Technical Brief Disposition of Comments Report

Research Review Title: *Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings*

Draft review available for public comment from May 13, 2016, to June 9, 2016.

Research Review Citation: Chou R, Korthuis PT, Weimer M, Bougatsos C, Blazina I, Zakher B, Grusing S, Devine B, McCarty D. Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings. Technical Brief No. 28. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 16(17)-EHC039-EF. Rockville, MD: Agency for Healthcare Research and Quality. December 2016. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Comments to Research Review

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Comments on draft reviews and the authors' responses to the comments are posted for public viewing on the Web site approximately 3 months after the final research review is published. Comments are not edited for spelling, grammar, or other content errors. Each comment is listed with the name and affiliation of the commentator, if this information is provided. Commentators are not required to provide their names or affiliations in order to submit suggestions or comments.

The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

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Commentator & Affiliation	Section	Comment	Response
AMCP (Academy of Managed Care Pharmacy) Susan A. Cantrell	General	The Academy of Managed Care Pharmacy (AMCP) thanks the Agency for Healthcare Research and Quality (AHRQ) for its work in developing strategies to address the growing opioid epidemic in the United States and for the opportunity to provide comments in response to the draft technical brief titled "Medication-Assisted Treatment (MAT) Models of Care for Opioid Use Disorder in Primary Care Settings." AMCP commends AHRQ for recognizing the important role that pharmacists can play in MAT and recommends that AHRQ consider supporting legislation to expand the ability of non-physician practitioners, including qualified nurse practitioners, physician assistants, and pharmacists, with appropriate training and state licensure to prescribe buprenorphine for opioid addiction. In addition, AMCP encourages AHRQ to include recommendations related to team-based care and education on diversion prevention strategies prior to finalization.	Thank you for your comment.
AMCP (Academy of Managed Care Pharmacy) Susan A. Cantrell	General	AMCP believes that a holistic, comprehensive, and multi-stakeholder approach among health care providers and patients is necessary to truly address the opioid epidemic. AMCP is committed to resolving issues associated with the opioid epidemic and has established an Addiction Treatment Advisory Group which will evaluate current gaps and barriers to addiction treatment services and develop recommendations to improve patient care. AMCP will share the recommendations and findings from the advisory group with AHRQ and other stakeholders.	Thank you for your comment.
AMCP (Academy of Managed Care Pharmacy) Susan A. Cantrell	General	AMCP is a professional association of pharmacists and other practitioners who serve society by the application of sound medication management principles and strategies to improve health care for all. The Academy's 8,000 members develop and provide a diversified range of clinical, educational, medication and business management services and strategies on behalf of the more than 200 million Americans covered by a managed care pharmacy benefit.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
AMCP (Academy of Managed Care Pharmacy) Susan A. Cantrell	General	AMCP commends AHRQ for recognizing the value of incorporating a pharmacist in MAT through physician-pharmacist collaborative models in which patients are managed using medication therapy management (MTM). In addition to advocating for the role of the pharmacist in a collaborative care model, AMCP encourages AHRQ to work with Congress to find a mechanism for expanding the definition of a qualified practitioner under section 303(g)(2) of the Controlled Substances Act to include additional providers, such as qualified nurse practitioners, physician assistants, and pharmacists. Enabling non-physician practitioners to prescribe buprenorphine, with the appropriate training and state licensure, is critical to expanding opioid abuse disorder treatment to a greater number of individuals throughout the nation.	Thank you for your comment. The need to evaluate prescribing of buprenorphine by non-physician providers is described as a future research need.
AMCP (Academy of Managed Care Pharmacy) Susan A. Cantrell	General	Prior to finalization of the draft technical brief, AMCP encourages AHRQ to work collaboratively with other federal agencies, such as Health and Human Services (HHS), the Centers for Diseases Control and Prevention (CDC), and the Food and Drug Administration (FDA), providers, pharmacists, and patients to develop a holistic, comprehensive, and multi-stakeholder approach to address the opioid epidemic. In the spirit of collaboration, AMCP also encourages AHRQ to include a recommendation to work collaboratively and communicate effectively with the patient's care team, including pharmacists and other health care providers who provide patient care and psychosocial services, to ensure a holistic and comprehensive approach to the patient's individualized treatment. Furthermore, AMCP urges AHRQ to consider the inclusion of training and education programs for qualified physicians to minimize the risk of diversion of buprenorphine and provide sound medication management.	Thank you for your comment. The issue of buprenorphine diversion is noted in the Ethical, Equity, and Costs section (pg 37) and also in the section discussing pharmacist-based strategies (pg 43)

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AMCP (Academy of Managed Care Pharmacy) Susan A. Cantrell	General	AMCP appreciates your consideration of the concerns outlined above and looks forward to continuing work on these issues with AHRQ.	Thank you for your comment.
APhA (American Pharmacists Association) Thomas E. Menighan	General	On behalf of the American Pharmacists Association ("APhA") we appreciate the opportunity to provide input on the Agency for Healthcare Research and Quality's ("AHRQ") Draft Technical Brief: Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings (hereinafter, "Brief"). APhA, founded in 1852 as the American Pharmaceutical Association, represents more than 62,000 pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care. APhA members provide care in all practice settings, including community pharmacies, hospitals, long-term care facilities, community health centers, physician office practices, managed care organizations, hospice settings, and the uniformed services.	Thank you for your comment.
APhA (American Pharmacists Association) Thomas E. Menighan	General	APhA regards medication-assisted treatment ("MAT") an important component of a multipronged approach to addressing our Nation's epidemic related to the abuse and misuse of opioid medications and supports research regarding the pharmacist's role in MAT. APhA is committed to working with the AHRQ, and other federal agencies, Congress, state agencies and officials, health professionals and other stakeholders to identify ways to improve treatment of substance use disorder. We believe addressing this problem will require the unified and coordinated efforts of many diverse stakeholders, including health care professionals, patients and caregivers, community-based organizations, and federal, state, and local governments. APhA, like AHRQ, agrees that additional MAT research would help identify effective treatment components and determine methods to overcome barriers to implementation.	Thank you for your comment.

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APhA (American Pharmacists Association) Thomas E. Menighan	General	Pharmacists are often an underutilized health care resource despite their medication expertise and accessibility. As demonstrated by the lack of research inclusive of pharmacists relied upon in the Brief, pharmacists can be overlooked as potential members of a primary care team. Pharmacists today graduate with a Doctorate of Pharmacy degree, which requires six to eight years to complete, and have more medication-related training than any other health care professional. Advancement of the pharmacist's role in MAT for substance use disorders can help improve access and outcomes.[1,2] APhA encourages AHRQ to advance research regarding the role of the pharmacists in MAT treatment programs, as such a position aligns with AHRQ's desire to learn more about innovative approaches to MAT treatment.	Thank you for your comment. Pharmacy-based dispensing is noted as a future research need.
APhA (American Pharmacists Association) Thomas E. Menighan	General	Thank you for the opportunity to provide comments on the Brief and efforts to improve the research base regarding MAT models..	Thank you for your comment.

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APhA (American Pharmacists Association) Thomas E. Menighan	General	1 DiPaula, B.A. & Menachery, E. (Mar/Apr 2015). Physician-pharmacist collaborative care model for buprenorphine-maintained opioid-dependent patients, Journal of the American Pharmacists Association, 55(2), 187-192. 2 Raisch, W. (2002). Opioid Dependence Treatment, Including Buprenorphine/Naloxone, Pharmacology & Pharmacy, 36(2), 312-321. 3 Agency for Healthcare Research & Quality, Draft Technical Brief: Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings, (March 2016), p. 7, available at: https://www.effectivehealthcare.ahrq.gov/ehc/products/636/2225/opioid-use-disorder-draft-report-160513.pdf, last accessed June 7, 2016, states that 11 “Key Informants” were interviews and that the clinicians interviews were comprised of the following: on internal medicine/addiction, one family medicine/addiction, one addiction psychiatry, one psychology, one registered nurse. 4 Agency for Healthcare Research & Quality, Draft Technical Brief: Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings, (March 2016), p. 7, available at: https://www.effectivehealthcare.ahrq.gov/ehc/products/636/2225/opioid-use-disorder-draft-report-160513.pdf, last accessed June 7, 2016.	Thank you for your comment. We reviewed these references and found no additional studies that met inclusion criteria.

Commentator & Affiliation	Section	Comment	Response
APhA (American Pharmacists Association) Thomas E. Menighan (continued)	General (continued)	5 Agency for Healthcare Research & Quality, Draft Technical Brief: Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings, (March 2016), p. 7, available at: https://www.effectivehealthcare.ahrq.gov/ehc/products/636/2225/opioid-use-disorder-draft-report-160513.pdf, last accessed June 7, 2016, described the following four consistent components of MAT models of care: 1) pharmacological therapy; 2) provider and community educational interventions; 3) coordination/ integration of substance use disorder treatment and other medical/psychological needs; and 4) psychosocial services/interventions. 6 Agency for Healthcare Research & Quality, Draft Technical Brief: Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings, (March 2016), Table 2 p.16-20, available at: https://www.effectivehealthcare.ahrq.gov/ehc/products/636/2225/opioid-use-disorder-draft-report-160513.pdf 7 Use Disorder in Primary Care Settings, (March 2016), p. 36, available at: https://www.effectivehealthcare.ahrq.gov/ehc/products/636/2225/opioid-use-disorder-draft-report-160513.pdf, last accessed June 7, 2016. 8 Drug Enforcement Agency, Mid-level practitioners authorization by state, last updated May 24, 2016, available at: http://www.deadiversion.usdoj.gov/drugreg/practioners/mlp_by_state.pdf, providing a table that includes information about states (California, Massachusetts (institutional only), Montana, New Mexico, North Carolina and Washington) that allow pharmacists to prescribe controlled substances when working under a collaborative practice agreement.	

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APhA (American Pharmacists Association) Thomas E. Menighan (continued)	General (continued)	9 Agency for Healthcare Research & Quality, Draft Technical Brief: Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings, (March 2016), p. 36, available at: https://www.effectivehealthcare.ahrq.gov/ehc/products/636/2225/opioid-use-disorder-draft-report-160513.pdf, last accessed June 7, 2016, referencing DiPaula, B.A. & Menachery, E. (Mar/Apr 2015). Physician-pharmacist collaborative care model for buprenorphine-maintained opioid-dependent patients, Journal of the American Pharmacists Association, 55(2), 187-192. 10 Food & Drug Administration, Information for Pharmacists SUBOXONE® (buprenorphine HCl/naloxone HCl dihydrate, sublingual tablet) and SUBUTEX® (buprenorphine HCl, sublingual tablet), available at: http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM191533.pdf (last accessed November 16, 2015). 11 Substance Abuse and Mental Health Services Administration (SAMHSA), U.S. Department of Health and Human Services, (March 2015), Federal Guidelines for Opioid Treatment Programs, available at: http://store.samhsa.gov/shin/content/PEP15-FEDGUIDEOTP/PEP15-FEDGUIDEOTP.pdf, last accessed: May 18, 2016. 12 Meshkin, B., Lewis, K., Kantorovich, S., Anand, N. Davila, L. (2015). Adding genetic testing to evidence-based guidelines to determine the safest and most effective chronic pain treatment for injured workers, International Journal of Biomedical Science, 11(4), 157-165. 13 Bauer, I.E., Graham, D.P., Soares, J.C. & Nielson, D.A. (2015). Serotonergic gene variation in substance use pharmacotherapy: a systematic review, Pharmacogenomics, 16(11), 1305-1312.	

