A mixed-method comparison of physician-reported beliefs about and barriers to treatment with medications for opioid use disorder

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Abstract

Background Evidence demonstrates that medications for treating opioid use disorder (MOUD) —namely buprenorphine, methadone, and extended-release naltrexone—are effective at treating opioid use disorder (OUD) and reducing associated harms. However, MOUDs are heavily underutilized, largely due to the under-supply of providers trained and willing to prescribe the medications. Methods: To understand comparative beliefs about MOUD and barriers to MOUD, we conducted a mixed-methods study that involved focus group interviews and an online survey disseminated to a random group of licensed U.S. physicians, which oversampled physicians with a preexisting waiver to prescribe buprenorphine. Focus group results were analyzed using thematic analysis. Survey results were analyzed using descriptive and inferential statistical methods.

Results Study findings suggest that physicians have higher perceptions of efficacy for methadone and buprenorphine than for extended-release naltrexone, including for patients with co-occurring mental health disorders. Insurance obstacles, such as prior authorization requirements, were the most commonly cited barrier to prescribing buprenorphine and extended-release naltrexone. Regulatory barriers, such as the training required to obtain a federal waiver to prescribe buprenorphine, were not considered significant barriers by many physicians to prescribing buprenorphine and naltrexone in office-based settings. Nor did physicians perceive diversion to be a prominent barrier to prescribing either buprenorphine or extended-release naltrexone. In focus groups, physicians identified financial, logistical, and workforce barriers—such as a lack of addiction treatment specialists—as additional barriers to prescribing medications to treat OUD.

Conclusions Additional education is needed for physicians regarding the comparative efficacy of different OUD medications. Governmental policies should mandate full insurance coverage of and prohibit prior authorization requirements for OUD medications.

1. Background

1.1 Opioid Crisis

Recent indications suggest that the opioid crisis is worsening in many regards, after claiming 47,600 lives in 2017 (1). Between 2.3 and 6 million persons had an opioid use disorder (OUD) in 2017, only 20–40% of whom received addiction treatment (2). Behavioral health workforce-related strategies to expand access to and delivery of evidence-based treatment for OUD are critical to reducing opioid-overdose risks and mitigating drug-related harms (3, 4).

1.2 Treatment for Opioid Use Disorder

Medications for OUD (MOUD), often in combination with behavioral therapy, are considered the gold standard for treating OUD (5). Clinical trials have demonstrated that three MOUDs—methadone, buprenorphine, and extended-release naltrexone—reduce opioid use, overdose, and other adverse health

outcomes (6–10). For example, methadone and buprenorphine treatment were associated with 53% and 37% reductions, respectively, in all-cause mortality among patients with OUD as compared to those receiving no MOUD in the 12 months following nonfatal overdose (11). Buprenorphine availability starting in 2003 in Maryland also was associated with a 37% reduction in heroin overdose deaths (12).

1.3 Access to Treatment for Opioid Use Disorder

Evidence suggests that MOUD access and treatment fall vastly below patient need (13, 14), owing in significant part to an under-supply of providers prescribing these medications (4, 15). Methadone for OUD, only provided within opioid treatment programs (OTPs), has maintained a relatively flat supply over time(13, 14). Many states have fewer than 10 OTPs, facilities that are scarce in rural areas(16–18). In 2002, physicians became eligible to prescribe buprenorphine in non-specialty settings, provided they complete requisite training and obtain a waiver from the Substance Abuse and Mental Health Services Administration (SAMHSA)(19). Although this regulatory change has expanded access to buprenorphine treatment for OUD, 44% of counties still lack a physician with a buprenorphine waiver, and only 3% of all primary care physicians nationwide are authorized to prescribe buprenorphine for OUD (16, 20).Unlike methadone and buprenorphine, both opioid agonists, the newer extended-release naltrexone is an opioid antagonist and not a controlled substance; thus, it can be prescribed by any licensed prescriber.

Previous studies have identified numerous barriers to prescribing MOUD in office-based settings. The majority of such studies have focused on oral buprenorphine, finding salient barriers to include a lack of training for physicians in MOUD and addiction treatment, concerns about diversion, insurance barriers, and discomfort in treating patients with comorbid psychiatric conditions(15, 21–24). Fewer studies have examined extended-release naltrexone; current research suggests that insurance-related factors, the requirement that patients are completely opioid-abstinent for 7 to 10 days prior to initiation, inadequate staffing, and limited education for prescribing physicians are key barriers to prescribing this MOUD(10, 25–28). Even though methadone for OUD cannot be prescribed outside of OTPs, office-based physicians can refer patients to these facilities for methadone treatment; but little is known about frequency of and barriers to this referral process. Furthermore, few studies have directly compared physician beliefs about efficacy and barriers across all three MOUDs (9, 29, 30).

