

**Incorporation of Medication-Assisted Treatment with Buprenorphine into
Primary Care Practice**

By

Alexandra Koch & Vishalee Patel

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First Reader: Paul Chelminski, MD, MPH, FACP

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Second Reader: Sara Koenig, MD, MBA

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I. Abstract

In 2015, over 3.8 million people reported misusing prescription pain medication within the last month and over 5.1 million people in the United States admitted to using heroin at some point in their lives. Despite the widespread prevalence of opioid abuse, evidence-based treatments, such as medication-assisted treatment (MAT), have yet to be made widely available and easily accessible to patients. This program plan was designed to recommend strategies to effectively incorporate MAT into the primary care setting. Interviews were compiled from key informants at primary care clinics with successful MAT programs in the Chapel Hill, North Carolina and surrounding area in order to develop a model of practice transformation that could be applied to a primary care clinic that does not currently provide MAT services. Ultimately, the key factors to consider when implementing MAT in the primary care setting include: provider buy-in, the availability of behavioral support staff, and support of key administrative and support staff.

II. Background

The United States is in the midst of an opioid use epidemic, affecting people of all ages, races and socioeconomic backgrounds. Over 100 Americans die each day due to opioid overdose¹. Fortunately, an evidence-based approach to treating opioid use disorder exists in the form of medication-assisted treatment (MAT). MAT describes the use of medications in combination with counseling and other therapeutic modalities to provide a more holistic approach to substance abuse treatment². MAT is the therapeutic modality of choice for opioid use disorder (OUD)³. The primary medications used for the treatment of OUD include methadone, buprenorphine (as monotherapy or in combination with naloxone), and naltrexone. Unfortunately, some providers remain reluctant to prescribe this treatment for various reasons which include but are not limited to:

- 1). Apprehension regarding working with a patient population perceived to be difficult;
- 2). Fear of negative patient outcomes;
- 3). Fear of patient capacity being oversaturated by those wanting MAT;
- 4). Not wanting to engage in the extra effort to receive a waiver to prescribe.

In order to comprehend how these medications work and to understand why many providers are apprehensive to prescribe one opioid to treat the addiction to another, it is necessary to have a basic understanding of the history of opioids in the US and the pathophysiology of OUD.

History of Opioid Use

Opium-based elixirs have been employed for both their euphoric and pain-relieving effects since before the Byzantine times⁴. Morphine was first developed in 1804 by Friedrich Serturmer of Paderborn, Germany as he isolated and neutralized the active ingredient of opium with ammonia. Morphine was initially referred to as “God’s own medicine” for its seemingly safe and long-lasting effects⁴. However, it was soon observed that users become dependent on the drug. Morphine was then distilled by Heinrich Dreser with the goal of producing a drug without the addictive side-effects of morphine: diacetylmorphine⁵. This was later commercially introduced by the Bayer Company of Elberfeld Germany as “Heroin”⁵.

Heroin was used briefly as a step-down cure for morphine addicts until it was noted that heroin withdrawal symptoms paralleled those of morphine⁵. Unfortunately, by 1903, the US was facing a massive heroin addiction crisis⁵. In 1914, the Harrison Narcotics Tax Act was passed, which required doctors, pharmacists and other prescribers of narcotics to register and pay a tax in order to attempt to curb the prescription of opioids⁵. This piece of legislation was one of the first of its kind to bring awareness to clinicians about the “highly addictive nature of opioids” and regulate their use⁴. However, the Harrison Act was more pernicious in that it made prescribing an opioid to a patient in order to treat opioid addiction illegal. This aspect of the Act would later be amended to allow for prescribing of methadone, and later buprenorphine, for opioid use disorder. A decade later in 1924, the Heroin Act was passed, which made the importation, manufacture and possession of even medicinal heroin illegal⁴.

The late 1990s marked an era of increased lobbying by the pharmaceutical industry to increase the use of opioids for all pain types, not limited to cancer and terminal illness⁵. This lobbying lead to the Joint Commission on Accreditation of Healthcare Organizations incorporating pain as the “fifth vital sign” and the training of healthcare providers in pharmacological pain management^{1,7}. Concomitantly, pharmaceutical companies began aggressive manufacturing, marketing, and promotion of opioid painkillers⁶. Opioid painkillers, such as oxycodone, were marketed as reliably safe and efficacious with minimal monitoring

needs in the acute pain setting⁷. This led to a sharp rise in the number of opioid prescriptions written by healthcare providers⁷. Additionally, more potent and dangerous synthetic opioids, such as fentanyl, were developed and introduced into the market by both medical and non-medical pathways⁷. The result of these changes has been the opioid epidemic in which the US is currently entrenched⁷.

Physiology of opioid use

Opioids are defined as “natural and synthetic substances that act at one of the three main opioid receptor systems: mu, kappa, and delta”⁸. Most opioids primarily act on the mu-receptor. Kappa and delta opioid agonists have been shown to activate pain inhibitory pathways with fewer unwanted side effects than mu-opioid agonists⁹. The development of pharmacologic agents targeting kappa and delta receptors is still being heavily researched⁹. The kappa and delta receptors are thought to require specific states of inflammation, that may not always be present, to yield efficacious results⁹.

Activation of mu-receptors leads to a cascade of reward, analgesia and withdrawal⁸. These receptors are located both centrally and peripherally⁸. Activation of central mu-receptors have the potential to cause respiratory depression, analgesia, euphoria, and miosis⁸. Secondary messengers, including cyclic adenosine monophosphate (cAMP), are acutely decreased by opioid receptor activation and are chronically upregulated with long-term opioid use, resulting in a need for increased dosing to achieve the same analgesic effect⁸.

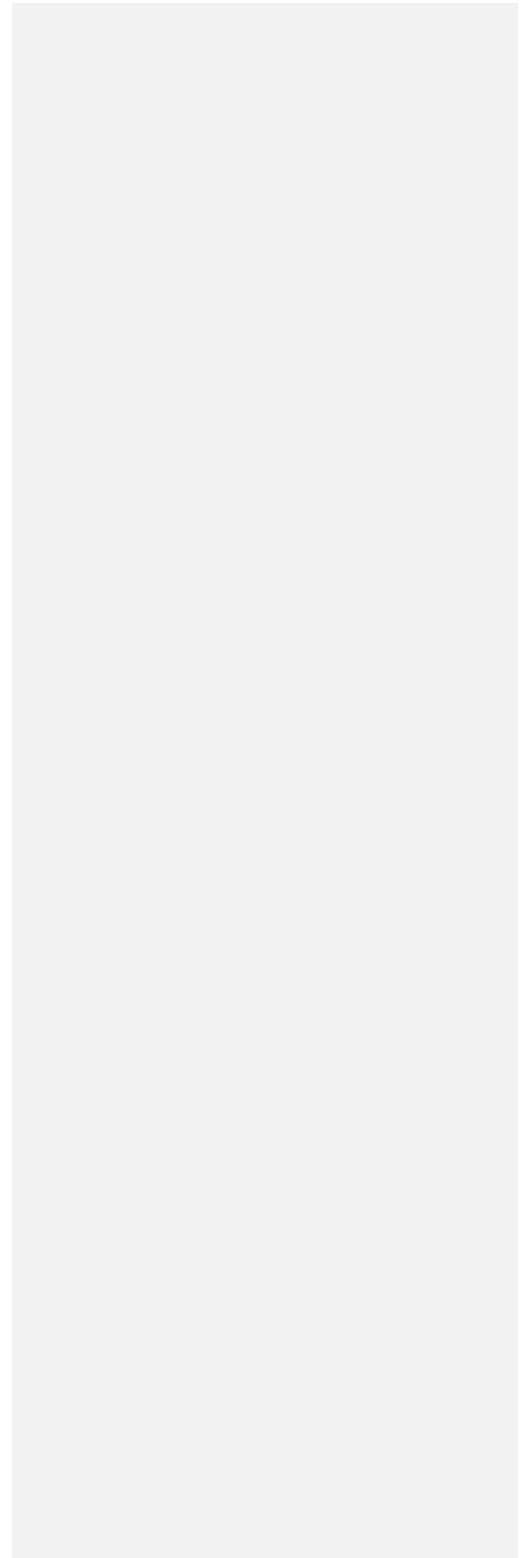
A plethora of compounds and subcategories fall under the umbrella term of “opioids,” including heroin, opium, and prescribed opioids. Prescribed opioids consist of subclasses including opiates (e.g. morphine and codeine- opioids containing alkaloid compounds), semi-synthetic synthetic opioids (e.g. oxycodone and hydrocodone), and synthetic opioids (e.g. fentanyl and methadone)⁸. In addition to these subclasses, opioids are further classified as agonists, partial-agonists or antagonists depending on their receptor binding and affinity⁸. The most commonly abused opioids (e.g. hydrocodone, oxycodone, codeine) are full agonists³. Broadly, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) incorporates opioid abuse and opioid dependence into one comprehensive disorder: opioid use disorder (OUD)³. OUD is a type of substance use disorder, defined as the state when “recurrent use of alcohol and/or drugs causes clinically and functionally significant impairment”, and “can

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involve misuse of prescribed opioid medications, use of diverted opioid medications, or use of illicitly obtained heroin”³. The DSM-V criteria emphasizes that the hallmarks opioid use disorder is use that leads to clinical impairment and personal harm in essential domains of daily life. We present the criteria in Text Box I.

