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Consensus Statement on Pain Management for Pregnant Patients with Opioid Use Disorder from the Society for Obstetric Anesthesia and Perinatology, Society for Maternal-Fetal Medicine, and American Society of Regional Anesthesia and Pain Medicine

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Abstract

Pain management in pregnant and postpartum people with an opioid use disorder (OUD) requires a balance between risks associated with opioid tolerance, including withdrawal or return to opioid use, considerations around social needs of the maternal-infant dyad, and the provision of adequate pain relief for the birth episode that is often characterized as the worst pain a person will experience in their lifetime. This multidisciplinary consensus statement between the Society for Obstetric Anesthesia and Perinatology (SOAP), Society for Maternal-Fetal Medicine (SMFM), and American Society of Regional Anesthesia and Pain Medicine (ASRA), provides a framework for pain management in obstetric patients with OUD. The purpose of

this consensus statement is to provide practical and evidence-based recommendations and is targeted to healthcare providers in obstetrics and anesthesiology. The statement is focused on prenatal optimization of pain management, labor analgesia and post-vaginal delivery pain management, and post-cesarean delivery pain management. Topics include a discussion of non-pharmacologic and pharmacologic options for pain management, medication management for OUD (e.g., buprenorphine, methadone), considerations regarding urine drug testing and other social aspects of care for maternal-infant dyads, as well as a review of current practices. The authors provide evidence-based recommendations to optimize pain management while reducing risks and complications associated with OUD in the peripartum period. Ultimately, this multidisciplinary consensus statement provides practical and concise clinical guidance to optimize pain management for people with OUD in the context of pregnancy to improve maternal and perinatal outcomes.

INTRODUCTION

Pain management in peripartum people with opioid use disorder (OUD) can be a complex and challenging issue, with sometimes competing aims of adequate analgesia and mitigation of risks and complications associated with OUD. The management of pain during pregnancy in this special population requires a comprehensive and individualized approach, taking into consideration the patient's history of opioid use, pain management, and potential impact on the fetus. Narrative review articles¹ and clinical guidelines for non-obstetric perioperative opioid use and OUD in pregnancy², as well as postpartum pain management³, are available. However, an evidence-based clinical guideline based on a systematic literature review and specifically focused on peripartum pain management among parturients with OUD is currently lacking.

The purpose of this clinical consensus statement is to provide practical and evidence-based recommendations for clinicians and healthcare providers, focused on peripartum pain management in people with OUD in key areas: 1) optimal management of medication for opioid use disorder (MOUD) in the peripartum period; 2) management recommendations to treat labor and delivery-related pain for people with OUD, treated or untreated; and 3) clinical interventions to optimize peripartum analgesic quality and adherence to substance use disorder (SUD) treatment goals throughout the peripartum period. The consensus statement is intended to be used by healthcare providers in obstetrics and anesthesiology. Three phases of pregnancy care are brought into focus in these consensus statements: prenatal optimization, labor analgesia and post-vaginal delivery analgesia, and cesarean anesthesia and post-cesarean delivery analgesia. Levels of evidence are presented with each recommendation, further highlighting specific needs where research is necessary to address knowledge gaps.

METHODS

A working group of subject matter experts in obstetrics, anesthesiology, addiction medicine, and acute and chronic pain from the Society for Obstetric Anesthesia and Perinatology (SOAP), American Society of Regional Anesthesia and Pain Medicine (ASRA), and Society

for Maternal-Fetal Medicine (SMFM) was convened. The group conducted a systematic scoping review in 2020 to identify all studies that examined peripartum pain management in pregnant people with OUD, either treated with MOUD or untreated. The systematic scoping review was guided by the Preferred Reporting Items for Systemic Reviews and Meta-Analysis extension for Scoping Review standards (PRISMA -ScR). Results from this systematic scoping review were published in 2022⁴. Original research, case studies, case series, cohort studies, letters to the editor, commentaries, white papers, published abstracts, and review articles in all languages were included. The PubMed and Embase database searches of this review yielded a list of 994 publications that was reduced to 84 full text publications⁴. The systematic scoping review broadly outlined studies identified but was not designed to provide study details or clinical recommendations for people with OUD.

