Brecher and Editors 1972; Courtwright 2001; Courtwright et al. 1989).

During the late 19th and early 20th centuries, U.S. society generally viewed iatrogenic addiction among women

and disabled war veterans sympathetically—as an unfortunate medical condition—and treated these groups with tolerance and empathy, particularly because neither group presented major social problems (Courtwright 2001). Doctors usually prescribed more opioids for these patients, and sanatoriums were established for questionable “cures” of the resulting addictions. The chronic nature of opioid addiction soon became evident, however, because many people who entered sanatoriums for a cure relapsed to addictive opioid use after discharge. In Eugene O'Neill's autobiographical drama “Long Day's Journey Into Night,” for example, his father refuses to return O'Neill's mother, who is addicted, to a sanatorium because he is aware of the addictive qualities of morphine and is resigned to the inevitability of relapse (Courtwright 2001).

By the end of the 19th century, doctors became more cautious in prescribing morphine and other opioids, and the prevalence of opioid addiction decreased. Small groups still practiced opium smoking, but most Americans regarded it as socially irresponsible and immoral. It is noteworthy, however, that heroin, introduced in 1898 as a cough suppressant, also began to be misused for its euphoric qualities, gradually attracting new types of users. This development, along with diffusion of the hypodermic technique of drug administration, which gained popularity between 1910 and 1920, had a profound effect on opioid use and addiction in the 20th century and beyond (Courtwright 2001).

The size and composition of the U.S. opioid-addicted population began to change in the early 20th century with the arrival of waves of European immigrants. Courtwright (2001) portrays most users of opioids of this period as young men in their 20s: “down-and-outs” of recent-immigrant European stock who were crowded into tenements and ghettos and acquired their addiction during adolescence or early adulthood. They often resorted to illegal means to obtain their opioids, usually from nonmedical sources and specifically for the euphoric effects. “Gone was the stereotype of the addicted matron; in its place stood that of the street criminal” (Courtwright 2001, p. 1).

The initial treatment response in the early 20th century continued to involve the prescriptive administration of short-acting opioids. By the 1920s, morphine was prescribed or dispensed in numerous municipal treatment programs (Courtwright et al. 1989).

Addictive use of opium, cocaine, and heroin, along with drug-related crime, especially in poor urban communities, increasingly concerned social, religious, and political leaders. The tolerance and empathy shown toward Civil War veterans and middle-aged women evaporated; negative attitudes toward and discrimination against new immigrants probably colored views of addiction. Immigrants and others who trafficked in and abused drugs were viewed as a threat. As detailed below, society's response was to turn from rudimentary forms of treatment to law enforcement (Brecher and Editors 1972; Courtwright 2001; Courtwright et al. 1989). For more on trends in the 1920s and 1930s, see “Early treatment efforts” below.

McCoy (n.d.) refers to a forced decline in opioid addiction during World War II, brought about by restrictions on shipping and strict port security, which produced a marked hiatus in global opium trafficking and caused the U.S. opioid-addicted population to drop to a historic low of about 20,000. Once smuggling resumed after the war, the population that had used opioids resumed the habit.

Another major change in the U.S. opioid-addicted population occurred after World War II. As many European immigrants moved from crowded cities, Hispanics and African-Americans moved into areas with preexisting opioid abuse problems, and the more susceptible people in these groups acquired the disorder (Courtwright 2001; Courtwright et al. 1989).

The post-World War II shift in the composition of opioid-addicted groups coincided with hardening attitudes toward these groups, leading some researchers to conclude that stigmatization of people with addiction disorders and their substances of abuse reflected, at least in part, class and ethnic biases. A portion of U.S. society appeared to view with disdain and fear the poor White, Asian, African-American, and Hispanic people with addiction disorders who lived in the inner-city ghettos (Courtwright et al. 1989).