Text Box 1



“A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring in a 12-month period”³:

1. Opioids taken in larger amounts or over a longer period than was intended;
2. A persistent desire or unsuccessful efforts to cut down or control opioid use;
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects;
4. Craving, or a strong desire or urge to use opioids;
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home;
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids;
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use;
8. Recurrent opioid use in situations in which it is physically hazardous;
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance;
10. Tolerance, as defined by either of the following:
 - a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect;
 - b. A markedly diminished effect with continued use of the same amount of an opioid;

*Note: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.
11. Withdrawal, as manifested by either of the following:
 - a. The characteristic opioid withdrawal syndrome (refer to Criteria A and B of the criteria set for opioid withdrawal);
 - b. Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms;
12. The severity of OUD can span from mild to severe, and treatment varies depending on this severity.
 - a. Mild: two to three criteria are met;
 - b. Moderate: four to five criteria are met;
 - c. Severe: six or more criteria are met.

*Adapted from DSM-5

Medication-assisted treatment (MAT) of opioid use disorder

Three compounds are utilized in medication-assisted treatment of OUD: methadone, buprenorphine, and naltrexone. Methadone is a full opioid agonist and has been used since the

1960s as maintenance therapy for moderate-severe OUD³. It is also used to treat severe chronic pain. When used for OUD, methadone may only be dispensed through a Substance Abuse and Mental Health Service Administration (SAMHSA) certified opioid treatment program (OTP)¹⁰. Typically, a patient becomes involved in an OTP—either inpatient or intensive outpatient—and is dispensed a daily dose of methadone determined to be appropriate for their prior opioid use by the medical director of the OTP. The patient is observed swallowing the methadone dose each day to ensure there is no diversion of medication. After a period of treatment stability, patients may be allowed to take doses of methadone at home but are still required to return to the OTP for regular follow up visits. One aspect of methadone treatment at OTPs that is problematic is that the medication is not technically prescribed by the OTP, but rather it is only dispensed. The methadone is also not reported to the state controlled substance registry. This means that outside providers cannot verify whether or not a patient is being treated with methadone at an OTP. According to a key informant, “this creates headaches because it provides incomplete clinical information that is essential to medical decision-making.”

Extensive research supports the efficacy of methadone treatment. In fact, it is marginally more efficacious in treating OUD compared to buprenorphine¹¹. Methadone is the first line treatment of OUD in pregnant patients, as there is a long history of use and it has been found to be safe for mother and fetus³. However, recent data now supports the use of buprenorphine during pregnancy. There are many limitations to the use of methadone. Its action as a full opioid agonist is a major concern, as the drug does have abuse potential and is more prone to cause lethal overdose due to respiratory depression when compared to buprenorphine. For this reason, methadone is a DEA Schedule II drug. Similar to other full agonists, chronic use of methadone can lead to hyperalgesia (abnormally heightened sensitivity to pain) in patients¹¹. Some studies have shown a “weak but significant risk” for cardiac arrhythmias, such as torsades de pointes, when taken as prescribed or in overdose at doses of up to 300 mg/day or above^{16,11}. Pathophysiology of these associated cardiac arrhythmias is not well-understood. In addition to the pharmacologic risks associated with potent full opioid agonists, there are regulatory and logistical constraints to providing methadone maintenance to patients with OUD. These probably constitute the largest obstacle to more widespread use of methadone for OUD. By law, treatment with methadone may only be obtained at an OTP under direct supervision.

The newer drug, buprenorphine is a partial opioid agonist that was discovered in 1966 but has only been FDA approved in the United States for OUD since 2002¹². The drug is also approved to treat severe pain and has been approved in the US for this indication since 1985¹². Buprenorphine may be prescribed by any clinician who has undergone required training and obtained a waiver from SAMHSA, in OTPs, clinician's offices, or other appropriate settings¹¹. Available formulations for the treatment of OUD include a sublingual tablet, sublingual or buccal film strips--with or without naloxone--and a long-acting implantable subdermal buprenorphine implant. The naloxone combination is used to prevent diversion of the drug. Naloxone has poor oral bioavailability and, if taken appropriately, only the buprenorphine component will be active. However, if the drug is injected, users will experience immediate opioid withdrawal as naloxone displaces buprenorphine or other opioids in the body from mu-receptors. Studies have shown buprenorphine to be nearly as effective as methadone in treatment of moderate-severe OUD and current recommendations do not prefer methadone over buprenorphine¹¹. Buprenorphine is safer than methadone, as its partial opioid agonist activity decreases the risk for abuse potential and lethal overdose due to respiratory depression. Furthermore, a major advantage of buprenorphine is the increased access to treatment for patients in comparison to methadone.

Naltrexone is a third option for treating OUD. In contrast to methadone and buprenorphine, naltrexone is a full opioid antagonist. It has been approved for the treatment of OUD since 1984¹¹. Naltrexone is not DEA scheduled and may be prescribed by any clinician in any appropriate setting. It is also used for alcohol use disorder and weight loss. Formulations include daily oral dosing and monthly long-acting injectable naltrexone. Current guidelines recommend the use of naltrexone for mild OUD or for highly motivated patients¹¹. Unlike buprenorphine or methadone, a patient must abstain from opioid use for at least 7-10 days in order to prevent the very unpleasant symptoms of precipitated withdrawal. This is one reason why naltrexone is not used as much as buprenorphine or methadone.

Prevalence of OUD

OUD affects people of all races, socioeconomic backgrounds, and ages. Risk factors for developing OUD among patients prescribed opioid analgesics include younger age, more severe pain, co-occurring mental disorders, and prior history of substance use disorder¹³. According to

the 2016 SAMHSA National Survey on Drug Use and Health (NSDUH), an estimated 11.8 million people in the US misused opioids in the past year, “including 11.5 million pain reliever misusers and 948,000 heroin users.” Approximately 2.1 million people suffered from OUD in 2016¹³. The rate of past year opioid misuse in 2016 was highest among people aged 18-25, at 7.3% of the population of that age group¹³. According to the NSDUH, among the main reasons cited for abusing prescription opioids in all age groups, 62.3% of participants noted “relieving physical pain” as their main reason¹³. In this same study, about half of participants obtained these medications from family or friends, whereas only 37.5% obtained their prescription through the medical system.

Over 100 million Americans suffer from chronic pain, making it a healthcare problem that affects more people than diabetes, heart disease, and cancer combined¹⁴. Some healthcare providers fear that chronic pain patients’ needs are being unmet due to “opiophobia,” an increasingly prevalent “phenomenon in which exaggerated concern about the risks associated with opioids prevent appropriate medical use of opioid analgesics”¹⁵. This can lead some chronic pain patients to seek relief outside the medical system, such as obtaining pain medications from friends or family, or trying illicit opioids for relief. Upon interviewing people who transitioned from abusing prescription opioids to heroin, it was noted that most users chose heroin due to its lower cost and easy availability¹⁶. Some users also attributed it to their physicians being “less willing to prescribe opioids as well as to increased attention to the issue by law enforcement”¹⁶.