In this mixed-methods study, we surveyed and conducted interviews with physicians to better understand and compare the facilitators and barriers they experience to prescribing (and referring, in the case of methadone) MOUDs. We hypothesized that prescriber beliefs about efficacy would be similarly positive for methadone and buprenorphine, with greater uncertainty expressed about the newer naltrexone, which has a less robust evidence base. We also hypothesized that perceived barriers to office-based buprenorphine prescribing would be most significant for physicians without a buprenorphine waiver and that opioid-abstinence would be a significant barrier to extended-release naltrexone treatment. However, we expected other barriers, like stigma and insurance-related hurdles, to be consistent across MOUDs studied.

2. Methods

To understand MOUD provision, barriers, and beliefs, we conducted a mixed-methods study that involved focus group interviews and an online survey disseminated to a random group of licensed U.S. physicians, which oversampled physicians with a preexisting waiver to prescribe buprenorphine. The Health Sciences and Behavioral Sciences Institutional Review Board at the University of Michigan approved this study (reference number HUM00159099). The questions were informed by a literature review of prescriber-perceived efficacy of and barriers to MOUD treatment.

2.1 Study Design

We developed the survey using Qualtrics™ software and piloted it among physicians in four states in the Spring of 2017 (n = 53). See Appendix B for survey questions. We administered the final survey online in two waves from July 11—September 8, 2017, and from October 25—November 18, 2017. The survey was emailed to a nationally-representative random sample of 4,010 physician prescribers, whose American Medical Association Masterfile contact and practice specialty information we purchased from Redi-Data.[52] The sampled population was divided among two groups of physicians: higher-frequency MOUD prescribers (n = 687, or physicians practicing addiction medicine and addiction psychiatry), and lower-frequency MOUD providers (n = 3,313, or physicians practicing in general medicine specialties less likely to have regular exposure to MOUD prescribing). A total of 157 emails were returned as undeliverable, reducing the overall sampled population to 3,853. Reminder emails were sent weekly and a $25 MasterCard gift card was offered an as incentive during the second wave of survey administration.

2.2 Survey Content

The survey examined provider-perceived barriers to and efficacy of the following MOUDs: oral buprenorphine, implantable buprenorphine, methadone, and depot injection extended-release naltrexone. We did not examine barriers to oral naltrexone prescribing, given its lack of efficacy for OUD due to low patient adherence(31) or to depot injection extended-release buprenorphine (Sublocade®) due to its recent Food and Drug Administration (FDA) approval(32). Questions about Probuphine®, a diversion-resistant subdermal buprenorphine implant, were included in this study; however, not enough prescribers expressed familiarity with this formulation to assess specific barriers to its utilization.

Participants were asked to rate 17 different potential barriers to prescribing buprenorphine or extended-release naltrexone on a Likert scale, with answers ranging from “not a barrier at all” (1) to “strong barrier” (4). If physicians indicated that they did not work with a particular medication (“N/A”), we removed these responses from the analysis. For buprenorphine, only those physicians who indicated they had a SAMHSA waiver were asked about their perception of barriers to that MOUD. Because this survey primarily targeted office-based physicians, rather than those working in an OTP, questions about specific barriers to prescribing methadone were not included. All respondents were asked questions about the efficacy of each MOUD on a Likert scale that ranged from “strongly disagree,” (1) to “strongly agree” (5).

2.3 Survey Statistical Analysis

We analyzed differences across average scores reported along each potential barrier to buprenorphine and extended-release naltrexone and, separately, across average scores reported about beliefs in MOUD efficacy using paired samples t-tests (with significance set at $\alpha = 0.05$). For all analyses, we also performed sub-analyses that involved independent samples t-tests to compare the responses of physicians who had a SAMHSA waiver to prescribe buprenorphine to those who did not. For this sub-analysis, we first performed Levene's Test for Equality of Variances to inform whether to assume equal variance between the groups; we assumed unequal variance if the test was significant at $\alpha = 0.05$ level.[55] A Bonferroni correction was performed to account for multiple testing for tests involving more than 7 comparisons.