Brecher and the Editors of Consumer Reports (1972) point out that, by the mid-1960s, the number of middle-class young White Americans using heroin was on the rise, as was addiction-related crime. By the 1970s, U.S. military involvement in Vietnam also was having an effect. From one-fourth (Brecher and Editors 1972) to one-half (Courtwright 2001) of American enlisted men in Vietnam were believed to have used or become addicted to heroin; however, White (1998) points out that the feared epidemic of heroin addiction among returning veterans did not materialize fully. He concludes, “Vietnam demonstrated that a pattern of drug use could emerge in response to a particular environment and that spontaneous remission could occur when the environment was changed” (p. 303).

By the 1980s, an estimated 500,000 Americans used illicit opioids (mainly heroin), mostly poor young minority men and women in the inner cities. Although this number represented a 66-percent increase over the estimated number of late 19th-century Americans with opioid addiction, the per capita rate was much less than in the late

19th century because the population had more than doubled (Courtwright et al. 1989). Nevertheless, addiction became not only a major medical problem but also an explosive social issue (Courtwright 2001; Courtwright et al. 1989).

By the end of the 1990s, an estimated 898,000 people in the United States chronically or occasionally used heroin (Office of National Drug Control Policy 2003), and the number seeking treatment was approximately 200,000 (almost double the number during the 1980s). The abuse of opioids that normally were obtained by prescription was a growing concern because of both their damaging effects and their potential as gateway drugs to other substance use. Treatment admission rates for addiction to opioid analgesics more than doubled between 1992 and 2001 (Substance Abuse and Mental Health Services Administration 2004), and visits to emergency rooms related to opioid analgesic abuse increased 117 percent between 1994 and 2001 (Substance Abuse and Mental Health Services Administration 2003b ).

## **Society's Changing Response**

### **The Harrison Narcotic Act of 1914**

The Pure Food and Drug Act of 1906, which required medicines containing opioids to say so on their labels, was the first national response to the changing image of people with addictions (Brecher and Editors 1972). The Harrison Narcotic Act of 1914 was the earliest significant Federal attempt to place strict controls on opioids and other substances (Brecher and Editors 1972). Although U.S. mercantile and trade interests were also at stake, the widely held perception that people with addictions generally were members of a White criminal underclass or a Chinese minority has been portrayed as an underlying motivation for the statute (Courtwright 2001; Courtwright et al. 1989). The Harrison Act was conceived not as a prohibition law but as a measure to regulate the manufacture, distribution, and prescription of opioids, coca, and their derivatives. Under the act's provisions, manufacturers, pharmacists, and physicians had to be licensed, keep records for inspection, and pay modest fees to the U.S. Department of the Treasury, referred to hereafter as Treasury.

The act permitted physicians and dentists to dispense or distribute opioids “to a patient ... in the course of [the physician's] professional practice only” (38 Stat. 786 [1914]). Although this provision permitted physicians to prescribe or dispense opioids so long as they kept the required records, Treasury interpreted the act as a prohibition on physicians' prescribing opioids to persons with addictions to maintain their addictions. (Treasury was the agency responsible for enforcing the Harrison Act as well as prohibition laws.) Treasury's position appeared to be that addiction is not a disease and the person with an addiction, therefore, was not a patient. It followed that any physician prescribing or dispensing opioids to such individuals was not doing so in the “course of his professional practice” (White 1998). In 1919, the United States Supreme Court upheld Treasury's interpretation. This interpretation and enforcement of the Harrison Act effectively ended, until well into the 1960s, any legitimate role for the general medical profession in medication-assisted treatment for Americans who had drug addictions (White 1998).

### **Early treatment efforts**

Until the 1919 Supreme Court decision upholding Treasury's interpretation of the Harrison Act, numerous municipalities with large numbers of residents who were opioid addicted were operating treatment clinics in which morphine was prescribed or dispensed. Some clinics prescribed heroin and cocaine (Courtwright et al. 1989). These early OTPs varied in how they functioned; some provided detoxification treatment and others adopted a maintenance policy (Courtwright 2001; Gewirtz 1969). Perhaps the best known of these early OTPs were the Department of Health program in New York City, where those with addictions were detoxified with decreasing doses of heroin and morphine, and the program established by Dr. Willis Butler in Shreveport, Louisiana, which not only detoxified patients but also maintained some of them on morphine (Courtwright et al. 1989).