Compared to heroin use rates from the 2014 and 2015 NSDUHs, heroin use in 2016 has remained stable¹³. While heroin use remained stable, overdose rates from synthetic opioids (e.g. fentanyl and fentanyl analogues) doubled between 2015 and 2016¹⁷. This is likely due to the influx of fentanyl and fentanyl analogues like carfentanil into the black market, specifically between July to December of 2016 in the Northeastern US¹⁸. Heroin users unwittingly use these chemicals and overdose, as fentanyl and carfentanil are exponentially more potent than heroin.

Impact of Opioid Use Disorder

According to the National Institute on Drug Abuse, as of March 2018, more than 115 Americans die daily due to opioid overdose¹. This number does not take into account the number of patients that die or suffer from complications from intravenous drug use (IVDU), such as HIV/AIDS, hepatitis C, or other infectious sequelae of IVDU. Also, not included in this

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statistic are the number of babies that suffer from neonatal abstinence syndrome due to maternal opioid use during pregnancy or die of prematurity secondary to maternal opioid use. The economic burden of the current US opioid epidemic is estimated by the CDC to be “\$78.5 billion a year, including the costs of healthcare, lost productivity, addiction treatment, and criminal justice involvement”¹.

Given the thousands of opioid overdoses and heavy economic burden of the opioid epidemic, President Donald Trump declared the opioid epidemic a “national public health emergency” on October 26th, 2017¹⁹. This declaration allows the federal government to create temporary positions within the Department of Health and Human Services (HHS) to focus on the opioid crisis and, in theory, makes federal public health funding more accessible to states in need. Many public figures believe that this response is not sufficient, and they have criticized the federal government for not classifying the opioid epidemic as a “National Emergency” under the Stafford Act. This would unlock supplemental funds from the Federal Disaster Relief Fund to be used to fight the opioid epidemic, rather than redeploying funds from existing federal programs. Despite these criticisms, the declaration does emphasize the importance of improving access to care for those with OUD. The declaration states that the federal government will work to “expand access for certain groups of patients to telemedicine for treating addiction; provide new flexibilities within HIV/AIDs programs...” and “announce a new policy to allow treatment at more facilities”¹⁹.

Barriers to Care

A problematic finding from the 2016 NSDUH is that while 26 million people ages 12 and older were noted to have a “need for substance use treatment in the past year,” only 1.4% of this population received any substance use treatment¹³. That means that only, 360,000 patients have access to SUD care. Many patients who are dependent on prescription opioids and seeking treatment note a variety of barriers to access: high costs, limited access to facilities, and lack of information²⁰. These barriers are substantial. Relieving them will require a determined coordinated approach and systematic set of solutions. These include the following: systems that ease financial burdens on patients; open communication between healthcare providers and patients in order to decrease stigma, promote education, and deter fear of being reprimanded and losing access to pharmacotherapy²¹. Clinic-based interventions—such as naloxone prescription

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and counseling on how to reverse overdose using naloxone for those prescribed chronic opioid therapy and access in the primary care setting to MAT—have the potential to reduce the occurrence of overdose related deaths²². Despite MAT’s potential to produce improved patient outcomes, uptake of office-based MAT by physicians has been disappointing. Both patient and healthcare provider factors explain this.

For patients, **cost** presents a significant barrier to accessing care for those with OUD. These costs are not simply limited to the actual cost of the medication but include the cost of physician visits, transportation, counseling services, lab testing, emergency detoxification, and ongoing service referrals by the prescribing physician. The extent of the coverage of these costs by insurance is widely variable. The Affordable Care Act (ACA) has included at least some level of services directed at Substance Use Disorders as a part of its Essential Health Benefits. Essential Health Benefits are a set of 10 categories that health insurance service plan must cover under the ACA. Commercial insurance coverage of OUD treatment depends on several factors including “medical necessity, whether medications are covered, if there is a required co-payment, if buprenorphine is on the plan’s approved medication list”²³.

ACA provisions have also broadened Medicaid coverage for adults and state capacity to address the opioid epidemic. Reports from the Kaiser Foundation indicate the Medicaid currently covers 38% of nonelderly adults with opioid addiction. A 2013 review of Medicaid Policies showed that 50 Medicaid programs have included buprenorphine-naloxone in their approved preferred drug lists. For those that are uninsured, access to affordable provisions of MAT depends on whether local community clinics offer these services in the first place. The out of pocket cost of a 30-day supply of buprenorphine-naloxone is approximately \$150, but can increase to as much as \$600 depending on the dose²⁴. This cost can also vary greatly, depending on the drug prescribed (generic vs. brand, combo product vs. mono product, etc...). While insurance plans vary, insurance coverage of MAT for OUD generally imposes greater restrictions compared to MAT for alcohol use disorder²⁵.

Goals of Research

The primary goal of this project will be to focus on a needs assessment evaluating the following question: How can MAT with buprenorphine be better incorporated into the primary

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care setting, and what barriers exist in accomplishing this? “Primary care” will be defined following the definition of the American Academy of Family Physicians in Text Box 2.

Text Box 2

Primary care is that care provided by [clinicians] specifically trained for and skilled in comprehensive first contact and continuing care for persons with any undiagnosed sign, symptom, or health concern (the “undifferentiated” patient) not limited by problem origin (biological, behavioral, or social), organ system, or diagnosis.

Primary care includes health promotion, disease prevention, health maintenance, counseling, patient education, diagnosis and treatment of acute and chronic illnesses in a variety of health care settings (e.g. office, inpatient, critical care, long-term care, home care, day care, etc.). Primary care is performed and managed by a personal [clinician] often collaborating with other health professionals, and utilizing consultation or referral as appropriate. Primary care provides patient advocacy in the health care system to accomplish cost-effective care by coordination of health care services. Primary care promotes effective communication with patients and encourages the role of the patient as a partner in health care.²⁶

This evaluation will examine primary care clinics that have successfully incorporated MAT into practice to determine what barriers these clinics faced, how these barriers were overcome, and what factors led to the clinics’ success. These clinics are UNC Aycock Family Medicine and Piedmont Health Chapel Hill Community Health Clinic. This assessment will be done utilizing key informant interviews of MAT providers at the aforementioned clinics. A brief assessment will also be conducted of a primary care clinic that plans to incorporate MAT into their practice, Piedmont Health Prospect Hill Community Health Clinic. Key informant interviews will be conducted of providers at this clinic to evaluate expected barriers and to determine strategies to overcome these barriers.

III. Methods

Published Literature Review

A preliminary literature review was conducted to better understand the extent and scope of current research efforts being made regarding efficacious implementation of MAT into the primary care setting. Search engines that were used included: PubMed, Google Scholar, Cochrane Library, and EmBase. MeSH Terms used included the following:

1. Buprenorphine-naltrexone
2. Suboxone
3. Extended-release naltrexone
4. Medication-assisted treatment
5. Opioid use disorder
6. Primary care
7. Barriers
8. Interdisciplinary management
9. Addiction medicine
10. Behavioral medicine
11. Medication-assisted treatment
12. Opiate substitution treatment
13. Opioid partial agonists
14. Opioid-related disorders
15. Substance-related disorders

The literature review provided foundational knowledge regarding the pathophysiology, epidemiology, and treatment options of opioid-use disorder and the utilization of MAT. The literature review also revealed the feasibility of incorporating MAT into primary care and the barriers that exist to do so. A variety of implementation models were explored during the literature review, including the Office-Based Opioid Treatment (OBOT) model, Massachusetts nurse care manager model, Hub and Spokes model, and ED Initiation of OBOT model (Table 1)²⁷. See Table 2 for a summary of systematic reviews analyzed during the literature search. Quality of systematic reviews was analyzed utilizing AMSTAR bias tool (Appendix B).

Key Informant Interviews

We identified 6 key informants and interviewed them during three separate interviews and an email questionnaire. Key informants were selected based on their expertise and experience using MAT in a primary care setting. These key informants were comprised of physicians (family medicine, internal medicine and addiction medicine, all practicing in primary care settings), social workers, and a care manager.

