

# Using Medication Assisted Treatment to Treat Opioid Use Disorder: Learning from Past Experience to Guide Policy

Mark W. Parrino

## Executive Summary

The increasing prevalence of opioid use disorder (OUD) in the United States has led to an ongoing public health crisis. At the present time, more than 150 Americans die each day of opioid-related overdoses. This epidemic of opioid overdose deaths, first characterized by prescription opioid misuse, has transitioned into heroin and fentanyl use.

Medication assisted treatment with methadone and buprenorphine has been shown to be effective in helping individuals addicted to heroin or other opioids stabilize their lives and reduce their illicit drug use. Naltrexone also is an effective medication for some opioid addicted individuals as well as for those with alcohol dependence.<sup>(1)</sup> The OUD crisis has led to an increasing demand for medication assisted treatment through opioid treatment programs (OTPs) and office-based opioid treatment via the Drug Abuse Treatment Act of 2000 (DATA 2000). Treatment capacity, however, must be further expanded to meet the growing demand, especially in rural and other underserved areas.

The American Association of Treatment of Opioid Disorders (AATOD) presents this policy paper to address some of the issues that impact the development of future policies in the use of medications in OUD treatment and the prevention of opioid overdose. These issues include:

1. Should treating OUD be viewed as a public health intervention with the principal component of care and treatment being the utilization of federally approved medications (methadone, buprenorphine, and extended release injectable naltrexone)?
2. Should resources be prioritized to treating OUD with medications and additional clinical services?
3. Should there be coordination to organize service delivery to treat this illness through a continuum of service delivery components?
4. Should there be a better connection/coordination between DATA 2000 practices and OTPs to address treatment capacity and facilitate interfacility referrals from one practice to the next?

This paper provides a historical perspective of the nation's current policies for delivering medication assisted treatment for OUD. By understanding the system and principles of care that guide how medication assisted treatment is delivered today, policymakers can develop future policies that offer greater stability, are based on evidence, and reflect best practices.

## Brief History of Opioid Addiction Treatment in the United States

In the late 1960s and early 1970s, media and public health reports warned about heroin addiction in large metropolitan cities among lower socio-economic groups. This led different cities throughout the United States to quickly open up methadone treatment programs, now referred to as OTPs, during the 1960s.

The foundation of methadone maintenance treatment was developed by Dr. Vincent Dole and his associates Dr. Marie Nyswander and Dr. Mary Jeanne Kreek at Rockefeller University in the mid-1960s. In the book, *Addicts Who Survived: An Oral History of Narcotic Use in America, 1923-1965*, Dr. Dole wrote,

“The problem was one of rehabilitating people with a very complicated mixture of social problems on top of a specific medical problem, and that [practitioners] ought to tailor their programs to the kind of problems they were dealing with. The strength of the early programs as designed by Marie Nyswander was in their sensitivity to individual human problems. The stupidity of thinking that just giving methadone to solve a complicated problem seems to me beyond comprehension.”<sup>(2)</sup>

In 1972, the Food and Drug Administration (FDA) published regulations for methadone treatment programs. However, there were no formal treatment guidelines until the Substance Abuse and Mental Health Services Administration (SAMHSA) published *Treatment Improvement Protocol #1: State Methadone Treatment Guidelines* in 1993.

In March 1990, the General Accounting Office (GAO) issued the report, *Methadone Maintenance—Some Treatment Programs Are Not Effective; Greater Federal Oversight Needed*, which was sent to the Chairman, Select Committee on Narcotics Abuse and Control, House of Representatives. The report noted that in spite of FDA and the Drug Enforcement Administration (DEA) having responsibility for methadone maintenance treatment programs since 1972, FDA’s oversight was lacking. This finding underscored the disparity of quality care offered through OTPs including subtherapeutic dosing and insufficient program services.