2.4 Qualitative Data Collection and Analysis

To complement the survey data, we convened 3 virtual focus groups of prescribers to provide more in-depth information regarding MOUD provision in an office-based setting. Each focus group lasted approximately one hour and together they involved a total of 7 participants. Participants were drawn from the National Council for Behavioral Health member organizations, although participation was not limited to active MOUD prescribers. Participants were drawn from mid-size and large cities across the country. Through these focus groups we elicited strategies for, as well as barriers to, providing MOUD. We coded and analyzed focus group transcripts, using thematic analysis methodology(33), for themes using *Excel* and *NVivo 12* software. Several themes emerged, the most prominent of which were related to the prevalence and impact of barriers to MOUD.

3. Results

3.1 Survey Results

3.1.1 Survey Respondent Characteristics

In total, 151 physicians completed the survey, 119 of whom reported their specialty. The majority of respondents were medical doctors (83%); most of those remaining identified as doctors of osteopathy (15%). Approximately 41% were female. 27% of respondents were high-frequency MOUD prescribers and 32% were low-frequency MOUD prescribers. Additional File Table 1 lists respondent specialties. Respondents most frequently specialized in family medicine (34%), followed by addiction medicine (25%) and anesthesiology (15%). The remaining specialties represented each made up less than 3% of the total (Additional File Table 1). Most respondents primarily practiced in outpatient primary care clinic settings (25%) or outpatient specialty clinics (14%), while only 5% practiced in an OTP. 35% reported that their practice facility was affiliated with or within a not-for-profit health center or hospital, 23% with an academic medical center, and 23% with a for-profit health center or hospital (Additional File Table 2).

Table 1
Comparison of Provider-Perceived Efficacy of Buprenorphine vs. Extended-Release Naltrexone

	Mean of the difference	95% Confidence Interval		Significance
		Lower	Upper	
MOUD decreases risk of death from opioid overdose	0.558	0.230	0.885	0.001*
MOUD decreases cravings for opioids	0.925	0.510	1.339	< 0.001 *
MOUD decreases rates of relapse	0.360	0.012	0.708	0.043 *
MOUD works well in patients with co-occurring mental health disorders	0.440	0.081	0.799	0.017 *
MOUD efficacy is improved by adding mental health counseling	0.089 9	-0.0979	0.2756	0.001*

Table 2
Comparison of Provider-Perceived Efficacy of Extended-Release Naltrexone vs. Methadone

	Mean of the Difference	95% Confidence Interval		Significance
		Lower	Upper	
MOUD decreases risk of death from opioid overdose (n = 50–56)	− .333	− .618	− .048	.023 *
MOUD decreases cravings for opioids	− .731	-1.121	− .341	.000 *
MOUD decreases rates of relapse	− .380	− .655	− .105	.008 *
MOUD works well in patients with co-occurring mental health disorders	− .420	− .784	− .057	.024 *
MOUD efficacy is improved by adding mental health counseling	.109	− .116	.334	.335

45% of respondents indicated that they had a SAMHSA buprenorphine waiver, although a small proportion were not currently using it (n = 6/104). 40% of physicians with SAMHSA waivers could serve up to 100 patients. 76% of prescribers reported that they had not obtained the Risk Evaluation & Mitigation Strategy (REMS) certification to implant Probuphine® as treatment for OUD and did not plan to in the future (n = 77/101); 11% had the certification but were not currently implanting Probuphine® (n = 11/101); and no respondents had the certification and were implanting Probuphine.

45% of respondents indicated that no one in their practice currently prescribed extended-release naltrexone; only 22% indicated that they or someone else in their practice prescribed the medication. Only

16% of respondents answering the question indicated they often or always referred patients with OUD for methadone treatment, while 48% said they “sometimes” and 29% “never” did so.

3.1.2 Provider Attitudes and Beliefs about MOUD Efficacy

Survey respondents had overall positive impressions of buprenorphine, extended-release naltrexone, and methadone for OUD treatment. However, there were some distinctions in beliefs about efficacy of the specific MOUDs. Respondents believed that buprenorphine decreases opioid cravings more than extended-release naltrexone (mean score 4.5 vs. 3.6, $p < 0.005$, Table 1). Respondents believed that buprenorphine, to a greater degree than extended-release naltrexone, decreases the risk of fatal opioid-overdose (mean score 4.3 vs. 3.8, $p = 0.001$, Table 1), decreases relapse (mean score 4.2 vs. 3.8; $p = 0.043$, Table 1), and works well in patients with co-occurring mental health disorders (mean score 4.2 vs. 3.8, $p = 0.017$, Table 1). Respondents also believed that methadone, to a greater degree than extended-release naltrexone, decreases opioid cravings (mean score 4.3 vs. 3.6, $p < 0.001$, Table 2), decreases risk of fatal opioid-overdose death (mean score 4.1 vs. 3.7, $p = 0.023$, Table 2), decreases relapse (mean score 4.2 vs. 3.8; $p = 0.008$, Table 2), and works well in patients with co-occurring mental health disorders (mean score 4.2 vs. 3.8, $p = 0.024$, Table 2). When comparing physician perspectives about buprenorphine and methadone to treat OUD, respondents believed that buprenorphine is slightly more effective than methadone in decreasing the risks of opioid-overdose death (mean score 4.3 vs. 4.0, $p = 0.035$, Table 3).