Interviews were loosely structured and were conducted by two researchers, with one facilitating the conversation with primarily predetermined questions and the other taking notes. Predetermined questions addressed MAT models of care, important factors to successfully establishing MAT care at the clinic and patient level, and barriers to incorporating MAT into the primary care setting as ascertained from the preliminary literature review (Appendix A). Additional questions were asked during the interview based on informant responses. One to three key informants were involved per interview, including at least one licensed or soon-to-be-licensed MAT provider per clinic. Interview 1 involved a physician who has not yet incorporated MAT into his practice. Interviews 2 and 3 included two separate primary care clinics that utilize differing models to incorporate MAT into patient care. Audio recordings of these interviews were transcribed, analyzed, and summarized by each researcher following each interview. The email questionnaire was sent to two key informants at one primary care clinic that had not yet implemented MAT into their practice but had plans to begin doing so in the near future. Answers to each questionnaire were analyzed and summarized by each researcher following the collection of all responses.

Intervention Mapping for Program Plan Development

The ultimate goal of this publication is to develop a program plan for primary care clinics planning to incorporate medication assisted treatment into practice. In order to develop this program plan, the authors utilized the Intervention Mapping Protocol by Bartholomew et al²⁸. The Intervention Mapping website describes the protocol as “a planning approach that is based on using theory and evidence as foundations for taking an ecological approach to assessing and intervening in health problems and engendering community participation”²⁹. The approach consists of six basic steps, involving conducting a needs assessment, creating logic models for both the problem and the proposed change, program production and evaluation (Table 3). The authors conducted the steps described in Table 3 to produce a program plan suitable for the target users.

IV. Results

Literature Review Findings

Results from our literature search provided background knowledge to the authors regarding OUD and the use of MAT. As discussed above, the advantages and disadvantages of different models of care were reviewed²⁷. Two systematic reviews were examined during the literature search, a 2011 review by Amato et al and a 2017 review by Gowing et al^{32,33}. Amato et al reviewed 35 randomized controlled trials and controlled clinical trials of patients with OUD to evaluate the effectiveness of psychotherapy plus agonist maintenance treatment versus agonist maintenance treatment alone³². Agonist treatments utilized in the reviewed studies included methadone, buprenorphine, and LAAM. The authors found that adding psychosocial interventions to standard agonist maintenance treatment did not offer any statistically significant benefit, in terms of retention in treatment, abstinence from opioid use, compliance, and psychiatric symptoms. The primary limitations of this systematic review is that most of the studies reviewed were conducted at specialty treatment centers (as opposed to primary care clinics). This limitation is important, because it limits generalizability of the findings. Patients of an experienced addiction medicine provider at a specialty treatment center may not benefit from adding psychosocial interventions to medication treatment as much as patients at a primary care clinic.

Gowing et al analyzed 27 randomized controlled trials of patients with OUD to evaluate whether there is a difference in treatment completion rates in patients treated with buprenorphine maintenance therapy versus methadone maintenance therapy³³. The review did not find statistically significant differences in days of treatment completed or rates of adverse effects between either therapy. Limitations of the systematic review included varying routes of administration and dosages of buprenorphine, selection bias and early cessation in a few studies, and a primarily male study population.

Key Informant Themes

Provider Awareness and Motivation

Providers surveyed cited lack of general awareness regarding MAT, time constraints to receiving training for MAT, fear of negative patient outcomes, and lack of motivation as significant barriers to pursuing an MAT waiver. The need to treat chronic pain patients' substance dependence is also something that was cited

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as intimidating by the healthcare providers surveyed. Additionally, providers cited a general mistrust and wariness of a “fix-all” solution that buprenorphine has been marketed as because this is how opioids were marketed initially in the 1990s as the pharmacologic solution for chronic pain. In order to prescribe or dispense buprenorphine products in the treatment of OUD, clinicians are required to complete at least 8 hours of training (24 hours for advanced practice providers) and then apply for an MAT waiver³⁰. This training provides education about the drug and prescriber practices. Key informants that attended this training found it to be very informative for their practice.

Medicine is a changing and imperfect science. Clinicians are constantly facing the challenging task of staying up to date with advances in treatment options. This is especially true in primary care clinics where providers are managing large volumes of patients with many comorbidities, with short visit times and limited support resources. As the opioid crisis reaches monumental heights—enough so to be labeled as a national public health emergency—our key informants see the incorporation of treatment options such as MAT as an inevitable move in the primary care sphere. One key informant likened the apprehension of addressing OUD in the primary care setting to the treatment of mental health disorders such as depression. OUD, similarly to depression, often necessitates treatment with medication as well as adjuvant psychotherapy in order to be successful.

Identifying a lead provider who is familiar with the waiver training and the complexities of prescribing buprenorphine to high-risk patients is crucial to implementing this shift in the primary care setting. The providers interviewed found the waiver training extremely effective, but also cited having colleagues experienced in MAT as a valuable resource. For healthcare providers that may not have colleagues within their clinic that are experienced with MAT, key informants cited the importance of seeking local resources to guide MAT implementation efforts. Within the Chapel Hill/Carrboro community, the UNC ECHO for MAT project was cited as resource that provides such support. UNC ECHO for MAT is a project that partners with clinics to build internal capacity to

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incorporate MAT within the outpatient setting. UNC ECHO utilizes a multi-faceted approach to develop individualized clinic plans to train staff internally and to also build an external community support network to provide greater patient access to referrals and community resources ³¹.

In addition to utilizing knowledgeable and experienced MAT providers, having providers passionate about the treatment of OUD with buprenorphine is crucial. As our key informants mentioned, patients with OUD are complex and sometimes “difficult.” If a provider is not highly motivated and especially interested in working with such a population, successful incorporation of MAT into their practice’s standard set of services is unlikely to occur.

Stigma

A key component to increasing motivation to treat such patients is stigma reduction regarding OUD. The issue of stigma was repeatedly noted by our key informants as a significant barrier to be overcome. Key informants recollect that many providers at their respective clinics had concerns that implementing an MAT program would bring “difficult patients”. According to our key informants, providers and staff at the clinic have expressed concerns that “they don’t want these patients in the waiting room” and “worry that the practice will become a methadone clinic,” highlighting the generalized way in which many people view addiction, OUD, and chronic pain patients. Providers surveyed noted concern that once they become MAT trained that their patient panel will consist entirely of this type of patient population and the challenges that come with treating a patient that has a diagnosis of substance use disorder. These challenges were cited as non-compliance, mistrust, and “drug-seeking” behaviors.

One key informant compared patients with OUD to patients with any other chronic illness. For instance, treating patients with diabetes requires addressing issues such as medication and diet noncompliance and the often-psychosocial factors behind such noncompliance. Key informants emphasized the necessity of reframing addiction as a chronic neurologic illness, rather than a moral failing. Physiologically, opioids change the reward system of the brain and lead to “side-

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effects” such as “drug-seeking” behavior. Key informants emphasized the need to think of the negative behaviors of those with OUD as a manifestation of their chronic neurological illness. Thinking of substance use disorders in this way allows healthcare providers to have healthier therapeutic relationships with their patients in which they are able to establish boundaries, expectations, and not feel personally affected by non-compliance. Key informants emphasized that MAT with buprenorphine may promote remodeling of the brain through reduction in cravings which allows for the establishment of normal reward circuits. Unlike methadone, people on buprenorphine have minimal functional limitations, according to one key informant. Ultimately, according to a key informant, MAT with buprenorphine can allow patients to reintegrate into society as a productive and functional citizen.

Appropriate Patients and Referral Structures

Due to the high prevalence of OUD, MAT programs are extremely popular in the community. Invariably, most primary care clinics serve patients that are suffering from OUD, whether this condition is being directly treated or not. According to a key informant at a large area family medicine clinic, providers are “seeing these patients anyway.” Key informants recommended that providers begin incorporating MAT into their care by identifying which of their current patients may benefit from MAT. Starting with patients with which a clinician has already built rapport allows for a more seamless transition to providing MAT.

