

The Availability of Medication-Assisted Treatment for Opioid Addiction in Pennsylvania

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EXECUTIVE SUMMARY

This study assessed the barriers and opportunities that exist in expanding Medication-Assisted Treatment (MAT) services in Pennsylvania. It identified areas in Pennsylvania, particularly rural areas, that are underserved by MAT services, identified salient themes from MAT clinic administrators regarding barriers and opportunities, and assessed state and federal policies for their impact on MAT services.

MAT includes the use of methadone, buprenorphine, Suboxone, naloxone, and naltrexone in residential, behavioral, or outpatient programs, hospitals, and jails and prisons to help individuals suffering from opioid addiction to overcome withdrawal symptoms, cravings, and potential overdose.

The researchers used secondary data from the Pennsylvania Department of Drug and Alcohol Programs, a literature review, Geographic Information Systems (GIS), and surveys and interviews with MAT clinic administrators to complete the research, which was conducted in 2017-2018.

The research findings indicated there is substantial coverage for MAT services in the western portion of Pennsylvania. There is only some coverage in the central and eastern portions of the state, and a lack of MAT services along the northern and southern portions of Pennsylvania.

The research also found that those who seek emergency care and long-term treatment for opioids and who live in rural areas of Pennsylvania have limited access to care. Mobile clinics and outreach teams that provide MAT services could potentially be a major source of care in Pennsylvania given the state's rural nature.

Other barriers to accessing MAT services are lack of childcare and housing, lack of transportation, limited private insurance coverage, and limited funding for MAT services.

Another barrier faced by patients is the stigma against those with opioid use disorder and the use of MAT services.

The research found that many opportunities for expanding MAT services exist. These include directing additional funding from SCAs to MAT services, addressing stigma through education, and increasing childcare and public transportation services. The number and hours of operation for MAT clinics could also be increased. Pennsylvania county drug courts should allow MAT services to be provided to those drug court participants who have medically prescribed and monitored MAT plans.

Finally, strict enforcement of insurance regulations by the state could increase coverage for MAT services.

Combating heroin and opioid use disorders requires an “all-in” commitment. Pennsylvania has taken positive steps in the past few years to address the opioid epidemic and the increased need for addiction treatment services. It should continue to enforce laws and regulations enacted to provide coverage for mental health services for patients suffering from addiction and direct additional state and federal funding to support MAT services throughout Pennsylvania.

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INTRODUCTION

This research assessed the barriers and opportunities associated with the expansion of Medication-Assisted Treatment (MAT) for opioid abuse in Pennsylvania by: identifying rural areas underserved by MAT by employing Geographical Information Systems (GIS) modeling; analyzing barriers and opportunities to expanding MAT; reporting strategies used by states with large rural populations to combat the opioid abuse crisis; and, assessing the influence of state and federal policies on MAT service delivery.

The Opioid Crisis in the U.S.

Drug overdoses killed nearly 72,000 Americans in 2017 with the clear majority (58 percent) involving a prescription or illicit opioid. According to 2018 data from the Centers for Disease Control and Prevention (CDC), overdose deaths have increased in all categories of drugs examined for men and women, people ages 15 and older, all races and ethnicities, and across all levels of urbanization. These overdose death rates are driven by sharp increases in deaths involving synthetic opioids other than methadone, such as illicitly manufactured fentanyl (CDC, 2018). In 2016, the age-adjusted rate of overdose deaths increased significantly (21.5 percent) from 16.3 per 100,000 in 2015 to 19.8 per 100,000 in 2016. Opioids were involved in 42,249 (66.4 percent) drug overdose deaths (13.3 per 100,000 population) in 2016, representing a 27.9 percent rate increase from 2015 (CDC, 2018).

The opioid crisis has impacted rural areas especially hard. From 1999 to 2015, there was a rising death rate of drug overdoses in rural areas, with a prevalence rate that increased 325 percent, contrasting with the increase in the urban rate of 198 percent (CDC, 2017). The CDC has recommended that two public health interventions may address the crisis, including creating

better access to evidence-based substance abuse treatment, including MAT, and, using opioid prescribing education for chronic pain (CDC, 2017).

The Opioid Crisis in Pennsylvania

In 2017, 5,456 drug-related overdose deaths were reported by coroners and medical examiners in Pennsylvania. According to 2018 data from the federal Drug Enforcement Agency (DEA), this number represents a rate of 42 deaths per 100,000 people, and a 64 percent increase in overdose deaths from 2015 to 2017. In 2016, Pennsylvania had the fifth highest rate per 100,000 people (37.9) of overdose deaths nationally, and had the third highest number of overdose deaths (4,627). From 2015 to 2016, Pennsylvania had the fourth largest growth in overdose deaths among all states at 44.1 percent (CDC, 2017). Approximately 13 people per day died from a drug overdose in Pennsylvania in 2016 (DEA, 2017).

According to the DEA, the presence of fentanyl was present in more than 67 percent of drug-related overdose deaths in Pennsylvania in 2017, and the presence of fentanyl-related substances in overdose deaths rose almost 400 percent from 2015 to 2017 (DEA, 2018).

In Pennsylvania, for every fatal opioid overdose, there are an estimated 30 non-fatal overdoses (Frazier et al., 2017). According to the CDC, rural Americans are more vulnerable to prescription painkiller abuse and overdoses, and the rate of opioid-related overdose deaths in non-metro counties is 45 percent higher than in metro counties (2011).

Medication-Assisted Treatment

MAT is the use of medication with the combination of behavioral health services to treat substance use disorders and is part of a comprehensive service delivery system used to address

addiction (Substance Abuse and Mental Health Services Administration, 2018). There are three Food and Drug Administration (FDA) approved medications for the use in detoxification or maintenance treatment for opioid use disorder (OUD): methadone, buprenorphine, and naltrexone (SAMHSA, 2018).

MAT has been widely proven effective in helping patients recover from addiction. MAT has been “shown to be safe and cost-effective and to reduce the risk of overdose. In addition, some MAT increases patients’ retention in treatment, and they all improve social functioning as well as reduce the risks of infectious-disease transmission and engagement of criminal activities” (Volkow et al., 2014). The epidemic of prescription opioid overdose is highly complex and has barriers to contributing to low access and use of MAT services. Expansion and implementation efforts to enhance and continually develop current substance abuse service systems, such as MAT, is a crucial component of efforts to help patients recover from addiction (Volkow et al., 2014).

MAT uses five main FDA approved medications in the treatment of opioid dependence: methadone, buprenorphine (as oral “Subutex” or injectable “Buprenex”), Suboxone, naloxone (as oral “naloxone,” nasal spray “Narcan,” or injectable “Naloxone Hydrochloride”), and naltrexone (as oral “Naltrexone” or injectable “Vivitrol”) (American Addiction Centers, 2018).

The first drug used as part of the Medication-Assisted Treatment regime was naloxone, which was developed in the 1970s to prevent overdoses by the suppression of opioids (AAC, 2018; McLoone, 2017). Clonidine, an FDA approved medication for the treatment of high blood pressure, began being used “off label,” in rehabilitation centers in 1978. Like naloxone, Clonidine could quell withdrawal symptoms and cravings (Center for Substance Abuse Treatment, 2006).

Talwin NX (i.e. pentazocine with naloxone) followed in 1982 and was used to curb withdrawal symptoms, cravings, and impending overdose (Strassers, 2009). Naloxone is packaged with buprenorphine, as Suboxone, to offset the intense withdrawal symptoms that come with Naloxone's overdose reversing power (ACC, 2018b). Suboxone works in a similar manner to Talwin NX, but the risks for dependence and withdrawal are markedly lower (AAC, 2018b). The injectable form, Naloxone Hydrochloride, was released in 2014 and, Narcan, the nasal spray version, became available the very next year. Many lives have been saved now that first responders and family members of individuals suffering from opioid addiction have access to these medications, (AAC, 2018).

Administered intramuscularly, Vivitrol has the powerful ability to block the action of any opioids taken for up to one month (AAC, 2018; SAMHSA, 2016; Vimont, 2018). Vivitrol must be administered no sooner than the 7 to 10 days following methadone detoxification, otherwise withdrawal symptoms will occur.

Efficacy of MAT

Extensive research has shown that the three available medications have superior patient treatment outcomes when compared to non-medication-based treatment therapies (SAMHSA, 2005). When prescribed and monitored properly, MAT has proved effective in helping patients recover as well as being safe and cost-effective and to reduce the risk of overdose (Volkow et al., 2014). With the assistance of MAT, patients have increased retention in treatment leading to reduced mortality, improved social function, a reduced risk of infectious-disease transmission, and improved quality of life with a decrease in drug use (Knudsen, Abraham & Roman, 2011).

MAT and Rural Pennsylvania

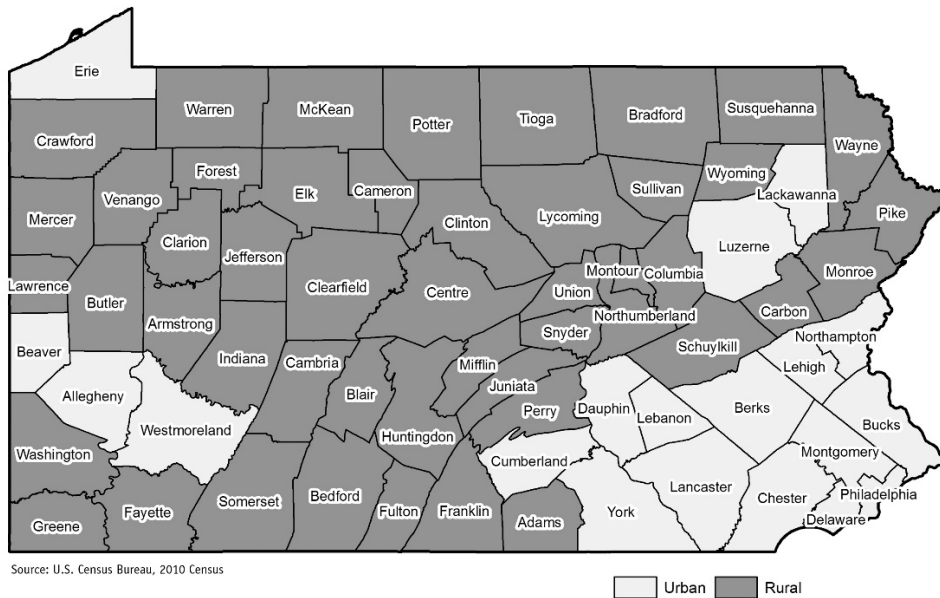
Rural Pennsylvanians face unique challenges when attempting to access MAT services. Forty-eight of Pennsylvania's 67 counties are rural, according to the Center for Rural Pennsylvania's rural/urban definition, which is based on population density (See Figure 1). Rural citizens with substance use disorder face additional challenges in accessing MAT services due to a variety of factors, including a limited number of MAT clinics and providers, and access within a 30-minute drive time to a MAT clinic.

Research supports the lack of addiction treatment services and providers in rural areas as a barrier to MAT services (Rigga, Monnatb, & Chavezc, 2018; National Rural Health Association, 2016). Rural providers, hospitals, clinics, and treatment professionals are often dispersed across large geographic areas, making access difficult, especially for patients who lack transportation (Rigga, Monnatb, & Chavezc, 2018).

Transportation is a key barrier to ongoing MAT treatment for patients who attempt to receive long-term MAT services. Transportation is especially critical for patients requiring daily visits to a clinic (Uebelacker, Bailey, Herman, Anderson, & Stein, 2016). A further added complication is when public transportation is limited or non-existent during weekends (Chatterjee, & Tishberg, 2018).

Research shows that the need for childcare services or the need to provide care for young children is also a key barrier for those seeking treatment for substance use disorder (Chatterjee, Yu, & Tishberg, 2018).

Figure 1: Rural and Urban Pennsylvania Counties



MAT Service Providers in Rural Pennsylvania

To provide MAT services, providers must first complete certain requirements to obtain specific medication prescribing privileges.

For example, methadone is prescribed through a specialized clinic that has received special federal approval to become a regulated Opioid Treatment Program (OTP) (Temple, 2018).

A physician prescriber of buprenorphine must complete an 8-hour training course before applying for a specialized DEA waiver, a process that usually takes 45 days. Special permission can be obtained for more immediate prescribing needs if the provider is licensed, has a DEA registration, and has completed the training (Temple, 2018).

The Comprehensive Addiction and Recovery Act of 2016 (CARA) made it permissible for nurse practitioners (NPs) and physician assistants (PAs) to also become prescribers. This provision was specifically designed to address MAT needs in rural areas. Now, these providers

follow the same steps as a physician to obtain waivers, but they must complete 24 hours of training rather than 8 (Temple, 2018).

Naltrexone can be prescribed by any licensed health provider.

Table 1 provides an assessment of the drugs that are part of MAT, the date of the Food and Drug Administration (FDA) approval, and the drug pros and cons for use as part of MAT.

