

# ***Draft Technical Brief***

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Number XX

## **Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings**

**Prepared for:**

Agency for Healthcare Research and Quality  
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**Contract No. [To be added for final report]**

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**AHRQ Publication No. xx-EHCxxx <AHRQ will provide>  
<Month Year>**

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## Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

This EPC evidence report is a Technical Brief. A Technical Brief is a rapid report, typically on an emerging medical technology, strategy or intervention. It provides an overview of key issues related to the intervention—for example, current indications, relevant patient populations and subgroups of interest, outcomes measured, and contextual factors that may affect decisions regarding the intervention. Although Technical Briefs generally focus on interventions for which there are limited published data and too few completed protocol-driven studies to support definitive conclusions, the decision to request a Technical Brief is not solely based on the availability of clinical studies. The goals of the Technical Brief are to provide an early objective description of the state of the science, a potential framework for assessing the applications and implications of the intervention, a summary of ongoing research, and information on future research needs. In particular, through the Technical Brief, AHRQ hopes to gain insight on the appropriate conceptual framework and critical issues that will inform future research.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

If you have comments on this Technical Brief, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to [epc@ahrq.hhs.gov](mailto:epc@ahrq.hhs.gov).

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## **Key Informants**

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

The list of Key Informants who provided input to this report follows:

**[List of Key Informants to be added for final]**

## **Peer Reviewers**

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report does not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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# Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings

## Structured Abstract

**Background.** Effective and innovative models of care for medication-assisted treatment (MAT) in primary care settings (including rural or other underserved settings) could facilitate implementation and enhance provision and uptake of agonist and antagonist pharmacotherapy in conjunction with psychosocial services for more effective treatment of opioid use disorders.

**Purpose.** The purpose of this Technical Brief is to describe promising and innovative MAT models of care in primary care settings, describe barriers to MAT implementation, summarize the evidence available on MAT models of care in primary care settings, and identify gaps in the evidence base.

**Methods.** We performed searches in electronic databases from 1995 to April 2016, reviewed reference lists, searched grey literature sources, and interviewed Key Informants. We summarized representative MAT models of care in primary care settings and qualitatively summarized the evidence on MAT models of care in primary care settings and identified areas of future research needs.

**Findings.** We summarized 12 representative MAT models of care in primary care settings, utilizing a framework describing the pharmacological component, the psychosocial services component, the integration/coordination component, and the educational/outreach component. Innovations in MAT models of care include the use of designated nonphysician staff to perform the key integration/coordination role; tiered care models with centralized intake and stabilization of patients with ongoing management in community settings; screening and induction performed in emergency department, inpatient, or prenatal settings with subsequent referral to community settings; community-based stakeholder engagement to develop practice standards and improve quality of care; and use of Internet-based learning networks in rural settings. Most trials of MAT in primary care settings focus on comparisons of one pharmacological therapy versus another, or on the effectiveness of different intensities or types of psychosocial interventions, rather than on effectiveness of different MAT models of care *per se*. Key barriers to implementation of MAT models of care include stigma, lack of institutional support, lack of prescribing physicians, lack of expertise, and inadequate reimbursement.

**Conclusions.** A number of MAT models of care have been developed and implemented in primary care settings. Research is needed to clarify optimal MAT models of care and to understand effective strategies for overcoming barriers to implementation. The models of care presented in this technical brief may help inform the individualized implementation of MAT models of care in different primary care settings.

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# Background

## Introduction

Opioid use disorder (OUD) has been identified by the Department of Health & Human Services as a national crisis.<sup>1</sup> OUD involves misuse or abuse of prescription opioids or illicit heroin, and is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)<sup>2</sup> as “a problematic pattern of opioid use leading to clinically significant impairment or distress.” In 2014, approximately 1.9 million Americans 12 years or older were estimated to have OUD due to prescription drugs and nearly 600,000 due to heroin use.<sup>3</sup> OUD is associated with decreased quality of life and increased morbidity and mortality. In 2013, an estimated 16,000 individuals died as a result of prescription opioid overdose (a 2.5-fold increase from 2001) and approximately 8,000 from heroin (a 4-fold increase from 2001).<sup>4</sup> These trends have occurred in conjunction with markedly increased rates of opioid prescribing for chronic pain;<sup>5-9</sup> in fact, the majority of heroin users now report that their first opioid of abuse was a prescription opioid, not heroin.<sup>10</sup> Challenges in the treatment of OUD include the relapsing nature of this condition, the frequent presence of psychological and medical comorbidities, and the disproportionate impact on those in socioeconomically disadvantaged settings with limited access to care.<sup>11,12</sup> Compared with OUD due to prescription drugs, OUD related to heroin is associated with additional risks from the high addiction potential of heroin, lack of control over drug purity, and increased risk of possibility of blood-borne disease transmission stemming from injection behaviors commonly used to take heroin (though prescription drugs may also be injected).

As noted in 1997 by a National Institutes of Health consensus panel, OUD “is a medical disorder that can be effectively treated with significant benefits for the patient and society.”<sup>13</sup> According to the Substance Abuse and Mental Health Services Administration (SAMHSA), Medication-assisted treatment “(MAT) is defined as the use of the Food and Drug Administration (FDA)-approved opioid agonist medications (e.g., methadone, buprenorphine products, including buprenorphine/naloxone combination formulations and buprenorphine mono-product formulations) for the maintenance treatment of opioid use disorder and opioid antagonist medication (e.g., naltrexone products, including extended-release and oral formulations) in combination with behavioral therapies to prevent relapse to opioid use. MAT includes screening, assessment (which includes determination of severity of opioid use disorder, including presence of physical dependence and appropriateness for MAT), and case management. MAT is to be provided in combination with comprehensive substance use disorder treatment, including but not limited to: counseling, behavioral therapies, other clinically appropriate services in order for individuals to achieve and maintain abstinence from all opioids and heroin, and, when needed, pharmacotherapy for co-occurring alcohol use disorder. MAT is to be provided in a clinically driven, person-centered, and individualized setting.”<sup>14</sup> MAT has been shown to be more effective than treatments that do not use MAT in reducing the frequency and quantity of opioid use<sup>15,16</sup> and may reduce the risk of overdose, improving social functioning, and decreasing criminal activity and infectious disease rates.<sup>17</sup> The purpose of the medication component is to block the euphoric and sedating effects of other opioids, reduce the craving for other opioids, and/or mitigate the symptoms of opioid withdrawal. Psychosocial interventions address the psychosocial contributors to OUD and may help improve retention in care. Examples of psychosocial interventions include individual therapy, group counseling, drug counseling, family behavior therapy, cognitive-behavioral therapy, motivational enhancement therapy, and assessment, coordination, and management of other medical and psychiatric care needs such as provision of general primary care or treatment



for other substances of abuse, human immunodeficiency virus (HIV) or hepatitis C virus (HCV) coinfection, or pregnancy.<sup>18</sup>

## **Current Practices**

The White House and the Department of Health & Human Services recently identified improved access to MAT as a key priority for reducing harms associated with OUD.<sup>1,19</sup> Prior to the Drug Abuse Treatment Act (DATA) of 2000, MAT using opioid agonists could only be provided through federally-approved opioid treatment programs and the partial opioid agonist buprenorphine was not yet approved for the treatment of OUD.<sup>20</sup> DATA 2000 enabled physicians to obtain a waiver and prescribe for treatment of OUD schedule III-V medications approved by the FDA for this purpose; currently the only such medication is buprenorphine (also available coformulated with the opioid antagonist naloxone). Under federal law, MAT patients must receive counseling, which can include different forms of behavioral therapy. Although DATA 2000 has increased access to buprenorphine in primary care settings, research indicates that access to and use of buprenorphine remains limited.<sup>4,21</sup> In many rural areas, for example, no buprenorphine prescribers are available.<sup>22</sup> Oral naltrexone, an opioid antagonist, has long been available for treatment of OUD and extended-release naltrexone is recently available as a monthly intramuscular injection. Naltrexone is not classified as a controlled substance and can be prescribed in primary care settings by any physician, physician assistant, or nurse practitioner, but its use has been limited. Methadone is a schedule II opioid that is dispensed in licensed opioid-treatment programs. Even in specialty substance use disorder settings, medications approved for MAT appear to be underutilized, with one study showing that MAT was used in only about one-third of patients.<sup>23</sup> Therefore, understanding the most effective and promising models of care and implementation strategies are critical for optimizing the impact of initiatives to expand access to MAT.<sup>1</sup>

## **Objective of Technical Brief**

The purpose of this Technical Brief is to describe the available literature on MAT models of care and methods for effective MAT strategies, and to identify and summarize key issues and gaps in the evidence base. A Technical Brief does not synthesize data on outcomes or grade evidence. Rather, it seeks to summarize what evidence is available, provide a conceptual or organizational framework to understand key components of the intervention of interest, highlight promising new and innovative strategies, describe barriers to implementation, and provide guidance regarding future research directions and priorities. The focus of the Technical Brief is on implementation of MAT in primary care settings, including rural or other underserved settings. Specifically, Guiding Question 1 provides an overview of MAT models of care, Guiding Question 2 describes the context in which MAT is implemented, Guiding Question 3 summarizes the current state of the evidence of MAT, and Guiding Question 4 addresses important issues and future directions for MAT. This technical brief is intended to help determine the scope of future research, such as a subsequent systematic evidence review on MAT.

## Guiding Questions

1. *Description/Overview of MAT for the Treatment of Opioid Use Disorder:*
  - a. What are the different types or models of care of MAT that have been proposed or used in clinical practice?
  - b. What are the potential advantages and disadvantages of these respective models of care?
2. *Context in Which MAT is Used:*
  - a. In what settings is MAT currently implemented?
  - b. Are there special considerations for implementing MAT in primary care, including rural or other underserved settings?
  - c. What are potential barriers to implementation, including resources needed, and how do barriers vary according to the setting?
  - d. What kinds of training, certification, and staffing are required for various MAT models of care?
3. *Current Evidence on MAT:*
  - a. What have published and unpublished studies reported on the use of and effectiveness MAT in primary care settings, including rural or other underserved settings? The technical brief will summarize the following information:
    - i. Patient population, including practice setting and country/location
    - ii. Details on MAT model of care, including the types of interventions used (specifics of pharmacological and nonpharmacological treatments), provider type/staffing needs, implementation strategy/mode of delivery, frequency, and other factors
    - iii. Study design/size
    - iv. Comparator used in comparative studies
    - v. Concurrent/prior treatments
    - vi. Length of followup
    - vii. Outcomes measured
    - viii. Adverse events/harms/safety issues reported
4. *Important Issues and Future Directions for MAT:*
  - a. What are promising new and innovative strategies in MAT models of care?
  - b. Given the current state of the evidence, what are the implications for the current level of diffusion and/or further diffusion of MAT?
  - c. What are the ethical, equity, and/or cost considerations that impact diffusion, decisionmaking, and/or conceptual thinking around MAT?
  - d. What are important areas of uncertainty for MAT?
  - e. What are possible key areas of future research on MAT, and what areas related to MAT warrant a systematic review?

## Methods

The Technical Brief integrates discussions with Key Informants with searches of the published literature and grey literature to inform the Guiding Questions.

### Discussions with Key Informants

We identified and interviewed 11 Key Informants (8 nonfederal and 3 federal) to represent broad and balanced perspectives relevant to MAT, with a focus on people with expertise or experience related to implementation in primary care settings, including rural or other underserved settings. The Key Informants represented the following stakeholder areas: researchers, clinicians, health policy, implementation, professional societies, patient groups, and federal representatives.

We organized and facilitated small group telephone discussions with the Key Informants (2 to 4 per call) to gain input on the Guiding Questions; group calls maximized efficiency and the relatively small number of Key Informants on each call allowed all representatives the chance to provide input. Members of our research team and the Agency for Healthcare Research and Quality (AHRQ) Task Order Officers also attended the calls. On the calls, we interviewed Key Informants using a semi-structured approach. Key Informants were asked to respond to predetermined questions targeted to different Key Informant perspectives, share more general insights, and interact with each other (**Appendix A**). The questions were used as a guide, but we asked additional or supplemental questions based on interviewee responses. We asked which MAT models of care are in use in primary care and other related settings, including models of care which are not described in the published literature, and asked Key Informants to describe the different components of the models and which components were particularly effective or promising, the current challenges or barriers to implementation, patient preferences, and future directions, including promising new and innovative models and strategies for implementation. We also asked about specific issues to be aware of when reviewing the literature, such as outcomes to be prioritized, meaningful length of followup, study design issues, and how MAT models of care vary in terms of intensity, goals, and components of care. Because we were particularly interested the feasibility and applicability of models of care implemented in one setting or population to others and about identifying models of care that may be particularly suitable for specific settings, including rural and other underserved settings, we focused the questions and discussions in that area. The calls were recorded, and the key points were summarized and shared with the group for clarification and additional input. We reviewed all of the Key Informant input regarding successful and promising MAT models of care and developed a framework for categorizing the different types of components in MAT models of care, to help organize and provide a structure for future research and discussions in this area. We then integrated feedback from the Key Informants with the expertise of our project team and evidence identified from the published and unpublished literature.

### Grey Literature search

To identify grey literature, the AHRQ Evidence-based Practice Center (EPC) Scientific Resource Center (SRC) sent email notification to relevant stakeholders about the opportunity to submit Scientific Information Packets (SIP) via the Effective Health Care (EHC) Web site.

In addition, we conducted searches of the grey literature. Specifically, we searched ClinicalTrials.gov and Health Services Research Projects in Progress (HSRProj) for ongoing

research, as well as Google Scholar, NIH Reporter, and Web sites of government agencies with MAT initiatives. The grey literature searches were used to primarily inform Guiding Question 3, but if information relevant to the other Guiding Questions was identified, it is also discussed in the report.