The GAO report provided several critical recommendations that guided future federal policy in this domain. “Standards should be based on results attainable from proven treatment approaches that combine appropriate doses of methadone and comprehensive rehabilitative services”.<sup>(3)</sup> The report also concluded that “greater program oversight is needed and should be based on performance standards.” Finally, the report made the following critical recommendation to federal agencies:

“To better monitor and assess methadone maintenance treatment programs we recommend that the Secretary of Health and Human Services direct the Food and Drug Administration or the National Institute on Drug Abuse, as appropriate, to: (1) develop result-oriented performance standards for methadone maintenance treatment programs, (2) provide guidance to

treatment programs regarding the type of data that must be collected to permit assessment of programs' performance, and (3) assure increased program oversight oriented toward performance standards.”<sup>(4)</sup>

After the GAO report was published, the FDA commissioned the Institute of Medicine (IOM) to conduct a comprehensive review of the federal regulations for methadone treatment programs. In its 1995 published findings, IOM recommended that the federal oversight of methadone treatment programs change from a process-oriented mechanism to a more patient-outcome mechanism. The IOM also concluded “that a need exists to maintain certain enforceable requirements in order to prevent substandard or unethical practices that have socially undesirable consequences.”<sup>(5)</sup>

### **Lessons Learned from Regulatory Oversight**

Following the release of the 1995 IOM report, the Department of Health and Human Services (DHHS) implemented a strategy to transition federal oversight from the FDA to SAMHSA. After years of strategic development, this transition occurred in 2001.

SAMHSA decided to use an accreditation oversight mechanism to monitor quality assurance in the OTPs primarily through the Joint Commission on Accountability of Healthcare Organizations (now the Joint Commission) and the Commission on Accreditation of Rehabilitation Facilities (CARF). Other accreditation entities such as the Council on Accreditation (COA) and the states of Washington and Missouri also became certified accreditation entities under the aegis of SAMHSA. The National Commission on Correctional Health Care implemented similar accreditation procedures for treatment in correctional settings.

While the federal government has provided guidelines and resources for evidence-based medication assisted treatment for OUD, it is important to note that the term “assisted treatment” reflects the view that medication alone is not generally thought to be sufficient to treat this complex disorder.

An article by Dr. Dole in the *Journal of the American Medical Association* in 1988 provides context for this view. In the article, Dr. Dole postulated that the high rate of relapse among addicts after detoxification from heroin use is due to persistent derangement of the endogenous ligand-narcotic receptor system and that methadone in an adequate daily dose compensates for this defect. Some patients with long histories of heroin use and subsequent rehabilitation on a maintenance program do well when the treatment is terminated. The majority, unfortunately, experience a return of symptoms after maintenance is stopped. The treatment, therefore, is corrective but not curative for severely addicted individuals. A major challenge for future research is to identify the specific defect in receptor function and to repair it. Meanwhile, methadone maintenance provides a safe and effective way to normalize the functioning of otherwise intractable narcotic addicts.<sup>(6)</sup>

## **Lessons Learned: The Value of OTP Services**

Dr. John C. Ball and his associates, in the article *Reducing the Risk of AIDS through Methadone Maintenance Treatment*, published in the 1988 Journal of Health and Social Behavior, cited two findings from a three-year NIDA-funded study of six methadone treatment programs in three Eastern cities that addressed program effectiveness:

“Although we had anticipated that there would be minor variations in outcome due to program differences, we thought that the dominant influence upon treatment success would be patients’ characteristics, such as length of addiction, employment history, prior criminality and severity of psychiatric symptoms. This expectation was not substantiated by the research findings; instead we found program treatment variables to be of paramount importance in reducing IV usage.<sup>(7)</sup>

It is a major finding that some methadone maintenance programs are markedly more effective than others in reducing IV drug use and needle sharing among their patients because these differences in treatment outcome are related to definite program variables. The more effective programs have high patient retention rates (especially long-term retention rates), high rates of scheduled attendance, a close, consistent and enduring relationship between staff and patients, and year-to-year stability of treatment staff. Conversely, the less- effective programs are characterized by poor patient attendance, inadequate methadone medication, and high rates of staff turnover. Effective and ineffective programs, however, did not differ with regard to patient characteristics.”

The conclusion here is that the program characteristics are more important in determining patient outcome than pre-treatment patient characteristics. These findings had a major impact on how federal authorities would provide guidance to OTPs, and they are equally applicable to DATA 2000 practices.