In this consensus, prenatal optimization and medication management (i.e., opioid agonists, partial agonists, and antagonists), labor analgesia and post-vaginal delivery analgesia, and post-cesarean delivery analgesia for peripartum people with OUD were assessed in detail based on the studies identified in the recently published systematic scoping review⁴. A working group from SOAP defined, by consensus, specific key questions that would be important and clinically relevant for peripartum pain management in pregnant people with OUD⁴. These clinically relevant management questions are summarized in Table 1⁴. Three smaller workgroups were assembled around the 3 phases of care in focus: prenatal optimization, labor analgesia and post-vaginal delivery analgesia, and post-cesarean delivery analgesia. These workgroups reflected expertise from anesthesiology, obstetrics, acute and chronic pain medicine, and addiction medicine. A steering committee of experts consisting of obstetric anesthesiologists (GL, BC, RL, RBG, BB), obstetricians (SO) and addiction medicine specialists (MT) oversaw activities of the three groups and reviewed all clinical recommendations generated for consistency. Areas of inconsistency were referred to the work groups for adjudication and consensus. The steering committee resolved any persisting discrepancies by consensus. The workgroups were instructed to use literature results available only from the systematic review to ground evidence synthesis and their clinical recommendations. Where evidence was lacking, and the experts judged it appropriate to apply available evidence from pregnant people without OUD or from non-pregnant people with OUD, that was specifically noted in the evidence review.

Despite a lack of high-quality evidence, the recommendations were grounded in the current and best available evidence based on the results of the systematic review. Bias was minimized by recusal and draft iterations that included viewpoints from the entire consensus group.

Each question was addressed using structured answers. Each answer aimed to provide a summary of all the evidence identified in the systematic review, and list specific evidence-based recommendations. The American College of Cardiology (ACC) and American Heart Association (AHA) Clinical Practice Guideline Recommendation Classification Systems⁵ were used to objectively evaluate each of the element's level of evidence. Table 1 summarizes key clinical recommendations for each clinical question.

Throughout this consensus statement, the terms “abuse” or “dependence” are used in reference to primary articles in which those terms are referenced. However, we highlight that the non-stigmatizing terminology “use disorder” is currently recommended and consistent with the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

RESULTS AND DISCUSSION

Prenatal Optimization

1. What medical co-morbidities are associated with opioid use disorder that can affect peripartum pain management?

Summary of the evidence: Several studies have shown that pregnant people with OUD have a higher prevalence of psychiatric co-morbidities that may influence peripartum pain management, such as depression and anxiety⁶. One study⁷ found that nearly one third of pregnant people enrolled in a SUD treatment program screened positive for moderate to severe depression and almost half reported symptoms of postpartum depression at 6 weeks after delivery⁸. Similarly, a prospective study in pregnant people (n=111) with OUD, found that 39.6% met the screening criteria for major depressive disorder, 43.2% for generalized anxiety disorder and 27.9% for panic disorder⁹. A retrospective study reported that pregnant people with OUD were 2.7 times more likely (prevalence ratio 95% CI: 2.5 to 3.2; $p < 0.0001$) to have depression and 2.7 times (95% CI: 2.4 to 3.1; $p < 0.0001$) more likely to have anxiety. In general, psychiatric co-morbidities are predictors for more severe postoperative pain and analgesic requirements. For example, one study¹⁰ found that pre-operative anxiety significantly increases the risk for more severe pain after cesarean delivery (OR: 1.60, 95% CI: 1.16-2.20, $p=0.004$). Similarly, another study¹¹ found that State Trait Anxiety Inventory, a validated questionnaire that evaluates state and trait anxiety, predicted total analgesic needs after cesarean delivery ($R^2 = 0.22$; $p < 0.01$). Other psychosocial factors, such as depressed mood, negative affect, and pain catastrophizing were also correlated with more severe postoperative pain and analgesic use in a systematic review reporting on 48 studies¹².

a. How can these medical co-morbidities be managed to improve peri-delivery pain outcomes?