## Published Literature Search

We searched, reviewed, and summarized the available literature on MAT for OUD in primary care settings to address Guiding Question 3. An experienced research librarian created search strategies for the following databases: Ovid Medline, PsycINFO, the Cochrane Library, SocINDEX, and CINAHL. The search strategies are available in **Appendix B**. Since addiction could not be treated in the primary care/non-addiction treatment settings until the year 2000, with the passage of the Drug Addiction Treatment Act (DATA) 2000, and due to the focus of the report in primary care settings and the large volume of abstracts, we restricted the start date for the searches to the year 1995 and later (to April 2016). The search was also used identify contextual evidence to supplement the Key Informant input obtained for Guiding Questions 1, 2, and 4. We also reviewed the reference lists of identified publications and solicited additional references from Key Informants to supplement electronic searches. Searches will be updated while the report is undergoing peer and public review in order to capture any recently added publications. If any new studies are identified from the update searches or arise as suggestions from the peer or public review, they will be added to the report prior to finalization.

We applied predefined screening criteria to identify the most relevant and authoritative evidence on MAT models of care in primary care settings. For Guiding Question 3, we focused on the following sources of evidence: 1) high-quality Cochrane systematic reviews of MAT; 2) randomized trials and cohort studies on the effectiveness of MAT models of care in primary care settings; 3) randomized trials evaluating the effectiveness of newer pharmacological therapies for MAT that could impact implementation or future models of care; and 4) randomized trials on the effectiveness of more intensive versus less intensive psychological interventions with MAT in primary care settings. To provide context for the other Guiding Questions, we also identified published and unpublished studies describing MAT models of care in primary care settings, including the setting for the model of care (e.g., urban vs. rural), patient characteristics (e.g., age, presence of comorbid conditions, OUD related to prescription opioids for chronic pain versus nonprescribed opioid use), and intervention characteristics (e.g., components of MAT models of care, including degree of coordination and intensity of psychosocial interventions). We also identified studies that provided contextual information on implementation strategies and barriers in primary care settings, including rural and other underserved settings. We excluded trials that focused on the dose or duration of pharmacological therapy, as the focus of this report was on MAT models of care, not on details regarding how pharmacological therapy should be provided.

All titles and abstracts identified through searches were independently reviewed for eligibility against our inclusion/exclusion criteria organized by PICOTS (population, intervention, comparator, outcome, timing, study design) (**Table 1**) by a trained member of the research team. Studies marked for possible inclusion by any reviewer underwent a full-text review. For abstracts without adequate information to determine inclusion or exclusion, we retrieved the full text and then made the determination. All results were tracked in an EndNote® database (Thomson Reuters, New York, NY). Each full-text article was independently reviewed by two trained members of the research team for inclusion or exclusion on the basis of the eligibility criteria. If the reviewers disagreed, conflicts were resolved by discussion and

consensus or by consulting another member of the review team. Results of the full-text review were also tracked in the EndNote® database, including the reason for exclusion for excluded full-text publications when they did not meet the eligibility criteria.

For Guiding Question 3, we summarized information from systematic reviews and primary studies that met inclusion criteria in summary tables. For systematic reviews, we summarized information on year of publication, the purpose of the review, search dates and databases searched, the number of studies included, populations and settings in the trials, MAT intervention characteristics, the type of studies included, how quality was rated for included studies, methods of synthesis, the total number of patients included, main findings (including harms), and limitations (including whether the studies were primarily performed in an opioid treatment program [OTP] or addiction specialty settings, whether the studies were conducted outside the United States, and other limitations). For randomized controlled trials, we summarized information on year of publication, comparisons evaluated, duration of followup, sample size, population characteristics, MAT model of care components, setting (including provider type and staffing if that information was provided), outcomes evaluated, and main findings.

For Guiding Question 1, we summarized data sources for the various MAT models of care, including published sources (with citations), unpublished sources (with URL information), and Key Informant input.

**Table 1. Inclusion and exclusion criteria for Guiding Question 3 on the efficacy and safety of MAT for OUD**

PICOT	Include	Exclude
<b>Populations</b>	Patients with OUD in primary care settings, including rural or other underserved settings	MAT in inpatient settings and licensed treatment centers or specialty addiction centers; MAT provided outside the United States, Canada, Europe, and Australia/New Zealand
<b>Interventions</b>	MAT (including the use of pharmacological therapy for OUD with psychosocial interventions) for OUD <sup>14</sup>	--
<b>Comparators</b>	1) MAT models of care in primary care settings vs. no MAT 2) MAT model of care vs. another MAT model of care 3) MAT model of care with more intensive psychosocial interventions vs. less intensive psychosocial interventions 4) MAT model of care with newer pharmacological component vs. placebo/no medication or vs. established pharmacological component	Studies that focused on dose or duration of pharmacological component of MAT
<b>Outcomes</b>	Measures of use or access Substance-use-related outcomes, including mortality, overdose, substance use Nonsubstance-use-related outcomes, including quality of life, functional status, work status, engagement in criminal activity, rates of unplanned pregnancy, acquisition or transmission of infectious conditions, and others; in pregnant women, maternal and fetal health outcomes	--
<b>Timing</b>	Any	--
<b>Study Design</b>	Cochrane systematic reviews Randomized controlled trials Cohort studies and case-control studies for comparisons #1 and #2	Nonsystematic reviews Studies without original data Non-English language Nonhuman

MAT = medication-assisted treatment; OUD = opioid use disorder; PICOTS = population, intervention, comparator, outcome, timing, study design.

**Note:** Intervention uses the SAMHSA definition for MAT.

# Findings

## Overview

By definition, MAT involves the use of opioid agonists or antagonists to assist in treatment of OUD. Two medications are currently used in the United States in office-based settings for treating OUD: buprenorphine (with or without naloxone) and naltrexone (as daily oral or extended-release formulations). Medications that have been used in primary care settings in other countries but are not available for treatment of OUD in office-based settings in the United States include methadone and sustained-release morphine; in the United States, methadone can currently only be dispensed for treatment of OUD in licensed opioid treatment programs or in rare research or demonstration settings.

We interviewed eleven Key Informants: five were clinicians with experience treating OUD or in administration of office-based MAT (one internal medicine/addiction, one family medicine/addiction, one addiction psychiatry, one psychology, one registered nurse), four had expertise in policy and implementation (three of these were from federal agencies, specifically the Health Resources and Services Administration/HIV and AIDS Bureau [HRSA/HAB], the SAMHSA, and the National Institute on Drug Abuse [NIDA]), one was from an organization representing opioid treatment programs, and one represented the patient perspective who also directs a MAT clinic. The interviews were conducted over four phone calls, with two to four Key Informants participating in each call. Interviews lasted from 60 to 90 minutes and consisted of 8 to 12 questions. All interviews took place in February and March 2016. A summary of the interviews appears in **Appendix C**.

A summary of data sources for Guiding Question 1 describing various MAT models of care in primary care settings is shown in **Table 2**, with sources in **Table 3**. For Guiding Question 3, abstracted data for randomized trials and systematic reviews on MAT models of care in primary care settings are shown in **Tables 4 and 5**, respectively. We abstracted data from a total of 29 publications. A figure depicting the literature flow is available in **Appendix D**, and a full list of included and excluded studies is shown in **Appendixes E and F**, respectively.

## Guiding Question 1: MAT Models of Care

A number of MAT models of care in primary care settings were described in the literature and by Key Informants. A challenge in summarizing MAT models of care is that the models of care frequently had overlapping characteristics, and varied in the degree to which they were structured and adapted to specific settings. Key Informants consistently noted four important components of MAT models of care: 1) pharmacological therapy (currently, buprenorphine (with or without coformulated naloxone) or naltrexone (oral or extended-release); 2) provider and community educational interventions; 3) coordination/integration of substance use disorder treatment and other medical/psychological needs; and 4) psychosocial services/interventions. However, they also noted variability in the degree to which each of these components is addressed.

**Table 2** summarizes 12 representative models of MAT care and how they address these four key components. These models were selected based on their influence on current clinical practice, innovation, or because they focus on delivery of MAT in primary care in specific populations or settings (e.g., HIV or HCV-infected people, pregnant women, or in rural settings).

**Table 3** summarizes sources used to describe the model. Ten of the models were described in Key Informant interviews, six were described in the published literature (including 4 models evaluated in randomized controlled trials), and seven models were described in unpublished/grey literature sources.

In most (10 of the 12) models of care, buprenorphine was the main (and frequently the only) pharmacological therapy offered, with relatively little emphasis on provision of naltrexone in most models. Key Informants noted that in many office-based settings there was not a high demand for naltrexone (due in part to its mechanism of action as a pure opioid antagonist) and the perception that it might not be the optimal therapy for most patients, in the context of limited empiric data regarding its use in primary care. The degree to which educational/outreach interventions were formally incorporated in MAT models of care varied. For example, some models included little or no structured education or outreach, whereas in other models there was an explicit educational/outreach component. Nonetheless, most Key Informants noted that education is important for decreasing stigma associated with MAT among both clinicians and patients, increasing the number of buprenorphine-waivered clinicians, increasing buy-in from staff involved in treatment of OUD, and increasing understanding and uptake of MAT by patients.

Educational/outreach efforts included local stakeholder meetings for training and to establish and disseminate standards of care (Southern Oregon Model), mentored buprenorphine prescribing and Internet-based provider education and support (Project Extension for Community Healthcare Outcomes [ECHO]), training aimed at getting more physicians waived for use of buprenorphine, and education aimed at decreasing stigma and increasing use or uptake of MAT by clinicians, office staff, and patients (various models). One Key Informant noted that the SAMHSA-funded Physician Clinical Support System-Buprenorphine (PCSS-Buprenorphine), a Web-based resource designed to support physicians who prescribe buprenorphine by providing training and education and linking them with a national network of trained physician mentors, was instrumental in increasing the number of buprenorphine-waivered physicians during the initial expansion of MAT into office-based settings.<sup>24</sup> Now supplanted by the Prescribers' Clinical Support System-Medication Assisted Treatment (PCSS-MAT),<sup>25</sup> PCSS represents a method for providing physician education and support services that is widely available across geographic settings and in different models of care.

Key Informants consistently noted that coordination/integration of care is critical for successful delivery of MAT in primary care settings. Coordination/integration of care was an explicit component of all of the more structured MAT models of care. In six MAT models (Hub and Spoke, Office-based Treatment Model (OBOT), Massachusetts Nurse Care Manager Model, Buprenorphine HIV Evaluation and Support (BHIVES) Collaborative Model, Project ECHO, One Stop Shop), a specific nonphysician is designated with providing care integration and coordination for treatment of OUD and coordinating primary medical care and mental health needs. The care coordinator may also serve as the main point of contact for patients, allowing for less extensive physician-patient contact. In these models, physicians primarily prescribe buprenorphine, have less frequent face-to-face visits with the patient, and provide consultation as needed. The Key Informants viewed this type of “glue” person as critical for offloading the burden of care from physicians and allowing them to manage more patients with OUD successfully, with the provision that the glue person needs to have requisite skills and knowledge in treating OUD.

Key Informants also consistently noted that availability of psychosocial services is essential to successful MAT models of care, and noted that provision of counseling is required to meet requirements for office-based MAT as specified in DATA 2000. The degree to which psychosocial services are integrated into the MAT treatment setting, the intensity of psychosocial treatments, and the intensity of psychosocial services, varied even within programs implementing the same model of care. Key Informants disagreed on the types or intensity of psychosocial services required to implement successful office-based models of care in primary care settings. Some Key Informants considered models of care without integrated, comprehensive psychosocial services to be inadequate; other Key Informants noted that models of care that included brief counseling with medication treatment have been shown to be effective and that although such models might not represent the ideal, they may be easier to implement and already represent a great improvement in terms of access to care and treatment outcomes. Key Informants noted that the need for more intensive psychosocial services is likely to vary according to the setting and population treated and that models of care that do not have more intensive psychosocial services may find it difficult to manage more complex patients. In most MAT models of care, additional psychosocial services, including management of psychiatric comorbidities, group and individualized counseling, peer support, social and family support, and community support services are available on-site or nearby. In the Collaborative Opioid Prescribing (Co-OP) model, ongoing psychosocial services are provided by a partnering OTP. Although the Key Informants noted a preference for comprehensive, on-site psychosocial services, they noted that this was not always possible due to financial constraints or local availability of services. The One Stop Shop model represents a unique model in which MAT is provided in a preexisting mental health clinic with comprehensive psychosocial services and also provides primary care and other health services. Several models of care focus on identification and initiation of MAT in specific settings (e.g., emergency department, during hospitalization, or in prenatal care), with referral to ongoing treatment in community-based/primary care settings.

The following section describes the 12 representative models of care in more detail, including advantages and disadvantages of each.

## **Hub and Spoke Model**

The Hub and Spoke model was developed in Vermont.<sup>26-28</sup> The model consists of two levels of care, with the patient's needs determining the appropriate level. In this model, centralized intake and initial management, including induction of MAT, occur at a "hub" center with extensive addiction expertise and resources. The hub may or may not be an OTP. Following stabilization, patients who do not require ongoing management at the hub have their management transferred to "spokes" (i.e., clinics in the community for ongoing management). Buprenorphine has been the primary pharmacological component in the Hub and Spoke model. Vermont incentivized implementation of buprenorphine by funding online training for physicians to obtain buprenorphine waivers and providing other technical assistance to physicians prescribing buprenorphine. The Hub and Spoke model includes some educational outreach in the community to increase the number of buprenorphine waived physicians. Coordination and integration occurs between the hub and spoke as well as within each spoke site, and is typically carried out by a registered nurse, clinician case manager, or other "care connector" (e.g., via peer-to-peer support or behavioral health workers). Psychosocial services are embedded within spoke sites, including social workers, counseling, and community health teams. The hub provides



consultative services to manage more clinically complex patient, support tapering off MAT, or to refer to an OTP (or dispense methadone if the hub is an OTP) if needed.

An important advantage of the Hub and Spoke Model is the centralized care provided during initiation of MAT, when patients may benefit most from the additional expertise and resources available at the hubs. Centralized intake and initial management allow the hubs to identify patients who may not be suitable for management in community-based practices. The established relationships between the hub and spokes promote ongoing coordination and integration, including efficient consultation with the hubs and transfer of care back to the hub as needed. Within the spoke sites in this model of care, the use of designated nonphysician “care connectors” at the spoke sites and availability of embedded psychosocial services are important advantages over models in which the coordination/integration roles are less well defined or in which psychosocial services are not available on-site. A potential disadvantage of the Hub and Spoke model is that a hub with the appropriate expertise and resources may not be available in all settings that wish to implement a MAT model of care. In addition, the handoff from the hub to the spokes could introduce some discontinuity of care, though this could be mitigated through appropriate coordination. Also, the spokes in the Hub and Spoke model are likely to vary in the degree of expertise and types of services provided.