When accepting new patients who have a desire to try MAT, key informants emphasized the capacity that clinicians have in choosing the patients that they deem appropriate for MAT therapy in the primary care setting. Key informants cited patient motivation to recover and complexity of a potential patient’s substance use disorder as two of the most influential factors as to whether a patient is accepted into their programs. For a novice MAT provider, it is recommended to have specific criteria for selecting patients that the provider feels could be safely managed on MAT. Patient motivation may be a factor that is difficult to quantify. Having a screening and application process may be useful in

discerning patients that have the self-initiative. Also, patients may have to wait weeks to months for an MAT appointment. This wait often “weeds out” less motivated patients, according to our key informants. However one key informant points out that “this “weeding-out” approach implicitly has more risk of patient harm and death due to delay in treatment.”

One aspect of providing MAT in primary care that our key informants highlighted as especially important is a practice having the ability to discern which patients are appropriate to accept into the program and which patients necessitate referral to a higher level of care. Just as with patients with other chronic illnesses, Key informants emphasized the ability that MAT providers have to refer patients with OUD to higher levels of care if needed.

Adequate Support Staff

Key informants varied in terms of the necessities of support staff which they found to be adequate in establishing and maintaining an MAT program within the primary care setting. Generally, key informants found that staff education prior to introducing MAT into the primary care setting is important. Explaining to clinic staff the basics of MAT and relevant protocols (and modifications) is crucial. Emphasizing the need to treat these patients in a humane way is critical and sharing success stories of patients who have benefited from MAT may be helpful, according to key informants.

Having an in-house social worker within a primary care clinic was cited as an invaluable resource to implementing MAT. Responsibilities of an MAT social worker or psychologist would include conducting screening interviews for patients interested in beginning MAT, conducting brief follow-up therapy as needed, and disseminating resources to patients to save MAT providers time. An in-clinic social worker or psychologist allows MAT prescribers to ultimately see more patients, according to our key informants. Having established adjuvant behavioral health resources (whether located in-clinic or nearby) was cited as an essential component to address co-occurring mental health disorders in patients with OUD. An in-house social worker or psychologist is able to not only assist

with connecting patients to behavioral health resources, but also in handing-off key information regarding patient history and medical care to the MAT provider to allow for seamless and informed continuity of care.

Institutional Buy-In/Cost

On an institutional level, “buy in” is an essential component to the incorporation of MAT in the primary care setting. Buy-in is not only essential at the level of high-level administration, but also for physicians working at the clinic and support staff. Though many community practices are not “profit driven,” such practices do operate on very tight budget margins. MAT in primary care must be implemented in a fashion that does not undermine already tenuous fiscal sustainability. A financial model that demonstrates program sustainability, and profitability to a certain extent (at minimum, no sunken costs) is an important aspect to consider when vying for institutional buy-in. Depending on the access to insurance of the MAT patient population at a specific institution, organizations may need to consider a plan in terms of absorbing potential costs from services that uninsured patients may incur.

Program Planning Steps

Logic Model of OUD, Plan Objectives, and Logic Model of the Change

As mentioned previously, OUD is a widespread problem that affects various populations and impacts not only the user’s quality of life, but also the overall health of the community. A logic model for the problem of OUD is included in Appendix C. While the entire United States is currently entrenched in an epidemic of opioid use and dependence, this program plan is most applicable to the treatment of adult patients in primary care practices in the Piedmont region of North Carolina. All of our key informants practice in this area and recommendations are based on this environmental/population context. Other regions of the state and country have different populations and environmental determinants that may make this program plan less effective.

The ultimate goal of this program plan is to incorporate MAT into primary care practice; in effect, reaching more patients suffering from OUD with an evidence-based treatment method and making treatment more easily obtainable and affordable. Secondary outcomes of this plan are: increasing the number of patients with OUD in remission, decreasing the number of lower acuity patients seen by specialty practices (e.g. psychiatry), decreasing the cost of care by offering treatment by primary care providers, decreasing negative health outcomes of untreated OUD (e.g. needle-borne illnesses, bacterial complications, cardiac complications, mental health issues, etc...), among others. Expected outcomes of the program plan are described in Table 4.

In order to accomplish the primary goal, attain the desired secondary outcomes and observe the expected outcomes of this program plan, it is necessary that change occur at different points in the healthcare system. The performance objectives for the change outcomes are broken down by ecological level: personal (patient), interpersonal, organizational (the participating healthcare practice), community, and societal. The term “performance objectives” refers to what specifically needs to be done in order for the expected outcomes to be met. These performance objectives are described in Table 4. The italicized text in Table 4 refers to the ecological levels, outcomes and objectives highlighted as most relevant to this program plan. The performance objectives listed in Table 4 are not all-inclusive, and certainly additional factors are patient dependent.

A logic model for the proposed change is included in Appendix D. Key components of the logic model include change objectives, behavioral and environmental change outcomes, and the desired health problem outcome. Change objectives include treatment co-occurring mental and physical health conditions (including chronic pain), prescription monitoring and appropriate prescribing, education, among other factors (See Appendix D). Behavioral change outcomes include preventing initiation and abstinence of substance abuse, among others. Environmental change outcomes occur on the personal, community and societal levels. Personal-level change outcomes include healthier, drug-free relationships. Community-level outcomes include safe living spaces, drug-free

workplace, among others. Societal-level outcomes include improved socioeconomic status and freedom from discrimination. The overarching health problem outcome is remission from OUD.

Program Plan Design, Production and Implementation Plan

Different models exist of MAT implementation in the primary care setting, as discussed previously (see Table 1). The institutions at which our key informants practice did not specifically model their MAT prescribing around an existing model of care. One of the clinics that had incorporated MAT into their workflow functions similar to the Office Based Opioid Treatment model with the assistance of a social worker care manager for screening interviews and psychotherapy. The other clinic that has incorporated MAT into practice also functions similar to the Office Based Opioid Treatment model, although the MAT prescriber at this practice is not a primary care physician but instead an addiction medicine specialist practicing at a primary care office. These differences highlight the idea that there are various methods to tailor the specific model by which MAT is offered at an individual clinic to the intricacies of that specific clinic. Additional important themes in offering MAT in the primary care setting noted by our key informants are discussed above in the section “*Key Informant Interview/Questionnaire Themes.*”

Potential users of this program plan include primary care practices treating adults with OUD in which at least one provider will offer MAT. Ideally, a practice would have multiple providers offering MAT. However, based on the success of one of the clinics examined in which only one provider offers MAT, we propose that it is possible to provide quality care to patients with OUD as long as at least one provider offers MAT and is supported by the clinic. Desired outcomes and performance objectives for program use are italicized in Table 4. Prior to embarking on any of the following recommended steps (Table 5) for incorporating MAT into practice in a primary care office, an interested practice should develop a financial model addressing how MAT will be offered in a cost-effective manner. As previously discussed, many patients who need MAT are

Commented [CPR12]: I think that the prevailing attitude is that a sustainable MAT program must have at least several prescribers who are waived and active at any given time. Did this surface in your interviews? Although the ECHO project does strive to create a community of waived practitioners, clinical decisions for any group of patients are ultimately delivered at the practice level. Clinical care is not sustainable without redundancy and overlap of services. Think of it this way, would it be possible for me to deliver excellent diabetes care (which to my astonishment the statistics show I do) without a large element of clinic support, including other providers licensed to prescribe? No. This is consistent with your contention that OUD is a chronic disorder. Bottom line, for sustainable, longitudinal care, a single MAT provider is not sufficient in any given clinic.

either underinsured, uninsured, or otherwise financially burdened. The practice will need to determine how it will absorb the costs of such patients. Providing MAT need not be economically profitable, but offering such care should not be significantly burdensome or costly. This paper will not address a detailed economic strategy for implementing MAT effectively, as that is beyond the scope of this practice transformation model.

Based on the considerations of providing MAT in the primary care setting highlighted by our key informants and background research on the topic, the authors recommend that a practice base their MAT practice on the Office Based Treatment Model and tailor treatment to unique clinic and patient needs (Table 1). The practice should also strongly consider hiring a social worker or psychologist, to provide in-house psychological services and screening interviews. If no behavioral health professional will be available to patients at the clinic, a relationship must exist between the MAT provider and a local behavioral health professional such that patients can be easily referred for timely service as needed. This aspect of our proposed practice transformation model is based on the recommendation of key informants to have easily accessible psychological services. As previously mentioned, the finding by Amato et al that psychosocial interventions do not add a statistically significant benefit to medication treatment is not generalizable to primary care clinics.