Table 3
Comparison of Provider-Perceived Efficacy of Buprenorphine vs. Methadone

	Mean of the Difference	95% Confidence Interval		Significance
		Lower	Upper	
MOUD decreases risk of death from opioid overdose (n = 63–71)	.265	.019	.511	.035 *
MOUD decreases cravings for opioids	.121	− .105	.347	.288
MOUD decreases rates of relapse	.062	− .166	.289	.590
MOUD works well in patients with co-occurring mental health disorders	− .016	− .240	.208	.888
MOUD efficacy is improved by adding mental health counseling	.159	− .057	.376	.146

When comparing beliefs about MOUD efficacy among physicians with and without a SAMHSA waiver, some significant differences emerged across medications. Waivered physicians agreed less strongly that buprenorphine is effective in treating opioid dependence in pregnant women, as compared to non-waivered physicians (mean score 3.58 vs. 4.42, $p < 0.001$, Additional File Table 3). Waivered physicians believed that extended-release naltrexone treatment decreases the rate of relapse to a greater degree than non-waivered physicians (mean score 3.57 vs. 4.03, $p = 0.037$, Additional File Table 4). Finally, waivered physicians, as compared to non-waivered physicians, believed less strongly that methadone decreases

risk of opioid-overdose death (mean score 3.66 vs.4.31, p = 0.003, Additional File Table 5); decreases opioid cravings (mean score 3.87 vs. 4.50, p = 0.002, Additional File Table 5), decreases rates of relapse (mean score 3.66 vs. 4.40, p = 0.001, Additional File 5), and is effective in treating OUD in pregnant women (mean score 3.48 vs. 4.47, p < 0.001, Additional File Table 5).

Table 4
Comparison of Provider-Perceived Barriers to Buprenorphine vs. Extended-Release Naltrexone

	Mean of the Difference	95% Confidence Interval		Significance
		Lower	Upper	
Concerns about diversion (n = 34–37)	1.000	0.667	1.333	0.000 *
Lack of patient interest	-0.417	-0.877	0.044	0.075
Law enforcement oversight	0.486	0.157	0.816	0.005
Professional licensing board oversight	0.457	0.177	0.738	0.002 *
MOUD* patients would unfavorably affect my patient mix	0.182	-0.091	0.454	0.184
My co-workers do not support provision of MOUD in my practice	0.111	-0.099	0.322	0.291
Managers/ admin. do not support provision of MOUD in my practice	-0.114	-0.445	0.217	0.487
Reimbursement rates for MOUD	-0.545	-0.998	-0.093	0.02
Insurance prior authorization requirements	-0.405	-0.853	0.042	0.075
Insufficient training	-0.200	-0.571	0.171	0.281
Insufficient time	0.167	-0.265	0.598	0.439
Insufficient staff support	0.143	-0.231	0.517	0.443
Insufficient experience	-0.188	-0.621	0.246	0.385
Insufficient resources for patient psychosocial support within community or in my practice	0.200	-0.161	0.561	0.268
Insufficient resources for patient detoxification within the community or in my practice	-0.265	-0.652	0.122	0.173

Table 5
Comparison of Perceived Efficacy of Extended-Release Naltrexone among SAMHSA-Waivered Physicians to Non-Waivered Physicians