Commentator & Affiliation	Section	Comment	Response
APhA (American Pharmacists Association) Thomas E. Menighan (continued)	General (continued)	14 Gonzalez Callejas, D., Canadas Garre, M, Aguilera, M., Jimenez Varo, E. & Calleja Hernandez, M.A. (2013). Pharmaocogenetics of Opioids and Alcohol Addiction, Omics for Personalized Medicine, 335-363.	
APhA (American Pharmacists Association) Thomas E. Menighan	General	Although APhA was pleased to see that pharmacists were highlighted in the "New and Innovative Strategies" section[7] we believe it is important to highlight that pharmacists regularly play a role in treating patients receiving MAT, even if not directly included in the MAT model. Because pharmacists are a highly accessible health care provider, they are frequently a point of contact for patients, including those receiving MAT. As medication experts, pharmacists engage with other health care practitioners to provide medication recommendations, such as dosing and tapering services and regularly interact with patients, potentially identifying patients in need of substance use disorder treatment. Federal regulations, such as 42 CFR Part 2, which addresses confidentiality for patients with substance abuse disorder, can impede patient care beyond the walls of an opioid treatment program or primary care setting. As the health care system moves to better coordinated and integrated care, APhA encourages AHRQ to include in its research pharmacists in MAT models and how MAT models function within the broader health care community.	Thank you for your comment. We did not describe all of the potential staff members involved in providing medication-assisted treatment models of care. Pharmacy-based models are described in the New and Innovative Strategies section and research in this area is noted in the future research needs section. Pharmacy-based models are described in the New and Innovative Strategies section and research in this area is noted in the future research needs section.

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APhA (American Pharmacists Association) Thomas E. Menighan	General	Currently, 48 states and the District of Columbia allow pharmacists to enter into collaborative practice agreements with physicians and other prescribers to provide advanced care to patients. According to the Drug Enforcement Agency[8] six states allow pharmacists to prescribe Schedule III, IV and V controlled substances under a collaborative practice agreement. In addition, as described in the Brief, pharmacists are partnering with physicians to provide MAT.[9] Within these arrangements, pharmacists have taken the lead in developing treatment plans, communicating with patients, improving adherence, monitoring patients, identifying treatment options and performing tasks to alleviate the physician's burden. Thus pharmacists have both the knowledge and experience to provide MAT but opportunities are limited because of regulatory barriers that impede access. Since approximately 86 percent of Americans live within 5 miles of a pharmacy, APhA has encouraged Congress and federal agencies to allow pharmacists to be eligible for a DATA waiver to help increase access to treatment and care in areas with limited options. AHRQ could play a vital role in expanding the pharmacist's role in MAT by fostering research and innovative models that test the effectiveness of pharmacist-led MAT.	Thank you for your comment. Pharmacy-based models are described in the New and Innovative Strategies section and research in this area is noted in the future research needs section.

Commentator & Affiliation	Section	Comment	Response
APhA (American Pharmacists Association) Thomas E. Menighan	General	Considering broad stakeholder interest in expanding access to MAT, it is of utmost importance to remember that pharmacists are the most accessible health care professionals who are medication experts that provide patient care. As the Food & Drug Administration ("FDA") noted specifically concerning suboxone and subutex, "pharmacists will play a role in the delivery of opiate addiction treatment…"[10]. Additionally, SAMSHA's 2015 Federal Guidelines for Opioid Treatment Programs considers pharmacists' role in providing MAT by stating, "Some aspects of medication-assisted treatment services may be provided by an authorized health care professional other than a physician such as an advanced practice nurse, physician assistant, or advanced-practice pharmacist."[11] Given the important role of the pharmacist, the need for more pharmacist-specific research, and the view that pharmacist-provided care is a component of MAT, APhA urges AHRQ to include pharmacists in future research endeavors and highlight their role in any future iterations of the Brief.	Thank you for your comment. Pharmacy-based models are described in the New and Innovative Strategies section and research in this area is noted in the future research needs section. We added a sentence to the Facilitators and Barriers section noting that pharmacists could play a role in dispensing, monitoring for adherence and diversion, and patient education.
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	The American Society of Addiction Medicine (ASAM) thanks you for the opportunity to comment on this draft technical brief on medication-assisted treatment models of care in primary care settings. Established in 1954, ASAM is a professional society representing more than 3,800 physicians and associated professionals dedicated to increasing access and improving the quality of addiction treatment; educating physicians, other medical professionals and the public; supporting research and prevention; and promoting the appropriate role of physicians in the care of patients with addiction.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	We applaud your efforts to increase access to medication-assisted treatment (MAT) by exploring models of care that can increase the number of providers willing to provide substance use disorder treatment. By increasing the evidence base for various models of care of MAT for opioid use disorder (OUD), this document should help to document the importance of MAT in the treatment of OUD. Each of the models presented has the potential to increase access to MAT. Support for state or regional efforts to match these models with existing infrastructure, geography and patient needs could help ensure that these models can be expanded to maximum effect.	Thank you for your comment.
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	A number of issues have reduced availability of MAT, both from addiction specialists and primary care providers. Among these issues are limited reimbursement for addiction treatment services, arbitrary, non-evidence based regulations restricting patient access to medications used to treat addiction and inadequate training of providers in addiction treatment.	Thank you for your comment. These issues are discussed in the Facilitators and Barriers section.
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	When reimbursement is not sufficient, providers cannot treat patients with addiction, even when clinical supports are available to the providers. Under many payment models, addiction specialists who consult with primary care providers cannot be reimbursed for their services without physically seeing the patient. Without payment systems that recognize the inputs provided by supporting addiction specialists, these models cannot be sustained. Primary care providers also need adequate reimbursement to be willing to accept patients with above-average psychosocial needs. We urge you to emphasize that inadequate reimbursement is and likely will remain a significant barrier to OUD treatment, in all models of care.	Thank you for your comment. Issues related to reimbursement are discussed in the Facilitators and Barriers section.

Commentator & Affiliation	Section	Comment	Response
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	Additionally, as noted in the brief, prior authorization requirements can be a barrier to care. Especially when combined with low reimbursement rates, utilization management that requires extensive administrative time and effort discourage providers from offering MAT services.	Thank you for your comment.
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	State regulations that limit coverage of MAT for a set length of time or impose dosage restrictions are also barriers to care. As noted in this brief, many payers implement arbitrary duration limits on MAT. Increased research on optimal dosage and duration would be welcome to help counter regulations that set arbitrary, discriminatory limits to treatment. However, even with improved knowledge of optimal duration and dosage, providers should retain the ability to prescribe dosages that meet each individual patient's needs and not be hindered by regulations or policies that mandate a maximum dosage or duration.	Thank you for your comment. This is discussed as a Barrier, and also as a Future Research need.
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	Regulations that limit the number of patients that addiction specialists and other waivered physicians can treat with buprenorphine also contribute to the lack of adequate addiction treatment. A suboptimal number of physicians with waivers to prescribe buprenorphine also contribute to limitations on treatment. Lack of provider education in addiction can lead physicians to be uncomfortable treating patients with addiction. Inadequate reimbursement can also make it difficult for a physician to maximize patient load if every buprenorphine visit results in a loss to the practice.	Thank you for your comment. This is discussed in the Facilitators and Barriers section.
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	Regulations on telemedicine can also restrict or limit the potential of the models presented in this brief. Restrictions on prescribing controlled substances and other limitations on telemedicine can limit access to addiction specialists for rural patients and primary care providers.	Thank you for your comment. Issues with telemedicine are noted in the Barriers section and also highlighted as an area of Future Research Need.

Commentator & Affiliation	Section	Comment	Response
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	The recent approval of a long acting, extended release buprenorphine will have an effect on patients and providers providing care in these MAT models. Many of these models can be enhanced or expanded when long-acting buprenorphine can be used. Rural patients, patients who must travel for work or with mobility limitations will benefit from reduced need to visit a physician for a prescription and then visiting a pharmacy for buprenorphine. When combined with psychosocial supports and therapy, including via telemedicine, extended release buprenorphine, when adequately paid-for, has the potential to enhance nearly all of these models of MAT in primary care.	Thank you for your comment. As noted in the Guiding Question 3 section of the report, we identified no trials of buprenorphine conducted in primary care settings. Implantable and injection forms of buprenorphine are highlighted as an area of Future Research Need (pg 46).
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	With improved access to MAT, it is critical that high-quality care is being delivered. This may require the development of new quality of care indicators for use of MAT in primary care settings. ASAM has developed Standards of Care and Performance measures that apply to any physician assuming the responsibility for caring for addiction. We are currently in the validating and testing phase for our performance measures. We also recently developed a National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. Our guideline addresses the research needed to better understand optimal duration and doses of treatment. Suboptimal care can result in buprenorphine diversion and other negative consequences and we are working to address this concern through education and with state medical boards.	Thank you for your comment. This is highlighted as a Future Research Need in the first bullet.
ASAM (American Society of Addiction Medicine) R. Jeffrey Goldsmith	General	Once again, we want to thank you for the opportunity to review and comment on this draft report on medication-assisted treatment models of care for opioid use disorder in primary care settings	Thank you for your comment.
Bright Quang	General	<Comment redacted>	The reviewer shared details about their personal experience.

Commentator & Affiliation	Section	Comment	Response
CleanSlate Centers **Amanda Wilson** **Gregory C. Marotta** **Kelly J. Clark**	General	Over the last few years, we have seen the opioid epidemic devastate lives and fill our hospitals and jails with people in need of compassionate, high-quality care and treatment. Unfortunately, there are numerous barriers that make it difficult, if not impossible, for many of those struggling with the disease of addiction to access the type of treatment they need and that will work for them in a safe, caring environment. These barriers include stigma and misinformation, lack of funds to pay for treatment, loss of family support or housing, and many more.	Thank you for your comment.
CleanSlate Centers **Amanda Wilson** **Gregory C. Marotta** **Kelly J. Clark**	General	We sincerely appreciate the work the Agency for Healthcare Research and Quality is doing to better understand opioid addiction and identify solutions that will help people reclaim their lives and ultimately end the opioid epidemic in the United States. Since 2009, CleanSlate Centers has provided treatment to more than 18,000 people suffering from addiction to opioids or alcohol. We have made it our mission to help people overcome their addiction by providing safe, high quality and effective care through evidence-based medicine for opioid addiction treatment.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
CleanSlate Centers **Amanda Wilson** **Gregory C. Marotta** **Kelly J. Clark**	General	For this reason, we applaud the AHRQ for examining models of public and grant funded care for opioid addiction utilizing medication assisted treatment in a primary care setting. After reviewing the recent draft report titled "Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings" and appendix, we were surprised that CleanSlate Centers is specifically mentioned in the summary of a discussion with an unidentified informant on page C-9 of the appendix which reads: "On the other hand, some physician groups are doing a lot of prescribing and not a lot of treatment/follow-up. The Clean Slate Addiction Treatment and Rehabilitation Centers in Massachusetts are a for-profit community of physicians who do a lot of prescribing and not a lot of treatment. They put a lot of buprenorphine in the hands of patients who need more structure. Patients from OTP say they can't handle the prescriptions." This anecdotal statement is inaccurate and does not reflect the CleanSlate program of care, which includes individualized treatment plans for each patient consisting of appropriate medication treatment prescribed by physicians, clear accountability and supportive counseling. We utilize a full diversion control protocol – monitoring drug tests for nor-buprenorphine levels, random call backs, random pill counts and drug tests, checking not only the state's Prescription Drug Monitoring Programs but also utilizing a commercial product which provides information about medications fills across state lines. Patients are seen weekly in treatment for several months until they are stable, then bi-weekly, up to monthly when they are doing well and adherent to their treatment plan.	Thank you for your comment. The Key Informant interview summaries have been removed from the report appendix.