In order for a clinic to effectively implement MAT into its workflow, it is critical that potential barriers be addressed prior to providers beginning to offer MAT. To accomplish this, the first step a practice should take would be to provide an in-house informational session for providers to learn about MAT and OUD. This training would address the following issues:

1. Increase provider awareness of MAT for OUD and its application in the primary care setting.
2. Review the epidemiology and pathophysiology of OUD and how MAT helps.

3. Discuss the types of patients suitable for MAT and factors to consider before accepting a new MAT patient, such as medical/psychiatric comorbidities, polysubstance use, support systems and motivation.
4. Explain that MAT is not a “quick-fix” solution, but rather an evidence-based treatment that works alongside individual or group psychotherapy to increase chances of remission from OUD.
5. Discuss potential benefits for patients and success stories.
6. Point out community resources for MAT providers and patients, such as the UNC ECHO Clinic.
7. Discuss all available treatment options for OUD and provide information on where to refer if a patient requires a higher level of treatment.
8. Explain the steps and requirements of MAT DATA-2000 waiver training.
9. Address concerns that providers may have about offering MAT or working in a clinic that offers MAT.

Interested providers would then proceed to become waiver trained and certified to begin providing treatment with MAT. Ideally, the buprenorphine waiver training will be offered in-house and paid for by the practice, to alleviate the perception some providers have that waiver training is time-intensive and expensive. Prior to beginning to offer MAT to patients, providers should review their current patients and determine which patients may be suitable for MAT. The practice should determine whether or not they would like to accept new patients for MAT. If the practice will accept new patients, the next step would be to develop a screening process for identifying appropriate patients. This will be provider/practice dependent, but general factors for consideration include patient motivation for sobriety, prior treatments, comorbidities or other substance use, and patient support system.

In addition to offering an informational session for providers, before incorporating MAT into care a practice should offer an in-house training for staff members (medical assistants, nurses, etc...). This training should accomplish the following objectives:

1. Review the basics of OUD.

2. Address stigma and potential biases about patients with substance-use disorders.
3. Explain the function of MAT and how it will be provided in the clinic.
4. Discuss any potential changes that may occur to the daily functioning of the clinic.
5. Address concerns that staff may have.

After all employees at the clinic have been educated and concerns have been addressed, current patients deemed appropriate may be offered MAT for OUD. If deemed appropriate by the clinic/providers, new patients may be accepted for MAT. To ensure quality care and efficiency, the clinic should periodically evaluate the effectiveness of their MAT program and adjust as necessary.

Program Evaluation Methods

To evaluate the effectiveness of an MAT program, a clinic should periodically review its outcomes and processes in a standardized and organized manner. This is most effectively accomplished by providing all healthcare providers and staff involved in the MAT program a survey with specific questions. A separate survey should be provided to MAT providers and support staff, as different issues are faced by each group. The clinic should write their own survey questions to address practice-specific issues, but the following indicators should be addressed:

1. Number of patients receiving MAT
2. Patient success
 - a. Abstinence from opioid use, as measured by urine drug screen
 - b. Compliance with buprenorphine treatment, as measured by urine drug screen
 - c. Involvement in treatment, as measured by attendance rate for medication-management appointments and for behavioral health appointments

- d. Patient well-being, measured by provider perception, patient self-report, patient employment status
- 3. Provider effectiveness, success and barriers
 - a. Number of MAT visits per evaluation period
 - b. Estimated or calculated length of average MAT visit
 - c. Provider perception of success
 - d. Provider report of barriers faced
- 4. Staff perception of success and barriers

In addition to the above indicators of success, the practice should also evaluate the economic health of their program and determine if any changes are necessary. This evaluation should take place at least annually.

V. Summary and Implications

The utilization of MAT with buprenorphine in combination with behavioral health services is an evidence-based approach to treating OUD. The integration of this treatment modality in the primary care setting would allow it to become more accessible to patients. In order to establish MAT with buprenorphine in the primary care setting, a variety of factors must be addressed. These factors include but are not limited to: institutional buy-in, appropriate patient referral structures, provider motivation and awareness, adequate support staff, stigma, and more. Practice transformation is always complex and following the aforementioned practice transformation model is not expected to be an easy process; however, the proposed model aims to break down the complexity of OUD into pieces that can be considered and addressed in a stepwise fashion. The transformation model describes a systematic framework for addressing these factors and implementing MAT into a primary care practice workflow, provided that important resource constraints can be overcome.

One potential issue that clinics may face when implementing an MAT program following the above practice transformation model is creating a model that is economically feasible (i.e. no sunken costs) for the practice. As previously mentioned, discussion of such a model is beyond the scope of this paper, but an adequate economic model will consider potential insurance reimbursement for services and the potential economic implications of providing care to underinsured patients. Another barrier that practices should anticipate facing is that prevailing

Commented [CPR13]: What you describe here was definitely not simple. Practice transformation is always complex, even for medical problems that are not as inherently challenging as chronic disease with behavioral dimensions. (I know this from experience.) What you do provide a structured systematic approach that breaks down the complexity of the OUD into pieces that can be considered and addressed step by step—hence your very useful logic models. I think you should address this in the summary. "Practice transformation" is an accepted technical term. Your might weave it into your arguments from the beginning because this is what you are proposing.

payment mechanisms to resource and reimburse clinics for in-house behavioral medicine are often inadequate. In the case that this is an issue, practices may consider developing a relationship with a nearby behavioral health provider such that timely referrals for services can be made in lieu of having in-house services. Implementing any kind of institutional change, such as creating an MAT program, is a process that must be repeatedly evaluated in order to continue successfully. The importance of periodic program review using the proposed program evaluation methods should not be underestimated. Topics reviewed in such an evaluation should at a minimum include both patient and provider outcomes (perceived and objective), as well as staff perception of the program.

There exist many potential implications for patients and practices when incorporating MAT with buprenorphine into the primary care setting. Obviously, the anticipated outcome is improved patient care and remission of OUD. However, our key informants noted that many patients treated with MAT in the primary care setting benefit beyond treatment of their OUD. One hope in providing care in a primary care clinic is that patients will interface more often with the healthcare system and have other chronic care or preventative health measures addressed at their visits. A worry voiced by a key informant is that prescribing buprenorphine in the primary care setting may lead to diversion of the drug. However, if diversion is an issue when prescribing buprenorphine, it is an even larger issue when prescribing opioids for pain management in the primary care setting, which is done much more often and with medications that are potentially more dangerous. The issue of diversion is controversial, but is an important topic for further research.

Future research into treatment of OUD in the primary care setting is necessary to continue to improve patient outcomes and encourage the development of sustainable models of care. Suggested areas of research include the use of telemedicine for MAT maintenance visits, a comparison of patient outcomes among different MAT models, management of patients with OUD and concomitant chronic pain disorders, and the use and efficacy of longer-term medication formulations (e.g. implantable and injectable buprenorphine). In addition to the necessity of further research into this ever-relevant area of medicine, policy changes are needed at the national and private levels to ensure that patients in need of services can access care. As previously discussed, many have criticized President Donald Trump's designation of the US opioid crisis as a "national public health emergency" as insufficient. Reclassifying the crisis as a

“National Emergency” under the Stafford Act would allow additional funds to be utilized, rather than reallocating funds from existing federal programs. Changes in insurance reimbursement for MAT for OUD that decrease barriers to the use of such medications as buprenorphine would also be immensely helpful for patients. Ideally, uninsured and underinsured patients would be able to access care and medications at a community clinic. In order for this to be possible, additional funding needs to be available for clinics offering such services. This is a very important area of future research and policy change.