Table 1: Substances Comprising Medication Assisted Treatment

Drug	Date of FDA Approval	Pros	Cons
Methadone	1964	<p><u>Efficacy</u></p> <ul style="list-style-type: none"> • Methadone maintenance treatment (MMT) has a positive impact on treatment retention and suppression of substance abuse (Rosic, et al., 2017) • National Institute of Drug and Alcohol (NIDA) 2017 data show patients receiving methadone treatments are 33% more likely to have clean opioid drug test results as well as being nearly five times more likely to stay in treatment when compared to control groups (NIDA, 2017) 	<p><u>Dispensing</u></p> <ul style="list-style-type: none"> • Highly regulated and may only be dispensed by an opioid treatment program (OTP); MMT OTPs can include hospitals, intensive outpatient facilities, and short-term or long-term residential treatment facilities • Regulations require counseling when undergoing MMT <p><u>Side Effects</u></p> <ul style="list-style-type: none"> • Significant adverse events include respiratory depression, cardiac arrhythmias, and other life-threatening risk factors <p><u>Relapse</u></p> <ul style="list-style-type: none"> • High risk of relapse after discontinuation, so a long-term treatment plan is necessary for most patients
Buprenorphine	<ul style="list-style-type: none"> • 2002 • 2016-implants • 2017-extended release injectable formulation 	<p><u>Prescribing</u></p> <ul style="list-style-type: none"> • Qualifying physicians can prescribe if they receive special training, obtain a SAMHSA waiver, and obtain a unique DEA registration number • Qualified physicians can prescribe buprenorphine as a treatment for opioid addiction in various settings, including offices, community hospitals, health departments, and correctional facilities (SAMSA, 2016) <p><u>Availability</u></p> <ul style="list-style-type: none"> • Prescribing regulations have greatly increased the number and type of settings where medication is available; new settings include non-OTP outpatient addiction treatment 	<p><u>Prescribing</u></p> <ul style="list-style-type: none"> • Lack of physicians trained and waived to treat patients with the drug, especially in rural underserved areas <p><u>Cost</u></p> <ul style="list-style-type: none"> • Buprenorphine costs almost twice as much as methadone on a yearly basis

Drug	Date of FDA Approval	Pros	Cons
		programs, as well as general medical and mental health practices or clinics (office-based opioid treatment). OTPs can also provide buprenorphine <u>Fewer side effects</u> <ul style="list-style-type: none"> • Less likely than methadone and other full agonists to cause respiratory depression in an accidental overdose 	
Naltrexone	1984	<u>Prescribing</u> <ul style="list-style-type: none"> • Physicians, nurse practitioners (NPs), and physician assistants (PAs) may prescribe or order for administration by qualified staff members without additional waiver requirements <u>Fewer side effects</u> <ul style="list-style-type: none"> • Well tolerated with few adverse effects <u>Opioid and alcohol treatment</u> <ul style="list-style-type: none"> • FDA approved for treatment of alcohol use disorder and therefore may be useful for patients with both OUD and alcohol use disorder 	<u>Compliance</u> <ul style="list-style-type: none"> • Oral form not widely used due to low rates of patient acceptance and high rates of nonadherence (leading to a lack of efficacy) <u>Cost</u> <ul style="list-style-type: none"> • More expensive than methadone and buprenorphine

Please see Appendices A, B, and C for a complete assessment of the pharmacological drugs associated with MAT services.

GOALS AND OBJECTIVES

This study had four specific goals. The first was to estimate the current number of treatment programs and individuals receiving MAT in rural and urban Pennsylvania. To accomplish this goal, the researchers:

1. Conducted a comprehensive review of MAT service center data from the Pennsylvania Department of Drug and Alcohol Program (DDAP), and demographic data from ESRI, as well as the list of SAMHSA-accredited MAT programs. Each service center was contacted to confirm the accuracy of the information.

2. Conducted key informant interviews with managers and clinicians from a representative sample of MAT centers in urban and rural Pennsylvania.
3. Created a comprehensive list of MAT centers in Pennsylvania along with the estimated number of individuals receiving care. MAT centers were identified that may be part of a hospital or health system, or which exist as stand-alone facilities, including mobile clinics.

The second goal was to analyze cost reimbursement for MAT services in rural and urban Pennsylvania. To accomplish this goal, the researchers:

1. Conducted key informant interviews with managers and health care professionals at MAT centers and state agencies to assess cost reimbursement for MAT service delivery and the associated barriers and opportunities. Salient themes in the interviews were used to identify key sources of cost differences, barriers, and opportunities that exist in rural and urban regions, ownership types, and within the different modes of MAT service delivery.

The third goal was to identify barriers and opportunities related to the expanded use of MAT in rural and urban Pennsylvania. To accomplish this goal, the researchers:

1. Conducted a thorough review of the existing literature, state and federal regulations, and best practices in MAT service delivery. This review served to identify policy, regulatory, and financial barriers and opportunities for expanded access to MAT services in rural and urban areas.
2. Conducted key informant interviews with managers and health care professionals from MAT centers to confirm and assess barriers and opportunities in the delivery of MAT services.
3. Identified barriers and opportunities related to the expanded use of MAT in rural and urban Pennsylvania.

4. Identified rural and urban geographically isolated areas with limited access to MAT services that might be suitable for mobile clinics and new treatment facilities.

The fourth goal was to identify the public policy implications and relevant recommendations regarding barriers and opportunities in the delivery of MAT services. To accomplish this goal, the researchers:

1. Identified relevant public policy implications of the expanded use of MAT services.
2. Performed in-depth analysis of state and federal legislation, regulation, and reimbursement policies that would influence expanded MAT services.
3. Conducted interviews of health care professionals at MAT centers and state agencies regarding the impact of these policies in the delivery of MAT services.
4. Identified barriers and opportunities from a public policy perspective, to the expanded access and availability of MAT services.

METHODOLOGY

The research used data from DDAP for both the quantitative and spatial analysis portion of the study. The May 2016 data were used to estimate the current number of treatment programs and individuals receiving MAT services in rural and urban areas. Statistical software was used to analyze the data to identify descriptive statistics of MAT programs based on capacity and occupancy rates. This information allowed for the examination of statistical differences between urban and rural areas, and among the different regions of the state in terms of MAT service capacity and occupancy rates.

The DDAP data were cross-referenced with SAMHSA's list of certified opioid treatment programs (OTP) for Pennsylvania.

Literature Review

Pennsylvania faces an opioid crisis that affects its urban and rural counties. A review of the literature revealed that a 30-minute driving time was a common baseline for adequate access to medical care and treatment. However, there was a gap in the literature with respect to opioids and service delivery. While the more urban areas surrounding major cities have treatment centers that are within approximately 30 minutes from the population, rural Pennsylvania has limited access to a 30-minute drive to a MAT treatment facility. The literature review suggests that those living in rural Pennsylvania who seek care and long-term treatment for opioids have limited access to that care.

Geographic Access and GIS

Geography is a critical component of the study of access to care. Cummins, Curtis, Diez-Roux and Macintyre (2007), in their comprehensive analysis and review of the literature in health and geography, believe environmental conditions influence health and health behavior. Access to medical treatment facilities is key in combating opioid addiction. Methadone clinics treat opioid addiction via medication so that the affected person does not have to fight withdrawal symptoms. Methadone clinics are necessary for long-term treatment care. No discussion of geography and medical access would be complete without mentioning the importance of Geographic Information Systems (GIS) within the broader study of the geography of health (Gatrell & Loytonen, 1998). The availability of GIS has created an interest in the location of health care services and the development of geographically-based health interventions to improve the public's health (Cromley & McLafferty, 2012). Using GIS, Wong,

Lee, and Lin (2010) determined that having clinics within an attainable location for affected persons is vital for their rehabilitation.

GIS provides the capability of handling large amounts of data. Spatially analyzing the information makes GIS a great tool to use in the fight against the opioid epidemic in Pennsylvania, as GIS has tremendous visual capabilities for pinpointing where there is a major gap between service availability and need.

Mobile Service Provision

Pennsylvania is a large state where the population is widely dispersed and in which most of the counties have been classified as rural.

For many residents of some rural counties, access to medical services is limited.

Mobile health can provide a major return on investment and help reduce costly visits to the emergency department (Oriol, et al., 2009). This current opioid crisis continues to tax the healthcare system and emergency departments as large numbers of overdose victims show up in hospital emergency departments. There are many examples of healthcare providers using mobile clinics to provide care to medically underserved areas across the country (Skillman, et al., 2010). For example, in California 30 percent of mobile programs targeted rural populations (Carr, Isong, & Weintraub, 2008).

Pennsylvania Services

Mobile MAT services are provided in Pennsylvania by Positive Recovery Solutions (PRS). PRS was established in 2013 and started as a brick and mortar facility in Washington, Pa. Originally, it provided patients with buprenorphine but expanded its services to also offer

Vivitrol. PRS started its mobile van service in July 2015 and contracted with three counties, Blair, Armstrong, and Indiana. It gave seven injections in its first month. It now operates in 26 counties, and, at the time of the research, was planning to offer services in six more counties and provide around 350 injections a month. PRS drives to a physical address where it provides medication and counseling to patients. Patients are required to drive to the mobile unit location to receive care. PRS has 14 county jail projects and is the sole source contract for the Pennsylvania Department of Corrections. PRS is trying to expand to the eastern borders of Pennsylvania and, at the time of the research, had plans to offer services in 14 other states, including Maryland, Ohio and Florida.

Based on the information from its website, it provides a variety of services including the following: medical management of Vivitrol, assistance with comprehensive treatment plans, long-term behavioral health counseling for opioid dependence, prevention of relapse to opioid addiction following opioid detox, coordination of medical services for drug court participants, and case management.

Specific regions in Pennsylvania also have Additional Recovery Mobile Outreach Teams (ARMOT), which are a collaboration of the Armstrong-Indiana-Clarion Drug and Alcohol Commission (AICDAC), the Armstrong County Memorial Hospital (ACMH), Clarion Hospital and the Indiana Regional Medical Center. ARMOT is federally funded by the Health Resources and Services Administration (RHIhub, 2018). According to the Rural Health Information Hub (RHIhub, 2018), ARMOT is made up of mobile case managers and recovery support agents who travel to hospitals, emergency departments, and psychiatric units to meet with patients who need substance use disorder services. These mobile case managers offer comprehensive care

assessments for substance use disorder treatment services, along with referrals and links to treatment providers and support services.

ARMOT also provides education to patients, family members, and hospital staff to deal with issues of stigma related to opioid addiction.

In 2016, Pennsylvania Governor Tom Wolf announced the implementation of the Centers of Excellence, which would offer MAT services to those with opioid-related substance abuse disorder in Pennsylvania. The Centers act as “navigational hubs” for Medicaid patients seeking treatment and treat the patients’ substance abuse, mental health (to address the underlying causes of addiction), and physical health. The state provided an initial \$15 million and the federal government provided \$5 million in funding for the Centers.

Phone Survey and GIS Spatial Analysis

To assess the need for MAT facilities in rural Pennsylvania, the research analyzed the overall number of facilities, capacity, operational features, and services provided using state databases and phone survey questions.

A working database was compiled from the facilities included in the study. The sources of information included DDAP, SAMHSA’s list of Accredited MAT Clinics and ESRI’s list of MAT clinics. These listings were then categorized as rural or urban as defined by the Center for Rural Pennsylvania (See Figure 1). One hundred and sixty facilities were defined as rural MAT sources.

To verify their status as currently open and functioning, the researchers’ confirmed the names, addresses, and telephone numbers for the 160 rural facilities through online tools and in-person corroboration. The researchers found that many entries were incorrect in the SAMHSA

database and a small number of facilities were no longer operational. Addresses and phone numbers were inaccurately reported, as well as the type of MAT services provided for patients.

After duplicate listings, incorrect addresses, or closed facilities were removed, the database was narrowed to 120 listings.

The researchers called the 120 rural facilities and asked them to participate in a 12-question survey regarding their MAT status and operational description. The researchers made three attempts with each facility to complete the survey. In total, 92 facilities completed the survey: 24 did not respond to the calls, two facilities declined to participate, and two were unable to fully complete the survey. Overall, the response rate was 80 percent. The interviewee (the clinic office manager or clinic director) was asked to describe the facility's MAT status, the types of MAT offered, services offered, profit status, major source of reimbursement, and types of physicians employed.

It should be noted that many potential participants felt uncomfortable answering questions about their facility, or were unable to provide the information necessary to respond.

Only data from the clinics that provided MAT (43) were used for the GIS analysis. Each one of the addresses was taken and geocoded. Geocoding is the process of taking physical addresses and converting them to latitude and longitude coordinates so that they appear as physical points on a map.

Qualitative Interviews and Survey Data of MAT Programs

MAT clinic director key informant interview data were obtained through primary data collection. Semi-structured interviews were conducted with 17 directors of MAT programs (in rural and urban Pennsylvania and rural Vermont, Rhode Island, and Ohio) to identify major

themes. Administrators were recruited by calling the clinic directly and explaining the study and its purpose. Clinics were selected with the goal of having a representative sample of both rural and urban clinics.