Commentator & Affiliation	Section	Comment	Response
CleanSlate Centers Amanda Wilson Gregory C. Marotta Kelly J. Clark (continued)	General (continued)	We are extremely proud of our track record and of the patient lives we have saved over the last six years. CleanSlate Centers was the inaugural recipient of SAMHSA's Science in Service Award for Office Based Opioid Treatment. We've been featured in the New England ICER report, and are proud to be partnered with organizations like Geisinger Health System and Health Plan, the Addiction Medicine Medical Fellowship Program at Brown University, and the Coalition to Stop Opioid Overdose to address the needs of patients and their communities. Our Massachusetts community partners in care include Hampden County Corrections, Beth Israel Deaconess Hospital in Plymouth, and Franklin Recovery Center in Greenfield. These partnerships are the result of our track record and our strong commitment to continually improving the care we provide and our reputation for successfully treating patients within the larger medical community in our area. Based on our record and the anecdotal and inaccurate nature of the opinion included in the report, we respectfully ask that AHRQ remove this reference as it does not correctly describe our treatment program and is not based on fact or supporting data. Additionally, we welcome an opportunity to meet with a representative of the Agency for Healthcare Research and Quality to discuss our work and ways we can help support your efforts.	
CleanSlate Centers Amanda Wilson Gregory C. Marotta Kelly J. Clark	General	Again, we sincerely appreciate the important work AHRQ is doing to help address the opioid epidemic in our country. We also thank you for your consideration of our request to remove the above reference from the report, and we look forward to meeting with a representative of AHRQ in the coming weeks.	Thank you for your comment. The Key Informant interview summaries have been removed from the report appendix.

Commentator & Affiliation	Section	Comment	Response
Daniel Pomerantz, Montefiore New Rochelle Hospital	General	While the report recognizes that stigma is an important obstacle to the adoption of effective treatments for OUD, the use of the term 'Medication-assisted treatment' (MAT)perpetuates the mostly false idea that treatment of OUD without medication is an effective alternative for most patients with OUD. Lifestyle modification is an important part of the treatment of lipid disorders, diabetes and hypertension, but in those illnesses, we talk about pharmacologic treatments and non-pharmacologic treatments, not medication-assisted treatments, because the professional community assumes that treatment relying on non-pharmacologic methods alone will be ineffective in the majority of cases. The construct of MAT carries with it the implicit assumption that effective treatment for most patients is possible without medication. An assumption that is, at best, unproven, and is, mostly likely, false.	Thank you for your comment. We agree that the term "medication-assisted treatment" may be misleading since it could imply that medications are an ancillary part of treatment. However, medication-assisted treatment remains a widely used term, is well understood, and has been defined by SAMHSA, and helps distinguish medication-based from non-medication based detoxification/abstinence approaches. We added to the Background section of the Intro: "It has been suggested that the term medication-assisted treatment is misleading because it implies that medications play an adjunctive role in treatment for opioid use disorder, and that it would be more accurate to simply refer to multimodal therapy for opioid use disorder as "treatment." In this report, we use the term medication-assisted treatment because it is widely used, well understood (as defined by SAMHSA), and to help distinguish medication-based from non-medication based (e.g., detoxification/abstinence) approaches. The term medication-assisted treatment is not meant to imply that medications play an ancillary role in treatment; rather, medications are central to the concept of effective multimodal treatment for opioid use disorder."
Janice Kauffman	General	I think this is a very thorough Technical report capturing a tremendous about of information and thought. Thank you for inviting me to be a Key Informant.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
Joseph Walsh	General	An overall concern is - Is the Goal of these Services, to ultimately ensure 'Graduation' from MAT ? Those of us in Recovery from addiction know there is No 'Graduation' from Recovery. However, it is a widely-held Principal that while changing 'Flavors' of Chemical Dependence (MAT), has and does save lives, its Long-Term success, (measured in Years), is largely undocumented. Our collective Experience as a Community of Addicts/Abusers in Recovery has been that while MAT is effective as a Bandage, fatal overdoses are all too prevalent for MAT Patients. The importance of continuous and effectively incorporated PSR, and Addict Peer Support in Recovery from Chemical Dependence cannot be over-emphasised.	Thank you for your comment. The Technical Brief does not address discontinuation of medication-assisted treatment, and arbitrary dose and duration limits are noted as an issue.
NASTAD (National Alliance of State and Territorial AIDS Directors) Murray C. Penner	General	The National Alliance of State and Territorial AIDS Directors (NASTAD) appreciates the opportunity to comment on the draft Agency for Healthcare Research and Quality (AHRQ) technical brief on Medication-Assisted Treatment (MAT) Models of Care for Opioid Use Disorder in Primary Care Settings. NASTAD represents public health officials who administer state and territorial HIV and hepatitis prevention and care programs nationwide. NASTAD has long been concerned about the holistic healthcare needs of people who use drugs and recognizes the important relationship between treatment for substance use disorders and infectious disease prevention and care.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
NASTAD (National Alliance of State and Territorial AIDS Directors) Murray C. Penner	General	NASTAD commends AHRQ for its research and work compiling the MAT in Primary Care Settings guidelines. The BHIVES care model as well as the supporting evidence outlined in the guidelines suggest that prescribing MAT within HIV and hepatology care settings is a promising practice as MAT lowers risk of transmission and increases retention in care. The other 11 care models suggest that the same is true of primary care settings. In general, NASTAD supports the draft guidelines and encourages AHRQ to quickly finalize and disseminate the guidelines to expand necessary treatment. NASTAD believes that a combination of technical assistance and research are necessary to further address the barriers of stigma, lack of institutional support, lack of prescribing physicians, and inadequate reimbursement described in the guidelines. We call on AHRQ to continue providing evidence-based practices to support MAT.	Thank you for your comment. Note that this is a Technical Brief, an overview of the evidence, and not a guideline. This is not intended to provide guidance about how to implement or deliver medication-assisted treatment, or how to administer medications for opioid abuse. AHRQ does not provide evidence-based practices about medication-assisted treatment.
NASTAD (National Alliance of State and Territorial AIDS Directors) Murray C. Penner	General	NASTAD agrees that rural populations need additional attention in MAT policy, and we encourage AHRQ to recommend building partnerships with existing systems of care experienced in reaching rural and other hard to reach populations, such as utilizing the Ryan White program to support people who use drugs living with HIV in rural areas. NASTAD supports suggestions in the guidance to develop models of care for adolescents, particularly models that address the syndemics of opioid overdose and hepatitis C infection that greatly affect youth who inject opioids. NASTAD commends AHRQ for addressing health equity in the guidelines, but we are concerned that the guidelines do not address racial and ethnic health disparities. We call on AHRQ to include future research that addresses racial inequities in MAT access and supports the development of evidence-based programs that target people of color who may be disproportionately affected by Opioid Use Disorders and hepatitis C.	Thank you for your comment. Note that this is a Technical Brief, an overview of the evidence, and not a guideline. This is not intended to provide guidance about how to implement or deliver medication-assisted treatment, or how to administer medications for opioid abuse. AHRQ does not provide evidence-based practices about medication-assisted treatment.

Commentator & Affiliation	Section	Comment	Response
NASTAD (National Alliance of State and Territorial AIDS Directors) Murray C. Penner	General	NASTAD and other national technical assistance providers are working to address drug and MAT-use stigma by training health departments, community-based organizations, and medical providers on harm reduction and cultural competency, including targeted media campaigns. NASTAD works to bolster health department support for MAT with people who inject drugs (PWID) through the publication of informational materials and by encouraging AIDS Drug Assistance Programs (ADAPs) to include MAT on their formularies. According to NASTAD's ADAP Formulary Database User's Guide, 12 ADAPs currently include buprenorphine on their formularies.	Thank you for your comment.
NASTAD (National Alliance of State and Territorial AIDS Directors) Murray C. Penner	General	Additionally, national technical assistance providers are urging Members of Congress to reduce federal barriers that complicate prescribing capacity. Health department programs are beginning to integrate and work across systems as well as with payers to ensure adequate reimbursement. Research and information on activities such as these that aim to reduce barriers described in the guidelines are appreciated as a next step.	Thank you for your comment. Note that this is a Technical Brief, an overview of the evidence, and not a guideline. This is not intended to provide guidance about how to implement or deliver medication-assisted treatment, or how to administer medications for opioid abuse. AHRQ does not provide evidence-based practices about medication-assisted treatment.
NASTAD (National Alliance of State and Territorial AIDS Directors) Murray C. Penner	General	We understand that the insidious combination of stigma, silence, and legal restrictions surrounding the overall health of people who use drugs in the U.S. has contributed to avoidable HIV and hepatitis infections, in addition to countless deaths as a result of overdose. This crisis requires an honest and critical examination of our efforts, explicit identification of effective public health programs for people who use drugs, and a sharpening of our focus so that we can prevent new infections and overdose among people who use drugs, support long term recovery, and ensure health promotion opportunities are in reach for people who use drugs in our communities.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
NASTAD (National Alliance of State and Territorial AIDS Directors) Murray C. Penner	General	Thank you for supporting opportunities to improve the lives of people who use drugs. Expanded federal investment to support prevention and care services for people who use drugs is paramount to the work of NASTAD and its members and improving the guidelines for MAT prescribing is just one of the many avenues to improve our nation's public health and promote the health of our most vulnerable communities.	Thank you for your comment. Note that this is a Technical Brief, an overview of the evidence, and not a guideline. This is not intended to provide guidance about how to implement or deliver medication-assisted treatment, or how to administer medications for opioid abuse. AHRQ does not provide evidence-based practices about medication-assisted treatment.
NASTAD (National Alliance of State and Territorial AIDS Directors) Murray C. Penner	General	We appreciate your attention and consideration of these comments.	Thank you for your comment.
Paul Bowman, NAMA Recovery (National Alliance for Medication Assisted Recovery)	General	<Comment redacted>	The reviewer shared details about his personal experience with medication-assisted treatment.
Peer Reviewer #1	General	This report is very useful. It has gaps in addressing extended release naltrexone. While I doubt you will find delivery models that are different from those you have highlighted, it might be a good idea to talk with a couple key informants that have more experience with it and could balance the discussion of barriers in particular.	Thank you for the comment. We revised (pg 22, 2nd to last paragraph) to clarify that we did not identify any published data on utilization of extended release naltrexone for opioid use disorder, but that Key Informants noted that use is variable. We did not identify additional distinct models focusing on extended-release naltrexone, and added research on models of care focusing on extended release naltrexone as a gap (pg 39).
Peer Reviewer #2	General	Overall a helpful summary of the various creative approaches currently being taken in different treatment settings and geographic locales, to extend the use of MAT to target opioid use disorders.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #2	General	However, I was disappointed in the lack of detail regarding basic logistics on who does what. I would have liked more information on the nuts and bolts of how these treatment settings are organized within primary care: who is doing the prescribing, who is doing the educating, who is checking the PDMP, how often is the PDMP being checked, who is ordering the urine tox screens, how often is the urine tox screen being checked, what diagnostic codes are being used, who is doing the billing, what kind of reimbursement rate are they getting, how are prior authorizations handled, who is administering the psychosocial intervention, how is it being paid for, etc., etc? I think this nitty gritty stuff is essential when thinking about the feasibility of further implementation. One way to do this is track a single sample patient in each clinic through time, with a graphic that shows all the different types of providers they come in contact with, how much time they spend with each provider, how long between providers, any monitoring done/labs drawn and at what intervals.... I loved the idea of a 'glue person', but how does this actually work?	Thank you for the comment. The level of detail requested by the reviewer in terms of tracking who is doing each of these specific tasks and the amount of time required was not available from Key Informant interviews or published material, and the processes are likely to vary within clinics using the same model. We also do not feel that this was the purpose of this Technical Brief, which was intended to describe key elements for successful/promising medication-assisted treatment models of care.
Peer Reviewer #2	General	I also think there should have been a more in depth analysis and discussion of how to prevent diversion and misuse of buprenorphine, since this continues to be a major and valid concern about extending the use of buprenorphine. How is misuse or diversion being monitored/detected/protected against, in these various treatment settings? What is happening in each of these settings when misuse is detected? Are patients fired from the clinic? Is their contract with the clinic renegotiated? If so, how? These are the real life situations that make treating this population so challenging, and where learning how other institutions are handling it would have been helpful.	Thank you for the comment. Prevention of diversion was not brought up by the Key Informants or in published materials as a key or distinguishing component of different medication-assisted treatment models of care. However, as a general issue in provision for medication-assisted treatment this was brought up by several Key Informants, and the need for research on methods to prevent diversion is noted as a research need (pg 39).