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VII. Tables

Table 1. Overview of select MAT models of care for OUD in primary care

Model	Summary	Components
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		Pharmacotherapy	Education/Outreach	Coordination of care	Psychosocial	Other
OBOT (Office Based Opioid Treatment)	Buprenorphine prescribed by PCPs who complete DATA 2000 waiver training	Primarily buprenorphine/naloxone	Not a major component; Provider Clinical Support Service for MAT available to mentor primary care providers	A non-physician clinic staff member sometimes used to coordinate MAT prescribing and integration with primary and mental health care.	Physician, psychologist, social worker or other counseling at least monthly; Other psychosocial services vary, including integrated CBT and motivational enhancement therapy; some psychosocial services off-site.	—
Massachusetts nurse care manager	A primary care-based model that teams nurse care managers with primary care physicians; nurse care managers generally perform initial screening, intake, education, observed/supports induction, follow-up, maintenance, stabilization, and medical management with the physician and team	Primarily buprenorphine-naloxone, with recent addition of extended-release naltrexone	A training program exists to get more physicians (especially residents) and faculty on board. The Department of Public Health trains staff on best practices. Nurse care managers receive 8 h of training in MAT, shadowing in model MAT site, site visits, e-mail and telephone support, case review, quarterly training, and an addiction listserv.	Nurse care managers (registered nurses or family NPs) manage 100 to 125 patients alongside primary care clinicians, with assistance from a medical assistant. Alternatively, care partners (usually persons with a master's degree) assist the primary care staff with screening, brief intervention, and referral to treatment.	Psychological services are integrated on-site or nearby	Patients who require a higher level of care can be expedited into an OTP, assistance with transfers of care, and day-support programs
Hub and Spokes	Centralized intake and initial management (buprenorphine induction) at "hub"; patients are then connected to "spokes" in the community for ongoing management	Primarily buprenorphine-naloxone	Outreach to prescribers in the community to increase the number of buprenorphine-waivered physicians	Coordination/integration between hub and spoke as well as within each primary care site spoke. Registered nurse clinician case manager and/or care connector (peer or behavioral health specialist) for coordination/integration of care at spokes.	Embedded in spoke sites, including social workers, counseling, and community health teams.	Hubs provide consultative services and are available to manage clinically complex patients; support tapering of MAT; or prescribe methadone, if needed

Commented [CPR14]:

ED Initiation of OBOT	ED identification of OUD; buprenorphine-naloxone induction initiated in ED; coordination with OBOT, nurse with expertise in buprenorphine working in collaboration with PCP	Buprenorphine-naloxone	Not a major component	OUD identified in ED and patients started on buprenorphine therapy and connected to ongoing OBOT provided by physicians and nurses for 10 wk, then transferred to office-based ongoing maintenance treatment or detoxification.	"Medical management" counseling visits with physician and nurse	—
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(Adapted from Chou R, Korthuis PT, Weimer M, et al. *Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016.)

Table 2. Details of Systematic Reviews

Author, year	Purpose of review	Number of included studies	Population characteristics	Intervention characteristics	Types of studies included	Methods for synthesizing results of primary studies	Total number of patients	Findings	Limitations
Amato, 2011	To evaluate the effectiveness of psychotherapy plus agonist maintenance treatment vs. standard treatment for opioid dependence	35	OUD (drug of choice not specified); setting not described (appears mostly specialist centers); USA, Germany, Malaysia, China, Scotland	Any psychosocial intervention plus any agonist vs. agonist treatment alone; medical interventions were methadone, buprenorphine, LAAM; models of care not described	RCTs, CCTs	GRADE; meta-analysis done	4319	No significant advantage of adding psychosocial interventions for retention in treatment and at follow-up, abstinence from opiates during treatment or at follow-up, compliance, psychiatric symptoms, and depression. Also, no significant difference in outcomes comparing psychosocial approaches.	Focused on effectiveness of psychotherapy interventions in addition to standard interventions; Setting not described (appears mostly specialist centers); 31 studies in USA
Gowing, 2017	Analyze if there is a significant difference between the number of days of treatment	27	OUD due to heroin or other opioids; setting not described	Buprenorphine maintenance vs. methadone; models of	RCTs	GRADE; meta-analysis done	3048	BUP and MET have similar potentials to alleviate opioid	BUP routes of administration and doses varied; authors identified selection bias

	completed and if there is a difference in the number of patients that complete treatment if treated with buprenorphine or methadone			care not described				withdrawal symptoms, with neither treatment having significantly more adverse effects than the other.	and early cessation as issues in three of the six studies; review included a relatively small number of participants that were primarily male
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(Adapted from Chou R, Korthuis PT, Weimer M, et al. *Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016.)

Table 3. Intervention Mapping Steps

Step 1: Logic Model of the Problem	<ul style="list-style-type: none"> Conduct a needs assessment to create logic model of problem Describe context for intervention (population, setting, community) State program goals
Step 2: Program Outcomes/Objectives; Logic Model of Change	<ul style="list-style-type: none"> State expected outcomes for behavior/environment Specify performance objectives for outcomes Select determinants for outcomes Create logic model of change
Step 3: Program Design	<ul style="list-style-type: none"> Generate program themes, components, scope, sequence Choose theory- and evidence-based change methods Select/design practical applications to deliver methods
Step 4: Program Production	<ul style="list-style-type: none"> Refine program structure Prepare plans for program materials Pretest, refine and produce materials
Step 5: Program Implementation Plan	<ul style="list-style-type: none"> Identify potential program users State outcomes/performance objectives for program use Design implementation interventions
Step 6: Evaluation Plan	<ul style="list-style-type: none"> Write effect and process evaluation questions Develop indications and measures for assessment Specify evaluation design Complete evaluation plan

(Adapted from Bartholemew et al (2016). *Planning health promotion programs: An Intervention Mapping approach* (4th ed). Hoboken, NJ: Wiley.)

Table 4. Expected Outcomes and Performance Objectives of Program Plan

Ecological Level	Expected Outcomes	Performance Objectives
Personal behavioral	Patients... <ul style="list-style-type: none"> Abstain from recreational substance use <i>Engage in behaviors that</i> 	Patients... <ul style="list-style-type: none"> Make the decision to seek treatment for substance use disorder <i>Have transportation/access to treatment</i>

	<p><i>promote their sobriety</i> (e.g. individual/group therapy, 12-step program, etc...)</p> <ul style="list-style-type: none"> • <i>Take buprenorphine at prescribed dose and frequency</i> 	<p><i>center and pharmacy</i></p> <ul style="list-style-type: none"> • <i>Have the financial means/insurance to afford treatment</i> • Avoid places, people and triggers that may lead them to engage in substance use • Have a support system that assists them in maintaining sobriety
Interpersonal environmental	<ul style="list-style-type: none"> • Intimate partners/family members support patients in abstaining from substance use and in adhering to buprenorphine treatment • Peers do not encourage substance use 	<ul style="list-style-type: none"> • Intimate partners/family members/peers do not use recreational substances
Organizational environmental	<p>At healthcare facilities...</p> <ul style="list-style-type: none"> • <i>Policies, programs, and facilities exist to assist substance-dependent people in achieving and maintaining sobriety</i> 	<p>At healthcare facilities...</p> <ul style="list-style-type: none"> • <i>MAT is offered at primary care clinics</i> • <i>Providers have been waiver-trained to provide buprenorphine treatment</i> • <i>A behavioral medicine specialist (e.g. social worker, psychologist, etc...) is available as needed (e.g. at the clinic, by referral, etc...)</i> • <i>Staff has been trained to assist substance-dependent patients</i> • <i>Policies and procedures have been developed specifically for MAT at the clinic</i>
Community environmental	<ul style="list-style-type: none"> • <i>Care for substance use disorder is easily accessible to patients</i> • Health ordinances encourage treatment of substance use disorders • Community groups exist that encourage sobriety (e.g. group therapy, 12-step groups) • <i>Substance use disorder is not stigmatized, but instead viewed as a treatable illness</i> 	<ul style="list-style-type: none"> • <i>MAT is available at primary care clinics, as opposed to solely by specialty practitioners</i> • Public transportation is easily accessible to transport patients to clinics offering treatment
Societal environmental	<ul style="list-style-type: none"> • Legislation, law enforcement and regulations encourage rehabilitation and treatment of substance use disorders • <i>Resources are allocated for rehabilitation and treatment</i> • <i>Policies, programs, and facilities exist to assist substance-</i> 	<ul style="list-style-type: none"> • Funding is available for clinics offering MAT

	<i>dependent people in achieving and maintaining sobriety</i>	
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Table 5. Program Steps