## **Lessons Learned in Favor of Clinical Support Services**

The recent update of the *Principles of Drug Addiction Treatment* from the National Institute on Drug Abuse (NIDA) underscores the point that medications are an important element of treatment for many patients, especially when combined with counseling and other behavioral therapies. NIDA further emphasized this point in its statement that “effective treatment attends to multiple needs of the individual, not just his or her drug abuse. To be effective, treatment must address the individual’s drug abuse and any associated medical, psychological, social, vocational, and legal problems.”<sup>(8)</sup> NIDA also noted,

“Many drug addicted individuals also have other mental disorders. Because drug abuse and addictions – both of which are mental disorders – often co-occur with other mental illnesses, patients presenting with one condition

should be assessed for the other(s). And when these problems co-occur, treatment should address both (or all), including the use of medications as appropriate.”<sup>(9)</sup>

## **Federal Guidance/Clinical Treatment Recommendations**

While NIDA’s principles provided a basic foundation for the treatment of this complex disorder, the underlying issue was how often would such principles be put into clinical practice using comprehensive treatment protocols. SAMHSA addressed this issue by applying NIDA’s principles for the treatment of this complex disorder in *Treatment Improvement Protocol #43 (2005): Medication Assisted Treatment for Opioid Addiction in Opioid Treatment Programs*, *Treatment Improvement Protocol #63: Medications for Opioid Use Disorder (2018)*<sup>(10)</sup>, and the *Federal Guidelines for Opioid Treatment Programs* published in March 2015.

SAMHSA’s *Treatment Improvement Protocol #43 (2005)* includes a discussion of whether opioid addiction is a medical disorder or a moral problem. Decades of findings support the view that OUD is a medical disorder that can be treated effectively with medications administered under conditions consistent with their pharmacological efficacy and when treatment includes comprehensive services, such as psychosocial counseling, treatment of co-occurring disorders, medical services, vocational rehabilitative services, and case management services.<sup>(11)</sup>

The *National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use*, published by the American Society of Addiction Medicine in 2015, further reiterates the point that treatment serves as a path to recovery in the following statement:

“Psychosocial treatment is recommended in conjunction with many pharmacological treatments of opioid use disorder. At a minimum, psychosocial treatment should include the following: psychosocial needs assessment, supportive counseling, links to existing family supports, and referrals to community services.”<sup>(12)</sup>

## **The Use of Buprenorphine to Treat Opioid Use Disorder**

At the end of the 1990s, medication development research and clinical trials at NIDA enhanced the medication arsenal beyond methadone. The introduction of buprenorphine and other new medications led to the passage of the DATA 2000, which was signed into law by President Clinton at the end of his second administration. DATA 2000 reversed the Harrison Narcotic Act of 1914, which prohibited physicians from treating OUD, and expanded access to care and the use of schedule III, IV, and V opioids for OUD treatment. NIDA and SAMHSA invested considerable funds in research and in the training of practitioners to provide office-based opioid treatment.

## **DATA 2000 Practices: The Forgotten Value of Oversight**

Through DATA 2000 policies, the treatment of OUD utilizing buprenorphine became available through accessible medical practice settings. The decision to not have any federal oversight for DATA 2000 practices was an attempt to “normalize addiction treatment” so clinical practitioners could treat this illness without the “regulatory burden” for OTPs. This also was the intent of legislation that limited practitioners to treat no more than 30 patients at one time. Subsequent legislation, however, raised the number of patients qualified practitioners could treat through individual DATA 2000 practices to up to 275.

### **Lessons Learned from Treatment Expansion**

There has been a great deal of federal and state legislative and policy-making activity since 2015. While new legislation is moving the system in a positive direction, unintended challenges that may develop in the future must be addressed proactively. Major elements of current policy debates include how to expand access to treatment for OUD; who will pay for such treatment; who will coordinate such service delivery systems; and how will service delivery expand into other areas of criminal justice, including drug courts and correctional facilities. A major challenge will be developing a workforce to support such expansion.

Based on the history of OUD treatment, it is clear that comprehensive services are necessary for the majority of people in treatment, especially when treatment begins. As patients become stabilized, the focus on what services are needed to continue recovery will inevitably change based on individual patient experiences. It is also clear that increasing access to care and treatment requires quality of care assessments and monitoring, as well as continuous quality improvement at the provider/facility level. In addition, medication diversion needs to be minimized, especially in the midst of an opioid epidemic.

### **The Diversion of Federally Approved Medications: Is it A Problem?**

Medication diversion in addiction treatment facilities has been an area of concern since the 1970s, when methadone was the exclusive medication used to treat OUD in the United States. By the 1980s, reports of methadone diversion from the nation’s OTPs became significant.