Interviewees in Pennsylvania were selected based on willingness to participate and geographic location. Ideally, the researchers tried to obtain interviewees in rural and urban regions. Personal interviews of directors were based on the methodology and approach of Hambrick and Mason (1984). The clinic director was interviewed and the interviews were transcribed and coded. Major themes of the interviews were documented and categorized to create a qualitative study of the barriers, opportunities, and lessons learned in delivering MAT services in Pennsylvania.

Interviews were conducted with three directors of MAT clinics in rural Vermont, Rhode Island, and Ohio. These states have successfully implemented strong evidence-based MAT programs (CMS, 2014). The list of SAHMSA-licensed MAT treatment facilities was used to contact facility directors in Rhode Island, Vermont, and Ohio. The interviews were obtained by a convenience sample, as the program directors voluntarily agreed to participate in the interviews after being contacted because they were a licensed SAHMSA facility. The purpose of these interviews was to identify barriers and opportunities for expansion, while exploring some of the components of highly successful treatment programs. One clinic director from each state (Rhode Island, Ohio, and Vermont) was interviewed.

RESULTS

Phone Survey of MAT Centers in Rural Pennsylvania

Of the 92 facilities that completed the phone survey, only about half provided MAT services while the other half provided the counseling required when prescribing MAT (43 MAT, 43 counseling only). Three facilities did not have MAT onsite but contracted out to other providers for MAT services. Two facilities were not providing MAT at the time of the research but had scheduled plans to offer it in the future, and one facility was no longer providing the service (N=92) (See Figure 2).

In the MAT facilities, Suboxone (buprenorphine) was the most commonly prescribed medication, followed closely by Vivitrol (naltrexone) and methadone (26 Suboxone, 24 Vivitrol, 16 methadone). Given the advantage of Suboxone and Vivitrol to be taken in settings other than designated opioid treatment clinics, it was not surprising that these two medications were the more commonly prescribed. The advantages of Suboxone can also be shown in its cost-effectiveness and safety profile. Suboxone is significantly less likely to cause respiratory depression, a potentially deadly side-effect of methadone (Thomas et al., 2014; Thomas et al., 2015), and has a significantly lower cost than Vivitrol; Vivitrol has no generic form, resulting in a higher cost than other substance abuse medications (Hartung et al., 2014).

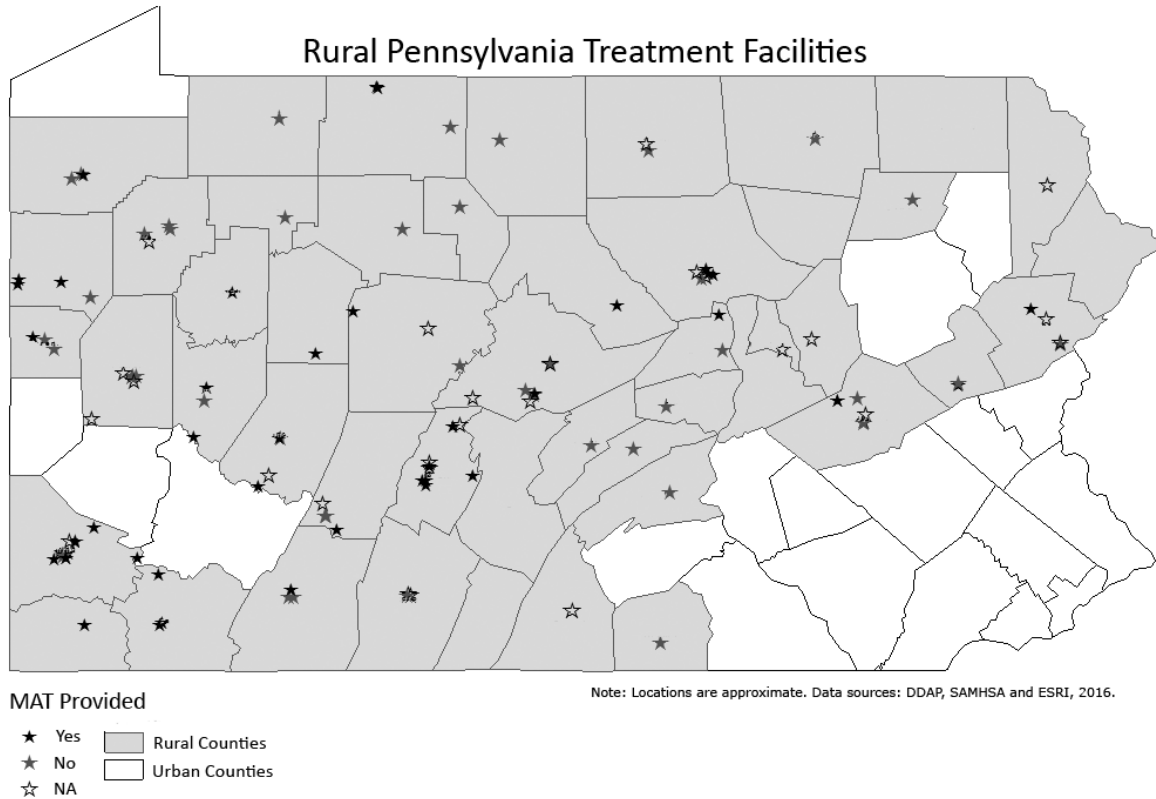
By far the most common form of reimbursement for services came from Medicaid (35 MAT facilities, 26 non-MAT facilities). Only four MAT facilities listed Medicare as a top payer. A few listed private insurance or self-pay as common forms of reimbursement (eight private insurance, two self-pay), 10 listed Community Care Behavioral Health, eight listed county money, and five listed Value Behavioral Health.

Although the results from facility interviews showed a direct split between providers of MAT and providers of drug and alcohol counseling services, all facilities were significantly more likely to provide outpatient services than inpatient (68 and 23, respectively). Facilities that provided MAT services were more likely to have inpatient services than those who provided counseling services alone (MAT facilities: 28 outpatient, 15 inpatient; non-MAT facilities: 37 outpatient, six inpatient).

Within all inpatient facilities, client capacity ranged from 10 to 275 beds, with a median of 36 and mean of 77.5. Most facilities were on the smaller end, ranging from 10 to 42 beds. A majority reported a constant maximum capacity, with only a handful stating lower than 100 percent. Facilities under 100 percent capacity were largely in the 90-99 percent range, with only two facilities reporting the lowest occupancy rate of 80 percent.

In terms of operational structure, facilities that did not provide MAT services were more likely to be non-profits (29 nonprofit, 15 for-profit) compared to an almost equal split in profit status among sites that did provide MAT (22 nonprofit, 24 for-profit). Non-MAT facilities were also more likely to have only certified drug and alcohol counselors employed at the facility, rather than a medically-trained doctor (physician, psychiatrist, psychologist, medical director, etc.) (Non-MAT: 26 certified drug and alcohol counselors only, 18 medically trained doctors employed). Most MAT sites employed at least one medically-trained physician, which is congruent with the increased medical and legal requirements of supplying MAT.

Figure 2



Geographic Information Systems Analysis

This section of the study used GIS mapping to determine MAT accessibility to mobile facilities and traditional “brick and mortar” MAT centers in each county.

Rural Counties and MAT Mobile Coverage

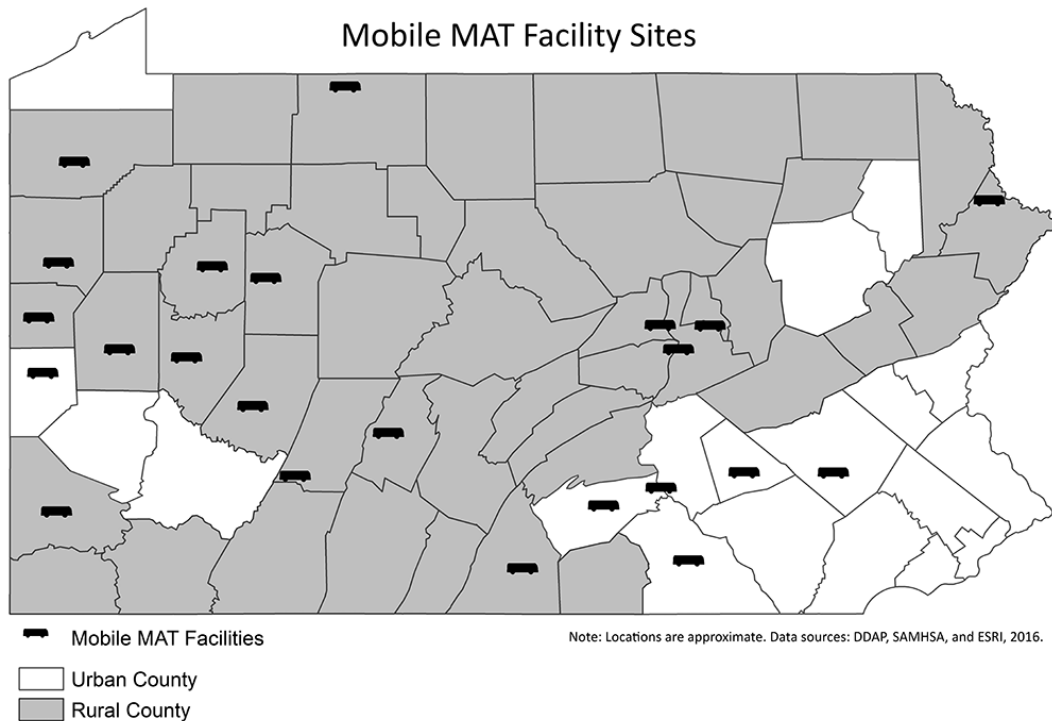
Figure 3 represents the mobile MAT facilities located within the rural Pennsylvania. As mentioned previously, PRS drives to fixed address locations, and patients are required to drive to these locations to receive care. The map displays 23 mobile sites where PRS was providing MAT services in Pennsylvania at the time of the research; six sites cover urban counties. The mobile facilities were mostly located in the western portion of Pennsylvania. There was no mobile coverage in central Pennsylvania, which contains Centre, Clinton, Fulton, Huntingdon, Juniata,

Mifflin, and Potter counties. There is also a gap in coverage in the northeast region of Pennsylvania, including Bradford, Sullivan, Susquehanna, and Tioga counties.

The rural counties where PRS provides MAT services include Armstrong, Blair, Butler, Cambria, Clarion, Crawford, Franklin, Indiana, Jefferson, Lawrence, McKean, Mercer, Montour, Northumberland, Pike, Union, and Washington. The mobile MAT sites within these counties also encompass at least one neighboring rural or urban county.

The rural counties without a mobile MAT site that have coverage from a nearby county's mobile MAT site are Adams, Bedford, Centre, Clearfield, Clinton, Columbia, Elk, Forest, Greene, Lycoming, Perry, Schuylkill, Snyder, Somerset, Venango, Warren, and Wayne. The rural counties without access to mobile MAT service are Bradford, Cameron, Carbon, Fayette, Fulton, Mifflin, Monroe, Potter, Sullivan, Susquehanna, Tioga, and Wyoming.

Figure 3

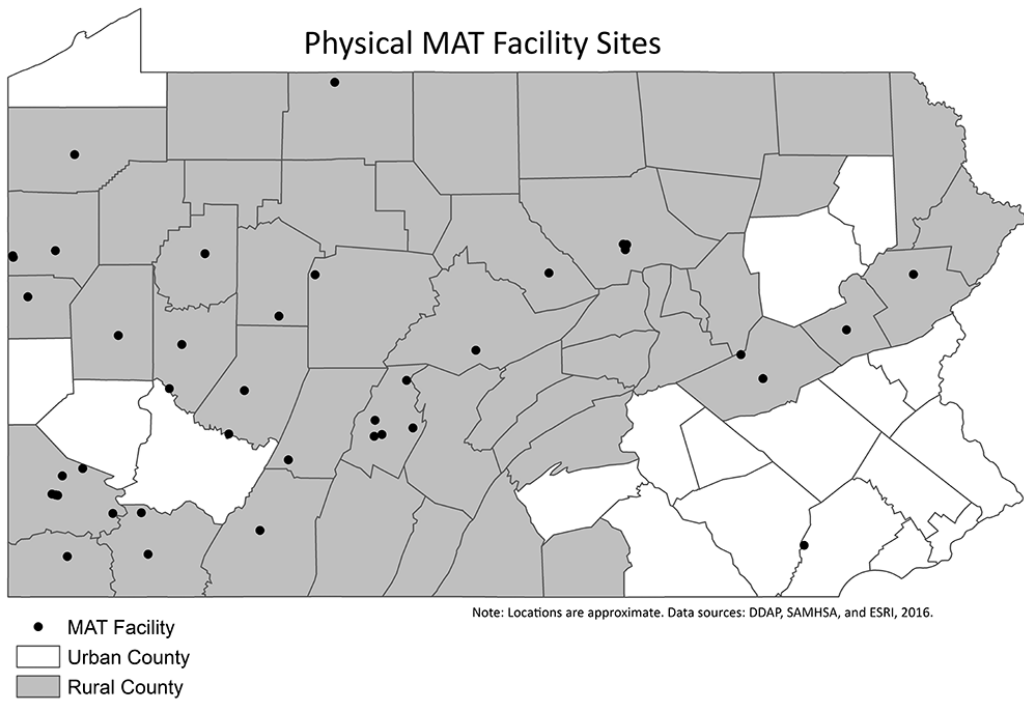


Rural Counties and MAT Physical Sites

Figure 4 represents the brick and mortar MAT clinics located in rural Pennsylvania. The physical MAT sites are clustered in western Pennsylvania, with a line of coverage in the middle of the state extending from the southwest to the northeast. Another cluster is in the central eastern section of the state.