		Mean Difference	95% Confidence Interval		Significance
			Lower	Upper	
Concerns about diversion	Equal variances not assumed	0.697	0.259	1.135	.003 *
Lack of patient interest	Equal variances assumed	0.054	-0.571	0.678	.864
Law enforcement oversight	Equal variances not assumed	0.564	0.076	1.051	.025
Professional licensing board oversight	Equal variances not assumed	0.950	0.315	1.585	.005
Extended-release naltrexone patients would unfavorably affect my patient mix	Equal variances not assumed	0.701	0.129	1.274	.018
My co-workers do not support provision of extended-release naltrexone in my practice	Equal variances not assumed	0.526	-0.005	1.057	.052
Managers/administrators do not support provision of extended-release naltrexone in my practice	Equal variances not assumed	0.833	0.145	1.522	.019
Reimbursement rates for extended-release naltrexone	Equal variances assumed	0.302	-0.477	1.081	.439
Insurance prior authorization requirements	Equal variances not assumed	0.194	-0.421	0.810	.528
Insufficient training	Equal variances assumed	1.214	0.616	1.812	.000 *

		Mean Difference	95% Confidence Interval		Significance
			Lower	Upper	
Insufficient time	Equal variances assumed	1.399	0.886	1.912	.000 *
Insufficient staff support	Equal variances assumed	1.128	0.526	1.729	.000 *
Insufficient experience	Equal variances assumed	1.475	0.903	2.047	.000 *
Insufficient resources for patient psychosocial support within the community or in my practice	Equal variances assumed	1.493	0.982	2.005	.000 *
Insufficient resources for patient detoxification within the community or in my practice	Equal variances assumed	1.508	0.945	2.071	.000 *

3.1.2 Provider Perceptions of Barriers to Office-based MOUD Prescribing

Figure 1: **Perceived Barriers to Buprenorphine and Extended-Release Naltrexone**

Figure 1 summarizes prescriber beliefs about barriers to prescribing buprenorphine and extended-release naltrexone in office-based settings. The most common barrier to prescribing buprenorphine, according to buprenorphine-waivered physicians (n = 47 respondents), was insurance prior authorization requirements (22%), followed by insufficient staff support (16%). Lack of support by managers/administrators at the practice was most commonly identified as a non-barrier (73%), followed closely by insufficient training (69%). As with buprenorphine, a commonly cited barrier to prescribing extended-release naltrexone (n = 97 respondents) was insurance prior authorization requirements, as well as the lack of community resources for patient detoxification (each 16.5%). Concern about diversion was the most commonly identified non-barrier to prescribing extended-release naltrexone (42%). Paired sample t-tests revealed statistically significantly different responses along only two barriers to prescribing buprenorphine versus extended-release naltrexone: concerns about diversion (mean score 2.2 vs. 1.2, $p < 0.001$, Table 4) and professional licensing board oversight (mean score 1.7 vs. 1.2, $p = 0.002$, Table 4).

We also compared waivered and non-waivered prescribers' perception of barriers to extended-release naltrexone. Waivered providers, as compared to non-waivered ones, were more concerned about the following with respect to extended-release naltrexone to treat OUD: diversion (mean score 1.83 vs. 1.13, $p = 0.003$, Table 5), insufficient training (mean score 2.76 vs. 1.55, $p < 0.001$, Table 5), insufficient time (mean score 2.82 vs. 1.42, $p < 0.001$, Table 5), insufficient staff support (mean score 2.77 vs. 1.65, p <

0.001, Table 5), insufficient experience (mean score 3.04 vs. 1.57, $p < 0.001$, Table 5), insufficient resources for patient psychosocial support (mean score 3.04 vs. 1.55, $p < 0.001$, Table 5), and insufficient resources for patient detoxification (mean score 3.25 vs. 1.74, $p < 0.001$, Table 5).

3.2 Focus Group Results

3.2.1 MOUD Efficacy

Participants in the focus groups provided more detail on many aforementioned themes; a list of selected quotations by theme is available in Additional File Table 6. With respect to MOUD efficacy, focus group participants noted disparities in the evidence base for different MOUDs. According to one focus group participant, “[t]he evidence base behind [extended-release naltrexone] right now is actually really limited. And it’s one of the things that makes me the most nervous when we talk about [MOUD], lumping them all together.” This perception was borne out by survey results that indicated greater belief in the efficacy of methadone and buprenorphine as compared to extended-release naltrexone.

3.2.2 Logistical and Financial Barriers

The focus groups also highlighted financial and logistical barriers to providing MOUD treatment. For example, participants raised concerns about the staff time and cost of acquiring necessary continuing education to provide MOUD, as well as the difficulties in ensuring a practice’s financial sustainability across the diverse MOUD billing codes and reimbursement rates. One provider stated that running an OUD program would lose money for their practice (quote 1a, Additional File Table 6). Providers also noted difficulties in establishing necessary workflows for providing MOUD, particularly in the context of multidisciplinary teams (quote 3c, Additional File Table 6). Finally, many focus group participants cited the lack of addiction treatment providers within their community as a significant barrier to patients (quote 2a, Additional File Table 6).