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #2	General	Any analysis of the opioid problem in the primary care setting has got to take on the vexing question of what to do with patients on chronically high and unsafe doses of opioid analgesics, who nonetheless do NOT meet strict criteria for an opioid use disorder, for example because they have only ever taken the medication as prescribed, and their doctors, once upon a time, prescribed a lot. I would have found it helpful to know how other primary care clinics are tackling this problem. Is anyone willing to use Suboxone off-label for pain to help this high risk population who nonetheless does not identify as having as "opioid use disorder"?	Thank you for the comment. Use of buprenorphine in patients with chronic pain without opioid use disorder was outside the scope of this report. The need for research on management of patients with opioid use disorder and concomitant pain is included as a future research need (pg 38).
Peer Reviewer #3	General	There are some real problems with this document.	Thank you for the comment. We responded to specific comments from this peer reviewer.
Peer Reviewer #3	General	1. Misstated information-it turns out that the Hub and Spoke model does NOT function as described. In working with Vermont and the CMS IAP, it has become clear that while the early model was as described in fact initiation most often occurs in the SPOKES, not the Hub. For further information the authors may want to talk with Beth Tanzman in Vermont.	Thank you for the comment. We revised to clarify that an initial assessment is used to determine whether patients are appropriate for management in a hub or spoke, and to clarify the roles of the hubs and spokes in this model.
Peer Reviewer #3	General	2. No State is mentioned related to Medicaid Health Homes MAT. in fact, Rhode Island has implemented that model with methadone I believe, not sure about other medications.	Thank you for the comment. We did not list the states that have initiated the Medicaid Home because it was unclear which, if any, have been implemented in primary care settings. We revised to note that implementation in Rhode Island has been in opioid treatment programs only; in Maryland, it has been in opioid treatment programs or psychiatric clinics.
Peer Reviewer #3	General	3. The integrated prenatal MAT model is implemented by Spectrum Health in Michigan and should be discussed.	Thank you for the comment. The description of the integrated prenatal medication-assisted treatment model is meant to apply to different clinics and settings. We were unable to identify any published information specifically regarding the Spectrum Health model or how it may differ from the general information provided on the integrated prenatal model in the report.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #3	General	4. Related to training, Missouri has long ago implemented a training program at the State level for all clinicians providing MAT for which they get a certification. Especially important for counselors.	Thank you for the comment. We did not add a reference to the Missouri program to the report as it does not appear to be linked to a specific model of care. In addition, education and training are available in a number of other states and it wasn't clear how Missouri's program differs. The Technical Brief describes a number of educational and training programs linked to specific models of care (e.g., Physician Clinical Support System, Project Extension for Community Healthcare Outcomes).
Peer Reviewer #3	General	5. I take it AHRQ descided there was to be no discussion of coverage and benefits and how these affect models of care. I think that is a big error.	Thank you for the comment. Reimbursement and coverage are noted as a barrier to implementation across models (pg 24). We also describe financial sustainability of the Massachusetts Nurse Care Manager model as a potential advantage given reimbursement policies in that state (pg 11).
Peer Reviewer #4	General	The need to expand access to medication-assistant treatment (MAT) for the treatment of opioid use disorders (OUDs) demands that primary care providers play a more prominent role in delivery of this treatment than has been the case up to now. Most MAT is delivered by addiction specialists (internists, psychiatrists, opioid treatment programs) and only about 1 in 5 opioid addicts receive MAT. Understanding how to better develop MAT capacity within primary care settings requires a synthesis of a diverse literature as well as stakeholder experience which this technical brief attempts to do.	Thank you for the comment. Yes, this is the purpose of the technical brief.
Peer Reviewer #5	General	Overall this is an excellent report that is extremely comprehensive and well-written. This will become an important reference for all future work (teaching and research) regarding this topic. Well done.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	General	I have tried to stop referring to medications for opioid use disorders as Medication Assisted Treatment based on the following article: Friedmann PD, Schwartz RP. Just call it "treatment". Addiction science & clinical practice. 2012 Jun 9;7(1):1. We don't refer to treatments for other chronic diseases as Medication Assisted Treatment. I do believe it contributes to the continued stigmatization of this therapy for this problem.	Thank you for your comment. We agree that the term medication-assisted treatment may be misleading since it could imply that medications are an ancillary part of treatment. However, medication-assisted treatment remains a widely used term, is well understood, and has been defined by SAMHSA, and helps distinguish medication-based from non-medication based detoxification/abstinence approaches. We added to the Background section of the Intro: "It has been suggested that the term medication-assisted treatment is misleading because it implies that medications play an adjunctive role in treatment for opioid use disorder, and that it would be more accurate to simply refer to multimodal therapy for opioid use disorder as "treatment." In this report, we use the term medication-assisted treatment because it is widely used, well understood (as defined by SAMHSA), and to help distinguish medication-based from non-medication based (e.g., detoxification/abstinence) approaches. The term medication-assisted treatment is not meant to imply that medications play an ancillary role in treatment; rather, medications are central to the concept of effective multimodal treatment for opioid use disorder."

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	General	For completeness may want to consider a more detailed description (only mentioned as a topic for further research) of "Methadone Medical Maintenance" which is methadone offered in non-OTP settings e.g., primary care. see references Salsitz EA, Joseph H, Frank B, Perez J, Richman BL, Salomon N, Kalin MF, Novick DM. Methadone medical maintenance (MMM): treating chronic opioid dependence in private medical practice--a summary report (1983-1998). The Mount Sinai journal of medicine, New York. 1999 Dec;67(5-6):388-97. Merrill JO, Ron Jackson T, Schulman BA, Saxon AJ, Awan A, Kapitan S, Carney M, Brumback LC, Donovan D. Methadone medical maintenance in primary care. Journal of General Internal Medicine. 2005 Apr 1;20(4):344-9. Harris KA, Arnsten JH, Joseph H, Hecht J, Marion I, Juliana P, Gourevitch MN. A 5-year evaluation of a methadone medical maintenance program. Journal of substance abuse treatment. 2006 Dec 31;31(4):433-8.	Thank you for your comment. Guiding Question 3 includes a section on methadone treatment (pg 33). We reviewed the studies suggested by the reviewer but they did not meet inclusion criteria because they are observational. We added these references to the future research needs sections bullet on methadone in primary care settings, noting that these are observational studies.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	General	One issue that is not well covered (only briefly mentioned in the "Areas of Uncertainty and Future Research Needs" is the ability to manage both OUD and chronic pain with buprenorphine in primary care. while this is not well studied it is a major issue as pain is so common in patients with OUDs and a potential motivator for practitioners to become waivored to prescribe (Alford DP, German JS, Samet JH, Cheng DM, Lloyd-Travaglini CA, Saitz R. Primary care patients with drug use report chronic pain and self-medicate with alcohol and other drugs. J Gen Intern Med. 2016;31:486-491) (Rosenblum A, Joseph H, Fong C, Kipnis S, Cleland C, Portenoy RK. Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. JAMA. 2003;289:2370-2378.) (Jamison RN, Kauffman J, Katz NP. Characteristics of methadone maintenance patients with chronic pain. J Pain Symptom Manage. 2000;19:53-62.) (Barry DT, Savant JD, Beitel M, Cutter CJ, Moore BA, Schottenfeld RS, Fiellin DA. Pain and associated substance use among opioid dependent individuals seeking office-based treatment with buprenorphine–naloxone: A needs assessment study. Am J Addict. 2013; 22(3): 212-217.)	Thank you for your comment. We added references to the Alford and Barry studies to the Future Research Needs bullet on management of opioid use disorder in patients with chronic pain. We did not add the other studies since they were not in primary care/office-based settings. To the Special Populations section of Guiding Question 3, we added a sentence noting the lack of trials on medication-assisted treatment for opioid use disorder due to prescription opioids.