The rural counties that host the physical MAT sites are Crawford, Mercer, Lawrence, Butler, Clarion, Armstrong, Jefferson, McKean, Indiana, Washington, Greene, Fayette, Somerset, Cambria, Blair, Centre, Clinton, Lycoming, Schuylkill, Carbon, and Monroe.

Figure 4



Key Informant Interview Summaries and Thematic Analyses

Although each MAT clinic in Pennsylvania exists in a unique environment and context, common themes emerged from the interviews with the clinic administrators. The emergent themes are summarized below. Only those themes that were discussed by the majority of the Pennsylvania clinic directors are reported. Themes that were mentioned by all the directors are noted. Any information that could be used to identify the MAT clinic or its administrator(s) was removed.

Theme 1: Transportation to MAT clinics is a barrier to access for patients receiving treatment, especially in underserved rural areas.

All participant administrators said the lack of transportation is a barrier for patients in reaching MAT clinics. This barrier exists in urban and rural areas. For example, it exists in urban areas when clinics are located a distance from public transportation. Women with small children experience the added hardship of transporting their children in a stroller. The time required to travel via public transportation means that young children are possibly in transit for several hours daily, which oftentimes creates a very challenging scenario for the client seeking treatment. A further added complication is when public transportation is limited or non-existent during weekends.

Access to transportation is especially critical for those who are undergoing methadone maintenance treatment (MMT), which may require daily dosage.

All the rural clinic administrators reported that clients residing in underserved areas of Pennsylvania experience the hardship of driving 30 minutes or more to a MAT clinic. The lack

of access may be especially difficult for those who require daily treatment as part of their MMT services.

Theme 2: Stigma against MAT services represents a significant barrier in receiving treatment with MAT services.

All administrators reported that patients must overcome the barrier of stigma, which may arise from family members, employers, law enforcement officers, drug courts, healthcare professionals and clinicians, and even support groups such as Narcotics Anonymous and Alcoholics Anonymous.

Abstinence-Only Therapy: Clinic administrators reported that some of their colleagues support an abstinence-only approach and, therefore, advocate against MAT treatment strategies. Such colleagues also refused to accept MAT clients in meetings of Narcotics Anonymous and Alcoholics Anonymous.

Even within the MAT services, patients who are on methadone are subject to more stigma versus those who are taking Vivitrol.

The stigma against MAT may arise from a lack of training regarding its effectiveness. Counselor training on medications has been effective at reducing bias against MAT therapies, and improving rates of adoption (Abraham et al., 2011; Aletraris et al., 2016). Incomplete information on MAT treatment, specifically methadone and buprenorphine, is a leading source of confusion among counselors regarding their effectiveness (Aletraris et al. 2016).

Employers: According to clinic administrators, stigma is a barrier for patients receiving MAT services as it leads employees to hide their condition from their employers for fear of losing their employment and, therefore, their employer-sponsored health insurance.

The Americans with Disabilities Act (ADA) provides protection to those who have substance-abuse disorders—but it cannot assist employees who are not diagnosed (Earnshaw, Smith, & Copenhaver, 2013). Studies show that individuals with substance-abuse disorders suffer greater rates of job loss. Consequently, job instability and income loss are associated with poor retention in MAT programs (Earnshaw, Smith, & Copenhaver, 2013).

Drug Courts: Stigma against MAT services also is shown in drug courts where judges and parole officers restrict access to MAT services. While some drug courts are more accepting of such treatment, administrators report that many patients do not continue their MAT treatment due to being imprisoned without access or because being drug free is a condition of their parole.

While methadone is made available to people who experience chronic pain within jails and prison systems, some drug courts still prohibit methadone and buprenorphine. Drug courts that do permit MAT treatments anticipate diversion of MAT medications due to a perception that MAT may aid and abet some illicit drug use (Matusow et al., 2013).

Medical Providers: All clinic administrators identified the stigma against MAT services by medical providers due to either ignorance or previous negative experiences with patients receiving MAT treatment.

Family Members: Administrators report that some relatives prefer their family members to be admitted to an abstinence rehab facility instead of a MAT clinic for their opioid addiction. This preference is also related to the family members' desire to have the patient out of their house and in an inpatient facility.

Research in this area finds that individuals suffering from opioid dependence frequently experience stigmatization by friends, family, and coworkers (Earnshaw et al., 2013).

Theme 3: The lack of childcare represents a significant barrier for patients receiving MAT services.

Administrators report that many patients have small children in their care. Caring for children represents a significant challenge for patients using public transportation to travel to and from the clinic, as well as their participation in individual and group counseling sessions. The children's care needs represent significant challenges for the clients. Many MAT clinics do not have the resources to provide childcare for the patients. Furthermore, administrators who wish to provide childcare face a dilemma if patients do not want their children exposed to the environment or if it exposes the clinic to liability risk.

Theme 4: The lack of coverage of MAT services by private insurance plans in Pennsylvania poses a significant barrier to patients receiving care.

All clinic administrators reported that the lack of coverage for MAT services by private insurance companies poses a significant barrier to patients receiving care. The effort and resources needed for patients to appeal and pursue reimbursement for services acts as a deterrent. Private insurance may provide coverage for services that are categorized as pain management, but insurers tend to either resist or deny coverage for MAT services. This despite the passage of the Mental Health Parity and Addiction Equality Act, effective January 2010. Administrators noted that it is ironic that health insurance companies resist providing coverage for MAT services given that they provide coverage for prescription pain killers.

Theme 5: Single County Authorities (SCAs) are gatekeepers for funding MAT services, and they provide relatively limited funding for MAT services.

Clinic administrators perceived a bias by some SCAs against MAT services. If MAT services are funded by the SCAs, there seems to be a preference promoting Vivitrol, and not methadone or Suboxone, among patients regardless of its appropriateness for the patient.

Theme 6: Lack of clinics in underserved areas serve as a barrier for patients receiving MAT services.

All rural clinic directors interviewed identified the lack of clinics or a lack of clinic capacity as a barrier for patients receiving services. Patients living in underserved rural areas without transportation to a clinic site, which could be miles away, feel this lack of access acutely. This is especially a hardship for patients who must travel to clinics once a day for treatment and counseling.

Qualitative Data from MAT Centers/Clinicians from Neighboring States that Have Had Successful Expansion and Use of MAT Centers

The researchers conducted interviews with MAT clinic service providers and/or program directors from Rhode Island, Vermont, and Ohio.

Lessons Learned

The successes revealed in the interviews were: the positive effects of increased community engagement and the importance of the “medical home” to increase access to treatment. Barriers to MAT treatment were stigma, childcare, lack of consistent housing, and transportation. Future challenges are the increasing availability of fentanyl, the difficulty of

adequately treating patients that have used fentanyl, and projecting the future need/growth of MAT.

Each of the sites/states cited different challenges and best practices. However, it is clear from these interviews that the best model for MAT integrates the use of the “medical home.” Also, programs that are community-based and engage the larger community in understanding addiction, as well as the purpose and significance of MAT were more successful. For example, in Rhode Island, summer performance events, such as concerts, were held and focused on living a recovery lifestyle. These community-based events were focused on reducing stigma within the community, and therefore helped to open doors and get more people into treatment. The concerts were organized and sponsored by the municipal government and community recovery activists.

Vermont has focused significant effort into building relationships with community members by hosting MAT clinic open houses, where community members can see and tour the facilities, dispelling any myths about treatment facilities being “crack houses,” and creating an environment of transparency. The Vermont Department of Health and its MAT clinic directors have built bridges with local law enforcement, consistently participating in community forums and hosting community events at the MAT clinics. This focus on community engagement has led to decreased stigma surrounding MAT and seeking assistance for addiction.

An excellent example of evidence-based methods is focusing on shifting MAT from a clinic to a “medical home” is Vermont’s hub and spoke model. The hub and spoke model integrates addiction treatment into its existing primary care framework. Hubs are regional specialty opioid addiction treatment centers, and spokes are general medical and specialist settings, including primary care practices that are equipped to treat opioid use disorder and receive consultation and support from hubs. All Medicaid beneficiaries receiving treatment in the

hub and spoke model have a primary care patient-centered medical home and access to Medicaid health home services delivered by staff at the hubs and spokes.

Vermont designed a robust evaluation of the hub and spoke model, and early results are promising. One analysis estimated cost-savings for Medicaid due to the reduction in the overuse of health services, such as emergency department visits. Although waitlists for treatment remain in two areas, the number of people served has more than doubled. Providers report that they can now provide the necessary wrap-around services needed to treat addiction (ASTHO, 2017).

In Ohio, the MAT clinic director participant worked at the Veterans Administration (VA). Since the VA is the largest integrated health care system in the U.S., it had similar successes in getting patients into treatment, and providing wrap-around services that are needed to treat addiction. In Rhode Island, the clinic director participant emphasized the importance of providing integrated treatment for patients that involves mental, physical, and addiction health care. Providing integrated care has shown to be successful in all three of the interview locations, Vermont, Rhode Island, and at the VA in Ohio.

Barriers to Access for MAT Services

All clinic directors that were interviewed cited transportation, childcare, lack of consistent housing, and stigma as major barriers to receiving MAT treatment. In Vermont, the state provides van/bus transportation to and from treatment facilities for all rural patients that live a maximum of 1 hour from the treatment facility. The Vermont hub and spoke model solves many long-term transportation issues because, after intensive treatment at the hub locations, patient care is managed at the spoke locations, which are much closer to the patient's home.

Transportation was a barrier to treatment in all three interview locations as they are similarly, largely rural states.

Childcare was also a major barrier for patients. In Vermont, childcare was the most common reason given for patients to miss MAT clinic appointments. In response to this barrier to care, one opioid treatment program in Vermont has started to offer on-site childcare for patients.

Lack of consistent housing was also cited as a barrier to treatment. In Rhode Island, a housing-first intervention has been shown to be effective in stabilizing patients, and has achieved a 90 percent success rate in housing chronically homeless people. Also, methadone is given in Rhode Island prisons for 30-90 days, which greatly assists incarcerated people in overcoming addiction.

Stigma is a significant barrier to MAT treatment. Specifically, the clinic director in Ohio cited significant issues of stigma with drug courts not seeing MAT as an effective therapy. In Vermont and Rhode Island, the clinic directors reported substantial issues with stigma from the families of patients and the patients of MAT clinics themselves.

Future Challenges for MAT Services and Patients

Future challenges are the increasing availability of fentanyl, the difficulty of adequately treating patients that have used fentanyl, and projecting the future need/growth of MAT services. All three interview locations stated that fentanyl was becoming a much more significant issue when addressing addiction treatment. In Rhode Island, the clinic director indicated issues with the lack of knowledge in treating patients that have been using fentanyl, as well as increasing difficulty in stabilizing patients with safe levels of MAT after fentanyl use. It appeared that

Vermont had lower rates of fentanyl use than Rhode Island and Ohio, as Vermont reported fentanyl as a significant future issue.

All three interview locations expressed issues with estimating the trajectory of the long-term need for MAT facilities, creating difficulties when planning future expansion efforts. In each interview location, the clinic directors continue to see large numbers of people seeking MAT (2 percent of the population of Vermont in treatment currently). The increased use and availability of fentanyl, as well as amplified efforts to restrict opioid prescriptions, has led to more illicit opioid use, which has created significant issues in implementing MAT safely.

CONCLUSIONS

The U.S. is facing an opioid epidemic, and Pennsylvania has been heavily affected by the epidemic (CDC, 2017). Pennsylvania has developed new education programs, created partnerships among public and private agencies and organizations, and altered or passed new laws and regulations to fight this epidemic.

However, access to affordable MAT services for opioid addiction remains limited by various federal and state policies and regulations. For MAT to be successful in helping as many individuals as possible, policies, programs, and education to support and promote MAT are needed at all levels of the healthcare system (Opioid Task Force, 2017).

Table 2 provides a detailed summary of the relevant federal and state policies, regulations, and programs and their implications for the delivery of MAT services. Every effort was made to provide the most current impact of federal and state legislation on MAT services for Pennsylvania residents.