Courtwright and others state that Treasury regarded these clinics as a threat to its antimaintenance philosophy. By the early 1920s, it had succeeded in closing them through legal pressure, critical inspections, and threats. The last program to be closed was Dr. Butler's in Shreveport (Courtwright 2001; Courtwright et al. 1989).

In the 1920s, an increase in crime related to the acquisition of illicit opioids was reported in cities throughout the country. In 1929, Congress appropriated funds to establish two new treatment facilities, initially called “narcotics farms” (White 1998), in Fort Worth, Texas, and Lexington, Kentucky. The Lexington facility, which opened to patients in 1935, was renamed the U.S. Public Health Service Narcotics Hospital in 1936. These institutions detoxified patients with opioid addiction who entered voluntarily, and they also served as hospitals for prison inmates who had opioid addictions and were legally committed through a Federal court. The prescribed stay was about 6 months, although some patients stayed longer. Prisoners could stay for up to 10 years. These hospitals

offered social, medical, psychological, and psychiatric services in addition to detoxification and had a low patient-to-staff ratio (about 2 to 1), but the atmosphere was described as prisonlike, especially at the Lexington facility (White 1998). Two major followup studies showed the program to be a failure. One reported a relapse rate of 93 percent in 1,881 former patients over a 1.0- to 4.5-year followup period (Hunt and Odoroff 1962). The second found a relapse rate of 97 percent in 453 former patients over followup periods of 6 months to 5 years (Duvall et al. 1963). The Lexington hospital facility was turned over to the Bureau of Prisons in 1974 (Courtwright et al. 1989). Despite the failure of these programs, White credits the research conducted there with providing “much of the foundation upon which modern treatment advances were built” (White 1998, p. 126).

The increase in heroin addiction in New York City after World War II led, in 1952, to the establishment of Riverside Hospital for adolescents with addiction disorders. This program also proved to be a failure. A followup study in 1956 showed a high posttreatment relapse rate (e.g., at least 86 percent of patients admitted in 1955), and the Riverside facility was closed in 1961 (Brecher and Editors 1972).

### Experiment in civil commitment

Civil commitment is portrayed by Brecher and the Editors of *Consumer Reports* (1972) and White (1998) as legislation enabling those with substance addiction and those “in imminent danger of becoming addicted” (White 1998, p. 250) to be confined in rehabilitation centers without having first committed or been convicted of a crime. Civil commitment was instituted in California and New York in the 1960s to allay fears about addiction-related crimes against people and property in the inner cities. People with addictions could be committed to facilities through a voluntary process that included a medical examination to validate the presence of an addiction, or they could be committed for 3 years when arrested on a misdemeanor charge, as an alternative to a jail sentence. The civil commitment program instituted in New York in 1966 turned out to be exceedingly expensive, and the positive results were minimal (Brecher and Editors 1972; Inciardi 1988). The great majority of those admitted, treated, and paroled to aftercare programs dropped out of these programs, and they usually could not be located. A review of California's civil commitment experience in the 1960s showed that five of every six patients committed for addictions and subsequently placed on aftercare relapsed, were rearrested, dropped out of treatment, died, or were removed from the program by writs of habeas corpus (Joseph 1988; Joseph and Dole 1970).

Although statutes permitting involuntary commitment might remain on the books in some States, such laws rarely have been used to commit people who abuse substances and who are not under criminal justice jurisdiction (Anglin 1988). Court decisions after the 1960s generally have required that an individual be a danger to himself or herself or others before the legal system can use involuntary commitment (e.g., *O'Connor v. Donaldson*, 422 U.S. 563, 1975).

### The search for alternatives

In New York, death rates associated with the injection of heroin increased from 7.2 to 35.8 per 10,000 deaths between 1950 and 1961 (Frank 2000; Joseph et al. 2000). In the 1960s and 1970s, more than 150,000 names were added to the Narcotics Register in New York City. (The Narcotics Register, active from 1967 to 1974, was a list of known or suspected persons with addictions.)