Commentator & Affiliation	Section	Comment	Response
Peter Friedmann	General	I would like to propose that AHRQ abandon the term "medication-assisted treatment" which implies that the medication itself is not treatment. When we treat diabetes we don't speak of "medication-assisted dietary therapy" -- we say they are on insulin treatment and a diet is part of the overall treatment plan. Similarly, as opioid medication is the primary active ingredient of treatment for opioid use disorders --rigorous studies have demonstrated that the psychosocial counseling provides limited additional benefit -- we should speak of agonist treatment, medication therapy, pharmacotherapy or just treatment (Friedmann & Schwartz, 2012: http://ascpjournal.biomedcentral.com/articles/10.1186/ 1940- 0640-7-10). To do otherwise continues to stigmatize medical treatment of opioid addiction.	Thank you for your comment. We agree that the term "medication-assisted treatment" may be misleading since it could imply that medications are an ancillary part of treatment. However, medication-assisted treatment remains a widely used term, is well understood, and has been defined by SAMHSA, and helps distinguish medication-based from non-medication based detoxification/abstinence approaches. We added to the Background section of the Intro: "It has been suggested that the term medication-assisted treatment is misleading because it implies that medications play an adjunctive role in treatment for opioid use disorder, and that it would be more accurate to simply refer to multimodal therapy for opioid use disorder as "treatment." In this report, we use the term medication-assisted treatment because it is widely used, well understood (as defined by SAMHSA), and to help distinguish medication-based from non-medication based (e.g., detoxification/abstinence) approaches. The term medication-assisted treatment is not meant to imply that medications play an ancillary role in treatment; rather, medications are central to the concept of effective multimodal treatment for opioid use disorder."

Commentator & Affiliation	Section	Comment	Response
Richard Saitz, Boston University School of Public Health	General	I believe AHRQ has a very important opportunity to lead by not perpetuating a misleading term in the title and throughout the report. "Medication-assisted" suggests that somehow medication is helping some other more important or more effective treatment. Instead medication is the treatment and in fact it is often not possible to detect an incremental benefit of ancillary treatments such as counseling when tested in randomized trials. We would never call medication treatment of hypertension or diabetes "medication-assisted" treatment despite the fact that these conditions also respond to behavioral approaches. Perpetuating the myth that medication is simply assisting treatment serves to perpetuate stigma for medication treatment, implies that somehow it is not as effective as it is, and it can serve as a serious barrier to care when practitioners only provide medication treatment when it is in the context of assisting some other treatment, and withhold it otherwise. Please see this call in an international journal to "just call it treatment." http://ascpjournal.biomedcentral.com/articles/10.1186/1940- 0640-7-10 and another international leading high impact factor journal which encourages calling it what it is--opioid agonist treatment (yes there are other medications like antagonists that can simply be called medications, medication treatment) http://www.thelancet.com/journals/lancet/article/PIIS0140- 6736(15)60750-4/abstractPlease do not miss this opportunity to lead and to improve care for people during this epidemic by inappropriately labeling this life-saving treatment.	Thank you for your comment. We agree that the term “medication-assisted treatment” may be misleading since it could imply that medications are an ancillary part of treatment. However, medication-assisted treatment remains a widely used term, is well understood, and has been defined by SAMHSA, and helps distinguish medication-based from non-medication based detoxification/abstinence approaches. We added to the Background section of the Intro: “It has been suggested that the term medication-assisted treatment is misleading because it implies that medications play an adjunctive role in treatment for opioid use disorder, and that it would be more accurate to simply refer to multimodal therapy for opioid use disorder as “treatment.” In this report, we use the term medication-assisted treatment because it is widely used, well understood (as defined by SAMHSA), and to help distinguish medication-based from non-medication based (e.g., detoxification/abstinence) approaches. The term medication-assisted treatment is not meant to imply that medications play an ancillary role in treatment; rather, medications are central to the concept of effective multimodal treatment for opioid use disorder.”

Commentator & Affiliation	Section	Comment	Response
Sybil Marsh	General	My observations through many years as a buprenorphine/naloxone prescriber and educator is that while many physicians learn how to prescribe buprenorphine, few are doing it. There is much confusion about the role of buprenorphine in overdose deaths and about its potential diversion. Physicians fear doing harm to patients, and to themselves, both through self recrimination if they leave the buprenorphine the prescribed is implicated in the patient's death, and through punitive oversight, at the level of the state medical board or at the level of the criminal justice system. Primary care physicians were encouraged some years ago to increased her prescribing of methadone for chronic pain. This prescribing and misuse of this medication resulted in a significant number of unintentional overdose deaths. Primary care physicians were then discouraged from prescribing methadone for pain. I would be surprised if any embracing of primary care use of methadone as MAT will ever occur. Studies done in "single issue" addiction medicine/psychiatry settings felt to recognize a burden of chronic pain in the opiate dependent population, and defer its management to primary care. I appreciate that this review identifies that issue. As a staff physician in a methadone assisted treatment program, I note new clients presenting who barely meet any criteria for an opiate use disorder, but who have high tolerance for the opiate medication that is apparently helpful for the chronic pain, and who have been referred in the best cases and abandoned in the worst, by their opiate prescribers. Surprisingly, many respond positively to the forced travel outside their homes, socialization, clear expectations, contingencies, and empathetic supportive counseling the received there.	Thank you for your comment. The issue with most buprenorphine waivered physicians being well below their allowed quota is noted in the Facilitators and Barriers section.

Commentator & Affiliation	Section	Comment	Response
Sybil Marsh (continued)	General (continued)	This observation might make a case for centralizing treatment of patients with chronic pain who appear to benefit from an opiate in a way that would decrease potential for misuse and diversion of that medication, problems that feed the need for MAT.	
Bright Quang	Background	<Comment redacted>	The reviewer shared details about their personal experience.
Janice Kauffman	Background	Current Practices: 1st paragraph, pg.#2 "Under Federal law, MAT patients must receive counseling" This statement is true for MAT - methadone treatment but not DATA 2000. DATA 2000 recommends but does not require counseling. I would suggest changing the language to reflect this. It states "the practitioner has the capacity to refer the patient for appropriate counseling and other appropriate ancillary services" Title XXXV Waiver Authority for Physicians Who Dispense or Prescribe Certain Narcotic Drugs for Maintenance Treatment or Detoxification Treatment, 10/17/00, pg. 1 (www.samhsa.gov) I would also suggest in the same paragraph for comprehensiveness sake that methadone is a schedule II opioid that is dispensed in license and 'accredited' opioid treatment programs."	Thank you for the comment. We revised to be clear that physicians are required to attest to the capacity to refer for counseling services.
Paul Bowman, NAMA Recovery(National Alliance for Medication Assisted Recovery)	Background	<Comment redacted>	The reviewer shared details about his personal experience with medication-assisted treatment.
Peer Reviewer #1	Background	page 8 line 24-28: of the three items comparing heroin to prescription pain medication, only the variability of dose or purity is really a difference. Propose restating: Lack of control over purity leading to high variability in dose is an additional concern with heroin as compared to prescription opioids.	Thank you for the comment. Revised as suggested.
Peer Reviewer #1	Background	line 41: MAT is to be provided in combination ... should read Medication is to be provided in combination...	Thank you for the comment. Revised as suggested.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	Background	line 46-47: MAT has been shown to be more effective than treatments that do not use MAT... should read MAT has been shown to be more effective than treatments that do not use medication	Thank you for the comment. Revised as suggested.
Peer Reviewer #1	Background	line 50-51: Remove the word other: block the euphoric and sedating effects of opioids, reduce the craving for opioids. Not all medication is an opioid but using other implies it is	Thank you for the comment. Revised as suggested.
Peer Reviewer #1	Background	line 54-56: Revise Examples of psychosocial interventions include individual therapy, group counseling, drug counseling, family behavior therapy, cognitive-behavioral therapy, motivational enhancement therapy.... to read cognitive-behavioral therapy, motivational enhancement therapy, and other evidence-based psycho-social interventions in individual, group or family counseling settings...	Thank you for the comment. Revised as suggested.
Peer Reviewer #1	Background	page 9 line 22: I do not believe there is evidence for oral naltrexone for OUD, only for extended release naltrexone. Oral naltrexone is used for AUD only.	Thank you for the comment. The label for oral naltrexone indicates that it is "indicated…for the blockade of the effects of exogenously administered opioids. Naltrexone…has not been shown to provide any therapeutic benefit except as part of an appropriate plan of management for addiction." Studies of oral naltrexone for opioid use disorder have been performed, but have not been effective, thought to be due to poor compliance. We revised (pg 2) to note that oral naltrexone is rarely used for opioid use disorder, also (pg 29, 2nd paragraph from bottom) to note that Key Informants noted that oral naltrexone is rarely used for opioid use disorder, given the lack of studies showing effectiveness and low compliance. Evidence on oral naltrexone for opioid use disorder is summarized on pg 26; as we noted, no trial was conducted in primary care settings.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #2	Background	Page 8 of 130. Line 9: Good to avoid the term "abuse" in favor of "misuse" "overuse" or "addictive use".	Thank you for the comment. The DHHS website (www.hhs.gov/opioids/about-the-epidemic) refers to opioid "abuse" and SAMHSA (www.samhsa.gov/atod/opioids) also refers to abuse and misuse of opioids, so we kept the term abuse here; however, to the extent possible we tried to use the term "opioid use disorder" as consistent with DSM-V (the DSM-V definition is provided in this sentence).
Peer Reviewer #2	Background	Line 21: Should include in the "challenges in the treatment of OUD" the risk of death even when taking opioids as prescribed.	Thank you for the comment. The mortality associated with opioid use disorder is described earlier in this section.
Peer Reviewer #2	Background	Line 26: This statement is incorrect. Heroin is no more addictive than many prescription opioids. I would delete this sentence.	Thank you for the comment. We revised to state "Lack of control over purity leading to high variability in dose is an additional concern with heroin as compared to prescription opioids," removing the reference to more addictive potential.
Peer Reviewer #2	Background	Page 9 of 130. Line 26: Might be good to clarify that methadone in pill form Rx'd for pain is not subject to the same constraints.	Thank you for the comment. Management of chronic pain without opioid use disorder is not within the scope of this Technical Brief.
Peer Reviewer #3	Background	There needs to be more discussion of methadone, long researched, but as you say available only in settings apart from both the specialty SUD treatment system and primary care. Not enough clarity about this in the document. It has some very serious implications. Research has shown that there is increased use of hospitals and ERs with patients in MTP...suggestive of poor health care.	Thank you for the comment. Methadone cannot be prescribed for opioid use disorder in primary care settings and is outside the scope of this review.
Peer Reviewer #4	Background	1. Throughout the background section there is a mixing of the terms psychological, psychosocial and psychiatric. I feel psychological co-morbidities are better termed psychiatric co-morbidities, and that psychological/psychosocial versus psychiatric treatment should be distinguished (the later utilizing medications).	Thank you for the comment. We revised "psychological comorbidities" to "psychiatric comorbidities" (pg 8). Also revised to note that psychiatric co-morbidities are common in patients with opioid use disorder and often require treatment with medications (pg 8).