Table 2: Summaries of Federal and State Policies/Regulations/Programs and Their Implications for Medication Assisted Treatment Services

Policy / Regulation / Program	State or Federal	Summary	Implications for MAT Service
<p>Governor Wolf and Public Health Emergency Declaration. January 2018 (Renewed April 4 and September 24, 2018).</p>	<p>State</p>	<p>The declaration includes 13 key initiatives categorized into three areas of focus to include: 1) enhancing coordination and data collection to bolster state and local response 2) improving tools for families, first responders, and others to save lives 3) speeding up and expanding access to treatment.</p>	<p>The declaration expands access to MAT in several ways: 1). It expands access to the Prescription Drug Monitoring Program (PDMP) to other commonwealth entities for clinical decision-making purposes 2). It waives the face-to-face physician requirement for Narcotic Treatment Program (NTP) admissions, which allows Certified Registered Nurse Practitioners (CRNP) or Physician Assistants (PA) to conduct initial intake reviews 3). It waives the regulatory provision to permit dosing at satellite facilities even though counseling remains at the base of the Narcotic Treatment Program 4). It waives annual licensing requirements for high-performing drug and alcohol treatment centers and 5). It waives separate licensing requirements for hospitals and emergency departments. While the declaration of public health disaster emergency expands access to treatment and addresses policy issues that were creating barriers to MAT services, the plan fails to address compliance issues, such as mandatory use of the PDMP, and fails to address incentives for provider participation, such as reimbursement. However, the provision that allows dosing at satellite facilities may</p>

Policy / Regulation / Program	State or Federal	Summary	Implications for MAT Service
			help to address the shortages of MAT service provision in rural areas.
Centers of Excellence for Medication Assisted Treatment	State	Centers of Excellence provide coordinated care for people with opioid-related substance use disorder. There are 51 Centers of Excellence (COE) throughout Pennsylvania. The goal of the COE is to integrate behavioral health and primary care into one setting, which is accomplished through a team-based strategy that facilitates care that focuses on the whole person. Medicaid eligible patients are the target patient population for the COE.	Centers of Excellence provide coordinated care for people with opioid-related substance use disorder. The goal of the COE is to integrate behavioral health and primary care into one setting, which is accomplished through a team-based strategy that facilitates care that focuses on the whole person. These centers work to ensure that people with opioid-related substance use disorders remain in treatment, receive follow-up care, and are supported within their communities. COEs in Pennsylvania are not strategically placed to benefit the maximum amount of people. Areas such as northwestern Pennsylvania and some parts of central Pennsylvania do not have any COE located within a reasonable, accessible distance. This means that individuals are either not receiving MAT because it is too far away, or they are receiving inadequate MAT services that do not follow-up with care or work to keep individuals in treatment.
Mental Health Parity and Addiction Equity Act	Federal	This act aims to mirror mental health and substance abuse coverage to medical/surgical coverage on insurance plans. This law applies to individual market plans, small employer funded programs (50 insured employees or less), larger	This act does not apply to smaller employer-funded plans grandfathered in before March 2010, church-sponsored and self-insured plans supported by state and local governments,

Policy / Regulation / Program	State or Federal	Summary	Implications for MAT Service
		employer funded programs (51 insured employees or more), Medicaid managed care programs, CHIP, and Medicaid Alternative Benefit Plans.	retiree-only plans, TriCare, Medicare, and non-managed care Medicaid. This limits the amount of people that can obtain the benefits of this act. Also, ambiguous wording has resulted in loopholes that have made it difficult for patients and providers to get prior authorization for MAT medications.
Pennsylvania Act 106	State	Act 106 requires minimum coverage for alcohol and substance abuse treatment upon a diagnosed certification of a medical problem and a referral from a licensed physician or psychologist. Act 106 covers up to 7 days of detoxification with four admissions per lifetime, a minimum of 30 days of residential treatment services per year, with 90-days maximum in a lifetime, a minimum of 30 sessions of outpatient or partial hospitalization services per year, with 120 maximums in a lifetime, and family counseling and intervention services.	Coverage for MAT services may be reduced because insurance companies will no longer cover costs after the minimum required amount of treatment days. Further, Act 106 acts as a barrier for patients requiring treatment for opioid abuse when patients must be diagnosed with a medical condition and be referred for treatments by a licensed physician. Patients that do not see a physician or psychologist may not receive services under Act 106.
Act 152 of 1988	State	Act 152 provides state funding for non-hospital residential detoxification and rehabilitation services. This program aims to assist individuals with residential rehabilitation, detoxification, and halfway house services. Single County Authorities (SCA) determine redistribution of these extra dollars for patients who require services.	Act 152 restricts funding for hospital detoxification and rehabilitation programs. This impacts the availability and access to MAT services. If an individual must travel a far distance to receive treatment, additional barriers develop such as transportation, child care, and available time.
Behavioral Health Services Initiative (BHSI)	State	BHSI was established to provide a safety net of state funding for individuals who were not eligible for Medicaid and had serious mental health	While 60% of the funding is distributed to alcohol and drug services, such as MAT, 40% is spent on mental health services.

Policy / Regulation / Program	State or Federal	Summary	Implications for MAT Service
		<p>or substance use disorders. Funds are allocated from the Office of Mental Health and Substance Abuse Services to SCAs. Funds for BHSI are split 60/40 between alcohol and drug services and mental health services.</p>	<p>Mental health services receive over \$600 million annually in funding from the OMHSAS, on top of the \$433 million in funding for state mental health facilities. By shifting the 60/40 distribution to have more or at least equal funding for drug and alcohol programs, more individuals would receive MAT.</p>
<p>Pennsylvania Department of Drug and Alcohol Programs (DDAP)</p>	<p>State</p>	<p>DDAP has successfully implemented programs that have expanded access to MAT, provided a platform for tracking opioid prescribing practices, and created partnerships with other organizations and government entities to prevent overdoses through naloxone and the Drug Take Back program.</p>	<p>DDAP needs to further educate communities and individuals on the dangers of opioid use. This would help increase the number of individuals willing to get MAT. Areas for education include opioid risks, stigma, the efficacy of MAT, and the importance and efficacy of naloxone.</p>
<p>Single County Authorities (SCAs)</p>	<p>State/Federal</p>	<p>Single County Authorities are county organizations that plan, coordinate, fiscally manage and implement the delivery of drug and alcohol prevention, intervention, and treatment services at the local level, primarily through contracts with drug and alcohol treatment service providers. SCAs are represented by the Pennsylvania Association of County Drug and Alcohol Administrators and receive state and federal money through contracts with DDAP.</p>	<p>Funds provided to Single County Authorities are not adequate to meet the demand for MAT services. Funding has been cut by 25% in recent years. Lack of adequate funding for treatment services impedes efforts aimed to address the opioid epidemic and the delivery of MAT services.</p>
<p>Drug Addiction Treatment Act of 2000</p>	<p>Federal</p>	<p>This act permits private physicians, nurse practitioners and physician assistants who meet explicit qualifications to treat opioid dependency with narcotic medication, buprenorphine, that is approved by the FDA in</p>	<p>Individuals who receive the waiver can only treat up to 30 patients per year with medication. After 1 year, a physician may submit a revised waiver to treat and prescribe medication to 100</p>

Policy / Regulation / Program	State or Federal	Summary	Implications for MAT Service
		treatment settings other than an opioid treatment program (OTP). This regulation gives those who do not have access to methadone clinics or do not meet criteria for treatment in an OTP an alternative to receive treatment with approved narcotic medications.	patients. This decreases the likelihood that a physician, physician assistant, or nurse practitioner can treat all individuals with medication that are seeking and in need of care.
The Safe Emergency Prescribing Act	State	This Act places limitations on emergency department and urgent care center MAT prescriptions. Specifically, health care practitioners may not prescribe more than a 7-day supply of an opioid drug product to an individual seeking treatment in an emergency department or urgent care center. Also, a health care practitioner may not prescribe refills of an opioid drug product in emergency departments and urgent care centers.	This act creates a barrier to access for MAT. Unfortunately, an urgent care center or emergency room may be the closest health care center for an individual, and since they cannot refill prescriptions or prescribe more than a 7-day supply, individuals may need to travel a much further distance for treatment.
Achieving Better Care by Monitoring All Prescriptions Program (Act 191 and 124)	State	This Act allows for the monitoring of all controlled substances. This is accomplished through the PDMP. This program gives prescribers and pharmacists access to a patient's controlled substance prescription medication history, and alerts medical professionals to potential dangers of over-prescribing, potential substance abuse, etc.	One barrier to successful implementation of the PDMP is compliance. With a large number of prescribers and dispensers using the PDMP it is challenging to monitor and ensure all necessary information is entered into the system. Also, overprescribing can still occur because prescribers who are treating individuals in an emergency department are not required to query the prescribing history of any drug.
Prescribing Opioids to Minors, imposing powers and duties, and imposing penalties (Act 125)	State	Act 125 regulates opioid prescribing to minors such that a prescriber may not prescribe a controlled substance containing an opioid unless the prescriber complies with section 52A04. A prescriber	The younger people are, the less likely they are to receive MAT. This could in part be due to providers' hesitation to treat minors with addiction. While Act 125

Policy / Regulation / Program	State or Federal	Summary	Implications for MAT Service
		<p>may not prescribe more than a 7-day supply of a controlled substance containing an opioid, unless medically necessary to treat a minor. Above all, a prescriber must obtain parental consent for a prescription containing an opioid.</p>	<p>provides regulations to ensure safe opioid prescribing among minors, it also might introduce a hesitation towards prescribing MAT to minors.</p>
<p>Drug Overdose Response Immunity (Act 139)</p>	<p>State</p>	<p>Known as the “Good Samaritan Act,” this law provides limited immunity from charge and prosecution for possession of drugs and drug paraphernalia for individuals seeking medical treatment related to an overdose. The act also provides limited immunity from charge and prosecution for persons who seek medical care in good faith for someone experiencing drug overdose, if certain conditions are met. Additionally, Act 139 expands access to naloxone by allowing medical professionals to dispense, prescribe, or distribute naloxone to family members, friends, and others who might be able to assist in an overdose. It also permits law enforcement officers, firefighters, and EMS personnel to carry and administer naloxone.</p>	<p>Some insurance companies require pre-authorizations and copays to cover naloxone. For example, individuals with medical assistance must obtain a prior authorization for Evzio Auto-Injector. Additionally, not all pharmacies have all types of naloxone readily available, and there may be a one to two-day lag time in dropping off the prescription and picking it up.</p>

POLICY CONSIDERATIONS

State government should continue to strictly enforce Act 106 of 1989, which mandates minimum benefits for alcohol abuse treatment and drug addiction treatment under most group insurance plans in Pennsylvania.

State government should also continue to strictly enforce the federal Mental Health Parity and Addiction Act of 2008, which requires the same health insurance coverage for mental health and/or substance use disorder conditions as patients would receive for coverage of medical/surgical services.

State government should closely monitor compliance with all state laws governing the medical education requirements for medical students and professionals to prescribe opioids, as well and those laws governing the prescription of opioids for juveniles and those seeking treatment at emergency departments.

All Pennsylvania county drug courts should allow MAT services to be provided to those drug court participants who have medically prescribed and monitored MAT plans.

State government agencies also should collaborate to address the numerous barriers that exist in rural Pennsylvania that hinder, or prevent, the use/benefit of MAT for those with a OUD. These barriers include: lack of transportation or child care; shortage of MAT sites/clinics and providers; counseling and support services for those with an OUD who also have co-occurring behavioral health conditions; and stigma within the health care industry and community regarding MAT.

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Appendix A: Methadone

Clinical Definition of Methadone

Methadone is defined as “a long-acting synthetic opioid agonist medication that can prevent withdrawal symptoms and reduce craving in opioid-addicted individuals” (National Institute of Drug Abuse (NIDA), 2018). It is typically administered daily “in oral solutions, tablet, and injectable forms” (Center for Substance Abuse Research (CESAR), 2016).

Methadone Maintenance Treatment (MMT) for opioid addiction has been available since 1964 and remains in high demand as a more effective alternative to abstinence-based treatment options (Volkow et al., 2014). The duration of treatment is indefinite and varies between individuals. Methadone is considered a maintenance medication; it is effective if a patient takes it. Some patients may begin to taper off methadone slowly until it is no longer needed, while others continue with MMT on a long-term basis.

Methadone has pharmacologic properties similar to morphine, heroin, and other opiates. It is μ -agonist, binding to and stimulating receptors in the brain. This property reduces painful symptoms of opiate withdrawal and blocks euphoric effects of opiate drugs such as morphine and heroin, as well as semi-synthetic opioids like oxycodone and hydrocodone (SAMHSA, 2016). This property is also known as cross-tolerance. Methadone, though, has incomplete cross-tolerance; users do not experience the euphoric high that they would with true opiates (Doverty et al., 2001).

Methadone may last (in the body) for up to 36 hours. This duration prevents a MMT patient from crashing before receiving their next dose and engaging in drug seeking behaviors (PEW Charitable Trusts, 2016).

Delivery Mechanisms and Federal and State Regulations

Methadone is recommended to be prescribed for individuals with high use patterns because it must be administered daily (Bruce, Kresina, Elinore & Katz, 2010). Patients are required to attend a methadone clinic daily to receive their medication. The clinic visit provides an additional level of clinical assessment since patients are also seen by a healthcare professional daily. Since patients remain dependent on methadone while receiving treatment, MMT is not considered an abstinence based treatment. “The goals of methadone treatment are to reduce or eliminate illicit opioid use and, as a result, to decrease its associated negative outcomes. For pregnant women, the goals of MMT include improved maternal and fetal outcomes” (Fullerton et al., 2014). For optimal results, patients seeking assistance with an opioid use disorder should participate in a comprehensive MMT program that includes counseling and participation in social support.