The IOM addressed methadone diversion in its 1995 report, *Federal Regulation of Methadone Treatment*, in which it stated that “The concerns for methadone diversion preceded the issuance of FDA methadone regulations in 1972, influenced the views of policymakers writing the regulations, and continues to shape the regulations today as thoroughly as does the concern for the medical use of methadone to treat opioid addiction.”<sup>(13)</sup> The report described how such diversion concerns influenced the development of “closed model”<sup>1</sup> treatment programs regulated by the federal government with strict time lines and criteria for granting and restricting take-home doses to patients.

---

<sup>1</sup> OTPs must file an application to operate, subject to the approval of SAMHSA and the DEA. The Congressional legislation bifurcated the regulatory oversight to DHHS and the DOJ.

Although the FDA transitioned its oversight of OTPs to SAMHSA in 2001, SAMHSA preserved the 8-point criteria that governed the provision of take-home medications to patients. These criteria include: absence of recent drugs of abuse, regular plan of attendance, absence of serious behavioral problems, absence of criminal activity, stability of the patient's home environment and social relationships, length of time in comprehensive maintenance treatment, assurance that take-home medication can be safely stored within the patient's home, and whether the rehabilitative benefit the patient derived from decreasing the frequency of clinic attendance outweighs the potential risk of diversion.<sup>(14)</sup>

In the late 1990s, practitioners in general practice settings increasingly prescribed methadone to treat pain. Studies determined that diversion was related to the prescribing of methadone to treat chronic pain, not take-home medication from OTPs. For example, federal officials along with epidemiology, pain management, and addiction treatment experts attending SAMHSA's National Assessment of Methadone Associated Mortality of 2003 acknowledged the correlation between increased distribution of methadone through pharmacies for pain management with the increase in methadone-associated overdose deaths and reached consensus that the increase in these deaths was not associated with addiction treatment in OTPs. Additionally, in 2006, researchers at the Centers for Disease Control and Prevention suggested that the increase in deaths involving methadone was related to physicians increasingly prescribing the drug for pain. The researchers reported that the increase in deaths tracked to the increase of methadone use for pain management rather than its use in OTPs.<sup>(15)</sup>

Five national reports, three from SAMHSA (2003<sup>(16)</sup>, 2007<sup>(17)</sup>, 2010<sup>(18)</sup>), one by the Department of Justice National Drug Intelligence Center (2007)<sup>(19)</sup>, and one by the GAO (2009)<sup>(20)</sup>, also arrived at a similar conclusion. SAMHSA's 2003 report states that "the data confirmed a correlation between increased methadone distribution through pharmacy channels and the rise of methadone associated mortality. This supports the hypothesis that the growing use of all methadone, prescribed and dispensed for the outpatient management of chronic pain, explains the dramatic increases in methadone consumption and the growing availability of the drug from diversion to abuse."<sup>(21)</sup> Furthermore, SAMHSA's three reports highlight the clear distinction between the oversight standards that restrict how take-home medications are administered and monitored in the OTPs versus the unrestricted use of methadone in a physician's office to treat pain. One might argue that the maturation of the treatment system, with greater vigilance in adhering to the promulgated federal and state regulations governing the provision of take-home medication, reduced the diversion of methadone from the OTPs.

The 2009 GAO report *Methadone Associated Overdose Deaths—Factors Contributing to Increased Deaths and Efforts to Prevent Them*, which was sent to Congressional requesters, further reiterated that methadone diversion and subsequent overdose deaths were not attributable to OTPs.

## **Buprenorphine Diversion**

Although a number of published accounts related to buprenorphine diversion have caused concern, it is important to note that due to buprenorphine's pharmacologic properties, the medication rarely causes an overdose when used alone. Overdoses occur when buprenorphine is used with a benzodiazepine, alcohol, or other drug combinations.

There has been an interesting debate on whether buprenorphine diversion is a serious problem. A number of public health proponents have described the street diversion of buprenorphine as "therapeutic" because its use by individuals not in treatment results in an attempt at lay treatment of OUD. It also is important to point out that the development of depot formulations of buprenorphine will certainly restrict its diversion to illicit market channels.

AATOD's public position on this topic is that the diversion of any opioid at any time, and particularly during an opioid epidemic, is unwise. Our argument has always been that one cannot define a diverted opioid as being therapeutic.