## **Collaborative Opioid Prescribing (Co-OP) Model**

The Co-OP model was developed in Baltimore.<sup>29,30</sup> Similar to the Hub and Spoke model, initial intake, induction with buprenorphine, and stabilization is performed at a center (in the Co-OP model, this is an OTP). Patients are shifted to primary care clinics for ongoing MAT after stabilization on medication. Unlike the Hub and Spoke model, in the Co-OP model psychosocial services are generally provided concurrently on an ongoing basis by the OTP, rather than at the primary care site. Some outreach and education is performed by counselors involved in Co-OP to community physicians.

Like the Hub and Spoke model, an advantage of the Co-OP model is that initial evaluation and management occurs in a specialty center; in addition, the specialty center continues to provide psychosocial services following the handoff to the primary care site. Therefore, this model takes advantage of the expertise and resources available at the OTP on an ongoing basis. A potential disadvantage of the Co-OP model is that because ongoing psychosocial services are provided by the OTP, it may require relatively close proximity between the primary care sites and the OTP, which may not be available in all settings that wish to implement a MAT model of care. Also, because the OTP in the Co-OP model provides ongoing services, this could limit the number of patients that could be managed compared to the Hub and Spoke model, in which ongoing care for most patients is more dispersed and provided more independently within the spoke centers.

## **Office-Based Opioid Treatment (OBOT) (Yale)**

An early model for OBOT implemented at Yale has since been widely disseminated throughout the United States. OBOT utilizes a clinic coordinator glue person (typically a nurse) with expertise in buprenorphine who works in collaboration with a primary care clinician.<sup>31-33</sup> The glue person is instrumental for coordinating and integrating care, including primary care and mental health. Psychosocial services include regular brief counseling provided by the physician and glue person or other staff; other psychosocial services vary but can include integrated cognitive behavioral therapy or motivational enhancement therapy. Psychosocial services may be

located on-site or off-site. Initially, education and training of new buprenorphine prescribers was often done through the PCSS-Buprenorphine program (now available through PCSS-MAT), including mentoring by more experienced prescribers.

A key advantage of the OBOT model is its use of a glue person to coordinate care ongoing care. This provides an efficient way for the prescribing physician to manage more patients. The model also takes advantage of a training and mentoring resource available via the Web. Although regular brief counseling is a core aspect of this model, a potential disadvantage is that the availability of additional psychosocial services is highly variable, which could make management more difficult for more complex patients. In addition, coordination and ongoing relationships with OTPs appear relatively informal or undefined in this model.

## **Massachusetts Nurse Care Manager Model**

This model was developed in Massachusetts, where Medicaid reimburses Federally Qualified Health Center nurses for OUD care management.<sup>34-36</sup> This model is similar to the OBOT model in that a key aspect is the use of a nonphysician to coordinate and manage much of the care. Unlike the OBOT model, the Massachusetts model specifically uses nurse care managers who team with primary care physicians to provide MAT (primarily buprenorphine). The nurse care manager performs initial screening, intake and education, often with assistance from a medical assistant. One Key Informant described an adaptation of this model at a community-based healthcare system in Massachusetts in which a “care partner” (usually a master’s level individual who is not a nurse care manager) performs this role. This model utilizes a training program to get more primary care physicians involved in prescribing buprenorphine and education is provided on best MAT practices. Psychological services are integrated on-site or nearby, though the specific services that are available vary from site to site. Patients who require a higher level of care can be expedited into treatment in an OTP.

A key advantage of this model is that it utilizes a nonphysician to offload some of the burden from prescribing physicians, which in turn enables the prescribing physicians to manage more patients. This model also emphasizes training and education to engage more primary care physicians in prescribing buprenorphine. Another advantage of this model is that it may be more sustainable financially, because Medicaid reimburses federally qualified health center (FQHC) nurses in Massachusetts for OUD care management and the state supports additional coordination services using Block Grant resources; however, Key Informants noted that this is not the case in all states. A disadvantage is that the availability of psychosocial services and whether they are present on-site vary. In addition, the model is highly dependent on the availability of a skilled person who can assume the nurse care manager or analogous role effectively.

## **Buprenorphine HIV Evaluation and Support (BHIVES) Collaborative Model**

The BHIVES Collaborative Model utilizes the OBOT framework to provide a chronic care model for providing buprenorphine in HIV primary care settings.<sup>37-47</sup> Like the OBOT Model, a clinic coordinator glue person (typically a counselor or social worker) is essential for coordinating care, working in conjunction with the primary care provider. HIV care can be provided by the primary care provider or by another on-site provider in coordination with the primary care provider. BHIVES sites generally have on-site psychological services, including

individual counseling, though the types of services vary. HIV clinics coordinate with affiliated OTPs for patients switching to or from methadone. A HRSA<sup>48</sup> monograph promotes adoption of BHIVES in United States HIV clinics and BHIVES is considered the standard of care for engaging HIV-infected patients with OUD in treatment.<sup>49,50</sup>

An advantage of the BHIVES model is that it is specifically designed to address MAT, HIV care, and primary care within a single setting. It also has the same advantages as other models that utilize a glue person for chronic care management and coordination. A potential disadvantage is that the availability of on-site psychological services and the types of available services vary and are not well specified. In addition, it requires clinicians with expertise and knowledge in both MAT as well as HIV care, which may not be available in all settings. Though BHIVES implementation preceded PCSS, PCSS now includes physician mentors with expertise in HIV care, an educational model that could potentially be expanded for other chronic comorbid conditions.

## **Project Extension for Community HealthCare Outcomes (ECHO)**

Project ECHO, a model of care first developed in New Mexico, links primary care clinics in rural areas with a university health system utilizing an Internet-based audiovisual network for mentoring and education<sup>51-53</sup> regarding an array of medical conditions. The University of New Mexico developed a module for supporting rural primary care providers in MAT management. It emphasizes nurse practitioner or physician assistant based screening with referral to a collaborating physician for initial and ongoing MAT, typically with buprenorphine. Counseling and behavioral therapies are offered from all ECHO team members. Complex patients can be referred for further assessment and/or evaluation at an OTP. There is also an emphasis on recruitment of physicians for buprenorphine waiver training and provision of continuing medical education in OUD.

An important advantage of the ECHO model is that it enhances the ability of rural primary care clinics to provide MAT through its Internet-based mentoring and educational network. The ECHO model may be considered a rural adaptation of the Hub and Spoke or Co-OP models, in that it engages the expertise of a “hub” center to assist in provision of MAT. A potential disadvantage of the ECHO model over traditional tiered care models is that due to the geographic distance between the primary care sites and the hub, initial intake and assessment does not occur at the centralized hub, due to the dispersed and rural settings in which care is provided. Rather, all care, including initial intake and assessment, occur at the primary care sites. The limited availability of on-site or face-to-face expertise in MAT could pose challenges for the management of complicated or high-risk patients. The ECHO model appears to have been successful in expanding access to MAT in New Mexico, which is near the top among states in buprenorphine-waivered physicians per capita and has had more rapid growth in the number of waivered physicians practicing in rural areas than in other areas of the United States since its initiation in 2005.<sup>51</sup> In addition, the ECHO model focuses on utilizing mid-level care providers for performing initial screening, which may be critical for expanding access to MAT in many rural settings. There is also a strong emphasis on provision of psychosocial services in the ECHO model. The ECHO model is a tele-education/tele-consulting approach considered distinct from telemedicine, as there is no direct doctor-patient relationship between off-site experts and patients, who are de-identified. A potential advantage of this approach is that it only requires basic, widely available teleconferencing technology and does not require the high startup costs required for Health Insurance Portability and Accountability Act (HIPAA)-compliant

telemedicine expansion or the sustainable funding necessary to purchase and maintain telemedicine technology and services. A potential disadvantage is the lack of direct contact between off-site experts and patients; which could make it more difficult to manage complicated patients and obtain reimbursement for providing consultative expertise.

## **Medicaid Home Model for Those With Opioid Use Disorder**

The Medicaid Home Model is a flexible model that provides MAT with behavioral health therapies that are integrated with primary care delivered in Medicaid Home clinics.<sup>54,55</sup> Provider and community education is emphasized to increase uptake (by clinicians and patients) and to decrease stigma. A core aspect of this model is that core psychosocial services are required (i.e., comprehensive care management, care coordination, health promotion, comprehensive transitional care/followup, individual and family support, and referral to community and social support services). Some telehealth services are also offered, though their availability and use vary. Implementation of Medicaid Home Models differs from state to state with differences in how the models are structured and overlap with other models of care described in this section.

An advantage of the Medicaid Home Model is that it requires care coordination and a set of core psychosocial services. In addition, a Key Informant noted that provider and community education are emphasized as key aspects of this model. The flexibility of this model is an advantage in enabling service delivery and provision to vary according to the needs and resources of the particular setting. At the same time, the flexibility of the model may be viewed as a disadvantage in that some aspects (e.g., who provides coordination/integration, who performs initial screening and assessment) are not standardized or well defined.

## **Southern Oregon Model**

The Southern Oregon Model is an example of a local and informal model for delivery of MAT in a rural primary care network. It focuses almost exclusively on buprenorphine. A notable characteristic of the Southern Oregon Model is that it has utilized regular meetings of stakeholders (including regional Medicaid-accountable care organizations) for education, training, and development of practice standards around the prescription of opioids for chronic pain and addiction treatment. Coordination or integration of care is variable and often limited, though an on-site clinical social worker is available. Access to OTPs for complex patients is not formally integrated.

An advantage of this model is that it is a grass-root, community-based effort, which may promote buy-in from clinicians and those in the community. This could serve as a model for implementation of MAT in rural settings where there may be increased stigma associated with MAT and resistance to its use. However, a number of key components of this model are not yet well defined, and a Key Informant noted that psychosocial services and coordination/integration of care is often limited. The Key Informant also noted that the relationship with the local OTP is suboptimal and at times office-based MAT is viewed as a competitor rather than a partner by the OTP.

## **Emergency Department (ED) Initiation of OBOT**

This model focuses on the ED identification of OUD, with buprenorphine induction initiated in the ED.<sup>56</sup> Patients are connected to ongoing OBOT for 10 weeks, then transferred to ongoing,

office-based maintenance treatment or detoxification. Brief “medical management” counseling is performed by physicians; other psychosocial services vary.

An advantage of this model is that it identifies patients who might benefit from MAT and may not have access to primary care, or only sporadic access. Initiation of buprenorphine in the ED also appears to increase retention in care rates versus a simple referral. A potential model disadvantage is that it focuses on ED screening and initiation of treatment, and the model of care for ongoing management in primary care settings is not well defined. However, the ED initiation model could be used to “feed” into one of the office-based models of care described above in a more formal manner, depending on what is available in the community.

## **Inpatient Initiation of MAT**

This model involves the identification of OUD in the hospital, with initiation of MAT (methadone, buprenorphine, or naltrexone) during the hospitalization by a multidisciplinary addiction consult service.<sup>57</sup> Patients are connected with primary care or specialty addictions care, where treatment continues following hospital discharge. In some programs, when relevant, there is a buprenorphine “bridge” clinic for stabilization prior to transitioning to primary care. Ongoing psychosocial services are provided at primary care sites. A variation of this model involves identification of OUD in the hospital and brief counseling, with facilitated referral to a community-based clinic for induction of MAT and ongoing care following hospital discharge.<sup>58</sup>

Like the model involving ED initiation, an important advantage of inpatient screening and initiation is that it identifies patients with complex morbidity and high risk of mortality who otherwise may have had limited or no access to MAT. Likewise, inpatient initiation appears to enhance retention in care rates versus simple referral for outpatient initiation of MAT after hospitalization. Like the ED initiation model, this model of care focuses on the inpatient aspect, but could be linked to one of the office-based models of care described above for ongoing management. Patients initiated on methadone would not be eligible for referral to office-based care.

## **Integrated Prenatal Care and MAT**

This model involves the provision of prenatal care to pregnant women who are treated with buprenorphine in primary care. Women receive prenatal and postpartum care, with care continued in an office-based setting after birth. Psychosocial services are provided on-site as well as through affiliated OTPs.

Like the models of ED and inpatient MAT initiation, this model can identify women who might benefit from MAT with limited or no access to care who come into contact with the medical system for prenatal care. In addition, women may be more amenable to MAT in the prenatal setting due to concerns about the fetus and the desire to integrate care in one location. An additional advantage of this model is that it provides ongoing care in the postpartum period, providing additional continuity. Outcome studies suggest that there is a reduction in Neonatal Abstinence Syndrome when pregnant women with OUD are maintained with buprenorphine rather than methadone.<sup>59</sup> A potential disadvantage is the need to transition at some point to a setting that can provide ongoing, long-term care, unless the office-based setting is equipped to do so; in one model (Oregon), ongoing care is provided through transition to a primary care clinic that can provide MAT.

## **One Stop Shop Model**

The One Stop Shop model was developed in response to an outbreak of HIV infection in rural Indiana due to sharing of infected syringes.<sup>60</sup> Based in an existing mental health clinic, it provides integrated care including management of HIV/HCV infection, MAT, mental health, and primary care needs, as well as other services including syringe exchange.<sup>61</sup> Peer navigators and social workers provide coordination with primary care providers. Because it is based in an existing mental health clinic, this model provides comprehensive on-site psychological services, including a visiting psychiatrist who is available on a weekly basis for consultation.

An advantage of this model is that it makes use of an existing mental health clinic to provide comprehensive integrated care, including extensive psychosocial services under a single roof. However, Key Informants noted that this model represents a unique response to the HIV outbreak and may not be reproducible in other settings due to the resources and unique clinical setting (i.e., an existing mental health clinic prepared to provide MAT) required.