By the middle to late 1960s, illicit-opioid-related mortality had become the leading cause of death for young adults from ages 15 to 35 in New York City. The number of serum hepatitis (now called hepatitis B) cases related to contaminated needles also was increasing. Record numbers of people with opioid addictions were arrested for drug-related crimes (e.g., possession, sales, robbery, burglary), and overcrowded jails had no effective method to ease detoxification (Inciardi 1988; Joseph and Dole 1970). By 1968, the Manhattan County Jail for Men (also known as the Tombs) had been wracked by riots blamed on poor living conditions, severe overcrowding, and lack of medical care for inmates with drug addictions.

As the incidence of addiction and related criminal activity rose dramatically in urban areas, concern grew in the legal and medical communities because increased incarceration had failed to stem the tide. The legal and medical professions were perturbed by the post-World War II rise in opioid addiction in the United States and the ineffectiveness of Federal regulatory policy. In 1958, a joint committee of the American Bar Association and the American Medical Association (AMA) issued a report recommending that an outpatient facility prescribing opioids to treat addiction be established on a controlled experimental basis (Brecher and Editors 1972).

Other groups voiced support for the concept of opioid maintenance programs. The New York Academy of Medicine recommended, in 1955 and again in 1963, that clinics be established in affiliation with hospitals to dispense opioids in a controlled manner to patients addicted to illicit opioids. In 1956, the AMA advocated a research project to investigate the feasibility of dispensing opioids in an OTP. In 1963, the Kennedy administration's Advisory Commission on Narcotic and Drug Abuse also recommended research to determine the

effectiveness of outpatient OTPs' dispensing of opioids to people addicted to opioids (Brecher and Editors 1972). In the early 1970s, faced with increased opioid-related drug use and crimes, the Nixon administration greatly increased funding to stem the supply of illicit opioids, primarily heroin, entering the United States. It also greatly increased funding for methadone maintenance, and the number of patients receiving methadone increased from 9,000 in 1971 to 73,000 in 1973 (Courtwright 2001). Support for opioid maintenance grew, especially because no effective psychosocial alternative existed to treat the large number of people with opioid addictions.

## Origins of Opioid Maintenance Therapy

### Development of Medications To Treat Opioid Addiction

#### Early rationale for methadone maintenance treatment

In 1962, Dr. Vincent P. Dole, a specialist in metabolism at The Rockefeller University, became chair of the Narcotics Committee of the Health Research Council of New York City. After studying the scientific, public health, and social ramifications of addiction in the city, he received a grant to establish a research unit to investigate the feasibility of opioid maintenance. In preparing for this research, he read *The Drug Addict as a Patient* by Dr. Marie E. Nyswander (Nyswander 1956), a psychiatrist with extensive experience treating patients who were addicted to opioids. She was convinced that these individuals could be treated within general medical practice. She also believed that many would have to be maintained on opioids for extended periods to function because a significant number of people who attempted abstinence without medication relapsed, in spite of detoxifications, hospitalizations, and psychotherapy (Brecher and Editors 1972; Courtwright et al. 1989). Dr. Nyswander joined Dr. Dole's research staff in 1964. Among others joining the team was clinical investigator Dr. Mary Jeanne Kreek.

These researchers realized that morphine, which is related to heroin, was not a good choice as an opioid maintenance drug because patients' social functioning was impaired by morphine's sedating effects (White 1998). Also, the short half-life of morphine required several injections per day, and, as tolerance developed, increasing amounts were needed over a short time for patients to remain stable (Brecher and Editors 1972). Other short-acting opioids, such as heroin, codeine, oxycodone, and meperidine (Demerol<sup>®</sup>), showed similar results (Dole 1980, 1988).

#### Development of methadone

With short-acting opioids eliminated as options for maintenance therapy, research focused on methadone. Methadone appeared to be longer acting and effective when administered orally. It also was selected on the basis of observations of its use in patients withdrawing from heroin and as an analgesic in the experimental treatment of pain (Dole 1980, 1988). In 1964, technology was not available to measure blood levels of heroin, morphine, or methadone to assess duration of action. Proof of the efficacy of methadone maintenance treatment depended on observation and recognition by researchers.