3.2.3 Negative Perceptions and Stigma

Focus group participants also emphasized the negative perceptions associated with treating patients with OUD and expressed a reluctance to take on this potentially challenging population. One provider raised concerns about practices, particularly large ones, attracting a patient population dominated by persons with OUD (quote 5c, Additional File Table 6). Providers did emphasize the importance of psychosocial support as a component of OUD addiction treatment services, in addition to MOUD (quote 5a, Additional File Table 6). Another participant said that providers do not feel comfortable talking with patients who screen positive for OUD, often lack the knowledge to provide behavioral health support, and do not have access to on-site support from counselors or psychologists/psychiatrists (quote 4a, Additional File Table 6).

4. Discussion

Our mixed methods study compared physician prescriber perceptions of efficacy and barriers to OUD treatment across three dominant MOUDs. In terms of barriers, we focused on office-based treatment settings (i.e., naltrexone and buprenorphine prescribing), but also asked about referral to methadone clinics. We also compared responses from those physicians with and without a waiver to prescribe buprenorphine. The survey data complemented by qualitative responses provides new and timely information on MOUD treatment beliefs and challenges.

Our study found that insurance barriers, specifically prior authorization requirements, were the most commonly cited barrier to buprenorphine and extended-release naltrexone prescribing. While few other studies have explored barriers to extended-release naltrexone prescribing (26, 30), partly owing to its relatively recent FDA-approval for OUD, other studies have likewise found that insurance requirements are a strong barrier to buprenorphine prescribing(21, 34, 35). By confirming results from these other studies, our study lends further support to the need for federal and state governments to intervene in decreasing insurance barriers to MOUD. For example, federal and state authorities should strengthen enforcement of parity laws and sanction violations related to inequitable non-quantitative treatment limitations applied to OUD treatment as compared to other chronic health conditions. These barriers may be quantitative (e.g., the number of days of treatment coverage) or non-quantitative barriers (e.g., types of treatment covered; fail first requirements or prior authorization requirements). Furthermore, given Medicaid's important role in ensuring OUD treatment (36), states should eliminate prior authorization requirements for buprenorphine and extended-release naltrexone covered by Medicaid programs.

Interestingly, we found that regulatory barriers were ranked lower than other barriers to buprenorphine prescribing, despite the existence of relatively unique regulations for buprenorphine prescribing such as patient limits and special education requirements. Possibly this is due to our sampling strategy, which oversampled physicians with a preexisting waiver to prescribe buprenorphine (approximately 40% of our sample) even though only approximately 2% of U.S. physicians have a waiver (20). Individuals who do not view buprenorphine prescribing regulations as a salient barrier may have self-selected into the group that has already obtained a waiver. Future studies should further examine the perception of regulatory barriers among a representative sample of physicians who have not yet obtained a waiver. Some previous studies may have oversampled physicians without a waiver; and physicians without a waiver may overestimate the difficulty of adhering to patient limits, completing special education requirements, and applying to SAMHSA for a waiver. Alternatively, over time, physicians may find it easier to meet regulatory requirements, especially as the availability of online education courses has increased. Also, the institutions in which physicians work may be increasing their support of buprenorphine prescribing over time, thereby giving physicians time and funds to complete the waiver process. Future studies should examine the impact of educational availability and institutional support on perceptions of regulatory barriers.

Our study found higher perceptions of efficacy in treating OUD for methadone and buprenorphine than for extended-release naltrexone. This discrepancy may be explained by greater awareness of methadone and buprenorphine (which were FDA-approved prior to extended-release naltrexone) and fewer published

studies about extended-release naltrexone—a point noted by focus group participants. Recently, some studies have found similar efficacy between buprenorphine and extended-release naltrexone for OUD (29, 37), while another more recent study found lower efficacy of extended-release naltrexone in terms of overdose protection (9); but these studies were unavailable or very recent when we implemented our survey. Additionally, since many physicians in our sample reported that no one in their practice was prescribing extended-release naltrexone, they may also have limited experiential knowledge of the medication. In other words, even if prescribers know that extended-release naltrexone has demonstrated efficacy in controlled trials, they may be unsure about its effectiveness in real world settings. However, our interpretation is limited by the fact that we did not ask survey participants whether they are currently prescribing extended-release naltrexone. Finally, our participants may feel that extended-release naltrexone is less effective for patients who are not yet opioid-abstinent (as required for extended-release naltrexone) and are unwilling or unable to do so, even though the medication may be effective for patients in other practices who have already completed the detoxification process.