## **The Importance of Treatment Coordination**

As our nation moves to increase access to treatment, care coordination becomes vitally important. In a previously published policy paper<sup>(22)</sup>, AATOD mentioned the Vermont Hub and Spoke Model<sup>2</sup>, one of the earliest treatment models to deal with this issue, and the use of health homes in Rhode Island and Maryland as means of coordinating care for patients in treatment. The success of these models resides in a central authority that works with providers to link services.

The co-op model is another treatment approach that is based on the success of the Vermont Hub and Spoke Model. As articulated by Dr. Kenneth Stoller and his colleagues at John's Hopkins in Baltimore, this approach provides an opportunity to coordinate care using the OTP as the hub site and DATA 2000 practices as the spoke.

Once again, it is important to point out that peer support recovery services are a key component of coordinated care and work effectively with OTPs and DATA 2000 practices as well as in hospital emergency departments and general medical practice settings.

## **Where We Are Today**

According to SAMHSA and the DEA, there are approximately 1,600 licensed and accredited OTPs in the United States. Wyoming is the only state without an OTP. It is estimated that over 400,000 patients are receiving treatment at OTPs. Additionally, by 2017, SAMHSA had approved over 45,000 DATA 2000 practitioners, however, only about

---

<sup>2</sup> The Hub and Spoke Model is characterized by a limited number of specialized regional addictions treatment centers, working in meaningful clinical collaboration with general medical practices. Specializing in the treatment of complex addiction, the regional centers (Hubs) provide intensive treatment to patients and consultation support to medical providers (Spokes), treating patients in the general practice community.

half are active prescribers. A number of factors contribute to this phenomenon, including low insurance reimbursement.

Comprehensive treatment protocols are critical as patients progress to maintenance therapy and recovery, especially in light of the focus on increasing access to medications with or without support services and the limited availability of support services.

By equipping law enforcement officials, such as sheriffs, with naloxone, first responders can administer this life-saving overdose prevention medication and bring revived individuals to emergency rooms rather than holding cells. Another emerging trend has been the development of programs for hospital emergency departments to engage opioid overdose patients in OUD treatment, such as using peer support recovery counselors to work in conjunction with emergency departments and substance use treatment facilities. The use of such trained peer support services is an integral part of the Vermont Hub and Spoke Model.

In addition, there is greater interest in treating OUD “behind the walls.” Correctional facilities are demonstrating increased expertise in initiating the use of medications to both prevent overdose during intake and to treat OUD during the period of incarceration and prior to release.

### **The Emerging Importance of Criminal Justice**

With the increased focus on expanding access to care through outpatient settings, the criminal justice system is assessing how it can better engage individuals who come before courts and/or are incarcerated. Drug courts are now working with OTPs and DATA 2000 practices more than ever, and the National Association of Drug Court Professionals has published a recommendation that patients continue treatment as long as they benefit from such care.<sup>(23)</sup> Still, some drug courts judges continue to require patients to withdraw from stabilizing medications despite evidence that both recidivism and overdose risk increase in response to this practice.

On the positive side, more correctional facilities are providing medication assisted treatment to inmates with OUD. The Connecticut Department of Corrections is one such case where correctional facilities throughout the state are diagnosing and treating inmates with OUD throughout their incarceration. Similarly, Connecticut’s counterpart, the Rhode Island Department of Corrections, works with treatment facilities, such as CODAC, providing access to all medications as part of its coordinated intervention efforts, which include maintenance, stabilization, and a “warm handoff” upon release. Both states have seen a significant reduction in recidivism, which means individuals do not return to the correctional system. Further, opioid mortality has dropped dramatically among the more than 50 percent of the inmates who are released to community-based practice settings and smoothly transitioned into an OTP or DATA 2000 practice for continued treatment. Without question, this kind of intervention, where inmates with OUD have access to treatment during incarceration and are referred to outpatient treatment facilities upon their release, should be replicated throughout the United States.

It is important to note that because it is impossible to treat this illness through arrests, an increasing number of sheriffs and other law enforcement officials have become an evolving force in supporting the use of treatment to quell the nation's OUD epidemic.