Methadone is highly regulated and may only be dispensed by an opioid treatment program (OTP) that is regulated at both the federal and state levels (PEW Charitable Trust, 2016). Certified OTPs operate under the federal oversight of the Substance Abuse and Mental Health Services Administration (SAMHSA) and the Drug Enforcement Administration (DEA); state methadone authorities also regulate treatment (Rinaldo, 2008). MMT OTPs can include hospitals, intensive outpatient facilities, and short-term or long-term residential treatment facilities (PEW Charitable Trust, 2016).

Although methadone is typically well tolerated, one reason it is highly regulated is its potential for overdose, especially when taken in combination with sedative-hypnotics. Over the past 30 years, multiple randomized clinical trials have demonstrated that methadone is a highly effective maintenance treatment in reducing opioid use. Doses of 60-100 mg/day of methadone

have been shown to be more effective than lower dosages in treatment. There is, however, a high risk of relapse after methadone discontinuation, so a long-term treatment plan is necessary for most patients.

Benefits of Methadone

Methadone is well researched and has proven to be effective in MAT (NIDA, 2015). “MMTs effectiveness studies show success in high treatment retention, in decreasing drug use, risk behaviors, comorbidity (HIV, viral hepatitis), mortality and criminality related, and in increasing employment rates and addicts’ quality of life” (Miranda, 2005).

“Methadone acts as a replacement therapy, mitigating withdrawal, reducing craving, and inducing tolerance to block the average dose of heroin for 24 to 36 hours. It is used both to assist in withdrawal and for maintenance” (Pecoraro, Ma & Woody, 2012).

Patients Most Appropriate for Being Prescribed Methadone

Factors favoring MMT as a viable treatment for patients include injection opioid use, pregnant or adolescent injection opioid users, previous treatment dropout with buprenorphine, or other risk factors for treatment dropout (unstable household, lack of social support, concurrent mental illness (Srivastava, 2017).

Women During Pregnancy

For pregnant women, studies have shown MMT’s efficacy to decrease pregnancy-related maternal and fetal morbidity among pregnant women with an opioid addiction (Fullerton et al., 2014). MMT has been associated with the risk of neonatal abstinence syndrome (NAS), a condition characterized by dysfunctionality of the autonomic nervous system, gastrointestinal tract, and respiratory system and by the irritability of the central nervous system. Babies born

with NAS often require a morphine detoxification treatment in the hospital. Infantile risk for NAS that develops among neonates of mothers who continued to use opiates and mothers with MMT fall within the same range (Fullerton et al., 2014). MMT during pregnancy was found to decrease illicit opioid use, increase rates of retention in treatment while pregnant, decrease pregnancy complications, and improve fetal outcomes overall (Fullerton et al, 2014).

Compliance/Success rates

MMT has a positive impact on treatment retention and suppression of substance abuse (Rosic, et al., 2017). MMT provided to individuals at adequate dose levels was significantly more effective than those receiving no medication treatment in retaining patients in the treatment program and reducing illicit opioid utilization (Fullerton, et al., 2014).

MMT has been found to be effective for decreasing illicit opioid use and successful follow through with treatment as well as being generally believed to reduce mortality risk among individuals with opioid dependence. There also may be evidence, although less concrete, regarding positive trends in secondary outcomes, such as mortality, and criminal activity (Fullerton, et al., 2014).

Regulations require counseling when undergoing MMT. Intermediate psychosocial counseling has shown to be more effective than low and high amounts of counseling. Methadone detoxification has appeared to be less effective than methadone maintenance, however, if done in conjunction with psychosocial counseling it may be more effective (Pecoraro, et al., 2012).

Treatment retention/Compliance/Cost effectiveness

National Institute of Drug and Alcohol (NIDA) 2017 data show patients receiving methadone treatments are 33 percent more likely to have clean opioid drug test results as well as

being nearly five times more likely to stay in treatment when compared to control groups (NIDA, 2017).

Masson et al. (2004) found the MMT group had an average retention rate of 310.7 days compared to 139.2 for the M180 (control) group. Overall, MMT participants incurred 13 percent more total health-care costs than the control group, and heroin use in the M180 group increased significantly. The authors concluded that although MMT incurred more in healthcare costs, it has proven to be more (clinically) effective and cost effective than the M180 (control) group (Masson et al., 2004).

Secondary outcomes (criminal activity, mortality)

Findings regarding secondary outcomes generally support that methadone has a positive influence on criminal activity associated with substance use, as well as an impact on mortality (Fullerton et al., 2014).

Barriers to Delivering Methadone Maintenance Treatment

Side-effects from MMT

Significant adverse events associated with methadone include respiratory depression, cardiac arrhythmias, and other life-threatening risk factors. These risk factors have contributed to increases in methadone-related deaths and some controversy about methadone. “Between 1999 and 2004, deaths attributed to methadone increased by 390 percent, an effect primarily related to increased utilization in pain clinics, as well as diversion.” Efforts to address the difficulties with methadone have resulted in the development of contextually specific guidelines to minimize the risk of death (Lowe, et al., 2010).

Protocols for safe treatment using methadone “require an appreciation for its pharmacology as well as individual medical, psychiatric, and behavioral factors that may affect the use of, or response to, methadone. Early identification of risk factors, conservative dose titration (adjustment of the dose until the medication has received its desired effect), and vigilance for adverse medication interactions may reduce methadone associated mortality in both MMT and pain populations” (Modesto-Lowe, Brooks, & Petry, 2010).

Methadone’s suppressive respiratory effect can be lethal when taken at inappropriately high doses. Some researchers speculate that instances of fatal overdose tend to occur in patients using methadone for the treatment of pain relief (SAMSA, 2016). They suggest that in these situations dosage may not be meticulously monitored as when methadone is used for treatment (Bart, 2012). Individuals who take methadone should never drink alcohol, because it could cause death (SAMSA, 2016).

Strength of Methadone

Methadone is a stronger and more aggressive form of treatment, so there should be greater care for precautionary methods during patient treatment (Srivastava,2017). Careful monitoring and a close relationship between doctor and patient are essential to its proper use (Cesar, 2016).

Withdrawal/Maintenance/Relapse

After a detoxification period, it is recommended that patients enter MMT as they develop tolerance to methadone. Should a patient discontinue MMT, they will experience withdrawal symptoms that mimic that of true opiates, putting them at high risk for relapse. Methadone withdrawal symptoms are slightly delayed and milder than that of true opiates. However, users

who attempt a life of strict abstinence after completing a medication-assisted detoxification program relapse at rates higher than those who enter a MMT program. Their dosage is adjusted under the supervision of medical professionals to find a maintenance dose appropriate for their tolerance level (Anderson and Kearney, 2000). Withdrawal symptoms may lead to relapse, and accidental overdose or death, which is why education and close monitoring are required when beginning treatment (Anderson and Kearney, 2000).

Comparison of MMT with Other MAT approaches

Buprenorphine

Study results display higher retention rates for patients receiving MMT. When comparing groups receiving equal dosages of MMT and buprenorphine, and with equal amounts of psychotherapy, results indicate that 80 mg of methadone is more effective in retention of individuals than buprenorphine. The greater the dosage of methadone, the more effective it is at retaining individuals, increasing treatment attendance adherence, and decreasing drug abuse. It appears that the greater the dosage of methadone the more effective it is in treating drug abuse compared to buprenorphine.

Peer Researched Review of Methadone

The following table provides a summary of peer reviewed studies related to the efficacy for methadone as a treatment in MAT options.

Table 3: Summary of Peer Reviewed Studies and Their Findings Regarding the Efficacy of Methadone as a Treatment in Medication Assisted Treatment Options

Study Title	Citation	Research Question(s)	Relative Findings
The Cost Effectiveness of Medication-Assisted Treatment for Opiate Addiction	<i>The Avisia Group.</i> Rinaldo, D. (2008)	What is the meaning of “cost-effectiveness” for Medication Assisted Treatment (MAT), including knowledge of the characteristics of the medications generally used to treat addiction and the public treatment systems that states use for medication-assisted treatment for opiate addiction.	Both methadone and buprenorphine were cost-effective treatments for opiate addiction.
Medication-assisted treatment and HIV/AIDS: aspects in treating HIV-infected drug users	<i>AIDS.</i> Bruce, R. D., Kresina, T. F., & McCance-Katz, E. F. (2010)	What are the issues associated with MMT for patients suffering from substance abuse and HIV-positive	Provides an overview of issues regarding the use of medication MMT for substance abuse and dependence among HIV-infected individuals. These issues include access to care and treatment, medication adherence, and drug interactions of prescribed treatments.
Medication-Assisted Treatment with Methadone: Assessing the Evidence	<i>Psychiatric Services.</i> Fullerton, et al., (2014)	What is the evidence for MMT’s effectiveness?	MMT is associated with improved outcomes for individuals and pregnant women with opioid use disorders. MMT should be a covered service available to all individuals.
Methadone maintenance patients are cross-tolerant to the antinociceptive effects of morphine	<i>Pain.</i> Doverty, et al., (2001)	How do the intensity and duration of antinociceptive responses compare at two pseudo-steady-state plasma morphine concentrations (C_{SS1} and C_{SS2}), between four patients?	Methadone patients are cross-tolerant to the antinociceptive effects of morphine, and conventional doses of morphine are likely to be ineffective in managing episodes of acute pain amongst this patient group.
Medication Assisted Treatment Improves Outcomes for Patients with Opioid Use disorder.	PEW Charitable Trust (2015)	Even though medication-assisted treatment (MAT) is the most effective intervention to treat opioid use disorder (OUD), why is it often unavailable to those in need (because of inadequate funding for treatment programs and a lack of qualified providers who can deliver these therapies)?	MAT is the most effective intervention to treat opioid use disorder (OUD) and is more effective than either behavioral interventions or medication alone.

Study Title	Citation	Research Question(s)	Relative Findings
Medication Assisted Therapies - Tackling the Opioid-Overdose Epidemic	<i>The New England Journal of Medicine.</i> Volkow, N., Frieden, T., Hyde, P., & Cha, S. (2014)	What are the best practices in addressing the opioid overdose epidemic from a MAT perspective?	Expanding access to MAT is a crucial component of the effort to help patients recover. It is also necessary, however, to implement primary prevention policies that curb the inappropriate prescribing of opioid analgesics — the key upstream driver of the epidemic — while avoiding jeopardizing critical or even lifesaving opioid treatment when it is needed.
The Science and Practice of Medication-Assisted Treatments for Opioid Dependence	<i>Substance Use and Misuse.</i> Pecoraro, A., Ma, M., & Woody, G. E. (2012)	How has opioid addiction treatment evolved - from humanitarian to scientific and evidence-based, the evidence-based supporting major medication-assisted treatments and adjunctive psychosocial techniques, as well as challenges faced by clinicians and treatment providers seeking to provide those treatments.	
Maintenance medication for opiate addiction: the foundation of recovery	<i>Journal of Addictive Diseases.</i> Bart, G. (2012)	What are the basic mechanisms of action and treatment outcomes for the three medications approved by the FDA for long-term treatment of opiate dependence: the opioid agonist methadone, the opioid partial agonist buprenorphine, and the opioid antagonist naltrexone?	Results indicate that maintenance medication provides the best opportunity for patients to achieve recovery from opiate addiction. Extensive literature and systematic reviews show that maintenance treatment with either methadone or buprenorphine is associated with retention in treatment, reduction in illicit opiate use, decreased craving, and improved social function.
Methadone deaths: risk factors in pain and addicted populations	<i>Journal of Internal General Medicine.</i> Modesto-Lowe, V., Brooks, D., & Petry, N. (2010)	What are the risk factors for methadone mortality in opioid dependent and pain populations? Evaluate the risk factors and present guidelines for initiating methadone treatment in these two populations to minimize the risk of death.	Early research with methadone maintained patients revealed that methadone fatalities occur primarily due to respiratory arrest during methadone induction and in the context of polysubstance use. To minimize fatalities, guidelines are presented for initiating methadone in opioid treatment and pain populations that consider the drug's pharmacology along with

Study Title	Citation	Research Question(s)	Relative Findings
			behavioral, medical and psychiatric risk factors.
Cost and cost-effectiveness of standard methadone maintenance treatment compared to enriched 180-day methadone detoxification	<i>Addiction</i> . Masson, et al., (2004)	How do the cost and cost effectiveness of MMT and 180 day methadone detoxification enriched with psychosocial services compare to one another?	Compared with enriched detoxification services, methadone maintenance is more effective than enriched detoxification services with a cost effectiveness ratio within the range of many accepted medical interventions and may provide a survival advantage. Results provide additional support for the use of sustained methadone therapy as opposed to detoxification for treating opioid addiction.

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Appendix B: Buprenorphine

The World Health Organization (WHO) reports that MAT with methadone or buprenorphine is the most effective for opioid use disorder (WHO, 2009). The WHO reports that MAT, combined with psychosocial assistance, was found to be the most effective for treating opioid abuse. When compared with detoxification or no treatment, the WHO finds that buprenorphine also significantly reduces drug use and improves treatment retention (WHO, 2009).