In an initial study, methadone was administered to two patients previously maintained on morphine. Once tolerance for daily doses of 50 to 120 mg was established, patients could function normally without the anxiety associated with drug craving (White 1998). During this research, the following important findings about methadone maintenance were noted, all supporting its efficacy and benefits (Dole 1980, 1988):

- Patients did not experience euphoric, tranquilizing, or analgesic effects. Their affect and consciousness were normal. Therefore, they could socialize and work normally without the incapacitating effects of short-acting opioids such as morphine or heroin.
- A therapeutic, appropriate dose of methadone reduced or blocked the euphoric and tranquilizing effects of all opioid drugs examined (e.g., morphine, heroin, meperidine, and opium), regardless of whether a patient injected or smoked the drugs.
- No change usually occurred in tolerance levels for methadone over time, unlike for morphine and other opioids; therefore, a dose could be held constant for extended periods (more than 20 years in some cases).
- Methadone was effective when administered orally. Because it has a half-life of 24 to 36 hours, patients could take it once a day without using a syringe.
- Methadone relieved the opioid craving or hunger that patients with addiction described as a major factor in relapse and continued illegal use.
- Methadone, like most opioid-class drugs, caused what were considered minimal side effects, and



research indicated that methadone was medically safe and nontoxic.

### Expansion of methadone maintenance from research project to public health program

In 1965, the initial research project on methadone safety and efficacy was transferred to Manhattan General Hospital in New York City (Brecher and Editors 1972). Because Dole and his colleagues knew that an independent evaluation of this new treatment would be necessary, a team headed by Dr. Frances Rowe Gearing was formed at Columbia University School of Public Health to evaluate patient progress as this treatment expanded. In general, the team found that patients' social functioning improved with time in treatment, as measured by elimination of illicit-opioid use and better outcomes in employment, school attendance, and homemaking. Most patients were stabilized on methadone doses of 80 to 120 mg/day. Most patients who remained in treatment subsequently eliminated illicit-opioid use. However, 20 percent or more of these patients also had entered treatment with alcohol and polysubstance abuse problems, despite intake screening that attempted to eliminate these patients from treatment (Gearing and Schweitzer 1974). Methadone treatment was continued for these patients, along with attempts to treat their alcoholism and polysubstance abuse. Further evaluation, research, and expansion of the program ultimately were recommended (Joseph and Dole 1970) and instituted. Methadone maintenance became a major public health initiative to treat opioid addiction under the leadership of Dr. Jerome Jaffe, who headed the Special Action Office for Drug Abuse Prevention in the Executive Office of the White House in the early 1970s. Dr. Jaffe's office oversaw the creation of a nationwide, publicly funded system of treatment programs for opioid addiction.

### Development of LAAM

Like methadone, levo-alpha acetyl methadol (LAAM) was classified as a U.S. Drug Enforcement Administration (DEA) schedule II controlled substance (i.e., having a high potential for abuse but also a currently accepted medical use) that creates a pharmacologic cross-tolerance for other opioids and therefore blocks their euphoric effects while controlling opioid craving. Whereas methadone suppressed opioid withdrawal symptoms for 24 hours or longer, LAAM achieved this effect for 48 to 72 hours or longer.

LAAM was first developed in 1948 by German chemists as an analgesic (Finn and Wilcock 1997). By the late 1960s, interest arose in LAAM as an alternative to methadone (American Association for the Treatment of Opioid Dependence n.d.). Between 1969 and 1981, 27 separate studies of more than 6,000 patients established LAAM's safety and efficacy (National Institute on Drug Abuse 1993a ). The U.S. Food and Drug Administration (FDA) approved LAAM for use in OTPs in July 1993 (National Institute on Drug Abuse 1993a ).

Later studies continued to confirm that LAAM was an effective alternative to methadone and was preferred by some patients (Glanz et al. 1997). However, in April 2001, based on reported LAAM-related disturbances in cardiac function, FDA and Roxane Laboratories, Inc., manufacturer of ORLAAM<sup>®</sup>, strengthened the warnings in LAAM product labeling (Haehl 2001). The American Association for the Treatment of Opioid Dependence has issued clinical guidelines for LAAM (American Association for the Treatment of Opioid Dependence n.d.). At this writing, only 3 percent of patients enrolled in maintenance programs in the United States are receiving LAAM (Substance Abuse and Mental Health Services Administration 2002a ).