**Table 2. Overview of MAT Models of Care for OUD in primary care (including rural or other underserved settings)**

Model	Summary	Pharmacological Component	Education/ Outreach Component	Coordination/ Integration of Care Component	Psychosocial Component	Other Component(s)
Buprenorphine-HIV Evaluation and Support (BHIVES) Collaborative Model	Chronic care model for providing buprenorphine in HIV primary care clinic setting	Buprenorphine	Patient and provider educational material available online	Treatment for OUD and primary care, including HIV care integrated in same setting. Clinical coordinator “glue person” coordinates care; works in conjunction with primary care provider. Provision of HIV care may be by the primary care provider or another provider working with the primary care provider	On-site psychological services variable, including individual and group counseling	Coordination with OTP for patients switching to or from methadone
Collaborative Opioid Prescribing (Co-OP) Model	Links opioid treatment programs with office-based buprenorphine providers; initial intake, induction, and stabilization performed at OTP then shifted to primary care clinic	Buprenorphine	Outreach performed by counselors to community physicians	Initial assessment, psychosocial treatment, and expert consultation initiated in drug treatment program and patients transitioned to primary care in federally qualified health center following stabilization	Provided concurrently via OTP, including ongoing counseling and monitoring	In Baltimore, supports to facilitate access to health coverage through Medicaid and to coordinate care through HealthCare Access Maryland
Emergency Department (ED) Initiation of OBOT	Model involving ER identification of OUD; buprenorphine induction initiated in ED; coordination with OBOT, nurse with expertise in buprenorphine working in collaboration with primary care clinician	Buprenorphine	Not a major component	OUD identified in ER and patients started on buprenorphine and connected to ongoing OBOT provided by physicians and nurses for 10 weeks, then transferred to office-based ongoing maintenance treatment or detoxification.	“Medical management” counseling visits with physician	

<b>Model</b>	<b>Summary</b>	<b>Pharmacological Component</b>	<b>Education/ Outreach Component</b>	<b>Coordination/ Integration of Care Component</b>	<b>Psychosocial Component</b>	<b>Other Component(s)</b>
Hub and Spoke Model (Vermont)	Centralized intake and initial management (buprenorphine induction) at “hub” and then patients connected to “spokes” in community for ongoing management	Primarily buprenorphine	Outreach to prescribers in the community to increase 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, behavioral health specialist) for coordination/integration of care at spokes.	Embedded in spoke sites, including social workers, counseling, and community health teams.	Hubs provides consultative services and available to manage clinically complex patients, support tapering off MAT, or prescribe methadone or refer to OTP, if needed
Inpatient Initiation of MAT	Model involving identification of OUD in the hospital and connecting patients to office-based MAT and primary care	Buprenorphine, naltrexone	Not a major component	MAT started by multidisciplinary addiction consult service during medical hospitalization and connected with primary care. Treatment continued in primary care; some programs have buprenorphine “bridge” clinic prior to transition to primary care.	Provided at primary care site	
Integrated Prenatal Care and MAT	Model providing prenatal care to pregnant women who are treated with buprenorphine	Buprenorphine	Not a major component	Primary care clinic provides MAT, as well as prenatal and post-partum care; care continued in office-based setting for 1 year after birth. In some programs women can work with doulas	Services provided on-site or via partnering OTP	



<b>Model</b>	<b>Summary</b>	<b>Pharmacological Component</b>	<b>Education/ Outreach Component</b>	<b>Coordination/ Integration of Care Component</b>	<b>Psychosocial Component</b>	<b>Other Component(s)</b>
Massachusetts Nurse Case Manager Model	A primary-care based model that teams nurse care managers with primary care physicians; nurse care managers generally perform initial screening, intake, education	Primarily buprenorphine	A training program exists to get more physicians, especially residents, and also faculty on board. DPH trains residential treatment providers on best practices.	Nurse care managers (RN or FNP) manage 100 to 125 patients alongside primary care clinicians, with assistance from a medical assistant. Alternatively, care partners (usually Master's level individuals) who assist the primary care staff with screening, brief intervention, and referral to treatment.	Psychological services are integrated on-site or nearby	Patients who require higher level of care can be expedited into an OTP
Medicaid Home Model For Those With Opioid Use Disorder	A flexible model that provides MAT in combination with behavioral health therapies and integrated with primary care.	Primarily buprenorphine	Provider and community education emphasized to increase uptake and decrease stigma	Required component, but mechanism of coordination varies	Six core psychosocial services are required: comprehensive care management, care coordination, health promotion, comprehensive transitional care/followup, individual and family support and referral to community and social support services.	Some telehealth services offered

<b>Model</b>	<b>Summary</b>	<b>Pharmacological Component</b>	<b>Education/ Outreach Component</b>	<b>Coordination/ Integration of Care Component</b>	<b>Psychosocial Component</b>	<b>Other Component(s)</b>
Office-based Opioid Treatment (OBOT) (Yale)	Glue person (typically nurse) with expertise in buprenorphine working in collaboration with primary care clinician	Primarily buprenorphine	Not a major component	Glue person (typically nurse) instrumental for coordinating and integrating care, including primary care and mental health	Physician counseling monthly; some psychological services provided on-site by glue person or other staff. Other psychosocial services vary, including integrated CBT, Motivational Enhancement Therapy; some psychosocial services offsite	
One Stop Shop Model	Integrated model based in mental health clinic to provide “one-stop” shopping including management of HIV/HCV infection and plans for MAT in progress	Primarily naltrexone	Education to increase number of waived physicians	Treatment for OUD, mental health, and primary care (including HIV/HCV care) provided in same setting. Peer navigators and social workers provide coordination with primary care providers	Centered in mental health clinic that provides comprehensive psychological services; psychiatrist once a week	Syringe exchange and other services also available

Model	Summary	Pharmacological Component	Education/ Outreach Component	Coordination/ Integration of Care Component	Psychosocial Component	Other Component(s)
Project Extension for Community Healthcare Outcomes (ECHO) (New Mexico)	Model of care for linking primary care clinics in rural areas with a university health system, emphasizing nurse practitioner or physician assistant screening and MAT (physician prescribing) combined with counseling and behavioral therapies.	Primarily buprenorphine	Mentored buprenorphine prescribing for providers, including Internet-based, audiovisual network for provider education. Free buprenorphine training provided several times a year. ECHO staff provide patient education one-to-one or in group setting.	NP/PA performs initial evaluation and screening educate patient and refer to collaborating physician for treatment. NP/PA performs monitoring treatment and followup appointments including labs, urine testing, monitoring, patient education and support and other coordination (e.g., vaccinations)	Counseling and behavioral therapies offered from all ECHO team members including CHWs, although CHWs and NPs provide education/support, psychosocial support including 12 step programs, crisis counseling, referrals, and relapse-prevention plans.	Refer any patients with high or moderate risk scores for opioid use to NP for further assessment and/or referral to OTP
Southern Oregon Model	A local and informal model for delivery of MAT in a rural primary care network	Almost exclusively buprenorphine	A group of local stakeholders from many perspectives who prescribe opioids (Oregon Pain Guidance) meets regularly to develop guidance and provide education.	Relatively limited support for coordination/ integration of care	On-site licensed clinical social worker with experience in treating patients for pain and addiction, not necessarily in MAT.	Access to OTPs for complex patients not formally integrated.

CBT = cognitive behavioral therapy; CHW = community health worker; DPH = Department of Public Health; ED = emergency department; ER = emergency room; FNP = family nurse practitioner; HCV = hepatitis C virus; HIV = human immunodeficiency virus; MAT = medication-assisted treatment; NP = nurse practitioner; OTP = opioid treatment program; OUD = opioid use disorder; PA = physician assistant; RN=registered nurse

**Table 3. Sources for MAT Models of Care**

Model	Published Literature	Grey Literature	Key Informant Interview
Buprenorphine HIV (BHIVES) Integrated Care Model	Altice, 2011 <sup>37</sup> Fiellin, 2011 <sup>39</sup> Korthuis, 2011 <sup>40</sup> Korthuis, 2011 <sup>41</sup> Lucas, 2010 <sup>42*</sup> Sullivan, 2006 <sup>44*</sup> Weiss, 2011 <sup>46</sup> Weiss, 2011 <sup>47</sup>	<a href="https://www.careacttarget.org/library/bee-hive-buprenorphine-program-tools">https://www.careacttarget.org/library/bee-hive-buprenorphine-program-tools</a> <sup>45</sup> <a href="http://buprenorphine.samhsa.gov/bwns/2010_presentations_pdf/19_Fiellin_2_508.pdf">http://buprenorphine.samhsa.gov/bwns/2010_presentations_pdf/19_Fiellin_2_508.pdf</a> <sup>38</sup> <a href="http://www.slideshare.net/SarahCookRaymond/buprenorphine-therapy-in-the-hiv-prima">http://www.slideshare.net/SarahCookRaymond/buprenorphine-therapy-in-the-hiv-prima</a> <sup>43</sup>	✓
Collaborative Opioid Prescribing (Co-OP) Model	Stoller, 2015 <sup>30</sup>	<a href="http://www.atforum.com/pdf/CoOPtalkforONDCP_SAMHSAAug2015Stoller.pdf">http://www.atforum.com/pdf/CoOPtalkforONDCP_SAMHSAAug2015Stoller.pdf</a> <sup>29</sup>	✓
Emergency Department (ED) Initiation of OBOT Model	D'Onofrio, 2015 <sup>56*</sup>	--	✓
Hub and Spoke Model (Vermont)	--	<a href="https://www.pccpc.org/initiative/vermont-hub-and-spokes-health-homes">https://www.pccpc.org/initiative/vermont-hub-and-spokes-health-homes</a> <sup>27</sup> <a href="http://www.healthvermont.gov/adap/documents/HUBSPOKEBriefingDocV122112.pdf">http://www.healthvermont.gov/adap/documents/HUBSPOKEBriefingDocV122112.pdf</a> <sup>28</sup> <a href="http://www.leg.state.vt.us/reports/2014ExternalReports/299315.pdf">http://www.leg.state.vt.us/reports/2014ExternalReports/299315.pdf</a> <sup>26</sup>	✓
Inpatient Initiation of MAT	Liebschutz, 2014 <sup>57*</sup>	--	--
Integrated Prenatal Care and MAT (Expert suggestion)	--	--	--
Massachusetts Nurse Case Manager Model	Alford, 2007 <sup>35</sup> Alford, 2011 <sup>34</sup> LaBelle, 2016 <sup>36</sup>	<a href="http://www.mass.gov/eohhs/gov/departments/dph/stop-addiction/get-help-types-of-treatment.html">http://www.mass.gov/eohhs/gov/departments/dph/stop-addiction/get-help-types-of-treatment.html</a> <sup>62</sup>	✓
Medicaid Home Model For Those With Opioid Use Disorder	-	<a href="https://www.medicaid.gov/Federal-Policy-Guidance/Downloads/CIB-07-11-2014.pdf">https://www.medicaid.gov/Federal-Policy-Guidance/Downloads/CIB-07-11-2014.pdf</a> <sup>54</sup> <a href="https://www.medicaid.gov/state-resource-center/medicaid-state-technical-assistance/health-homes-technical-assistance/downloads/hh-irc-health-homes-opiod-dependency.pdf">https://www.medicaid.gov/state-resource-center/medicaid-state-technical-assistance/health-homes-technical-assistance/downloads/hh-irc-health-homes-opiod-dependency.pdf</a> <sup>55</sup>	✓
Office-based Opioid Treatment (OBOT) (Yale)	Fiellin, 2002 <sup>33</sup> Fiellin, 2006 <sup>32*</sup> Fiellin, 2008 <sup>31</sup>	--	✓
One Stop Shop Model	--	<a href="http://www.lifespringhealthsystems.org/about-us/locations/">http://www.lifespringhealthsystems.org/about-us/locations/</a> <sup>61</sup>	✓
Project Extension for Community Healthcare Outcomes (ECHO) (New Mexico)	Komaromy, 2016 <sup>51</sup>	<a href="http://echo.unm.edu/wp-content/uploads/2014/10/Opioid-Abuse-and-Addiction-Management-Protocol.pdf">http://echo.unm.edu/wp-content/uploads/2014/10/Opioid-Abuse-and-Addiction-Management-Protocol.pdf</a> <sup>52</sup> <a href="http://www.aafp.org/news/chapter-of-the-month/20140930nmaf-chapspot.html">http://www.aafp.org/news/chapter-of-the-month/20140930nmaf-chapspot.html</a> <sup>53</sup>	✓
Southern Oregon Model	--	--	✓

\*Randomized controlled trial evaluating the model of care

## **Guiding Question 2: Settings In Which MAT Is Implemented**

MAT is currently implemented in a variety of primary care settings. As described above, models of care are implemented in general primary care settings as well as in settings in which primary care is integrated with management of other conditions (e.g., HIV, pregnancy, mental health). Certain models utilize the ED and inpatient settings to identify patients with OUD who could benefit from induction and referral to office-based treatment. Most studies on MAT in primary care settings have been conducted in centers that are either university-affiliated or hospital-based. Because of the need to expand access to the medically underserved and to support access to MAT in office-based settings for Medicaid beneficiaries<sup>54</sup> and in FQHCs,<sup>63</sup> aspects of MAT models of care developed in university-affiliated or hospital-based settings may be transferable to community-based settings, (e.g., use of a glue person for care coordination and initial management, association with a centralized center of excellence, focus on integration and coordination of care, and provision of psychosocial services).