Clinical Definition of Buprenorphine

Buprenorphine represents one of the latest advancements in MAT services. It is a medication that, in combination with counseling and behavioral therapies, provides a whole-patient approach to MAT. Buprenorphine is an agonist-antagonist drug. For MAT patients, the agonist's main targets are the μ -opioid receptors in the brain, which are activated when the opioid drug attaches to them. This opens up reward pathways in the brain, resulting in the release of endorphins to reduce pain and produce senses of pleasure and relaxation. As an antagonist, it binds to (but does not activate) endorphin opioid receptors and can block the activity of other agonists (SAMHSA, 2016).

Such pharmacologic properties do not produce the euphoria and sedation caused by heroin or other opioids, but do reduce or eliminate withdrawal symptoms associated with opioid addiction, as well as carrying a lower risk of abuse or misuse and overdose. Buprenorphine has a "ceiling effect;" after a certain point, taking more will not increase its effect. If a patient decides to abuse an opioid while taking buprenorphine, the buprenorphine actively blocks the opioid from reaching the receptors in the brain and producing strong, euphoric effects. Buprenorphine

also reduces cravings, prevents withdrawal symptoms and reduces the risk of respiratory depression (SAMHSA, 2016).

Buprenorphine received approval for clinical use for opioid addiction treatment in 2002 (SAMHSA, 2016). The Federal Drug Administration (FDA) approved buprenorphine products for MAT, including Subutex, Bunavail, Suboxone, Zubsolv, Buprenex, Subute and buprenorphine-containing transmucosal (diffused through the mucus membrane) products.

Buprenorphine comes in mono-product (buprenorphine only) form, which is mostly given to pregnant females, and in a combination product (buprenorphine/naloxone). The most common form is taken sublingually (under the tongue). Buprenorphine can be prescribed daily, weekly or monthly and used much like methadone in a maintenance pattern.

Buprenorphine is administered once symptoms of opioid withdrawal have begun. For longer term opioid addiction treatment, a combination of buprenorphine/naloxone is usually recommended. A once a month injection (Sublocade) was approved in the U.S. in 2017 and was available as of March 2018 (PR Newswire, 2018).

Delivery Mechanisms and Federal and State Regulations

Under the Drug Addiction Treatment Act of 2000, qualified U.S. physicians can prescribe buprenorphine as a treatment for opioid addiction in various settings, including offices, community hospitals, health departments, and correctional facilities (SAMSA, 2016). Physicians may prescribe buprenorphine after completing an approved eight-hour course and must request an amended controlled substance license from the Drug Enforcement Administration (DEA).

A physician can also prescribe doses that can be taken at home, although most successful treatments include a behavioral therapy aspect and regular clinic visits. Nurse practitioners or

physician assistants cannot prescribe buprenorphine, limiting its use in rural communities where these providers often serve.

Benefits of Buprenorphine

One of the benefits of buprenorphine is that it may be prescribed by a qualified physician in an office-based setting, improving access for patients.

Patients Most Appropriate for Being Prescribed Buprenorphine

Factors favoring buprenorphine-naloxone as the treatment of choice for patients include oral prescription opioid use, occupations requiring alertness (driving or operating machinery), or patients at risk of methadone toxicity (elderly, heavy alcohol users), patients with cardiac or respiratory compromised conditions, patients at risk of QT (irregularity in the heart's electrical cycle) prolongation (cardiac patients), or patients taking benzodiazepines or atypical antipsychotics. It is recommended that buprenorphine, along with behavioral therapy be used for HIV-infected opioid dependent patients because of its accessibility.

Convenient Settings and Access to Buprenorphine Maintenance Treatment (BMT)

Buprenorphine offers multiple benefits to those for whom treatment clinics are not preferred or are inconvenient. The wide safety margin associated with buprenorphine allows for it to be prescribed in treatment settings such as physicians' offices, and more conservative, traditional opioid treatment programs (OTPs). Buprenorphine is the first medication used to treat opioid dependency that is permitted to be prescribed in a physician's office; it can be dispensed or prescribed in the office, not requiring any further counseling to be involved in treatment. This

enables and establishes treatment in locations that were once scarce or nonexistent and expands treatment options to better meet patients' needs.

Effectiveness of BMT

The mild nature of buprenorphine's positive psychoactive effects has raised questions about its effectiveness for highly dependent patients who are actively seeking MAT for opioid abuse (Dole Research Team, 2006).

Dependency on BMT

Buprenorphine treatment carries the risk of causing psychological or physical dependence. Buprenorphine has a slow onset and a long half-life (the concentration of the drug that is half of the starting dose) of 24 to 60 hours. Once a patient has stabilized on the medication, there are three options: 1) continual use, 2) switching to buprenorphine/naloxone, or 3) medically supervised withdrawal.

Barriers to Delivering BMT

Physician Barriers to Providing BMT

Access to buprenorphine may be influenced by the perceptions of physicians who are permitted to prescribe it for patients. Among those who were prescribing it for their patients during the study, concerns were noted including medication misuse, time constraints, and lack of available mental health or psychosocial support services (Medical Express, 2017).

Among those physicians who were permitted to prescribe buprenorphine but who were not at the time of the study, they reported the following barriers : lack of time and patient need,

resistance from practice partners, lack of specialty backup for complex problems, lack of confidence in their ability to manage opioid use disorder, concerns about DEA intrusions on their practice, and attraction of drug users to their practice (Medical Express, 2017). Additional reasons given by physicians include the reluctance for having patients with substance abuse disorders and addictions in their office or from fear of being audited by the Drug Enforcement Administration (Moran, 2016).

Lack of Access in Rural Counties to BMT

Access to treatment with buprenorphine may be significant due to the lack of physicians trained and waived by the DEA to treat patients with the drug, especially in rural underserved areas. For instance, more than half of rural counties do not have a physician trained and waived by the DEA to treat opioid use disorder using BMT (Eureka, 2017).

Only about 3 percent of primary-care physicians in the U.S. have buprenorphine waivers. Not even half of counties—1,465 out of 3,143—have a physician who can prescribe the medication, according to an analysis published in the *Annals of Family Medicine* in 2015. This leaves 30 million Americans, 21.2 million of them in rural areas, living in counties without a physician who can legally prescribe buprenorphine (Whitman, 2016).

Comparison of BMT with other MAT Approaches

Metadone

Initial research indicated that BMT produced signs and symptoms similar to morphine use. Unlike morphine, research suggested that buprenorphine produced little physical dependence and mild withdrawal symptoms, even when withdrawn abruptly. Further research showed limitations in the treatment, including higher dropout rates. This may be due to slower

induction rates, the maximum allowed buprenorphine dose being too low, or patients' ability to terminate BMT more comfortably than MMT because of buprenorphine's milder withdrawal effects. Unlike methadone, buprenorphine is not as potent as a full agonist and causes less analgesia and euphoria from its usage.

Studies find that buprenorphine would be effective when compared with other medications at achieving adolescence adherence and sobriety. Buprenorphine effects in comparison to methadone are dose-related and highly comparable. For instance, Shiner et. al. (2017) found that the demographic characteristic of patients receiving buprenorphine and those receiving methadone differed along some key aspects. "Patients who received buprenorphine were younger and more likely to be rural, white, and married. Patients who received methadone were older, urban, unmarried, from racial and ethnic minorities, and more likely to see substance abuse specialists" Shiner et al., (2017).

Studies have also shown that there are cost differences between buprenorphine and methadone, with buprenorphine costing almost twice as much as methadone on a yearly basis. For patients who take buprenorphine daily, its cost is \$4,000 to \$5,000 per year; daily methadone costs \$2,600 to \$5,200 per year. The cost for buprenorphine in implant form is \$8,000 to \$12,000 per year (BupPractice, 2017).

Peer Reviewed Research of Buprenorphine

Buprenorphine has been shown to reduce substance abuse at a similar rate to methadone, but with fewer negative outcomes. Studies have been performed comparing buprenorphine maintenance treatment (BMT), methadone maintenance treatment (MMT) and a placebo. Both BMT and MMT treatments showed similar amounts of improvements of well-being and

reduction in substance abuse when compared to the placebo (Maremmani, 2007). One study found there was a significant and visible benefit in utilizing buprenorphine over methadone. The researchers recommended the administration of buprenorphine as a treatment for methamphetamine craving during methamphetamine withdrawal (Ahmadi and Jahromi, 2016).

Two randomized controlled studies examined the efficacy of buprenorphine in combination with substance-use counseling. One study found that persons 13 to 18 years old prescribed buprenorphine for a two-week period were more likely to continue medical treatment compared to those taking clonidine, a drug that alleviates the symptoms of opioid withdrawal and is used to treat adolescents with attention deficit hyperactivity disorder and anxiety disorders (Ming, 2011).

One dilemma with buprenorphine is that, due to its opioid agonist characteristic, it has the potential to be misused. Another study found that, among adolescence, BMT has a greater chance of aiding adolescents in achieving long-term sobriety (a more effective treatment option for this age group). The following table provides a summary of peer reviewed studies related to the efficacy for buprenorphine as a MAT treatment option.

Table 4: Summary of the Peer Reviewed Studies and Their Findings Regarding the Efficacy of Buprenorphine as a Treatment in Medication-Assisted Treatment Options

Study Title	Citation	Research Question	Relative Findings
Substance Abuse and Quality of Life over 12 months among buprenorphine maintenance treated and methadone maintenance treated heroin addicted patients	<i>Journal of Substance Abuse Treatment</i> . Maremmani, et al. (August 12, 2006)	What are the effects of methadone treatment and buprenorphine treatment on retention in treatment, urine drug testing results, psychiatric status, social adjustment, and quality of life among patients involved in long-term treatment	The results of this study show statistically significant improvements in opioid use, psychiatric status, and quality of life between the 3rd and 12th months for both medications

Study Title	Citation	Research Question	Relative Findings
		with the cited medications?	
Comparing the effect of buprenorphine and methadone in the reduction of methamphetamine craving: A randomized clinical trial	<i>Trials</i> . Ahmadi, J. and Jahromi, L. (2016)	What is the effectiveness of methadone and buprenorphine in the treatment of methamphetamine withdrawal craving over a 17-day treatment period?	There was a considerable reduction in the craving within each of the two groups but also between the groups. Buprenorphine is a safe, effective, and valuable medication for decreasing methamphetamine craving during methamphetamine withdrawal and more effective than methadone. The study authors recommend consideration of buprenorphine as a treatment for methamphetamine craving during methamphetamine withdrawal.
Trends in Opioid Use Disorder Diagnoses and Medication Treatment Among Veterans with Posttraumatic Stress Disorder	<i>Journal of Dual Diagnoses</i> . Shiner, B.; et al (2017).	What is the prevalence of diagnosed opioid use disorder and use of medications for opioid use disorder in a large cohort of patients with Post Traumatic Stress Disorder (PTSD)?	Opioid use disorder is an uncommon but increasing comorbidity among patients with PTSD. Patients entering VA treatment for PTSD have their opioid use disorder treated with opioid agonist treatments in large and increasing numbers. The study authors recommend additional research both on the epidemiology of opioid use disorder among patients with PTSD and on screening for opioid use disorder.
Development of the Self-efficacy for Medication Adherence for Buprenorphine (SEMA-B) Assessment	<i>Dissertations</i> . Krug, M. (2012). http://epublications.marquette.edu/dissertations_mu/188	Can the Self-Efficacy for Medication Adherence – Hypertension scale be adapted into the Self-Efficacy for Medication Adherence – Buprenorphine (SEMA-B)?	SEMA-B has adequate internal consistency and temporal stability and is comprised of multiple underlying factors related to specific aspects of buprenorphine treatment for opioid addiction.

Study Title	Citation	Research Question	Relative Findings
Buprenorphine Treatment for Opioid Addiction in the Primary Care Setting: Predictors of Treatment Success and Failure. Doctoral Dissertation: Harvard Medical School	Harvard. Drago, J., 2015.	What objective tools are available for physicians to use to analyze a given patient's prognosis for addiction treatment with buprenorphine?	The overall buprenorphine one-year success rate of 43.8% was on par with other studies in similar settings. However, a given patient's individual chances of success can vary greatly depending on certain characteristics. These trends are evident when single variables are investigated in isolation—for example, injection drug users, patients who are unemployed, are Hepatitis C positive, and who do not participate in drug counseling are less likely to succeed.

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Appendix C: Naltrexone

Clinical Definition of Naltrexone

Naltrexone is sold under the brand names ReVia and Vivitrol (among others). It is an opioid antagonist; it covers the body's mu-opioid receptors, so it does not deliver any euphoric (opioid) effects and does not lead to patient physical dependency or withdrawal (PEW Charitable Trusts, 2016). Naltrexone fully blocks the effects of opioids and requires individuals to have withdrawn from opioids 7 to 10 days before injections (or they will face immediate withdrawal symptoms) (SAMHSA, 2016). The lengthy withdraw period has influenced the use of naltrexone for MAT, in part due to the low motivation of many opioid dependent patients to endure the required withdraw period (Bruce et al, 2010).

Naltrexone is a prescription drug that can be administered in (twice) daily doses; it also comes in other forms that have different dosage schedules. Naltrexone improves treatment retention and abstinence in patients with opioid use disorders when taken orally (SAMHSA, 2016).