In 2003, Roxane Laboratories announced that it would stop producing LAAM on January 1, 2004 (Schobelock 2003), making LAAM's continued availability doubtful. This TIP continues to include basic, limited coverage of LAAM in discussions of opioid medications because of its clinical significance and relevance in MAT.

### Development of buprenorphine

Information on the development of the latest successful maintenance medication, buprenorphine, is in "DEA classification of buprenorphine" below and TIP 40, *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction* (CSAT 2004a ).

### Development of naltrexone

Naltrexone is the only pure opioid antagonist of the medications described here (see chapter 3). In the early 1980s, the National Institute on Drug Abuse (NIDA) completed initial testing of naltrexone to treat opioid addiction, and FDA approved naltrexone for this use in 1984. In 1995, naltrexone also received FDA approval as a preventive treatment for relapse to alcohol use among patients dependent on alcohol. Some opioid treatment providers have found that naltrexone is most useful for highly motivated patients who have undergone detoxification from opioids and need additional support to avoid relapse or who desire an expedited detoxification schedule because of external circumstances. Naltrexone also may benefit some patients in the beginning stages

of opioid use and addiction. Other patient groups frequently have demonstrated poor compliance with long-term naltrexone therapy, mainly because naltrexone neither eases craving for the effects of illicit opioids when used as directed nor produces withdrawal symptoms when discontinued (Tai et al. 2001).

### Public Policy Studies and Reports Since 1993

Analyses since the publication of TIP 1 have shown that maintenance treatment for opioid addiction is effective in both treatment outcomes and costs.

### California Drug and Alcohol Treatment Assessment

In 1994, the California Department of Alcohol and Drug Programs published the results of a pioneering large-scale study of the effectiveness, benefits, and costs of substance abuse treatment in California. Using State databases, provider records, and followup interviews with treatment participants, the study detailed the effects of treatment on participant behavior including drug and alcohol use, criminal activity, health, health care use, and income; the costs of treatment; and the economic value of treatment to society (Gerstein et al. 1994).

Among the California Drug and Alcohol Treatment Assessment's findings were the following:

- Treatment was cost beneficial to taxpayers, with the cost averaging \$7 returned for every dollar invested (Gerstein et al. 1994). "Each day of treatment paid for itself (the benefits to taxpaying citizens equaled or exceeded the costs) on the day it was received, primarily through an avoidance of crime" (Gerstein et al. 1994, p. iv). "Regardless of the modality of care, treatment-related economic savings outweighed costs by at least 4 to 1" (Gerstein et al. 1994, p. 90).
- Methadone treatment was among the most cost-effective treatments, yielding savings of \$3 to \$4 for every dollar spent. This was true for each major methadone treatment modality, but costs were lower in an outpatient OTP than in a residential or social modality (Gerstein et al. 1994).
- Patients in methadone maintenance showed the greatest reduction in intensity of heroin use, down by two-thirds, of any type of opioid addiction treatment studied.
- Patients in methadone maintenance showed the greatest reductions in criminal activity and drug selling, down 84 percent and 86 percent, respectively, of any type of opioid addiction treatment studied.
- Health care use decreased for all treatment modalities; participants in methadone maintenance treatment showed the greatest reduction in the number of days of hospitalization, down 57.6 percent, of any modality.

### Institute of Medicine

In 1995, the Institute of Medicine (IOM) produced a study titled *Federal Regulation of Methadone Treatment* (Institute of Medicine 1995). This study concluded that FDA regulations were inhibiting physicians from exercising their professional judgment; isolating methadone treatment from mainstream medicine, thereby depriving patients of important ancillary services; and discouraging research into new medications. This IOM study recommended that the Federal regulatory process be modified to

- Encourage programs to provide comprehensive services, such as individual and group counseling and medical care
- Emphasize the need for continuing clinical assessment throughout treatment
- End arbitrary restrictions on OTP practices.