DATA 2000 and the approval of buprenorphine in 2002 increased the availability of MAT by permitting waived physicians to prescribe buprenorphine for treatment of OUD. A 2006 report from SAMHSA on the effects of the DATA Waiver Program found that about 56 percent of waived physicians were from a nonaddiction specialty<sup>64</sup> (the proportion that were primary care providers was not reported). However, not all waived physicians actually prescribed buprenorphine. Among waived physicians, approximately two-thirds reported prescribing buprenorphine. As of 2016, 21,781 physicians in the United States were certified to provide buprenorphine treatment for up to 30 patients and 10,459 were certified to provide buprenorphine treatment for up to 100 patients (total 32,240).<sup>65</sup>

There is geographic variability in the United States in access to and utilization of MAT. One study found that buprenorphine use was highest in the Northeast (Vermont, Maine, and Massachusetts) and lowest in South Dakota, Iowa, and Kansas.<sup>66</sup> Many geographic areas in the United States continue to experience shortages in access to MAT in primary care settings especially for patients living in rural areas. A survey found that only 3 percent of primary care physicians in rural American had received a Drug Enforcement Administration (DEA) DATA waiver to prescribe buprenorphine for OUD. Although the proportion of the United States population residing in rural counties has declined substantially, about half of United States counties have no buprenorphine-waivered physicians, and it is estimated that more than 30 million people live in counties (predominantly in nonmetropolitan areas) without access to buprenorphine treatment.<sup>22,67,68</sup> One study estimated that the number of physicians with buprenorphine waivers (per 10,000 population) is about 7 to 9 times higher in urban compared with rural settings.<sup>69</sup> Another study found that states that opted to expand Medicaid following the passage of the Affordable Care Act and establish a state-based health insurance exchange experienced greater growth in the supply of buprenorphine-waivered physicians than states that did not take these actions.<sup>70</sup> In another study, states with increased Medicaid funding, more opioid overdose deaths, and specific state guidance for office-based buprenorphine use were associated with more buprenorphine-waivered physicians.<sup>68</sup>

## **Considerations and Barriers for Implementing MAT in Primary Care**

Our Key Informants and literature review identified a number of important considerations for implementing MAT in primary care. Insufficient institutional support is frequently cited as a

barrier to implementation.<sup>71,72</sup> Institutional support may include sponsored training, resources and staffing for coordination and integration of care, and provision of nonphysician staff with expertise in OUD to offload some of the burden from prescribing physicians. Primary care physicians also report important knowledge gaps in the area of addiction. These gaps reduce the likelihood that they will prescribe MAT unless they have ready access to addiction expertise (e.g., for complex patients). Addiction expertise could be accessed through telehealth initiatives (e.g., Project ECHO), mentored prescribing (e.g., PCSS-MAT), coordination with local OTPs or experts in addiction (e.g., Hub and Spoke model or Co-OP model), or other methods. Barriers to telehealth include substantial start-up costs to be HIPAA compliant, the need for ongoing resources for staffing and maintenance, and variable reimbursement. Implementing MAT also requires the integration of enhanced psychosocial services that may not be readily available in all primary care settings.

Another consideration is whether there are enough patients and sufficient reimbursement to justify the resources and time required to implement MAT in primary care settings. Key Informants noted that there needs to be a minimum number of waived physicians available to provide cross-coverage to avoid burn-out among prescribing physicians. In rural settings, Key Informants observed that travel time can be a significant barrier, with some patients facing a 2-hour commute to clinic; this can result in high travel costs and jeopardize the ability of patients to maintain employment.<sup>73</sup>

Key Informants and the literature describe other barriers to implementation of MAT in primary care settings.<sup>71,72,74</sup> A key barrier is the relative lack of physicians with an FDA waiver to prescribe buprenorphine for treatment of OUD. In December 2013, the average state had only eight waived physicians per 100,000 residents.<sup>75</sup> Increasing the limit on the number of patients that a physician could prescribe buprenorphine for OUD (currently 30 or 100) could be more effective at increasing buprenorphine use and access than increasing the number of substance abuse treatment facilities or increasing the number of waived physicians.<sup>75</sup> One study found that the greatest impact on the amount of buprenorphine prescribed was the number of waived physicians able to treat up to 100 patients with buprenorphine.<sup>69</sup> Although some Key Informants felt that the current patient limits could be a barrier to implementation, most primary care clinicians are not close to the prescribing limit and there are concerns that increasing the limits could result in suboptimal care. Most (70% to 95%) physicians prescribing buprenorphine never turned away any patient because of patient prescribing limits.<sup>76</sup> As noted above, there seems to be an unwillingness on the part of some physicians to prescribe even though they have a waiver.<sup>74</sup> The same survey found that about two-thirds of physicians with a buprenorphine waiver elected to not be included on the public Centers for Substance Abuse Treatment Locator List in 2008; among these, about two-thirds reported no prescribing of buprenorphine in the last 90 days. Among physicians on the Locator List, 86 percent reported prescribing in the last 90 days.

Key Informants consistently noted that stigma towards MAT remains an important barrier to implementation. Surveys of physicians<sup>74</sup> describe stigma as pervasive and present among physicians, clinic staff, patients, law enforcement, and the community. Key Informants noted that some patients do not even want to be in the same waiting room as patients who are receiving MAT. This could result in significant barriers due to the need to create separate clinic areas. In some states and other settings, abstinence is still viewed as a “better” treatment than MAT, despite evidence to the contrary. The perception persists that using an opioid agonist is replacing one addicting drug with another and promotes a preference for detoxification and abstinence

rather than agonist or antagonist therapy. In rural settings in particular, Key Informants noted that MAT is often discouraged due to these beliefs. The Key Informants noted a general lack of training and understanding<sup>74</sup> regarding MAT even among physicians, and emphasized the need for education of physicians as well as the community regarding the evidence on effectiveness of MAT in order to increase the number of buprenorphine waived physicians, increase uptake of MAT by patients, and increase buy-in among the community.

Other barriers to prescribing buprenorphine for OUD frequently cited in a survey of family physicians in Vermont and New Hampshire includes inadequately trained staff, insufficient time, inadequate office space, and cumbersome regulations.<sup>75</sup>

Reimbursement remains an important barrier.<sup>71</sup> For example, although Nurse Care Managers in the Massachusetts model are reimbursed for their services, people serving similar functions in other models are not necessarily reimbursed in the same way. In the Project ECHO model, off-site experts provide consultative expertise to primary care providers there is no doctor-patient relationship, and therefore these services are not reimbursable. Key Informants also noted variability in policies related to reimbursement of provision of telemedicine services in which there is an established, direct doctor-patient relationship. Without adequate reimbursement, Key Informants noted that implementation in many primary care settings is unsustainable financially. Key Informants also noted onerous prior authorization requirements as a barrier to prescribing buprenorphine, as well as arbitrary limits on the treatment duration and doses. A survey of 45 states found that in 2013, only 11 percent of states had Medicaid policies that excluded coverage for methadone and buprenorphine, whereas nearly three-quarters (71%) had policies to cover both buprenorphine and methadone in Medicaid enrollees.<sup>77</sup> However, there was also an increase in adoption of policies that could hinder access to buprenorphine or methadone, such as prior authorization requirements.

## **Training, Certification, and Staffing Needs**

DATA 2000 allows physicians to provide MAT using buprenorphine outside of licensed OTPs if they complete 8 hours of training and submit an application to receive a waiver. Physicians who obtain a waiver may be subject to periodic DEA audits of patient records (a potential barrier to obtaining a waiver). DATA 2000 further specifies that brief counseling be offered in conjunction with buprenorphine; this can be provided by the physician or nonphysician staff. Models that integrate treatment of OUD with management of other chronic conditions require expertise in management of those conditions; this can be provided by the same physician that is managing the OUD or by other clinicians (not necessarily a physician).

Additional staffing and training requirements vary depending on the model of care. Several models use a designated staff person to support the prescribing physician and serve as a main point of clinical contact. In the Massachusetts model, an RN Case Manager performs screening, supports the prescribing physician, and coordinates care and in Project ECHO, nurse practitioners and physician assistants assume similar roles. There are no formal certifications or trainings required to fulfill these roles, though DATA 2000 buprenorphine waiver trainings are open to and attended by nonphysicians. The success of such models is likely to depend to a large degree on the knowledge and skill that such people have in the area of addiction. Additional staffing largely depends on the types of psychosocial services that are offered and may include psychologists, social workers, peer counselors or mentors, psychiatrists, addiction specialists, and others.

## Guiding Question 3: Current Evidence on MAT

### MAT Models of Care

We identified six trials on the effectiveness of MAT models of care in primary care/office-based settings<sup>32,33,42,44,56,57</sup> (**Table 4**). Two trials compared buprenorphine with more intensive versus less intensive counseling in the OBOT (Yale) model.<sup>32,33</sup> One trial compared buprenorphine with more intensive versus less intensive counseling among HIV infected patients in the BHIVES model<sup>44</sup> and another trial of HIV-infected patients compared clinic-based buprenorphine in the BHIVES model versus case management and referral to an OTP.<sup>42</sup> One trial compared the Emergency Department Initiation of OBOT model with buprenorphine versus referral for treatment (with or without a brief intervention)<sup>56</sup> and one trial compared the Inpatient Initiation of MAT model with buprenorphine versus linkage to care.<sup>57</sup> No trial compared the effectiveness of one MAT primary care model versus another.

Detailed tables of included trials for Guiding Question 3 are available in **Appendix G**.

### Psychosocial Interventions

A number of trials have evaluated the comparative effectiveness of different psychosocial interventions given as a component of MAT. However, relatively few trials on psychosocial interventions have been conducted in office-based settings. A Cochrane review included 35 trials on the effectiveness of psychological therapies plus any agonist maintenance treatment as a component of MAT for OUD (**Table 5**).<sup>78</sup> Thirty-one trials were conducted in the United States; in six trials the pharmacological component was buprenorphine; the remainder evaluated methadone (no study evaluated naltrexone). Of the trials, only one was conducted in a primary care/community-based setting.<sup>32</sup> It compared standard medical management with brief (20 minutes/session) medically focused counseling versus extended medical management with more in-depth counseling (45 minutes/session) in patients prescribed buprenorphine and found no clear differences in effectiveness. We identified nine additional trials that evaluated the effectiveness of more intensive psychosocial interventions or compared one psychosocial intervention versus another in office-based settings (**Table 4**). The comparisons evaluated were internet-based community reinforcement approach plus contingency management versus contingency management alone,<sup>79</sup> cognitive behavioral therapy versus standard counseling,<sup>80,81</sup> network therapy versus standard medication management,<sup>82</sup> cognitive behavioral therapy plus directly observed, thrice-weekly buprenorphine versus physician management with weekly buprenorphine, brief versus extended counseling,<sup>83-85</sup> guided drug counseling plus standard medical management versus medical management alone,<sup>33</sup> and brief physician management versus brief physician management plus nurse-administered drug counseling and adherence management.<sup>44</sup> The evaluation of different comparisons makes it difficult to assess overall findings of the trials, but in most studies there were no clear differences in outcomes between different psychosocial interventions.

Detailed tables of included systematic reviews for Guiding Question 3 are available in **Appendix H**.



## Pharmacological Therapies

A number of trials evaluated the pharmacological component of MAT. In all trials, psychosocial interventions were also provided, though the psychological component was often not well-described. Relatively few trials were conducted in office-based settings. Some trials evaluated methadone and sustained-release morphine, which are not approved by the FDA for this indication. We included those medications in this section as they could inform future MAT strategies if they become available in the United States.

### Buprenorphine

A Cochrane systematic review on buprenorphine as a component of MAT included 31 trials (**Table 5**).<sup>15</sup> The trials in the review focused on the effectiveness of buprenorphine versus placebo or versus another medication, rather than the effectiveness of MAT models of care per se. In addition, the studies had characteristics that might impact applicability to MAT in United States primary care settings. Of the 31 trials, 15 were conducted in North America, and only two trials were clearly conducted in community-based settings. One trial<sup>86</sup> compared buprenorphine/naloxone versus buprenorphine versus placebo in a United States setting and the other trial<sup>87</sup> compared buprenorphine versus methadone in an Australian setting (**Table 4**). We identified trials of a newer implantable formulation of buprenorphine, but they were conducted in addiction settings and did not meet inclusion criteria for this report.<sup>88,89</sup>

### Naltrexone

For oral naltrexone as a component of MAT, a Cochrane review included 13 RCTs (**Table 5**).<sup>78</sup> Of these, four were conducted in the United States; all focused primarily on patients who had been recently incarcerated, with none clearly conducted in primary care settings. For extended-release naltrexone, another Cochrane review<sup>90</sup> (**Table 5**) included only one trial on effectiveness, which was conducted in an inpatient setting.<sup>91</sup> Although searches for the Cochrane review appear outdated (conducted in 2007), we identified no recent studies of extended-release naltrexone conducted in primary care settings.<sup>91-97</sup>

### Methadone

A Cochrane review of methadone as a component of MAT included 11 trials, but none were clearly conducted in primary care or community-based settings (**Table 5**).<sup>16</sup> We identified four trials not included in the Cochrane review that compared methadone maintenance in an office-based setting versus a methadone clinic setting (**Table 4**). Two studies were conducted in France<sup>98,99</sup> and two studies in the United States<sup>100,101</sup> The trials generally found that methadone maintenance in office-based settings was associated with similar outcomes as methadone maintenance in addiction treatment settings.