Injectable versions of naltrexone (Vivitrol) are available and are administered monthly. Extended release injectable naltrexone was approved by the Federal Drug Administration (FDA) in October 2010. Injectable naltrexone was developed to improve adherence; it allows for an extended release (SAMSA, 2012). Injections deter patients from missing or skipping doses (which might occur if patients were on a daily naltrexone schedule).

In a study comparing daily oral doses of naltrexone to monthly injections, researchers stated "by providing continuous exposure to naltrexone for several weeks following intramuscular (IM) injection, this long-acting naltrexone formulation may offer therapeutic benefit to patients who have trouble adhering to the daily administration schedule necessitated by

oral naltrexone therapy” (Dunbar, 2006). One advantage of injectable vivitrol is that it does not produce a high feeling for patients (Levy et al., 2017).

A promising new technology is a sub-dermal implant that releases naltrexone over time (potentially up to 6 months). It is a small device embedded beneath the skin. Initial studies suggest this form of naltrexone may encourage patient retention. More research is needed, however, to establish the safety and efficacy of naltrexone implants (Larney, et al., 2014). Continual research regarding implanted forms of long-acting, sustained-release naltrexone formulation has been conducted in Russia. This form of naltrexone contains 1,000 mg of naltrexone that is slowly released into the body for 3 months after being inserted subcutaneously in the abdominal wall through a minor surgical procedure. The implantable naltrexone studied appears to be a safe and more effective alternative to oral naltrexone and a placebo implant in helping to prevent relapse. The limitation of patient adherence is no longer an issue and the blockade provided by the implant is unlikely to be over-ridden.

The effectiveness of naltrexone is dependent on the individual’s level of motivation and support system because it does not provide a negative reinforcement (withdrawal) when the medication is stopped (Bruce et al., 2010).

Delivery Mechanisms

Naltrexone can be prescribed by any health care professional and can be given in pill form (ReVia or Depade) daily or as an extended release intramuscular injection (Vivitrol) once a month. Neither tolerance nor dependence develops with naltrexone (Krupitsky, Zvartau & Woody, 2010).

Benefits of Naltrexone

Advantages of naltrexone are that it is not a narcotic, not addictive, and can be utilized for alcohol- and drug-related addiction treatment. Studies assessing the effectiveness of naltrexone maintenance treatment (NMT) have demonstrated improvement in treatment retention and increases in the number of negative urine drug tests for opioids. Further research needs to be conducted to determine the effectiveness of NMT over time (SAMHSA, 2016).

Naltrexone provides benefits to patients by preventing opioid-addicted individuals from feeling the effects of opioids. Naltrexone may be helpful in highly motivated and carefully selected patients. However, a potential downside of the drug is that patients treated with naltrexone may be at increased risk of overdose death should relapse occur (Kolodny, et al., 2015).

Barriers to Delivery of NMT

High Motivation to be Treated with Naltrexone and Non-Compliance

A common issue with NMT is patient non-compliance; this limits the drug's ability to prevent relapse (Ling et al, 2012). Supervision in combination with therapeutic support is associated with higher rates of compliance. Naltrexone does not have an opioid component so it does not stop opioid cravings. Because of this, patients using naltrexone need to be highly motivated and have strong psychosocial support for successful treatment (Center for Substance Abuse Treatment, 2004).

Patients who receive comparatively more supervision while taking naltrexone have higher rates of success in their treatment when compared with those that have fewer days of supervised activity. For instance, researchers observed patients receiving naltrexone living in a supportive community environment and found those who received supervision 6 to 7 days per

week were more likely to have remained in NMT as well as opiate-free after 6 months. However, those who received supervision and interaction less than 3 to 4 days a week were significantly more likely to have discontinued naltrexone compliance and returned to illicit drug use after the 6-month observation period (Hulse, et al., 2000).

To counteract non-compliance, some studies have explored incentivizing patients to comply with their medication regimen through reward systems. One reason that patients struggling with opioid addiction continue to use is that opioids stimulate the brain's reward centers. NMT blocks these feelings, which contributes to the high rates of non-compliance. Studies have been designed to provide a substitute reward system and positively reinforce continued compliance with a participant's medication and abstinence from drug use. Groups of participants who were offered rewards showed significantly higher rates of compliance with their NMT than those in the control group, with almost half of the subjects completing treatment while only about a quarter of the standard group completed the 12-week treatment period (Carroll et al., 2001).

Research has concluded that naltrexone has been well tolerated with few adverse effects (such as mild cases of nausea). Those taking naltrexone reported fewer days of substance use and had fewer positive urine drug tests. A meta-analysis study found that NMT combined with psychosocial therapy was more effective than placebo in reducing opioid use and being incarcerated during treatment (Stotts, et al., 2009).

Study findings demonstrate that primary problems associated with oral naltrexone MAT is low adherence to the medication and poor retention in individual treatment. When compared with the rates of those in treatment with buprenorphine, perhaps the low retention and dropout rates could be associated with the ability of those receiving the naltrexone to terminate treatment

services with little to no adverse effects. There are few severe ramifications associated with ending naltrexone treatment, such as severe withdrawal symptoms, that could influence a patient's actions (Bart, 2012).

Opioid antagonists are not recommended for withdrawal management, it is suggested they be utilized for relapse prevention and abstinence treatment (PEW Charitable Trusts, 2016). Naltrexone's availability in different forms has arisen in research demonstrating taking it as a pill results in poor compliance and inadequate retention in treatment among patients (Pecoraro, Ma & Woody, 2012).

Cost

Naltrexone provided in an Opioid Treatment Program (OTP), including drug, drug administration, and related services, is estimated to be \$1,176.50 per month or \$14,112 per year. This cost is more expensive than methadone treatment, including medication, and integrated psychosocial and medical support services (assumes daily visits) at \$126 per week or \$6,552 per year and buprenorphine (including medication and twice-weekly visits) at \$115 per week or \$5,980 per year (NIDA, 2018).

Side Effects

Serious (but rare) side effects of NMT can include severe vomiting or diarrhea, and nausea. For some users, naltrexone may cause liver damage, allergic pneumonia, and infections or skin reactions. Naltrexone users should avoid drinking alcohol and using sedatives, tranquilizers, opioids, and all illicit drugs (SAMHSA, 2016).

Comparison of NMT with Other MAT Approaches

Methadone

Naltrexone is a k-antagonist. Rather than stimulating the opiate receptors in the brain, it blocks their function. This reverses any effect that opiates would have on the user. It also does not do much to suppress feelings of withdrawal. Some evidence shows a suppression of cravings, (Comer et al., 2006), however, this may be a result of negative reinforcement, which is the mechanism that the drug is intended to work through. When users take an opiate, the naltrexone will counteract euphoric feelings or high and may make them feel sick. Unlike methadone, if use of naltrexone is discontinued, users will not experience symptoms of withdrawal as one would with agonist-based treatment.

Naltrexone differs from methadone in that it does not have the addictive properties or produce physical dependence (Center for Substance Abuse Treatment, 2004). Antagonist treatment also removes the risk of overdose, abuse, and diversion that is possible when using agonists like methadone (Krupitsky, et al., 2011).

Buprenorphine

Many individuals choose naltrexone treatment, because it binds and blocks opioid receptors, helping them to reduce their addiction better than buprenorphine and methadone, which activate opioid receptors in the body that suppress cravings (SAMSA, 2016).

In comparison to buprenorphine, studies have found that oral naltrexone response is inferior. There are no comparative studies between methadone or buprenorphine and extended release naltrexone. “It has been observed that the 6-month retention rates following extended

release naltrexone are like 1-year retentions in methadone maintenance and thus non-inferiority studies of extended release naltrexone are needed” (Bart, 2012).

It could be argued that naltrexone is a hypothetically better alternative for MAT; however, low adherence and retention rates plague the effectiveness of its treatment, making methadone and buprenorphine the more common options for treatment of opioid dependency (SAMHSA, 2016).

Methadone and Buprenorphine

Unlike methadone and buprenorphine, naltrexone does not exhibit behavioral reinforcement in individuals without opioid tolerance and does not induce respiratory suppression (Bart, 2012).

Table 5 provides a summary of peer reviewed studies related to the efficacy of naltrexone as part of MAT services.

Table 5: Summary of Peer Reviewed Studies and Their Findings Regarding the Efficacy of Naltrexone as a Treatment in Medication Assisted Treatment Options

Study Title	Citation	Research Question(s)	Relative Findings
The association between naltrexone compliance and daily supervision	<i>Drug and Alcohol Review</i> . Hulse (2000)	What was the 6-month outcome status in 300 heroin users (aged 13–47 years) who started naltrexone maintenance in a community-based outpatient treatment program?	Observed patients receiving naltrexone living in a supportive environment and supervision for shorter periods of time were significantly more likely to have discontinued naltrexone compliance and returned to illicit drug use.
Targeting Behavioral Therapies to Enhance Naltrexone Treatment of Opioid Dependence: Efficacy of Contingency Management and Significant Other Involvement	<i>Archives of General Psychiatry</i> . Carroll et al., (2001)	What are contingency management strategies to enhance treatment retention, medication compliance, and outcome for naltrexone treatment?	Behavioral therapies can be used to address specific pharmacotherapies' weaknesses, such as noncompliance.
Opioid dependence treatment: options in pharmacotherapy	<i>Expert Opinion on Pharmacotherapy</i> . Stott, A., Dodrill, C., & Kosten, T. (2009)	What is the effectiveness of opioid treatments (including opioid agonists, partial agonists, opioid antagonists, and alpha-2-adrenergic agonists) targeted toward either detoxification or long-term agonist maintenance?	Naltrexone maintenance combined with psychosocial therapy was more effective than placebo in reducing opioid use and re-incarceration rates during treatment.
Injectable, Sustained-Release Naltrexone for the Treatment of Opioid Dependence: A Randomized, Placebo-Controlled Trial.	<i>Archives of General Psychiatry</i> . Comer, et al. (February 2006)	What is the safety and efficacy of sustained-release naltrexone in treating opioid dependence?	No main effect was found between groups for any of the drugs evaluated besides cocaine.
Medication-assisted treatment of adolescents with opioid use disorders	<i>American Academy of Pediatrics</i> . Levy, et al., (September, 2016)	Does the extended release characteristic of naltrexone increase patient adherence?	Policies, attitudes, and messages that prevent patients from accessing a medication that can effectively treat a life-threatening condition may be harmful to adolescent health.

Study Title	Citation	Research Question(s)	Relative Findings
Comparison of pharmacological treatments for opioid-dependent adolescents: a randomized controlled trial	<i>General Psychiatry</i> Marsch, L. A., W. K. Bickel, et al. (2005).	What effective opioid treatments exist for adolescents?	Buprenorphine has a greater chance of aiding adolescents in achieving long-term sobriety.
Maintenance medication for opiate addiction: the foundation of recovery	<i>Journal of Addictive Diseases</i> . Bart, G. (2012)	What are the basic mechanisms of action and treatment outcomes for the three medications approved by the FDA for long-term treatment of opiate dependence: the opioid agonist methadone, the opioid partial agonist buprenorphine, and the opioid antagonist naltrexone?	Results indicate that maintenance medication provides the best opportunity for patients to achieve recovery from opiate addiction. Extensive literature and systematic reviews show that maintenance treatment with either methadone or buprenorphine is associated with retention in treatment, reduction in illicit opiate use, decreased craving, and improved social function.
The effectiveness of telemedicine-delivered opioid agonist therapy in a supervised setting	<i>Drug and Alcohol Dependence</i> . Eibl, et al, (July 2017)	How do treatment outcomes for in-person versus telemedicine-delivered opioid addiction treatment compare?	Telemedicine may be an effective alternative to in-person opioid addiction treatment and has the potential to expand access to care in rural, remote, and urban regions.
The Science and Practice of Medication-Assisted Treatments for Opioid Dependence	<i>Substance Use and Misuse</i> . Pecoraro, A., Ma, M., & Woody, G. (2012)	How has opioid addiction treatment evolved - from humanitarian to scientific and evidence-based, the evidence bases supporting major medication-assisted treatments and adjunctive psychosocial techniques, as well as challenges faced by clinicians and treatment providers seeking to provide those treatments.	
Systematic review of the safety of buprenorphine, methadone and naltrexone	<i>WHO International</i> . Gray, A. (September 2007).	How safe are methadone, buprenorphine, and naltrexone for MAT treatment based on research studies?	Summary conclusions were provided for opioid treatment drugs methadone, buprenorphine, and naltrexone.
Trends in Receipt of Buprenorphine and Naltrexone for Opioid Use Disorder Among	<i>Journal of Adolescent Health</i> . (February 2017).	How often do youth with opioid use disorder receive buprenorphine or	Medication receipt has increased from 2001 to 2014, but only 1 in 4 individuals received buprenorphine or naltrexone. Younger individuals,

Study Title	Citation	Research Question(s)	Relative Findings
Adolescents and Young Adults, 2000-2014		naltrexone, and how has this changed over time?	females, and black and Hispanic youth were less likely to receive a medication.

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