Participants believed that buprenorphine is slightly more effective than methadone at preventing opioid overdose, although the scholarly literature suggests that their efficacy is comparable, with methadone being slightly more effective at retaining patients in treatment than lower doses of buprenorphine (38). Respondents may simply have been less familiar with the literature about methadone and with real-world effectiveness of methadone, since they cannot prescribe it in office-based settings. Additionally, patients who seek OUD treatment in office-based settings may have stronger pre-existing preferences for buprenorphine than for methadone(39, 40), making providers in such settings less likely to seek out education about methadone or to refer patients to methadone treatment.

Although little has been written about the appropriateness of prescribing methadone, buprenorphine, or extended-release naltrexone for individuals with co-occurring mental health disorders, our participants believed that methadone and buprenorphine are more appropriate than extended-release naltrexone for dual diagnosis patients. Possibly participants are aware that depression is an adverse event associated with extended-release naltrexone in about 10% of patients (41). The literature on extended-release naltrexone's efficacy in dual diagnosis patients may also be less developed because of its novelty in treating OUD and/or because participants are more risk averse to prescribing it. Furthermore, since individuals beginning extended-release naltrexone must be opioid abstinent for at least seven days, health practitioners may feel that this hurdle is too difficult for individuals with dual diagnosis to overcome. Given the correlation between OUD and mental health disorders (42), significantly more research is needed regarding the effectiveness of MOUD for individuals with dual diagnosis and barriers to prescribing MOUD for this population.

Non-waivered participants believed methadone is highly effective for pregnant women, but waivered participants had more negative beliefs about methadone's effectiveness in this population (mean score 4.47 vs. 3.48, $p < .0005$). Likewise, non-waivered participants believed buprenorphine is highly effective for pregnant women, but waivered participants had more negative beliefs about buprenorphine's effectiveness in pregnant women (mean score 4.42 vs. 3.58, $p < .0005$). Possibly the waivered survey

participants do not routinely treat pregnant women for OUD and are thus more risk averse to using MOUD; however, we did not ask survey participants what percentage of their patient panels consists of pregnant women. Both methadone and buprenorphine are effective for pregnant women with OUD (43, 44). Therefore, education about methadone's and buprenorphine's efficacy in pregnant women should be part of courses for obtaining a SAMHSA waiver, especially in light of increasing rates of OUD in pregnant women and of neonatal abstinence syndrome (45).

Participants were significantly less likely to identify diversion and licensing board oversight as barriers to extended-release naltrexone prescribing than to buprenorphine prescribing. This result is not surprising, since misuse or diversion of extended-release naltrexone is unlikely, given its office-based administration and lack of a psychoactive ingredient. Nevertheless, even for buprenorphine, participants did not, on average, believe diversion and licensing board oversight were strong barriers to prescribing (mean score 2.2 and 1.7 out of 5). However, our study oversampled waivered physicians; and physicians who have sought and obtained a waiver may as a group be less likely to have diversion or oversight concerns than physicians who have not sought and obtained a waiver. Nevertheless, real-world experiences of those actually waivered to prescribe buprenorphine are important to the extent they reflect that diversion is not a high concern with this medication, to refute longstanding stigma.

No participants were implanting Probuphine®, likely reflecting the novelty of the medication. Even though we included questions about Probuphine® in our survey, due to sample size limitations, not enough data was gathered to assess specific barriers to its utilization. Future studies should explore the extent to which the REMS certification serves as a barrier to prescribing Probuphine®, as well as barriers associated with the need to stabilize patients on oral buprenorphine prior to Probuphine® administration. Additionally, future studies should examine barriers to Sublocade® prescribing. To date the vast majority of studies of buprenorphine accessibility have been conducted on oral and sublingual formulations only.

Our study has several limitations. Our survey response rate was small relative to the population sampled, likely because the incentives offered were small and because this population may be experiencing survey fatigue. Complementing our survey results with focus group data that support our findings and offer additional insights helps to contextualize the survey responses. Our final sampled population over-represented physicians with a buprenorphine waiver, so our results may represent a bias in favor of MOUD treatment and more moderate perceptions of barriers related thereto. However, this may suggest that once prescribers become waivered and prescribe MOUDs, that the actual barriers to this treatment for OUD may be less substantial than previously perceived. Also, regulatory barriers may be less prominent to MOUD prescribing than they were in earlier years, and provider beliefs about efficacy largely track the evolving evidence base. Finally, we did not ascertain whether respondents were currently prescribing extended-release naltrexone, a potential variable related to perceptions of efficacy and barriers.