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #4	Background	2. In the first paragraph it is stated heroin has a significantly higher addiction potential than other opioids, which is not clearly established.	Thank you for the comment. We revised to take out the statement that heroin has higher addiction potential.
Peer Reviewer #4	Background	3. In the line "MAT is to be provided in combination with comprehensive substance abuse treatment including but not limited to: ..." should include mention of treatment of co-morbid psychiatric disorders as these re present in >50% of those with OUDs.	Thank you for the comment. We revised to note that psychiatric co-morbidities are common in patients with opioid use disorder and often require treatment with medications (pg 8)
Peer Reviewer #4	Background	4. It should be noted that DATA 2000 does not require co-delivery of psychosocial treatment, only that "physicians must attest that they have the capacity to refer addiction treatment patients for appropriate counseling and other non-pharmacologic therapies." The co-delivery of face-to-face counseling of some sort is more a standard of care.	Thank you for the comment. This sentence has been corrected (pg 10).
Peer Reviewer #5	Background	P8L9: would try to remove the DSM IV term "abuse" from the document as much as possible for example would edit to "...misuse of prescription opioids or use of illicit heroin"	Thank you for your comment. We revised this as suggested.
Peer Reviewer #5	Background	P8L26 would add mention of illicit fentanyl as example of increased risks associated with heroin use	Thank you for your comment. Based on comments from other reviewers, we focused the discussion on heroin risks to focus on uncertain purity. Use of prescription opioids could also lead to use of illicit fentanyl.
Peer Reviewer #5	Background	P8L49 could add normalize brain changes (Kaufman MJ et al. Psychiatry Res 1999)	Thank you for your comment. This sentence focuses on effects of medication-assisted treatment on clinical outcomes, so we did not add this.
Peer Reviewer #5	Background	P9.L17 Under federal law, MAT patients must receive counseling,...is this true? I thought the law stated providers mush have counseling available. In fact the studies on the benefits of counseling over medical management for OBOT patients is mixed (Weiss RD, Griffin ML, Potter JS, Dodd DR, Dreifuss JA, Connery HS, Carroll KM. Who benefits from additional drug counseling among prescription opioid-dependent patients receiving buprenorphine–naloxone and standard medical management?. Drug and alcohol dependence. 2014 Jul 1;140:118-22.)	Thank you for your comment. We revised to note that the requirement is for physicians to have access to counseling services.

Commentator & Affiliation	Section	Comment	Response
Peter Friedmann	Background	The attribution of models to specific institutions undervalues the significant contributions made by others and convergent evolution to the development of these effective models of care. For example, I don't think any one institution can take credit for developing the nurse care manager model of care.	Thank you for your comment. We attributed models to specific institutions or locales when the information from published articles and Key Informants was able to identify the original/main source. The Nurse Care Manager model is not attributed to a specific institution—it was a system primarily originally developed in Massachusetts.
Stephan Arndt, Iowa Consortium for Substance Abuse Research, University of Iowa	Background	If I am not mistaken, most of the research showing the benefit of MAT is based on studies involving heroin dependence. The reviews you cite summarize this "Buprenorphine is an effective medication in the maintenance treatment of heroin dependence, retaining people in treatment at any dose above 2 mg, and suppressing illicit opioid use (at doses 16 mg or greater) based on placebo-controlled trials." (Mattick et al, 2014). The text of the current report generalizes this to all opioid use disorder, although there is no evidence to support that generalization.	Thank you for your comment. We added a bullet noting that most on medication-assisted treatment has focused on patients with heroin use disorder, and research is needed on patients with prescription opioid use disorder as well.
Sybil Marsh	Background	I appreciate the identification of inadequate reimbursement, inadequate staff support, and stigma as impediments to extension of MAT and primary care settings.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
Ellie Grossman	Background/ Title	I would quibble with the term 'Medication-Assisted Treatment.' To be clear on terminology – this disease is opioid use disorder. It can be treated with a. psychosocial/psychotherapeutic interventions; b. medications, and c. a combination of items a and b. We do not have sufficient evidence to suggest that any one of these 3 approaches to treatment is clearly better than another; what evidence we do have suggests that medication may be the key ingredient. Using the term 'MAT' implies that 'treatment' is non-pharmacologic, and the medication is a 'bonus add-on.' Given the state of evidence, it would seem more accurate to just use the term 'Treatment' when we are talking about pharmacotherapy or counseling/behavioral modalities – and call this report 'Models of Care for Opioid Use Disorder in Primary Care Settings'	Thank you for your comment. We agree that the term medication-assisted treatment may be misleading since it could imply that medications are an ancillary part of treatment. However, medication-assisted treatment remains a widely used term, is well understood, and has been defined by SAMHSA, and helps distinguish medication-based from non-medication based detoxification/abstinence approaches. We added to the Background section of the Intro: "It has been suggested that the term medication-assisted treatment is misleading because it implies that medications play an adjunctive role in treatment for opioid use disorder, and that it would be more accurate to simply refer to multimodal therapy for opioid use disorder as "treatment." In this report, we use the term medication-assisted treatment because it is widely used, well understood (as defined by SAMHSA), and to help distinguish medication-based from non-medication based (e.g., detoxification/abstinence) approaches. The term medication-assisted treatment is not meant to imply that medications play an ancillary role in treatment; rather, medications are central to the concept of effective multimodal treatment for opioid use disorder."

Commentator & Affiliation	Section	Comment	Response
APhA (American Pharmacists Association) Thomas E. Menighan	Methods	While APhA appreciates AHRQ's efforts to engage stakeholders by interviewing "KeyInformants,"[3] which included physicians, a psychologist, a psychiatrist, and a nurse practitioner, we believe that AHRQ should include pharmacists in the pool of Key Informants when obtaining input on MAT and other health care and treatment programs to gather a more complete view of the current environment. As described in further detail below, pharmacists are the medication experts on the health care team and play a crucial role in treating patients, including those receiving MAT. Given that the Brief relies on only a few peer-reviewed studies that include pharmacists, it even more critical to include pharmacists as a Key Informant.	Thank you for your comment. The stakeholder perspectives for the Key Informants were determined with input from AHRQ.
Paul Bowman, NAMA Recovery (National Alliance for Medication Assisted Recovery)	Methods	<Comment redacted>	The reviewer shared details about his personal experience with medication-assisted treatment.
Peer Reviewer #1	Methods	May want to say something about how you selected key informants	Thank you for the comment. The Methods state "We identified and interviewed 11 Key Informants (8 nonfederal and 3 federal) to represent broad and balanced perspectives relevant to medication-assisted treatment, 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 revised to note that we selected clinicians who were primary care clinicians as well as those with expertise in management of addiction, and that Key Informants were asked to disclose conflict of interests (which were reviewed by AHRQ) prior to participation.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #2	Methods	Page 11 of 130. Line 38 typo.	Thank you for the comment. We revised the sentence by inserting the word "compared", so it is now, "…one setting or population compared to others" (pg 5 of the current Word version of report)
Peer Reviewer #3	Methods	I would have thought AHRQ staff would have reviewed all existing Guidelines for use of medications in SUD treatment since they all were based on systematic reviews of the literature. They are a glaring omission unless I missed something.	Thank you for the comment. The purpose of the Technical Brief was not to systematically review guidelines of use of medications for substance use disorder. As noted in the Methods, a focused overview of the literature was conducted. Note that this Technical Brief is not intended to provide guidance about how to implement or deliver medication-assisted treatment, or how to administer medications for opioid abuse. AHRQ does not provide evidence-based practices about medication-assisted treatment.
Peer Reviewer #4	Methods	I believe the guiding question capture what is needed to formulate plans moving forward to develop effective MAT delivery in primary care settings.	Thank you for your comment.
Peer Reviewer #4	Methods	Given the nascent level of literature in this field, and the resent explosion of gray literature in this area, the use of Key Informant Interviews to better organize and synthesize the extant data was critical. It is agreed that the focus on primary care models and those that explore delivery models rather than particular pharmacological comparisons was a valid approach.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
APhA (American Pharmacists Association) Thomas E. Menighan	Findings	Based on the content included in "Guiding Question 1: MAT Models of Care,"[4] only four broad components[5] were listed along with an "other component(s)" section. All five components can be interpreted very broadly and are not scaled, providing little insight to the actual variances that exist between models. When models are reviewed under the framework no information is given regarding the effectiveness or value of each component or the degree to which the component is provided.[6] While APhA applauds AHRQ's efforts to research and evaluate promising and innovative MAT models of care in primary care settings, we encourage AHRQ to better define the categories of program components noted in the Brief and limit what is included in the "other components" section to more clearly depict differences and similarities between models and convey findings in a manner that better informs decision-makers and future programs.	Thank you for your comment. The four categories are meant to provide a broad framework for the major components of medication-assisted treatment models of care. The Key Informants consistently agreed with this framework. The "other components" category is meant to be broad to capture other important issues that are not addressed in the four main components. Future efforts could refine our framework further.
APhA (American Pharmacists Association) Thomas E. Menighan	Findings	All models of care referenced in the Brief included education and outreach as a component. APhA believes it is imperative to find effective practices to best communicate public health information to the public, patients and their families, and health care providers; therefore, we support AHRQ's desire to include education and outreach in its research in effort to identify successful practices. Furthermore, we encourage AHRQ to work with stakeholders, including other federal and state agencies, to communicate these effective practices when identified.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
APhA (American Pharmacists Association) Thomas E. Menighan	Findings	Pharmacists are leaders in pharmacogenomics, a field which has gained attention in the context of pain management and substance use disorder treatment.[12,13, 14] Notably, the Brief does not mention any model that includes pharmacogenomics. There is a strong interest in this field and its role in the future of health care as demonstrated by numerous efforts from public and private stakeholders, such as President Obama's Precision Medicine Initiative. Thus, APhA recommends that AHRQ consider researching MAT models that include a pharmacogenomics component.	Thank you for your comment. We did not identify any model of care that included a pharmacogenomics component.
Ellie Grossman	Findings	Guiding Question 1 The distinction between the 'Massachusetts nurse care manager' model and the 'OBOT (Yale)' model seems minor, at best. Both systems are located in primary care and rely on some type of non-prescribing 'glue' person to guide patient care between physician visits, triage patients among different levels of care, and provide care coordination services. I might argue that the MA nurse care manager is merely one specific type of 'OBOT' model. Another model of care not mentioned here is that of group visits. In the Cambridge Health Alliance system (and also at Montefiore in NYC), several sites deliver OBOT-type of care primarily by group visits, similar to 'shared medical appointments' used to manage other chronic diseases in primary care. The groups may be led by a nurse care manager or therapist or social worker – or by a physician; physicians see patients briefly 1:1 alongside the group and prescribe medication, while the majority of the psychosocial part of the treatment is delivered by group discussions, support, and check-ins.	Thank you for your comment. The Office-based Opioid Treatment (Yale) and Massachusetts Nurse Care Manager models are similar but have enough distinct aspects to be discussed separately, in our opinion. The Massachusetts Nurse Care Manager model is more specific in designating nurse care managers as the "lead" and in setting up reimbursement policies, training, and education, and structuring care around this person; the Office-based Opioid Treatment (Yale) system is looser in terms of who functions in the "glue" role and what tasks they assume. The Cambridge Health Alliance model is discussed in the Massachusetts Nurse Care Manager as a variant of the Nurse Care Manager model (one of the Key Informants was based in the Cambridge Health Alliance).