### National Institutes of Health

In 1997, a National Institutes of Health (NIH) consensus panel called for expansion of methadone maintenance treatment. It identified such barriers as the public's misperception of persons who are opioid addicted not as individuals with a disease but as "other" or "different," the misperception "that [addiction] is self-induced or a failure of willpower and that efforts to treat it inevitably fail," and overregulation of methadone treatment that limits the flexibility and responsiveness of treatment programs (National Institutes of Health 1997b ). That panel called for the following:

- Federal leadership to inform the public that opioid addiction is a medical disorder that can be treated effectively, with significant benefits for the patient and society
- Access to methadone treatment for persons under legal supervision (e.g., probation, parole,

incarceration)

- Increase in funding for methadone maintenance treatment
- Reduction in unnecessary regulation of MAT, including
  - Replacement of FDA regulation and oversight of MAT with more effective, less expensive measures, such as accreditation, to improve the quality of methadone treatment
  - Revision of DEA regulations to eliminate the extra level of regulation placed on methadone compared with other schedule II opioids, thereby encouraging more physicians and pharmacies to prescribe and dispense methadone and making maintenance treatment available in more locations
  - Faster approval of new medications for MAT by FDA and the States
  - Expansion of the availability of maintenance pharmacotherapy to States and programs where it is currently unavailable.

## Regulatory History

For more than three decades, methadone's use to treat addiction has been subjected to extensive Federal, State, and local regulation. (For a detailed history of Federal regulation of methadone treatment, see [chapter 5](#) in the IOM report [1995] edited by Rettig and Yarmolinsky.)

### Laws Related to Controlled Substances as Addiction Treatment Medications

Congress has enacted several significant statutes since 1970 to limit and control the availability of psychoactive drugs and their use to treat addiction.

#### Controlled Substances Act (1970)

The Controlled Substances Act of 1970 (Public Law [P.L.] 91–513) requires all manufacturers, distributors, and practitioners who prescribe, dispense, or administer controlled substances to register with DEA. A physician seeking registration must meet certain standards established by the Secretary of Health and Human Services and must comply with regulations established by the U.S. Attorney General regarding security of opioid stocks and maintenance of records.

#### Narcotic Addict Treatment Act (1974)

In passing the Narcotic Addict Treatment Act of 1974 (P.L. 93–281), which amended the Controlled Substances Act, Congress recognized the use of an opioid drug to treat opioid addiction as critical and, for the first time in Federal law, defined “maintenance treatment.” To promote closer monitoring of programs that use opioids for maintenance treatment, the law required separate DEA registration by medical practitioners who dispense opioid drugs in the treatment of opioid addiction. Previously, any physician with a DEA registration could prescribe methadone for pain management or addiction treatment. This act also increased coordination between the U.S. Department of Health and Human Services (DHHS) and DEA. Under its provisions, before a practitioner can obtain registration from DEA, DHHS must determine that the practitioner is qualified according to established treatment standards.

The Narcotic Addict Treatment Act also established NIDA as an institute independent of the National Institute of Mental Health. Authority to regulate the treatment of opioid addiction was split between NIDA and FDA. NIDA became responsible for determining appropriate standards for medical, scientific, and public health aspects of drug abuse treatment. FDA received the authority to determine the safety and effectiveness of drugs and approve new drugs for opioid addiction treatment.

#### Drug Addiction Treatment Act (2000)

The Drug Addiction Treatment Act of 2000 (DATA [P.L. 106–310 div. BJ]) amended that portion of the Controlled Substances Act mandating separate registration for practitioners who dispense opioids in addiction treatment. It allows practitioners who meet certain qualifying criteria to dispense or prescribe schedule III, IV, or V controlled substances specifically approved by FDA for MAT. [Chapter 3](#) describes the specific requirements that physicians must satisfy under DATA provisions, including the requirement that physicians must have the capacity to refer patients for needed counseling and other ancillary services.



## DEA classification of buprenorphine

On October 8, 2002, DEA completed its evaluation of buprenorphine, classifying it as a schedule III drug (i.e., having potential for abuse and a currently accepted medical use in treatment but less potential for addiction than schedule II drugs). FDA made buprenorphine the first drug approved for treatment of opioid addiction in physicians' offices (CSAT 2004a ; Substance Abuse and Mental Health Services Administration 2003a ; see also chapter 3).