### Sustained-Release Morphine

A Cochrane review included three trials of sustained-release morphine as part of MAT (not approved by the FDA for this use), but none of the trials were conducted in primary care/office-based settings.<sup>102</sup>

## Special Populations

One Cochrane review evaluated the effectiveness of MAT in pregnant women, but evidence on effectiveness of FDA-approved office-based treatments for MAT was extremely limited (**Table 5**).<sup>103</sup> In addition, although three trials (sample sizes 18, 30, and 175) evaluated buprenorphine versus methadone maintenance treatment; none were conducted in primary care or community-based settings. One trial evaluated buprenorphine in community settings for treatment of OUD in young people (15 to 21 years of age), but did not meet inclusion criteria because it compared treatment for 12 weeks versus a 2 week taper.<sup>104</sup> A Cochrane review evaluated effectiveness of oral substitution treatment for OUD in injecting drug users on risk behaviors and rates of HIV,<sup>105</sup> but did not focus on medications approved for use in office-based settings and only included two trials in which patients were managed in primary care settings (**Table 5**).<sup>106,107</sup>

**Table 4. Trials for Guiding Question 3**

Model name Author, year	Comparators	Followup	N	Country	Population Characteristics	Findings
<b>MAT Models of Care</b>						
D'Onofrio, 2015 <sup>56</sup>	Screening and referral to treatment (referral) vs. screening, brief intervention, and facilitated referral to community-based treatment services (brief intervention) vs. screening, brief intervention, ED-initiated treatment with buprenorphine/naloxone, and referral to primary care for 10-week follow-up (buprenorphine)	30 days	329	USA	76.3% male mean age 31 years 34.3% use alcohol to intoxication	Among opioid-dependent patients, ED-initiated buprenorphine treatment vs brief intervention and referral significantly increased engagement in addiction treatment, reduced self-reported illicit opioid use, and decreased use of inpatient addiction treatment services but did not significantly decrease the rates of urine samples that tested positive for opioids or of HIV risk. These findings require replication in other centers before widespread adoption.
Fiellin, 2002 <sup>33</sup>	Buprenorphine and medication management (thrice-weekly sessions with a nurse and a monthly meeting with a physician) vs. buprenorphine and medication management plus drug counseling (not described)	13 weeks	14	USA	71% male mean age 36 years 79% with history/current alcohol dependence	Overall, patients reduced opioid-positive urine toxicology tests and good retention through maintenance; less patients in medication management group vs. medication management plus counseling group achieved greater than or equal to one week of opioid-free urine screens, though this difference was not statistically significant; A greater proportion of the medication management plus counseling group had opioid-free urine screens compared with the medication management alone group, though this difference was not statistically significant
Fiellin, 2006 <sup>32</sup>	Standard medical management (20 minutes with a nurse) and once-weekly medication dispensing (buprenorphine-naloxone) vs. standard medical management and thrice-weekly medication dispensing vs. enhanced (45 minutes with a nurse) medical management and thrice-weekly medication dispensing All groups met monthly with a physician	24 weeks	166	USA	78% male mean age 36 years	The efficacy of brief weekly counseling and once-weekly medication dispensing did not differ significantly from that of extended weekly counseling and thrice-weekly dispensing
Liebschutz, 2014 <sup>57</sup>	Detoxification plus referral vs. induction plus contact from long-term opioid agonist treatment staff that facilitated linkage to hospital-associated primary care buprenorphine treatment	6 months	139	USA	71.2% male mean age 41 years	Compared with an inpatient detoxification protocol, initiation of and linkage to buprenorphine treatment is an effective means for engaging medically hospitalized patients who are not seeking addiction treatment and reduces illicit opioid use 6 months after hospitalization. However, maintaining engagement in treatment remains a challenge.
Lucas, 2010 <sup>42</sup>	Clinic-based, nurse-administered treatment with buprenorphine-naloxone vs. case management and referral to an intensive opioid treatment program (referred treatment)	12 months	93	USA	72% male median age 45-46 years 73% positive for hepatitis C antibody 10% AIDS-defining opportunistic condition in previous 3 month	Participation in opioid agonist therapy was significantly higher in clinic-based buprenorphine than for referred treatment. Positive test results for opioids and cocaine were significantly less frequent in clinic-based buprenorphine than in referred treatment, and study participants receiving clinic-based buprenorphine attended significantly more HIV primary care visits than those receiving referred treatment. Use of antiretroviral therapy and changes in HIV RNA levels and CD4 cell counts did not differ between the 2 groups.

Model name Author, year	Comparators	Followup	N	Country	Population Characteristics	Findings
Sullivan, 2006 <sup>44</sup>	Buprenorphine/naloxone and physician management (brief, biweekly) vs. buprenorphine/naloxone and physician management plus once-weekly drug counseling and adherence management	12 weeks	16	USA	94% male mean age 47 years 29% reported one or more days of alcohol use in past 30 days 100% HIV positive 81% HCV positive	There was no difference in treatment retention or illicit drug use by counseling group; Overall, the proportion of opioid-positive weekly urine screens decreased substantially over trial; CD4 counts remained stable; viral load declined significantly; demonstrated feasibility of integrating buprenorphine into HIV clinical care for treatment of opioid dependence
<b>Psychosocial Interventions</b>						
Christensen, 2014 <sup>79</sup>	Buprenorphine and individual counseling plus contingency management (based on urine results linked to points for gift cards or money) vs. buprenorphine and individual counseling and contingency management plus internet-based community reinforcement approach Both groups had individual counseling every 2 weeks	12 weeks	170	USA	54% male 13% with concurrent alcohol dependence	Compared to those receiving contingency management-alone, community reinforcement approach recipients had more total days of abstinence and were less likely to drop out of treatment; prior treatment for opioid dependence moderated the additional improvement of community reinforcement approach for longest continuous days of abstinence
Fiellin, 2002 <sup>33</sup> (also a model of care)	Buprenorphine and medication management (thrice-weekly sessions with a nurse and a monthly meeting with a physician) vs. buprenorphine and medication management plus drug counseling (not described)	13 weeks	14	USA	71% male mean age 36 years 79% with history/current alcohol dependence	Overall, patients reduced opioid-positive urine toxicology tests and good retention through maintenance; less patients in medication management group vs. medication management plus counseling group achieved greater than or equal to one week of opioid-free urine screens, though this difference was not statistically significant; A greater proportion of the medication management plus counseling group had opioid-free urine screens compared with the medication management alone group, though this difference was not statistically significant
Fiellin, 2006 <sup>32</sup> (also a model of care)	Standard medical management (20 minutes with a nurse) and once-weekly medication dispensing (buprenorphine-naloxone) vs. standard medical management and thrice-weekly medication dispensing vs. enhanced (45 minutes with a nurse) medical management and thrice-weekly medication dispensing All groups met monthly with a physician	24 weeks	166	USA	78% male mean age 36 years	The efficacy of brief weekly counseling and once-weekly medication dispensing did not differ significantly from that of extended weekly counseling and thrice-weekly dispensing
Fiellin, 2013 <sup>80</sup>	Physician management (15-20 minutes weekly for the first 2 weeks, every 2 weeks for the next 4 weeks, and then monthly) with buprenorphine-naloxone or physician management with buprenorphine-naloxone plus CBT (up to 12 50-minute weekly sessions during the first 12 weeks of treatment)	24 weeks	141	USA	74% male mean age 34 years	The effectiveness of physician management did not differ significantly from that of physician management plus cognitive behavioral therapy.
Galanter, 2004 <sup>82</sup>	Buprenorphine plus medication management (2 individual sessions per week) vs. buprenorphine plus network therapy (1 individual and 1 group counseling session per week)	18 weeks	66	USA	76% male mean age 36 years	Network therapy led to significantly more negative urine toxicologies and more network therapy than medication management patients had positive outcome relative to secondary heroin use by the end of treatment

Model name Author, year	Comparators	Followup	N	Country	Population Characteristics	Findings
Moore, 2012 <sup>81</sup>	Buprenorphine and physician management (15 minute sessions weekly) vs. buprenorphine and physician management plus CBT (45 minute sessions weekly, depending on therapist availability)	12 weeks	55	France	74% male mean age 39 years	Analyses adjusting for baseline characteristics showed no significant differences between groups on retention or drug use based on self-report or urines. Patient satisfaction was high across conditions, indicating acceptability of CBT counseling with observed medication. The number of CBT sessions attended was significantly associated with improved outcome, and session attendance was associated with a greater abstinence the following week.
Sullivan, 2006 <sup>44</sup> (also a model of care)	Buprenorphine/naloxone and physician management (brief, biweekly) vs. buprenorphine/naloxone and physician management plus once-weekly drug counseling and adherence management	12 weeks	16	USA	94% male mean age 47 years 29% reported one or more days of alcohol use in past 30 days 100% HIV positive 81% HCV positive	There was no difference in treatment retention or illicit drug use by counseling group; Overall, the proportion of opioid-positive weekly urine screens decreased substantially over trial; CD4 counts remained stable; viral load declined significantly; demonstrated feasibility of integrating buprenorphine into HIV clinical care for treatment of opioid dependence
Tetrault, 2012 <sup>83</sup>	Physician management (brief, once every 2 weeks) vs. physician management plus enhanced medical management (45 minutes weekly; focused on drug counseling and adherence to anti-retroviral treatment)	12 weeks	47	USA	39% male mean age 47 years mean 4 days of alcohol use in past 30 days mean 12 years duration of HIV diagnosis 26% HCV positive	At end of trial, no difference between groups in percentage of opioid negative urines, maximum duration of continuous abstinence, or retention; the percentage of subjects with detectable viral loads decreased from baseline across both groups similarly; overall, providing extended counseling in this setting is feasible but does not provide detectable improvement in outcomes
Weiss, 2011 <sup>84</sup> Prescription Opioid Addiction Treatment Study (POATS)	Phase 1: Standard medication management (after initial session, 15-20 minutes weekly, then biweekly sessions with a physician) with buprenorphine/ naloxone vs. standard medication management with buprenorphine/ naloxone plus opioid dependence counseling (45-60 minute sessions with a counselor, twice weekly then biweekly) Phase 2 (extended treatment for those who relapsed): Standard medication management (2 visits first week, then weekly) with buprenorphine/ naloxone vs. standard medication management with buprenorphine/ naloxone plus opioid dependence counseling (twice weekly then biweekly)	Phase 1: 12 weeks Phase 2: 24 weeks	653	USA	60% male mean age 33 years 27% alcohol dependence during lifetime	During phase 1, only 6.6% of patients had successful outcomes, with no difference between standard medical management or standard medical management plus opioid dependence counseling. During phase 2, 49% attained successful outcomes, with no difference between groups. Success rates 8 weeks after completing the buprenorphine-naloxone taper (phase 2, week 24) dropped to 8.6%, again with no difference between groups.
Weiss, 2015 <sup>85</sup> Prescription Opioid Addiction Treatment Study (POATS)	See above	9 month treatment; 42 month followup	375	USA	56% male mean age 33 years old 3.7% with alcohol dependence in past year	Few participants had successful opioid outcomes in phase 1; almost half had successful opioid treatment in phase 2; addition of opioid dependence counseling to medication did not improve outcomes; one third of those in followup abstained and were not on agonist medication, one third were abstinent on agonist therapy and another third were using opioids (followup outcomes not described by group)

Model name Author, year	Comparators	Followup	N	Country	Population Characteristics	Findings
<b>Pharmacological Therapies</b>						
Carrieri, 2014 <sup>98</sup> See also Roux, 2012 <sup>99</sup>	Induction of methadone in primary care vs. specialty care	12 months	221	France	84% male median age 32 years 33% had hazardous alcohol consumption 2% HIV-positive 19% HCV-positive	Under appropriate conditions, methadone induction in primary care is feasible and acceptable to both physicians and patients. It is as effective as induction in specialized care in reducing street-opioid use and ensuring engagement and retention in treatment for opioid dependence.
Fiellin, 2001 <sup>100</sup>	Primary care-based methadone (weekly physician sessions and monthly counseling session) vs. narcotic treatment program-based methadone (1 to 3 sessions per week dose, weekly group counseling, and monthly individual counseling)	6 months	46	USA	65% male mean age 42 years 17% HIV-positive	There was no significant between-group difference on illicit drug use or patients with clinical instability; Significantly more office-based patients thought that quality of care was excellent; There were no group differences in functional status or use of health, legal, or social services; Overall, results supported feasibility and efficacy of transferring stable opioid-dependent patients to primary care for methadone maintenance
Fudala, 2003 <sup>86</sup>	Daily buprenorphine/naloxone vs. buprenorphine vs. placebo All participants received HIV counseling and up to 1 hour of individualized counseling per week; emergency counseling and referrals provided	4 weeks for efficacy; 52 weeks for safety	323 for efficacy; 472 for safety	USA	65% male mean age 38 years	Efficacy study terminated early due to greater efficacy of buprenorphine/naloxone and buprenorphine vs. placebo; Proportion of opiate-negative urine samples significantly less among both MAT groups vs. placebo; MAT groups reported significantly less opiate craving than placebo; Rates of adverse events similar in active-treatment and placebo groups; findings from open-label followup indicated combined treatment was safe and well tolerated
King, 2006 <sup>101</sup>	Routine care (methadone dispensing window for weekly doses and monthly counseling for 20 minutes) vs. methadone maintenance clinic (monthly observed dose, take home supply, monthly 20 minute counseling session with medical provider) vs. primary care based-methadone (monthly observed dose, take home supply, monthly 20 minute counseling session with office physician)	12 months	92	USA	62% male mean age 44 years	Generally low rates of drug use or failed medication recall with good study retention; No between-group differences on ASI scores; Treatment satisfaction was high in all groups and patients in all groups rated strong quality of therapeutic alliance; methadone medical maintenance patients in both office and clinic-based care initiated more new employment or social/family activities than routine care; most methadone medical maintenance patients reported a preference for office-based care compared with clinic-based
Lintzeris, 2004 <sup>87</sup>	Methadone vs. buprenorphine administered under naturalistic conditions by 18 community-based and 1 specialist-based sites by general practitioners and community pharmacists (Buprenorphine Implementation trial [BIT])	12 months	139	Australia	58% male mean age 30 years	Among methadone stabilized patients, mean retention time was similar between groups; among heroin users, there was a trend towards improved retention among those taking methadone compared with those on buprenorphine, though this was not statistically significant; There were significant reductions in heroin use in all groups over time and a trend toward lower heroin use among heroin users on buprenorphine

ASI = Addiction Severity Index; CBT = cognitive behavioral therapy; ED = emergency department, MAT = medication assisted treatment

**Table 5. Cochrane Systematic Reviews for Guiding Question 3**

Author, Year	Intervention Characteristics	Population and Setting	Countries	Types of Studies Included	No. of Included Studies No. of Patients	Findings	Limitations
Amato, 2011 <sup>78</sup>	Any psychosocial intervention plus any agonist vs. any agonist alone; methadone, buprenorphine, LAAM; models of care not described	OUD due to opiates (not specified); setting not described (appears mostly specialist centers)	USA, Germany, Malaysia, China, Scotland	RCTs, CCTs	35 studies 4319 patients	Comparing any psychosocial intervention plus maintenance pharmacological treatment to standard maintenance treatment, shows no significant advantage of adding psychosocial interventions for retention in treatment and at followup, abstinence from opiates during treatment or at followup, compliance, psychiatric symptoms, and depression. Also, there was no significant difference in outcomes comparing psychosocial approaches. Of note, standard pharmacological treatment generally offers counseling services.	Focused on effectiveness of psychotherapy interventions in addition to standard interventions; setting not described (appears mostly specialist centers); 31 studies in USA
Ferri, 2013 <sup>102</sup>	Slow-release oral morphine vs. other MAT medications; models of care not described	OUD due to heroin; Setting not described	Australia and Austria	RCTs, quasi-randomized (one study only provided conference abstract)	3 studies 195 patients	Limited evidence that sustained-release oral morphine is at least similar to other MAT medications for retention and other clinical outcomes	Focused on effectiveness of medications; trials with no description of setting; no studies in USA
Gowing, 2011 <sup>105</sup>	Buprenorphine, methadone, or LAAM for substitution therapy (alone or vs. others); models of care not described	OUD due to heroin; majority injecting drug users or with recent history (last 3 months); users of other injectable drugs also included; mostly specialist treatment centers	USA, UK, Australia, Italy, Germany, Canada, Malaysia, Ukraine with one study in multiple countries	RCTs, observational prospective studies, cross-sectional studies	38 studies 12400 patients	Oral substitution treatment with methadone or buprenorphine is associated with significant reductions in illicit opioid use, injecting use, and sharing of injecting equipment; also led to fewer drug users reporting multiple sex partners or exchanges of sex for money or drugs but no change in condom use; reduced drug risk behaviors led to reduced HIV; one study partially done in primary care showed significant reductions in proportion injecting, sharing injecting equipment, and having unprotected sex in those on methadone treatment.	Focused on effectiveness of medications on HIV and behaviors; 2 studies included primary care settings; 26 studies in USA
Lobmaier, 2008 <sup>90</sup>	Three depot and two implant formulations of naltrexone (10 of 17 depot studies used sustained release form) vs. placebo, different naltrexone doses, oral naltrexone, or methadone; in addition to medication, all patients offered relapse prevention therapy	OUD not specified; effectiveness study in outpatient setting	Australia, Germany, USA, Norway, Spain, UK	RCTs for effectiveness; prospective controlled and uncontrolled trials, case-series, and record-linkage for safety evaluation	1 study for effectiveness 60 patients for effectiveness	One study found high-dose naltrexone depot injections significantly increased days in treatment vs. placebo and vs. low-dose with no group differences on patients retained in treatment;	Focused on effectiveness and adverse events of medications; effectiveness study in outpatient setting (no further details); effectiveness study and most safety studies done in USA