## **Who Pays for Treatment**

Unless payors recognize that there is a need to reimburse treatment wherever patients receive care for their OUD, there will be no way out of this public health crisis. At the present time, 11 states<sup>3</sup> do not provide Medicaid reimbursement for OTPs. However, following recently passed legislation<sup>4</sup>, the Centers for Medicare and Medicaid Services will be developing a reimbursement model for Medicare beneficiaries receiving treatment in OTPs. Commercial carriers are also working to develop models to provide reimbursement to OTPs. This will take years to develop but the change appears to be positive.

## **Summary**

A recent article in the *New England Journal of Medicine* (July 5, 2018)<sup>(24)</sup> suggests that methadone might be made available in primary medical practice settings for the treatment of opioid dependence. AATOD recommends that this proposal should only be considered after careful, conservative, and thoughtful evaluation. As history and our policies have shown, we do not reject the public health model for increasing access to care for OUD, nor are we ignoring what has been learned about clinical standards of care to treat this illness. It is important to understand, however, the complexity of inducting a new patient into methadone maintenance treatment when developing policies for increasing access to medication assisted treatment. While methadone induction is discussed in SAMHSA's Treatment Improvement Protocols, it is critical that policymakers consider the unique pharmacology of methadone maintenance and the need to conduct a safe and medically effective assessment during induction

The value of an OTP is certainly evident during the induction phase due to the number of medical/nursing and counseling personnel. Induction must be conducted in an organized, therapeutic manner, and it requires enormous clinical vigilance through a well-coordinated team of professionals who are engaged and working with the patient.

Fifty-plus years of experience treating this population suggest that this is a complex illness confounded by other physical and behavioral health disorders, social and environmental stressors, victimization, stigma, and discrimination. Treatment and recovery support need to be particularly sensitive to these factors. For most, opioid addiction is the tip of the iceberg. Any and all treatment and recovery efforts depend on adequate, objective, and comprehensive evaluation and assessment and must be skillfully and carefully coordinated.

---

<sup>3</sup> Arkansas, Idaho, Iowa, Kansas, Louisiana, Mississippi, Montana, North Dakota, Oklahoma, Tennessee, Utah

<sup>4</sup> H.R. 6

## Conclusion

AATOD believes there are ways to have a safer “middle ground” for expanding access to treatment. When medications are needed to treat this disease, it is best to provide a comprehensive array of services for as long as the patient needs them. Both NIDA and SAMHSA have demonstrated that medication alone is rarely associated with long-term successful patient outcomes.

Given what has been learned about the unintended consequences of prescribing methadone for pain, as described earlier in this paper, AATOD’s view, from a policy standpoint, is that it is unwise to have primary care practitioners induct new patients onto methadone maintenance treatment or to consider using methadone to “detox” patients from opioids. While we believe these practices are countertherapeutic and dangerous, our judgment leads us to believe that primary care practitioners, working in conjunction with OTPs, could be valuable in treating fully stabilized patients. With this treatment model, the OTPs are the addiction specialty hub site and primary care practices become extensions of the OTPs. Linkage back to the hub site would provide accessibility to patients and providers for restabilization and increased recovery services and support as needed. Clearly, this model would need to be developed as treatment protocols are put into place to ensure safety and to not expose patients to unintended danger. Additionally, it is worth considering the prospect that some entities, such as Johns Hopkins, may utilize pharmacies to treat even more stabilized patients, as they do when patients pick up medications to treat any other chronic disorder.

In conclusion, we should not dismiss lessons learned over the past 50 years, nor should we try to marginalize the value of providing support services when using medications to treat OUD, as long as they are competently provided and well-coordinated

We must do all that we can to provide effective care to those who suffer with OUD. Stigma and discrimination are still major problems that loom over any effective public policy as our nation continues to struggle with the reality of OUD. Without question, a multi-year and effective public health education campaign is essential as all treatment programs and systems confront the problem of dealing with this chronic, public health epidemic.