Commentator & Affiliation	Section	Comment	Response
Ellie Grossman	Findings	Guiding Question 2 I would chime in that reimbursement is a key barrier for implementing OUD treatment in primary care – especially in terms of funding non-physician personnel and even in terms of reimbursing for urine toxicology tests, which must be performed frequently. Further, prescription prior authorization requirements are onerous and painful for this disease; if buprenorphine requires prior authorization, it is clear that there is no alternative medication on the formulary, and a patient who is motivated and entering treatment must be told to wait a few days for his insurance company (including Medicaid) to determine if he is allowed to receive treatment. It seems ridiculous for a health-care provider to have to tell an insurance company (Medicaid included) that 'well, heroin wasn't working well for him' on response to the typical prior-authorization question of 'how did he respond to prior medication trials?'. Insurance companies also seem to have a steady stream of non-evidence-based requirements for specific types of counseling, visit frequency, and/or urine toxicology testing in assessing for authorization of buprenorphine treatment – all of which delay obtaining approval for treatment and allow patients to slip through the cracks. When patients 'slip through the cracks' for this disease, they are potentially at risk for imminent death due to overdose; it seems unconscionable to permit non-evidence-based insurance company requirements to delay treatment to motivated patients.	Thank you for your comment. These issues are discussed in the Facilitators and Barriers section of the report.

Commentator & Affiliation	Section	Comment	Response
Janice Kauffman	Findings	Same comment as background, 1st paragraph, Pg.#7 in this section license and 'accredited' opioid treatment programs. This is important because accreditation is not required for operation in DATA 2000 practices. Guiding Question 1: MAT Models of Care. Pg.9 - Models of Care 2nd sentence "provision of counseling is required" should probably say "has the capacity to refer for counseling" as stated in DATA 2000 - I think this has different meaning and there is nothing that monitors that this is done. Pg.11 Massachusetts Nurse Care Manager Model second to last sentence, question of a typo -should this say on "most" instead of "best" MAT practices?	Thank you for the comment. On pg 14 (pg 7 in reviewer's comments), we added "accredited" as suggested. On pg 16 (pg 9 in reviewer's comments), we revised to state that capacity to refer to counseling is required under the Drug Addiction Treatment Act of 2000. On pg 18 (pg 11 in reviewer's comments), training in "best" practices is correct. We added a reference to the Maternal Opioid Treatment Human Experimental Research study, and also revised to note that these trials were conducted in opioid treatment program settings.

Commentator & Affiliation	Section	Comment	Response
Janice Kauffman (continued)	Findings (continued)	Pg.14 Integrated Prenatal Care and MAT. "Outcome studies suggest that there is a reduction in NAS when pregnant women with OUD are maintained on Buprenorphine..." I think you should also cite the MOTHERs Study (Addiction. 2012 Nov;107 Suppl 1:28-35 Maternal Opioid Treatment: Human Experimental Research (MOTHER)--approach, issues and lessons learned. Jones HE1, Fischer G, Heil SH, Kaltenbach K, Martin PR, Coyle MG, Selby P, Stine SM, O'Grady KE, Arria AM..) Guiding Question 2: Settings in Which MAT is Implemented. Pg.23 2nd full paragraph, Correction: "A key barrier is the lack of physicians with an 'DEA' not FDA waiver Guiding Question 4. Future Directions. Pg. 37 Consider adding to the last paragraph "Deductibles and co-pays in private and public insurance systems may be a barrier for patients to receive affordable comprehensive care. It could inadvertently support medication only treatment models. interventions." Pg. 39, 2nd bullet: last sentence "However, there is almost no evidence on injectable buprenorphine used in primary care." Just a thought, this is confusing to me. Are we talking about for treatment of addiction. My understanding was that injectable buprenorphine was approved by the FDA for pain management long before we even entertained sublinqual buprenorphine. I thought it was not approved for treatment of addiction. Is this what we mean here or are you talking about buprenorphine implants?	