## History of Methadone Regulation

### Federal regulation

In 1972, FDA issued regulations governing eligibility, evaluation procedures, dosages, take-home medications, frequency of patient visits, medical and psychiatric services, counseling, support services, and related details for methadone treatment programs. Several modifications were made to these regulations during the 1980s. Until 2001, FDA was responsible for approving these programs and ensuring compliance with FDA regulations.

As experience with the effectiveness of methadone grew, criticism of the 1972 FDA regulations increased from physicians, who complained that the regulations placed burdens on their practice of medicine, and from addiction treatment specialists, who pointed out that proscriptive regulations failed to leave room for treatment innovation. (See comments on the new rules in their proposed form [*Federal Register* 64:39812–39814].)

The movement away from a compliance orientation and toward an accreditation model was supported by a number of reviews, including the 1997 NIH consensus development conference on Effective Treatment of Opiate Addiction and the review of 1972 FDA regulations by IOM (Institute of Medicine 1995). Interest in accreditation grew because of its emphasis on self-assessment and improvement and on integration of quality assurance and performance elements developed by expert accreditation organizations. In addition, trends in national health care fueled movement toward accreditation. Many managed care organizations require all accredited health care practitioners to demonstrate quality care. Several States grant exemptions from State licensing requirements (called “deemed status”) to accredited health care facilities.

Final regulations issued by DHHS and the Substance Abuse and Mental Health Services Administration (SAMHSA) on January 17, 2001, effective May 18, 2001, govern the use of methadone and LAAM in both maintenance and detoxification treatments for opioid addiction. The 1972 FDA regulations were repealed, and a new accreditation-based regulatory system was created. The new system shifted administration and oversight from FDA to SAMHSA. The new regulations acknowledged that addiction is a medical disorder not amenable to one-size-fits-all treatment. They recognized that different patients, at different times, could need vastly different services.

Accreditation itself is a peer-review process that evaluates a treatment program against SAMHSA's opioid treatment standards and accreditation standards of SAMHSA-approved accrediting bodies (42 Code of Federal Regulations, Part 8). It includes site visits by specialists with experience in opioid pharmacotherapy and related activities.

The new regulations establish an entirely different regulatory and oversight structure for MAT. The DEA role remains the same, but FDA's authority to approve and monitor programs has been transferred to SAMHSA. Instead of detailed proscriptive rules, the new regulations set forth general certification requirements and Federal opioid treatment standards. These are elaborated in best-practice guidelines and in accreditation “elements” (or standards) developed by the SAMHSA-approved accreditation bodies. SAMHSA has employed a series of expert panels to develop guidelines for an accreditation-based certification system. Placing detailed practice criteria in accreditation standards rather than in regulations permits SAMHSA and the accreditation bodies to update the standards as needed.

The new regulations provide that, once a program is accredited, SAMHSA uses accreditation results along with other data to determine whether the program is qualified to carry out treatment under the standards in the regulations. SAMHSA maintains oversight of accreditation elements in its review of accreditation bodies' initial and renewal applications.

The consensus panel for this TIP expects the accreditation process to result in an integrated and individualized approach to services, increased patient satisfaction, better staff recruitment, enhanced community confidence and outcomes, and improvements in quality of care. The shift to accreditation enables SAMHSA to focus its oversight efforts on improving treatment rather than ensuring that programs are meeting regulatory criteria.

### States

The new Federal regulations preserve States' authority to regulate OTPs. Oversight of treatment medications remains a tripartite system involving States, DHHS/SAMHSA, and the U.S. Department of Justice/DEA.

States can monitor the same areas as Federal agencies, but State rules do not always echo Federal regulations. Some States have established medical recertification requirements for continuation of comprehensive, long-term MAT after a specified period. Other State and local requirements, such as certificates of need, zoning, and licensure, can affect the number, size, and location of OTPs. These regulations are not affected by the change in Federal regulations.

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