## References

---

1. NIDA. (2012b). Is the use of medications like methadone and buprenorphine simply replacing one addiction with another? Principles of drug addiction treatment: A research based guide, third edition. Retrieved from <http://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/frequently-asked-questions/use-medications-methadone-buprenorphine>
2. Addicts Who Survived: An Oral History of Narcotic Use in America, 1923-1965
3. GAO (Government Accountability Office). (1990). Methadone Maintenance Some Treatment Programs Are Not Effective; Greater Federal Oversight Needed. Available at <https://www.gao.gov/assets/150/148872.pdf>

4. GAO (Government Accountability Office). (1990). Methadone Maintenance Some Treatment Programs Are Not Effective; Greater Federal Oversight Needed. Available at <https://www.gao.gov/assets/150/148872.pdf>
5. Rettig, R.A., Yarmolinsky, A. (1995) Federal Regulation of Methadone Treatment. Institute of Medicine. National Academy Press
6. Dole, VP. (1988). Implications of methadone maintenance for theories of narcotic addiction. *Journal of the American Medical Association* 260:3025–3029
7. Ball, J.C., Lange, W.R, Myers, C.P, Friedman, S.R. (1988). Reducing the Risk of AIDS Through Methadone Maintenance Treatment. *Journal of Health and Social Behavior*, 29(3), 214-226
8. NIDA. (2012b). Is the use of medications like methadone and buprenorphine simply replacing one addiction with another? Principles of drug addiction treatment: A research based guide, third edition. Retrieved from <http://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/frequently-asked-questions/use-medications-methadone-buprenorphine>
9. NIDA. (2012b). Is the use of medications like methadone and buprenorphine simply replacing one addiction with another? Principles of drug addiction treatment: A research based guide, third edition. Retrieved from <http://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/frequently-asked-questions/use-medications-methadone-buprenorphine>
10. Substance Abuse and Mental Health Services Administration. Medication for Opioid Use Disorder. Treatment Improvement Protocol (TIP) Series 63, Full Document. HHS Publication No. (SMA) 18-5063FULLDOC. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2018
11. SAMHSA (Substance Abuse and Mental Health Services Administration. (2005). Medication-assisted treatment for opioid addiction in opioid treatment programs. Pub. No. (SMA) 05-4048. Treatment Improvement Protocol 43. U.S. Department of Health and Human Services. Rockville, MD
12. American Society of Addiction Medicine (2015). National Practice Guidelines for the Use of Medications in the Treatment of Addiction Involving Opioid Use.
13. Rettig, R.A., Yarmolinsky, A. (1995) Federal Regulation of Methadone Treatment. Institute of Medicine. National Academy Press
14. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration (2001) Federal Register/Vol. 66, No. 11 21 CFR Part 291, 42 CFR Part 8 Opioid Drugs in Maintenance and Treatment of Opioid Addiction
15. GAO (Government Accountability Office). (2009). Methadone-associated overdose deaths: Factors contributing to increased deaths and efforts to prevent them. Washington: U.S. Government Accountability Office. Available at <http://www.gao.gov/new.items/d09341.pdf>
16. SAMHSA (Substance Abuse and Mental Health Services Administration. (2004). Methadone-associated mortality: Report of a national assessment. U.S. Department of Health and Human Services. Publication No. (SMA). 04-3904
17. SAMHSA (Substance Abuse and Mental Health Services Administration. (2007). Methadone mortality: A reassessment. U.S. Department of Health and Human Services. Center for Substance Abuse Treatment. Draft paper

18. SAMHSA (Substance Abuse and Mental Health Services Administration. (2010). Methadone mortality: A 2010 reassessment. U. S. Department of Health and Human Services. Center for Substance Abuse Treatment. Draft paper
19. U.S. Department of Justice, National Drug Intelligence Center. (2007, November). Methadone diversion, abuse, and misuse: Deaths increasing at alarming rate. Product No. 2007-Q0317-001
20. GAO (Government Accountability Office). (2009). Methadone-associated overdose deaths: Factors contributing to increased deaths and efforts to prevent them. Washington: U.S. Government Accountability Office. Available at <http://www.gao.gov/new.items/d09341.pdf>
21. SAMHSA (Substance Abuse and Mental Health Services Administration. (2004). Methadone-associated mortality: Report of a national assessment. U.S. Department of Health and Human Services. Publication No. (SMA). 04-3904
22. Casper, K.L, Folland, A., Storti, S., Walters, V., Fulmer, A., Models of Integrated Patient Care Through OTPs and DATA 2000 Practices (2016). American Association for the Treatment of Opioid Dependence. SAMHSA Contract #HHSP233201400268P
23. Adult Drug Court Best Practice Standards (2013) National Association of Drug Court Professionals.
24. Samet, J.H., Botticelli, M., Bharel, M. (2018). Methadone in Primary Care - One Small Step for Congress, One Giant Leap for Addiction Treatment. *New England Journal of Medicine*, 379, 7-8