Commentator & Affiliation	Section	Comment	Response
Joseph Walsh	Findings	Psychosocial components- seems like intent is to place some emphasis here, and while the various Models incorporate Value of this piece; actual implementation appears too varied and vague to ensure uniformity and therefore across-the-board, intended Outcome. Also, One wonders about Uniformity and Standards of PSR (Psycho-social Rehab.), Practices. Which, if any, PSR Organizations/Practitioners have been, or are intended to be included in development/delivery of PSR Services ?	Thank you for your comment. The variability in psychosocial services in different models is highlighted in the report. We also summarize evidence noting that it is unclear if more intensive psychosocial services are more effective than less intensive interventions. The need for research to identify patients who would benefit from more intensive psychosocial services and to effectively target psychosocial services is highlighted in the Future Research Needs section.
Paul Bowman, NAMA Recovery (National Alliance for Medication Assisted Recovery)	Findings	<Comment redacted>	The reviewer shared details about his personal experience with medication-assisted treatment.
Peer Reviewer #1	Findings	page 14 line 47: double check if anyone really talked about oral naltrexone as a component of MAT for OUD rather than AUD. They may have been treating both and not clearly distinguished that they didn't use oral naltrexone for OUD. It is not an EBP for OUD and I am concerned that it appears to be included in this document as though it were	Thank you for the comment. Oral naltrexone is approved for prevention of opioid relapse. We revised to note that Key Informants noted that oral naltrexone is rarely used for opioid use disorder (pg 22, next to last paragraph) and evidence on oral naltrexone is summarized on pg 26 (no trials of oral naltrexone were done in primary care settings).
Peer Reviewer #1	Findings	page 15 lines 8-15 I wonder if you missed some key informants. In my experience, physicians seem to be comfortable with either agonists or antagonists and rarely use both. You may have not talked to the antagonist crowd and missed some information.	Thank you for the comment. We sought a broad range of stakeholder perspectives in the Key Informants, as described in the Methods (pg 4). We did include Key Informants with experience in prescribing opioid antagonists; e.g., one of the Key Informants has been involved in a model (the “One Stop Shop”) that focuses on extended-release naltrexone.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	Findings	Page 15 lines 15-22 Maybe education and outreach should not be considered key elements of MAT since they were not present in most of the models. I understand that your key informants felt they were important, but since you identified successful models that do not include it, I think the key informants may be confusing their roles with the role of treatment providers.	Thank you for the comment. Key Informants consistently noted that education/outreach is an important component and should be included as one of the core elements described for medication-assisted treatment models of care, so we think this should be kept. We noted that the degree to which education/outreach components were formally incorporated in models of care varied (pg 8, paragraph 2). Describing the education/outreach component does not necessarily mean that it is a necessary component of medication-assisted treatment Models of Care. Table 2, which highlights models felt to be successful or promising, indicate that education/outreach is not a major component for several models.
Peer Reviewer #1	Findings	page 20 line 15: we are not using the word stigma any more, but just calling it prejudice as stigma is more about the patient and prejudice is a clearer statement about another's attitude toward the patient	Thank you for the comment. We decided to keep the term as "stigma" since there is more research around stigma as a construct.
Peer Reviewer #1	Findings	page 29 line 24 nonaddiction should be non-addiction	Thank you for the comment. Per AHRQ style requirements, words starting with "non" are not to be hyphenated.
Peer Reviewer #1	Findings	Page line 20-54 This is an introduction section yet focuses solely on buprenorphine and leaves out extended release naltrexone. What is the rate of prescribing of Vivitrol in the mid-western states that have low use of buprenorphine? Or vice versa for the New England states? Might it just be variation in choice of treatment rather than a disparity in care?	Thank you for the comment. We revised to clarify that we did not identify published data on rates of utilization of extended release naltrexone for opioid use disorder (pg 22, 2nd to last paragraph).
Peer Reviewer #1	Findings	Page 30 Barriers section - many opportunities to replace the word stigma with prejudice	Thank you for the comment. We decided to keep the term as "stigma" since there is more research around stigma as a construct.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	Findings	There is nothing in this section about barriers to using extended release naltrexone, yet there are barriers that are related to reimbursement, storage of the medication, and other similar barriers to buprenorphine that should be included. On the other hand, there are no special waivers or training to provide extended release naltrexone.	Thank you for the comment. We revised to describe barriers to use of extended-release naltrexone (pg 24).
Peer Reviewer #4	Findings	A strength of the Findings was breaking down each model into the four components (pharm., 2) educational interventions, 3)coordination of care with medical/psychological [I'd prefer psychiatric and psychosocial] needs, and 4)psychosocial [I'd prefer psychiatric and psychosocial] interventions. Several areas of major importance common to a successful model include 1) importance of provider and community education, 2) a "glue" person to extend the ability of the prescriber to deliver care to the greatest number of patients, 3) a key need to address both psychiatric and psychosocial aspects of dysfunction in those with an OUD, 4) a role for some sort of centralized expertise to start and stabilize patients on MAT before hand off to more peripheral centers, 5) the role of whatever service provides MAT to screen for other mental health and medical issues and coordinate care of these other conditions.	Thank you for your comment. This comment summarizes the findings in the Models of Care section and summarized in the Discussion. We kept it as the “psychosocial” component since this is where the models seemed to differ in terms of what was offered/available.
Peer Reviewer #4	Findings	In other sections: a) Settings for MAT Delivery: The debate about whether increasing the number of waiver-trained physicians, or increasing the prescriber limit, will improve MAT penetration remained unanswered. delivery in rural areas was identified as a future challenge.	Thank you for your comment. The need for research to understand why waivered physicians do not prescribe and methods to increase prescribing is described as a future research need.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #4	Findings	b) Barriers to Implementation: summarized insufficient institutional support, knowledge gaps, complications of setting up tele-health, stigma, inadequate staff and/or staff reimbursement for case management, inadequate mental health resources and inadequate reimbursement. Training and staffing needs again left unclear what is an optimal approach in times of limited resources, though physician extenders are key in all models.	Thank you for your comment. This comment summarizes the section on Barriers to Implementation. We revised this section to note that inability of physician assistants and nurse practitioners to prescribe is a potential barrier to implementation.
Peer Reviewer #4	Findings	c) Current Evidence on MAT - unfortunately here there is little to summarize specific to primary care settings - the review is brief but accurate. Well noted was the lack of any clear guidance on the role of more vs. less intensive psychosocial interventions based on the literature, and reflected in varying opinions of the Key informants.	Thank you for your comment.
Peer Reviewer #4	Findings	d) Future Directions: Suggested new strategies include: more use of education to reduce stigma, increase provider training and acceptance, and improve penetration of MAT. Systems that use care coordinators and physician extenders (NPs, PA, pharmacists) are more practicable and allow for higher physician case-loads. Important is the integration of substance abuse care with total needs of the patient. Rural challenges require more Web-based educations and tele-health delivery and/or consultation. To improve penetration of MAT, increase training of prescribers, use of extended-release naltrexone and broader discussion of restructured financing, mental health staffing support etc. A final section on inequities in MAT availability point out difficulties for those in rural areas, adolescents, , and payer procedures limiting payment, access etc. Overall lack of societal funding for treatment of OUDs remains an issue.	Thank you for your comment. These comments summarize the findings in the Future Directions section.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	Findings	P21.L16 Inpatient Initiation section could add reference: (Shanahan CW, Beers D, Alford DP, Brigandi E, Samet JH. Seizing a “reachable moment”-A Transitional Opioid Program (TOP) for hospitalized opioid dependent patients. J Gen Intern Med. 2010; 25(8):803-8)	Thank you for your comment. We added this reference to the section on Inpatient Initiation of medication-assisted treatment. Because it focuses on initiation of methadone and management in an opioid treatment program, we did not add it to the Table listing sources for this model.
Peer Reviewer #5	Findings	In the Massachusetts Model - nurse care managers also provide ongonig care management including offer drop-in visits, same day visits, coordinate prior authorizations, communicate with pharmacists, coordinate perioperative care...	Thank you for your comment. We revised the section on the Massachusetts Nurse Care Manager model to specify some of these other roles of the nurse care manager.
Peer Reviewer #5	Findings	P29 Guiding Question 2: how does availability of MAT correspond with epidemiology of opioid use disorders...are the regions with high MAT access also areas with high OUD problems or is there a mismatch?	Thank you for your comment. We did not identify studies correlating availability of medication-assisted treatment with prevalence of opioid use disorder.
Peer Reviewer #5	Findings	P30L6 it is not so much as "off load some of the burden" on physicians but rather implementing team-based care where all staff work together on clinical work that is appropriate to their profession...e.g., physicians don't need to assess if a patient is in withdrawal in order to start bup/nx when there are validated scales (COWS) that nurses can follow	Thank you for your comment. We revised the Facilitators and Barriers section to include implementation of team-based care as one of the benefits of nonphysician staff with expertise in opioid use disorder. However, we retained the reference to offloading some of the burden from prescribing physicians, as this was brought up by a number of Key Informants as facilitating the ability to provide medication-assisted treatment.
Peer Reviewer #5	Findings	P30 Consideration and Barriers: I have heard that the fear of the DEA site visits (as per DATA 2000) as a barrier. The thought of having a DEA agent come to your practice unannounced is very disturbing to some. this is only mentioned briefly in the report without a potential remedy.	Thank you for your comment. We revised the Facilitators and Barriers section to note fear of Drug Enforcement Agency site visits as a barrier to obtaining a waiver (this was mentioned by several Key Informants).
Peer Reviewer #5	Findings	P31L38 the actual language in DATA 2000 for counseling is: "the practitioner has the capacity to refer the patients for appropriate counseling and other appropriate ancillary servicesa" this is different than what is stated in the document as "brief counseling be offered"	Thank you for your comment. We revised to be clear that Drug Addiction Treatment Act of 2000 required that physicians have capacity to refer for counseling.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	Findings	P46L20 in addition to Research to understand why buprenorphine waivered physicians don't prescribe, maybe conduct research on why waivered physicians DO prescribe...job satisfaction, able to concurrently manage OUD and chronic pain, being part of the solution to the opioid crisis???	Thank you for your comment. We added "factors associated with prescribing" to this Future Research Need bullet (pg 46).
Sybil Marsh	Findings	I wonder if you should broaden your definition of psychosocial supports. Primary care physicians and other patients well may learn and counsel about the patient's general well-being, family relationships , new and stressful life events, relapse potential and prevention in the course of the appointment with the patient, especially if that physician is also responsible for the patient's primary care, not just a buprenorphine dispensing machine. Patients generally do not have access to reimburse professional counseling on an unlimited basis. We should acknowledge and value the psychosocial contribution of the caregiver providing the buprenorphine, physician or other, as well as the role of mutual help programs that are accessible online and in remote communities.	Thank you for your comment. Physician counseling is considered a psychosocial intervention; e.g., in the Office-based Opioid Treatment model much of the counseling is done by physicians. Use of online or other programs were also considered
Peer Reviewer #2	Findings - Next Steps	Key areas of future research that were not included are: 1. Patients with cancer pain who are overusing opioids 2. Kids being treated with opioid analgesics, and their risks for misuse and addiction, especially given neuroplasticity etc.	Thank you for the comment. We revised the bullet on Future Research on management of patients with opioid use disorder and concomitant chronic pain to specific both cancer and noncancer pain. We also added a bullet on need for research on optimal medication-assisted treatment models of care for treatment of opioid use disorder in adolescents and children.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #4	Findings - Next Steps	The Future Research Needs points out the many knowledge gaps needed to develop better MAT delivery systems in primary care settings. As well, what is not discussed are the vast number of state, federal, and private agencies reviewing and summarizing the field of OUDs and how best to tackle them. Better coordination of the many efforts is needed to prevent wasting valuable times and resources. As an example, many state boards are seeking to develop training resources for prescriber sin their states, when PCSS-MAT and PCSS-O already exist, as does Project ECHO, to serve that role. Based on the report I believe the key steps needed NEST are 1) addressing the reimbursement issues to allow more viable models to be developed, 2) improve training of PCPs (and all prescribers in responsible opioid prescribing and screening for OUDs though licensing mandates 3) clarification of medico-legal and reimbursement issues for delivery of tele-mental health across state lines, to allow for use of expert consultation and prescribing in many underserved areas.	Thank you for the comment. We revised the section on "New and Innovative Strategies" to note that utilization of existing training and educational resources would be more efficient than developing new resources in each implementation setting. Reimbursement/financing is noted as an issue in the Ethical, Equity, and Cost section (pg 44). Research on telehealth and other Web-based efforts is noted in the Future Research Needs section (pg 45).
Peer Reviewer #5	Findings - Next Steps	Research questions listed are comprehensive	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
APhA (American Pharmacists Association) Thomas E. Menighan	Summary and Implications	The Brief provided limited details regarding health information exchange between practitioners. As health care delivery continues to evolve to more effectively utilize different practitioners and their expertise, we believe more research is needed regarding communication and information exchange. For pharmacists to assess appropriateness of prescribed medications, assist in the prevention of medication abuse and misuse, and support substance use disorder treatment, it is essential they have access to the patient's relevant health information and be able to exchange pertinent clinical information using health information technologies. Therefore, in effort to deliver more comprehensive and coordinated care, APhA requests AHRQ to explicitly address information exchange between DATA-waived physicians and pharmacists in the Brief and support research involving pharmacists' access to appropriate electronic health record information	Thank you for your comment. We added a sentence to the Facilitators and Barriers section noting that improvement in communication and exchange of health information could greatly facilitate implementation.
Paul Bowman, NAMA Recovery (National Alliance for Medication Assisted Recovery)	Summary and Implications	<Massachusetts Model>Program offered flexible treatment programs to meet individual needs of each patient, Able to continue work and develop meaningful relationships with family and others.	Thank you for your comment.
Peer Reviewer #3	Summary and Implications	Because of the misstatements about the Hub and Spoke and lttle information about Medical Health Homses and why the Rhode Island implementation so important given findings about health care for patients in methadone treatment, the summary and implications are off the mark.	Thank you for the comment. We revised the discussion of the Hub and Spoke model. The Rhode Island model has not been implemented in primary care settings (only in opioid treatment programs). Management of patients on methadone is outside the scope of this technical brief, which focuses on medication-assisted treatment models of care in primary care settings.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #4	Summary and Implications	The report accurately concludes that practical differences between different treatment settings may better determine what MAT service can be designed rather than a single "optimal" model. Integration of MAT with treatment of co-morbid mental/physical/psychosocial conditions of concern, a central role for care coordinators, and education of providers/community appear key to any program. The report accurately summarizes the fact we have lock-stock and barrel moved towards providing buprenorphine formulations over naltrexone formulations. It is hoped in 10 years we are not drawing parallels between prescribing of buprenorphine now to the prescribing of pain medications in the early 1990s. Though not explicitly stated, it is clear most patients started on buprenorphine have no "exit strategy."	Thank you for your comment. Barriers to use of naltrexone and need for research on naltrexone are noted in the report.
Peer Reviewer #5	Summary and Implications	Well written	Thank you for your comment.
Janice Kauffman	References	Add reference for: Jones HE1, Fischer G, Heil SH, Kaltenbach K, Martin PR, Coyle MG, Selby P, Stine SM, O'Grady KE, Arria AM..) Addiction. Maternal Opioid Treatment: Human Experimental Research (MOTHER)--approach, issues and lessons learned. 2012 Nov;107 Suppl 1:28-35.	Thank you for your comment. The Maternal Opioid Treatment Human Experimental Research trial does not meet inclusion criteria because it compared methadone vs. buprenorphine. Details about the clinic settings were limited but based on provision of methadone it is highly likely that this trial was conducted in OTP settings.
Paul Bowman, NAMA Recovery (National Alliance for Medication Assisted Recovery)	References	Boston NAMA Recovery. Peer recovery center, ALLRECOVERY meetings.	Thank you for your comment.
Janice Kauffman	Tables	Pg.17 Table 2 -Hub and Spoke (other considerations) Not sure that they prescribe methadone (technically can't do that), probably should be dispense in the OTP or omit and just say refer to an OTP.	Thank you for your comment. The Hubs are opioid treatment programs and can prescribe methadone.

Commentator & Affiliation	Section	Comment	Response
Janice Kauffman	Appendix	Appendix A: No recommendations Appendix B: No recommendations Appendix C: <Reviewer had comments about specific details in this appendix.> Appendix D: No recommendations Appendix E: add reference cited above "Jones HE1, Fischer G, Heil SH, Kaltenbach K, Martin PR, Coyle MG, Selby P, Stine SM, O'Grady KE, Arria AM..) Addiction. Maternal Opioid Treatment: Human Experimental Research (MOTHER)--approach, issues and lessons learned. 2012 Nov;107 Suppl 1:28-35." Appendix F: No recommendations.	Thank you for the comment. The Maternal Opioid Treatment Human Experimental Research trial does not meet inclusion criteria because it compared methadone vs. buprenorphine. Details about the clinic settings were limited but based on provision of methadone it is highly likely that this trial was conducted in opioid treatment program settings.
Peer Reviewer #1	Clarity and Usability	Generally it is well organized and clear. I think the lack of information on extended release naltrexone may be the result of the key informants you used and it is a big gap for the document.	Thank you for the comment. We revised to note the lack of data on rates of utilization of ER naltrexone (p 22) and describe barriers to use of ER naltrexone (p 24).
Peer Reviewer #1	Clarity and Usability	The conclusion and call for further research is clear and having a document that states that the best model may be defined by existing resources rather than the research is helpful for dissemination. I do not think the conclusion and recommendations would be changed by making the changes I have suggested, but I do think the document will appear more balanced.	Thank you for your comment.
Peer Reviewer #2	Clarity and Usability	I felt like the manuscript was vague and redundant at times, and could benefit from more specifics as I describe in general comments above.	Thank you for the comment. We responded to specific comments from this peer reviewer.
Peer Reviewer #3	Clarity and Usability	I think what is presented is presented clearly but there is a significant amount of missing information.	Thank you for the comment. We have responded to specific comments from this reviewer.
Peer Reviewer #4	Clarity and Usability	The report is very readable and clearly structured. The main points are well stated and supported by the extant literature, including grey literature. As noted above, the report raises as many questions as it answers but is a clear guide to future research needs.	Thank you for your comment.
Peer Reviewer #5	Clarity and Usability	the report is very well structured and organized and clearly presented.	Thank you for your comment.