Step 1	Develop a financial model describing: 1). How a practice will absorb the costs of MAT for financially burdened patients 2). How all aspects of care will be paid for without any sunken costs
Step 2	1). Hire in-house social worker or psychologist OR 2). Develop relationship with local behavioral health professional such that patients can obtain services in a timely manner.
Step 3	Host in-house information session for providers discussing MAT and OUD
Step 4	Host in-house buprenorphine DATA 2000 waiver training session for interested providers
Step 5	Potential MAT providers review current patients and determine which may benefit from MAT
Step 6	Practice/providers determine if new patient will be accepted for MAT treatment. If so: 1). Develop screening process for determining which patients will be accepted. 2). Determine who will conduct screening (behavioral health provider or MAT provider)
Step 7	Host in-house informational session for support staff discussing OUD, MAT and potential changes in clinic functioning
Step 8	1). Providers begin to offer MAT to current patients deemed appropriate AND 2). Begin accepting new patients for MAT, at clinic/provider discretion
Step 9	Clinic periodically evaluates effectiveness of its MAT program and makes adjustments to workflow as necessary

VIII. Appendices**Appendix A. Questions for Key Informants**

Clinic Perspective	Interview Questions
Has implemented MAT	<ol style="list-style-type: none"> 1. How and when was MAT implemented at this clinic? 2. What models did this clinic consider in the early stages? 3. What model does this clinic follow? 4. What were the barriers to implementing MAT at this clinic? 5. How did the clinic overcome these barriers (if able)? 6. What were some factors that contributed to the clinic's success?

	<ol style="list-style-type: none"> 7. In addition to the SAMHSA DATA 2000 waiver requirement to be able to prescribe buprenorphine, are there any additional requirements to prescribe at this clinic? 8. Have there been any barriers to providers becoming licensed to prescribe buprenorphine? 9. What do you think is the biggest reason providers choose to/not to become licensed? 10. Have you noticed stigma around MAT (among providers, staff or other patients) to be an issue at the clinic? 11. What is the biggest strategic barrier to incorporating MAT patients into this clinic? 12. How is insurance coverage for these services? 13. What have the results been like for patients at this clinic? 14. Are there restrictions on the types of patients accepted by the clinic (e.g. no psychiatric comorbidities, only OUD, etc...)? 15. What feedback have you received from providers regarding implementing MAT at the clinic? 16. What behavioral health resources are a part of this clinic's program? 17. What role does social work/care management play in this clinic's program? 18. Is there an educational/outreach component (among patients, providers, and/or staff) to the program?
Has not yet implemented MAT	<ol style="list-style-type: none"> 1. What barriers do you anticipate facing in incorporating MAT into practice? 2. How do you plan to overcome the aforementioned barriers? 3. What factors do you anticipate will contribute to the clinic's success? 4. What model of MAT is the clinic considering? 5. Have any providers completed the training to prescribe buprenorphine as of yet, or do any plan on becoming waived within the next 6 months? 6. What do you think is the biggest reason providers choose to/not to become licensed to prescribe buprenorphine? 7. Does the clinic plan on placing restrictions on the types of patients it will accept (e.g. no psychiatric comorbidities, only OUD, etc...)? 8. What feedback have you gotten from providers regarding plans to implement MAT at the clinic? 9. What behavioral health resources will be incorporate into the program? 10. What role will social work/care management play in the program? 11. Do you anticipate there being an educational/outreach component (among patients, providers, and/or staff) to the program?

Appendix B. AMSTAR Bias Analysis Tool for Systematic Reviews

1. *Amato L, Minozzi S, Davoli M, et al. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. Cochrane Database Syst Rev. 2011(10):CD004147. PMID: 21975742.*

Did the research questions and inclusion criteria for the review include the components of PICO?	Yes
Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	Yes
Did the review authors explain their selection of the study designs for inclusion in the review?	Yes
Did the review authors use a comprehensive literature search strategy?	Yes

Did the review authors perform study selection in duplicate?	Yes
Did the review authors perform data extraction in duplicate?	Yes
Did the review authors provide a list of excluded studies and justify the exclusions?	Yes
Did the review authors describe the included studies in adequate detail?	Yes
Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	Yes
Did the review authors report on the sources of funding for the studies included in the review?	Yes
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	Yes
If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Yes
Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Yes
Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes
If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	Yes
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Yes

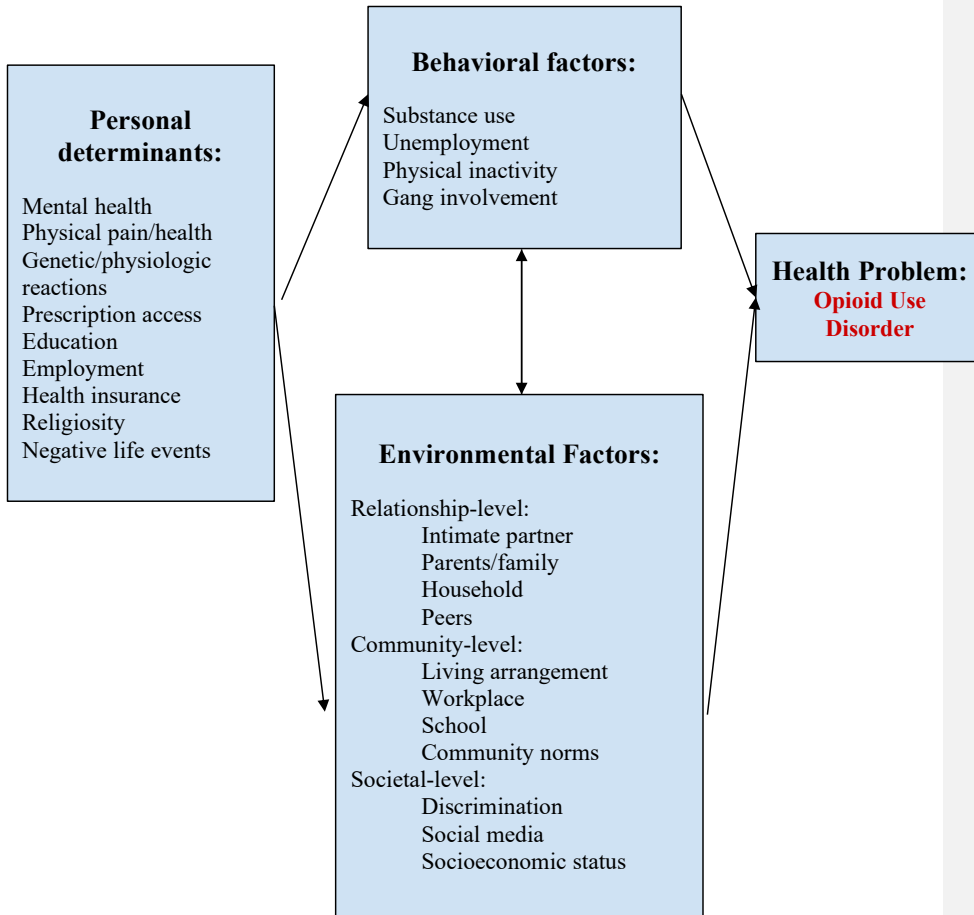
Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008.

2. Gowing, L., Ali, R., White, J.M., Mbewe, D. (2017) Buprenorphine for managing opioid withdrawal (Review). Cochrane Database of Systematic Reviews, Issue 2. Art No.: CD002025. doi: 10.1002/14651858.CD002025.pub5

Did the research questions and inclusion criteria for the review include the components of PICO?	Yes
Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	Yes
Did the review authors explain their selection of the study designs for inclusion in the review?	Yes
Did the review authors use a comprehensive literature search strategy?	Partial Yes
Did the review authors perform study selection in duplicate?	Yes
Did the review authors perform data extraction in duplicate?	Yes
Did the review authors provide a list of excluded studies and justify the exclusions?	Yes
Did the review authors describe the included studies in adequate detail?	Yes
Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies	Yes,

that were included in the review?	included only RCTs
Did the review authors report on the sources of funding for the studies included in the review?	Yes
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	Yes
If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Yes
Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Yes
Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes
If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	Yes
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Yes

Appendix C. Logic Model of Problem of Opioid Use Disorder



Appendix D. Logic Model of Proposed Change