Our findings suggest that there is room for improvement in OUD treatment education. For example, less is known about newer medications—especially implantable and injectable buprenorphine—and these are areas for further training. Also, MOUD treatment in pregnant women is not well understood and warrants

additional training. Finally, persistent insurance barriers to MOUD prescribing, including prior authorization, continue to merit attention and parity enforcement from regulators. Public payers can act as market leaders in generously covering MOUD and complementary treatment such that prescribers and patients do not perceive these as significant obstacles to effective care.

5. Conclusion

Our study compared physician beliefs about the efficacy of and barriers to three types of medications for OUD treatment. We found that physicians reported insurance barriers as more common than either regulations or diversion concerns for both oral buprenorphine and extended-release naltrexone. Physicians in our sample believed that oral buprenorphine and methadone have greater efficacy than naltrexone in treating OUD, which a recent study of comparative effectiveness with respect to overdose prevention (9). Physicians also believed that buprenorphine and methadone are superior treatments for patients with dual diagnoses – an underexamined issue in previous literature. Also, physicians in our sample believed that buprenorphine was more effective than methadone at treating OUD – a conclusion that may result in too few referrals to methadone treatment. Additional education for physicians about comparative efficacy of OUD treatment is needed.

Abbreviations

MOUD
medication for opioid use disorder
OUD
opioid use disorder

Declarations

Ethical Approval: The study was approved by the Institutional Review Board at the University of Michigan, reference number HUM00159099. All participants provided informed consent.

Consent for Publication: Not applicable

Availability of Data and Materials: Materials are available from the first author upon request. To protect the confidentiality of study participants, survey data and interview data is not available.

Competing Interests: Authors have no competing interests to report.

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Figures

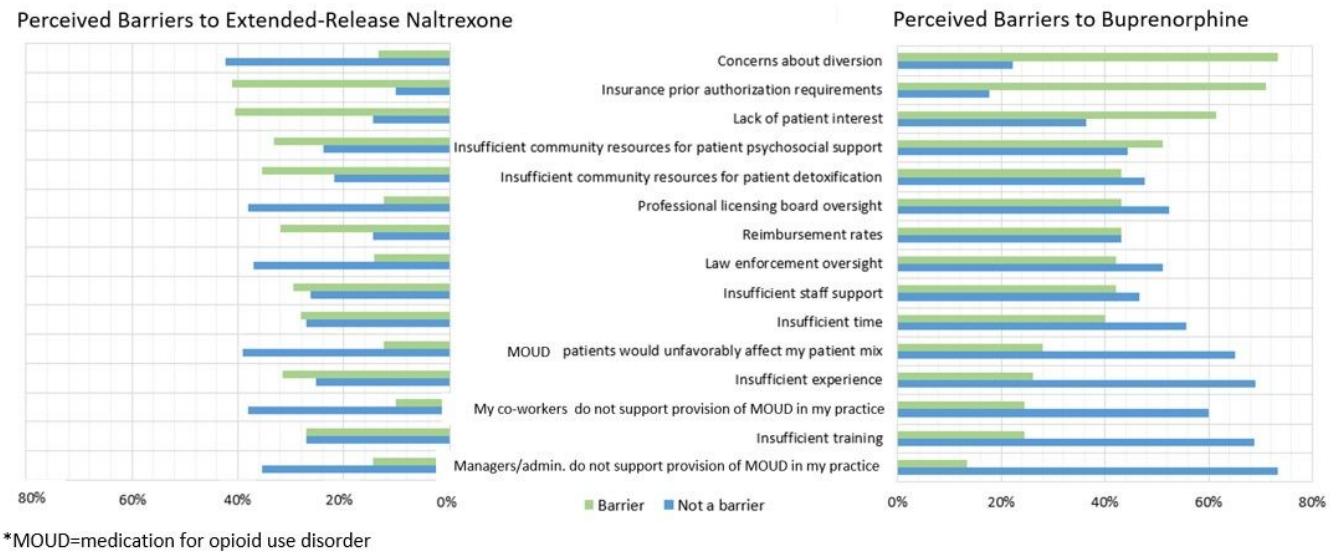

Figure 1

Perceived Barriers to Buprenorphine and Extended-Release Naltrexone Treatment

Supplementary Files

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