Author, Year	Intervention Characteristics	Population and Setting	Countries	Types of Studies Included	No. of Included Studies No. of Patients	Findings	Limitations
Mattick, 2009 <sup>16</sup>	Methadone maintenance vs. placebo or other nonpharmacological therapy (wait-list control, drug-free rehabilitation, detoxification); models of care not described (some studies included counseling in the intervention but this was not described)	OUD due to opioids (not specified); most studies done in specialist medical or research facilities (3 in prison setting)	USA, Australia, Hong Kong, Thailand, Sweden	RCTs	11 studies 1969 patients	Methadone was significantly more effective than nonpharmacological approaches in treatment retention and suppression of heroin use but not different in criminal activity or mortality	Focused on effectiveness of medication; no studies appear to have been done in primary care; 6 studies in USA
Mattick, 2014 <sup>15</sup>	Buprenorphine maintenance vs. placebo or methadone; models of care not described	OUD due to heroin or other opioids; settings not described	North America, Europe, Asia, Middle East, Australia	RCTs	31 studies 5430 patients	Buprenorphine was superior to placebo in participant retention at all doses; only high-dose buprenorphine (not low- or moderate-dose) was more effective than placebo in suppressing illicit opioid use; flexible dosed buprenorphine was less effective than methadone in participant retention with no group differences in suppression of opioid use; low-dose methadone was more likely to retain participants and limit opioid use than low-dose buprenorphine but high and medium-dose methadone were not more effective than high and medium-dose buprenorphine for participant retention and illicit opioid use	Focused on effectiveness of medications; setting not described; 15 studies from North America
Minozzi, 2009 <sup>108</sup>	Any maintenance treatment alone or in combination with psychological intervention vs. no intervention, other pharmacological or psychosocial intervention; models of care not described	OUD due to heroin; adolescents; outpatient	USA	RCTs and controlled clinical trials	2 studies 187 patients	Limited evidence that maintenance treatment was superior in patient retention but not in reducing illicit opioid use; Opioid use at 1 year followup was significantly lower in the maintenance group and more patients in this group were enrolled in other addiction treatment at followup	Focused on effectiveness of medications; outpatient setting (unclear if primary care); all trials done in USA



Author, Year	Intervention Characteristics	Population and Setting	Countries	Types of Studies Included	No. of Included Studies No. of Patients	Findings	Limitations
Minozzi, 2011 <sup>78</sup>	Oral naltrexone alone or in combination with psychosocial treatments vs. placebo, no intervention, other pharmacological treatments, or psychosocial treatments; models of care not described	OUD due to heroin alone or multiple drugs; outpatient only	USA, Israel, Russia, Italy, Spain, China, Malaysia, Germany	RCTs	13 studies 1158 patients	Oral naltrexone did not perform better than treatment with placebo or no agent with respect to abstinence and relapse, though naltrexone was favored for number of people reincarcerated. Naltrexone was not superior to benzodiazepines and buprenorphine for retention, abstinence, and side effects, though numbers retained in studies were generally low. In single study of naltrexone vs. psychotherapy, there was no statistically significant difference for abstinence and reincarceration. Overall, studies inadequate to evaluate oral naltrexone treatment for opioid dependence.	Focused on effectiveness of medications /interventions; includes psychotherapy as an intervention; outpatient trials (unclear if primary care); 4 trials in USA
Minozzi, 2013 <sup>103</sup>	Methadone vs. buprenorphine or slow-release morphine; models of care not described	Opiate addicted pregnant women (OUD not specified); inpatient and outpatient settings	Austria, USA, one multicounty trial (Austria, Canada, USA)	RCTs	4 studies 271 patients	Limited evidence of no significant differences between methadone and buprenorphine or slow-release morphine for all outcomes (child health status, neonatal mortality, treatment retention, and reducing substance use)	Focus on effectiveness of medications; 3 studies in outpatient setting (no further details); 2 studies done in USA
Rahimi-Movaghar, 2013 <sup>109</sup>	Various pharmacological therapies (alone or in combination with psychosocial interventions) compared to no intervention, detoxification, different doses of the same intervention, other pharmacologic interventions and any psychosocial interventions; models of care not described	OUD due to heroin; outpatient	Iran	RCTs	3 studies 870 patients	Higher doses of buprenorphine significantly increased the treatment retention rate compared with lower doses; No significant difference in maintenance retention rate between baclofen vs. placebo post detoxification.	Focused on effectiveness of medications; outpatient setting (unclear if primary care); no trials in USA (appears Asia-focused)

CCT = controlled clinical trial; LAMM = levo-alpha-acetylmethadol; OUD = opioid use disorder; RCT = randomized controlled trial

## Guiding Question 4. Future Directions

### New and Innovative Strategies

Key Informants uniformly noted that the most promising models of care are those that emphasize the integration of management of OUD with primary care and other medical and psychological needs. The chronic disease management paradigm is particularly suitable for populations with OUD who also have other conditions that require ongoing care, such as HIV or HCV infection.<sup>110</sup> The BHIVES model was specifically designed to integrate office based treatment with buprenorphine with HIV management. Some important innovations in implementation of MAT models of care include the use of a nonphysician glue person (e.g., OBOT [Yale], Massachusetts Nurse Care Manager model, ECHO Project), integration of more comprehensive psychosocial services (e.g., One Stop Shop, Medicaid Home Model), coordination and integration of office-based management with centralized centers of excellence (e.g., Hub and Spoke, Co-OP), and identification and initial treatment in ED, inpatient, or prenatal settings. Several Key Informants noted that models of care that also integrate education, training, and outreach, such as the Massachusetts Nurse Care Manager model, are important for increasing the pool of buprenorphine-waivered physicians, decreasing stigma, and increasing uptake of MAT, while also promoting higher quality care. Existing resources such as PCSS-MAT, which provides physician training and access to a national network of experts in MAT who can provide mentoring to those less experienced in prescribing buprenorphine, could be leveraged by models of care that lack resources for their own educational and training component; such resources were utilized successfully in the initial dissemination and expansion of office-based buprenorphine in the United States.

Recent MAT models focus on the identification of patients with OUD and initiation of treatment in the ED, inpatient and prenatal settings. These strategies can help identify patients with OUD who otherwise might not have access to primary care, have a higher prevalence of OUD (e.g., in the ED and inpatient settings), or facilitate initiation and engagement in treatment. Ideally, such models of care would be linked to an integrated, office-based model that can provide ongoing management.

In rural settings, major barriers to MAT include the lack of addiction and psychiatric expertise, distances that patients must travel to access care, lack of buprenorphine-waivered physicians, and negative attitudes and beliefs regarding MAT. Strategies to overcome these barriers include Web-based learning networks (e.g., Project ECHO), use of telemedicine for consultation with experts, utilization of nonphysician providers in key roles (e.g., screening, counseling, coordination of care, provision of primary care), and educational and outreach efforts. In the Southern Oregon Model, for example, local stakeholders meet regularly and discuss issues in management of OUD and develop practice standards using a collaborative model. One Key Informant has developed and evaluated computer-assisted delivery of cognitive behavioral therapy for addiction.<sup>111,112</sup> Resources such as these could supplement face-to-face psychosocial services and would not be constrained by geographical barriers. In rural settings, the availability of extended release formulations (e.g., currently approved extended-release naltrexone and emerging products such as implantable and injectable buprenorphine preparations) could potentially reduce the need for frequent visits, particularly in less complex patients who have long distances to travel, particularly if coupled with psychosocial services conducted over the phone or via the Web.

MAT models of care in primary care settings could also integrate pharmacist-based management strategies. A recent small (n=12 patients) pilot project evaluated a physician-pharmacist collaborative model in which patients were managed using a drug therapy management model.<sup>113</sup> The pharmacist conducted intake assessments and followup appointments and documented each interaction after debriefing with a physician, who appended additional notes as needed and cosigned records. The pharmacist was responsible for gathering data from outside providers and pharmacies regarding prescribed medications and results of urine drug testing. Prescriptions were written by the physician or called in by the pharmacist. In addition, the pilot study projected that the model would be cost savings for the health system. Another 2-year pilot study in San Francisco evaluated a tiered model with centralized induction and stabilization followed by management in a community-based center, with buprenorphine dosing and dispensing provided through a designated pharmacy.<sup>114</sup> The pharmacist at the dispensing pharmacy works in collaboration with the clinicians at the community center, with a secure database specifically designed to facilitate communication. However, for both models, details regarding the provision of psychosocial services and coordination of care within this model are limited.

## **Implications for Diffusion of MAT**

Key Informants consistently noted that MAT is effective in office-based settings, but access remains limited, particularly in rural settings. Increasing the number of buprenorphine waived physicians as well as the number of buprenorphine waived physicians who actually prescribe are critical for increasing the diffusion of MAT. Enhanced use of extended-release naltrexone could also increase diffusion of MAT since it does not require a waiver to prescribe and provides patients with additional options. As an opioid antagonist, naltrexone may be preferred by patients who do not wish to use opioid agonist or partial agonist therapy.

This report describes a number of MAT models of care viewed as effective or promising by Key Informants. Although evidence is lacking with regard to how one model of care performs compared to another, comparative effectiveness research may not be the most important determinant for informing further diffusion of MAT. Rather, the most effective model of care is likely to depend in part on the specific implementation setting, including unique characteristics of the target patient population (e.g., HIV infection, pregnant, or adolescent), what resources are available locally, and financing options. Implementation of the Hub and Spoke or Co-OP models, for example, requires a relatively local center of expertise in addiction that is willing to partner with community centers in an integrated model. A model developed for patients with HIV infection requires expertise in both OUD and HIV care. In rural settings, models of care that integrate Web-based training, consultation, and mentorship may be needed to overcome the lack of local expertise. One support model, for example, is the Oregon Addiction Education and Prevention Initiative, in which academic medical center addiction medicine specialists partner with accountable care organizations to conduct DATA2000 waiver training for rural primary care providers, who are then linked to PCSS and offered personal ongoing phone consultation support in MAT management. In some cases, effective diffusion of MAT may involve adaptation of an established model of care to the needs of the particular setting. For example, the Massachusetts Nurse Care Manager model represents an adaptation of the OBOT model developed at Yale and the BHIVES model represents an adaptation of the OBOT model for patients with OUD and HIV infection. Models of care could also integrate models that target different parts of the treatment process—i.e., models that involve ED or inpatient screening for

OUD and initiation of treatment could be integrated with models that provide ongoing care based on the Massachusetts Nurse Care Manager or Hub and Spoke models.

Given the barriers to implementing MAT in primary care settings, effective strategies for implementation are likely to require multifactorial interventions that involve partnerships between payers and clinics that use financing, contracting, policy change, process improvement to improve workflow, and customer input to facilitate organizational change. Although one such intervention (Advancing Recovery) has been shown to increase access to MAT in addiction treatment settings,<sup>115</sup> studies on the effects of Advancing Recovery in primary care settings are not yet available. Several Key Informants also commented that with increased diffusion of MAT comes the possibility for suboptimal provision of care. They noted the need for clear standards to measure the quality of care and ensure that care is adequate.

## **Ethical, Equity, and Cost Issues**

Key Informants noted equity issues with regard to access to MAT in rural areas due to lack of prescribing physicians, ongoing stigma, and lack of policy and funding support. Efforts to expand MAT in Medicaid programs and Federally Qualified Health Centers represent an opportunity to increase equity. Although evidence indicates that OUDs often begin during adolescence, no models of care have been developed to address adolescent populations. A multi-site clinical trial documented improved short-term outcomes for adolescents and young adults supported on buprenorphine compared to those who completed a brief taper.<sup>104</sup>

Key Informants consistently noted that MAT is effective and that it is important from an ethical standpoint that patients have access to these treatments and be provided with accurate information about the risks and benefits of MAT and alternative treatments. Key Informants noted that although substance use disorder benefits are included as Essential Health Benefits in the Affordable Care Act, insurers may try to avoid paying for MAT medications through onerous prior authorization requirements or arbitrarily limit the duration or dose of therapy.<sup>116</sup> Key Informants noted that prevention of buprenorphine diversion has been a major concern of some payers and providers and in some cases has impacted the ability to provide MAT, due to the effects of efforts to prevent diversion.

Key Informants also noted that financing remains a major issue in many settings. They noted that some models have been run largely by volunteers or are unable to remain financially viable due to inadequate reimbursement and a lack of state or other financial support. One Key Informant noted that some private clinics have gone bankrupt trying to work with Medicaid. Some Key Informants noted that the 100-patient limit for prescribing buprenorphine may make provision of MAT noneconomically viable for some physicians. Other Key Informants noted that some for-profit clinics involve several physician banding together to increase the number of patients treated and increase economic viability, but could result in provision of MAT which may not meet quality of care standards. Key Informants noted that showing that MAT is cost-effective or even cost-savings in the long run would be very helpful for convincing policymakers and clinicians to support and use MAT.

## Areas of Uncertainty and Future Research Needs

Key Informants noted a number of important areas of uncertainty regarding MAT that warrant additional research. These include:

- Research to identify factors associated with high quality care and how to measure it. Key Informants noted that with improved access to MAT it is also critical to insure that the quality of care that is delivered is high. This will require development of new quality of care indicators for use of MAT in primary care settings.
- Research on management of patients with OUD and concomitant chronic pain, benzodiazepine use, and/or alcohol use disorder (e.g., use of buprenorphine for transitioning off high doses of opioids in patients with chronic noncancer pain). Key Informants noted that treatment of OUD in patients who also have pain is a major challenge given the high prevalence of opioid prescribing. A systematic review of 10 studies of limited quality evaluated the role of buprenorphine for management of chronic pain, but only one study was conducted in primary care.<sup>117</sup>
- Research on effectiveness and safety of mid-level prescribing of buprenorphine, such as by nurse practitioners and physician assistants. Currently, DATA 2000 only permits physicians to prescribe buprenorphine for OUD. Allowing mid-level providers to prescribe buprenorphine could help improve access in rural areas with few or no physicians.
- Research to identify patients more likely to benefit from more intensive psychosocial services, and methods for effectively targeting specific types of psychosocial services. Key Informants noted that the need for more intensive psychosocial services is likely to vary. Understanding which patients require which services would be very helpful for designing and implementing effective models of care.
- Research to understand optimal methods for coordination and integration of care. Although Key Informants consistently noted that this is a critical component of successful MAT models of care, methods for coordination and integration of care varied among models and no study evaluated the effectiveness of different coordination and integration methods.
- Research to better understand the costs and cost-effectiveness of implementing MAT models of care. Key Informants noted that such research would be of particular importance for policymakers, and that such research should address societal outcomes impacted by OUD (e.g., ability to work, criminal activity) in addition to impacts on drug use.
- Research on effective methods implementation of MAT models of care in primary care settings and increasing uptake of MAT. Although some multicomponent implementation strategies appear to be effective for enhancing access, they have not yet been studied in primary care settings.<sup>115</sup>
- Research to better understand optimal duration and doses of treatment. Key Informants noted that this is particularly important because otherwise payers may (and sometimes do) impose arbitrary duration limits for MAT.
- Research on effectiveness of telehealth and Web-based training, mentoring, and educational resources. These would be particularly useful in rural and other settings where addiction and other expertise are not available locally. As noted elsewhere in this

report, one Key Informant described a Web-based cognitive-behavioral resource that has been developed<sup>111,112,118</sup> and another described psychiatric consultation using computer tablets.

- Research on effectiveness of alternative medications or formulations (e.g., implantable and injectable buprenorphine preparations). Key Informants noted that such formulations could reduce the frequency of followup, increase uptake and compliance, and mitigate barriers related to long travel distance. However, there is almost no evidence on injectable buprenorphine used in primary care settings.
- Research on effectiveness of methods for reducing diversion (e.g., use of extended-release medications, thrice weekly observed dispensing, or pharmacy-based dispensing). Pharmacy-based dispensing is done in Canada and Europe for buprenorphine and methadone prescribed in primary care and has been piloted in small studies in the United States.<sup>113,114</sup> Key Informants noted that preventing diversion has been a major concern of some payers and policymakers.
- Research to understand why buprenorphine-waivered physicians don't prescribe and methods to increase prescribing. The gap between the number of waivered physicians and the number prescribing indicates that there is substantial untapped capacity to prescribe buprenorphine.<sup>76</sup>
- Research to better understand patients who are appropriate for office-based treatment versus those who require treatment in an OTP. Key Informants noted that current methods to determine who is appropriate for office-based treatment are largely based on anecdotal experience.
- Research on patients who are more likely to benefit from extended-release naltrexone, and on comparative effectiveness of buprenorphine versus extended-release naltrexone. Key Informants noted that most models of care have focused on provision of buprenorphine, and there is very little evidence on use of extended-release naltrexone in primary care settings. Although there is evidence supporting the efficacy of extended-release naltrexone, Key Informants reported the perception that this treatment was not in high demand by patients and that some patients might not do well with opioid antagonist therapy. In addition, a recent study found a low rate of linkage to ongoing treatment with extended-release naltrexone following an initial injection during inpatient opioid detoxification.<sup>119</sup> On the other hand, Key Informants also suggested that expanding the medication choices for patients could increase uptake and that extended-release naltrexone may be associated with less stigma by some patients and providers.
- Research on effectiveness of methadone for office-based treatment. Methadone is not authorized under DATA 2000 but has been evaluated in office-based settings in some clinical trials in the United States<sup>100,101</sup> and is used in primary care settings in other countries. Primary care providers in Canada, parts of Europe, and some other countries prescribe methadone for directly observed daily dispensing in local pharmacies. This model has not been tested in the United States, but could expand access to OUD treatment while limiting diversion.

## Ongoing Studies

We identified several ongoing randomized trials of MAT models of care in primary care settings that may address some of the research gaps described above (**Table 6**). One ongoing trial compared effects of an organizational readiness intervention (including implementation tools and

activities) plus an integrated collaborative care service delivery intervention (based on a chronic care model) versus usual care for implementing substance use disorder treatment in primary care.<sup>120</sup> Two ongoing trials focused on MAT models of care that involve screening and initiation of MAT in emergency department<sup>121</sup> or inpatient<sup>122</sup> settings. One other trial compared effects of group visits (5 to 10 patients with primary care provider and behavioral specialists) versus usual care (individual visits) in patients receiving buprenorphine.<sup>123</sup>

**Table 6. Ongoing studies of MAT for OUD**

Reference	Setting	Study design, Interventions	Outcomes
<p><i>Substance Use Motivation Medication Integrated Treatment (SUMMIT) Study</i></p> <p>Ober, AJ. An organizational readiness intervention and randomized controlled trial to test strategies for implementing substance use disorder treatment into primary care: SUMMIT study protocol. <a href="http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4432875/">http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4432875/</a><sup>120</sup></p> <p>Watkins, K. Integrated collaborative care for substance use disorders. <a href="https://clinicaltrials.gov/ct2/show/NCT01810159">https://clinicaltrials.gov/ct2/show/NCT01810159</a><sup>124</sup></p>	Federally qualified health center and Venice Family Clinics	<p>RCT</p> <p>Integrated collaborative care vs service as usual</p> <p>Details: combined effect of both an organizational readiness intervention, consisting of implementation tools and activities and an integrated collaborative care service delivery intervention, based on the Chronic Care Model</p> <p>Also, mixed methods study (pre-post analysis)</p>	<p>Service system outcomes: patient-centered care, utilization of substance use disorder treatment, utilization of health care services and adoption and sustainability of evidence-based practices</p> <p>Patient outcomes: substance use, consequences of use, health and mental health, and satisfaction with care</p>
<p>Bogenschutz, M. Comparing interventions for opioid dependent patients presenting in medical emergency departments. <a href="https://clinicaltrials.gov/ct2/show/NCT02586896?term=NCT02586896&amp;rank=1">https://clinicaltrials.gov/ct2/show/NCT02586896?term=NCT02586896&amp;rank=1</a><sup>121</sup></p>	Opioid dependent patients in medical emergency departments	<p>RCT</p> <p>Brief strengths-based case management vs. screening, assessment and referral alone</p>	<p>Initiation of and engagement in treatment for opioid dependence</p> <p>Opioid and other substance use</p> <p>Initiation and engagement in participants with higher levels of environmental instability at baseline</p> <p>Quality of life</p>
<p><i>Group Buprenorphine Maintenance Treatment (G-BMT) Study</i></p> <p>Fox, A. Buprenorphine group medical visits in primary care. <a href="https://clinicaltrials.gov/ct2/show/NCT02526212?term=NCT02526212&amp;rank=1">https://clinicaltrials.gov/ct2/show/NCT02526212?term=NCT02526212&amp;rank=1</a><sup>123</sup></p>	Primary care	<p>RCT</p> <p>Group visits (90 minutes; 5-10 patients simultaneously receive care from a multidisciplinary team of a generalist physician and a behavioral specialist) vs. treatment as usual in primary care (individual visits including protocol of BMT intensification, which includes increased visit frequency, referral for mental health counseling, and referral to addiction treatment specialist); both buprenorphine</p>	<p>Opioid abstinence</p> <p>Retention in treatment</p> <p>HIV risk behaviors</p> <p>Acceptability</p> <p>Feasibility</p>
<p>Stein, M. Linking opioid-dependent patients from inpatient detoxification to primary care. <a href="https://wwwcf.nlm.nih.gov/hsr_project/view_hsrproj_record.cfm?NLMUNIQUE_ID=20132453&amp;SEARCH_FOR=((%22primary%20care%22))%20AND(buprenorphine)%20OR(naltrexone)">https://wwwcf.nlm.nih.gov/hsr_project/view_hsrproj_record.cfm?NLMUNIQUE_ID=20132453&amp;SEARCH_FOR=((%22primary%20care%22))%20AND(buprenorphine)%20OR(naltrexone)</a><sup>122</sup></p>	Recruiting illicit opioid users during detoxification and linking them to primary care-based treatment	<p>RCT</p> <p>Buprenorphine, initiated during inpatient detoxification and continued after discharge vs. buprenorphine detoxification</p>	<p>Illicit opioid use</p> <p>Emergency department and hospital utilization</p>

MAT = medication-assisted treatment; OUD = opioid use disorder; RCT = randomized controlled trial.



## Summary and Implications

A number of MAT models of care have been developed and implemented in primary care settings. Key Informants noted that MAT models of care could be described using a framework focusing on the following four components: 1) pharmacological therapy; 2) psychosocial services; 3) integration of care; and 4) education and outreach. This report describes 12 representative/key models of care utilizing a framework based on these four components. Although other models of care have been developed, in many cases sources to understand their components could not be identified, or it was difficult to determine how they differed from the representative models. A challenge in understanding current MAT models of care is the limited published data on most models. No study has compared the effectiveness of one MAT model of care in primary care versus another; rather, most trials have focused on specific components, in particular which medication was used and the type of psychosocial services provided. However, the ideal model of care for a particular setting is likely to depend on a number of local factors, such as the expertise available, the population being served, proximity to an addiction center of excellence, reimbursement policies, geographic factors, and others. Several Key Informants noted that efforts to implement MAT have often failed due to poor reimbursement or because the model was financially unsustainable for other reasons. Therefore, decisions about MAT models of care may best be individualized to address the unique milieu of each implementation setting. In some situations, it may be appropriate to utilize elements of different models of care (e.g., implement nurse care manager-based coordination of care within a Hub and Spoke model of care) or to link models of care (e.g., ED or inpatient based screening and initiation of treatment linked with an office-based model of care for ongoing management).

Regarding the pharmacological therapy component, most MAT models of care in primary care settings to date have focused on provision of oral buprenorphine. Although implantable buprenorphine has been evaluated for treatment of OUD and is awaiting FDA approval, research on its use in primary care settings is lacking. Similarly, although extended-release naltrexone has been shown to be effective in addiction treatment settings, research on its use in primary care settings is extremely sparse. Provision of additional pharmacological therapy choices for MAT has potential advantages in terms of expanding patient choices, reducing risk of diversion, and decreasing need for frequent followup in appropriate patients.

Key Informants consistently noted that the psychosocial services component is critical for any MAT model of care, but there is uncertainty about whether brief counseling (as required by DATA 2000) is sufficient, or whether more extensive psychosocial services should be routinely available. In addition, many different types of psychosocial services beyond brief counseling are available and it is uncertain which services should be prioritized when implementing a model of care. Although most evidence suggests that more intensive psychosocial services are not associated with superior outcomes to standard counseling, Key Informants noted that some patients require more intensive psychosocial services and that research is needed to identify higher-risk patients who would benefit from such services. Although Key Informants generally agreed that psychosocial services are best provided on-site, some models of care utilize services via an affiliated OTP or through telehealth/Web-based resources.

A core component of successful MAT models of care is the integration/coordination component, in order to manage issues related to OUD as well as psychological, medical, and primary care needs. Key Informants viewed successful integration of care as critical for the success of any MAT model of care. The MAT models of care that were viewed as particularly successful utilized a designated nonphysician staff member in the integration/coordination role,

reducing the burden on the physician while increasing practice efficiency and permitting more patients to be effectively and safely treated.

Although the education and outreach component was not as well-defined in some models, this was viewed by Key Informants as critical for reducing stigma associated with MAT, increasing the pool of prescribing physicians, and increasing uptake, particularly in settings in which stigma is still high. Education was also viewed as critical for improving standards and quality of care. Our survey of MAT models of care indicated a number of approaches to education and outreach, including a Web-based learning network and educational resources, internet-based mentoring by more experienced physicians, meetings of community stakeholders, in-person educational sessions with patient and clinician educational sessions, and others.

Particular challenges in rural settings include a lack of waived buprenorphine physicians, limited access to addiction expertise, persistent stigma associated with MAT, and long travel times for patients. Models of care developed in rural settings have attempted to address some of these issues by utilizing a Web-based learning network and accessing a national network of mentoring physicians. Other strategies that could be helpful include use of longer-acting medication formulations to reduce the number of followup visits in appropriate patients, use of telemedicine, engagement of community stakeholders, and use of online interventions such as Web-based cognitive-behavioral therapy.

Key Informants noted a number of important areas of uncertainty with regard to MAT models of care in primary care settings, including methods for measuring quality of care, how to assess patients to better individualize care, optimal psychosocial components of MAT, effectiveness of mid-level prescribing, enhancing access to and uptake of MAT in primary care settings, effectiveness of newer or alternative medications for OUD, optimal medication dosing strategies, cost and costeffectiveness, methods for reducing diversion, effective implementation methods, optimal methods for coordination and integration of care, and effectiveness of telehealth and telemedicine approaches. Research in these areas would be helpful for informing future efforts at dissemination and expansion of MAT in primary care settings. In the meantime, this technical brief describes a number of MAT models of care that have been developed and implemented in such settings, which may help inform further efforts at individualized implementation of MAT.

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