Summary of the evidence: While several reports have advocated for referral to psychology, e.g., for cognitive behavioral treatment, and psychiatry for simultaneous treatment of these psychiatric co-morbidities,^{13, 14} there are no studies evaluating the outcome associated with such interventions specifically for pain outcomes.

Clinical Recommendation: Pregnant people with OUD frequently have psychiatric co-morbidities that may increase risk for more severe pain and increased analgesic requirements in the peripartum period (Level B-NR). Screening for psychiatric co-morbidities should be performed during pregnancy in accordance with ACOG recommendations for all prenatal people¹⁵ (Class I, Level B-NR). Referral for appropriate multidisciplinary care may be beneficial to achieve optimal care for these patients (Class IIa, Level C-EO). Although interventions such as cognitive behavioral therapy for pain management have been recommended by some, data are lacking on the effectiveness of such interventions for pain outcomes in pregnant people with OUD (Class IIb, Level B-NR).

b. What other substance use disorders are associated with opioid use disorder that can affect peripartum pain management?

Summary of the evidence: Pregnant people with OUD are at increased risk of use of other substances, including tobacco, cannabis and alcohol^{2, 16}. One study¹⁶ compared patients with OUD being screened for opioid agonist treatment with pregnant people without substance use disorder, and found that patients with OUD were four times more likely to smoke versus pregnant patients without SUD (88% vs 22%; $p < 0.01$). In a retrospective analysis of more than 120,000 deliveries in Maine⁸, pregnant people with OUD were 16.8 times more likely to have other drug abuse or dependence compared to pregnant people without OUD (Prevalence Ratio (PR) 95% CI: 13.4-20.9; $p < 0.0001$). Notably, the OR for cannabis use was 5.2 (95% CI: 4.6 – 5.9; $p < 0.0001$), for nicotine use 6 (95% CI: 5.9 – 6.2; $p < 0.0001$) and for alcohol use disorder 8.5 (95% CI: 5.8 – 12.5; $p < 0.0001$).

Nicotine and cannabis use have been associated with increased postoperative pain and analgesic requirements. Nicotine is a central nervous system stimulant with analgesic properties. Nicotine withdrawal during the peripartum period can increase pain perception and analgesic requirements¹⁷. A retrospective chart review including 1,899 patients without OUD undergoing cesarean delivery found that tobacco use was associated with increased likelihood of experiencing postoperative severe pain (OR 2.52; 95% CI: 1.17 – 5.44)¹⁸. One study¹⁹ reported pain recovery patterns after surgery in 530 parturients scheduled for elective cesarean delivery. The authors collected worst pain intensity scores daily for 60 days after surgery and cluster analysis of the data revealed 6 distinct trajectories of recovery from pain, with Cluster 1 having the lowest pain burden and Cluster 6 having the highest pain burden. Smoking status was found to be a predictor of cluster membership with a higher pain burden. Similarly, for vaginal birth, a retrospective study including 9,038 people undergoing vaginal delivery found that smoking increased the need for postpartum opioid analgesia (OR: 1.48; 95% CI: 1.24 - 1.77)²⁰.

No evidence is available in the obstetric literature regarding the effect of cannabis or cannabinoids on peripartum pain management.

Clinical Recommendation: Use of other substances is common in pregnant people with OUD (Level B-NR). Screening for and discussion about opioid use and other substances is recommended (Class I, Level B-NR), and cessation services including nicotine replacement therapy should be offered in accordance with ACOG recommendations²¹ (Class I, Level B-NR).

2. Prenatal Anesthesiology Consultation

a. Should all pregnant people with OUD have a predelivery anesthesiology consult?

Summary of the evidence: No studies measured the effects of a prenatal anesthesia consult on delivery outcomes. OUD in pregnancy is associated with a significant increase in maternal morbidity and mortality particularly if OUD is untreated. Given the significant increased risk of obstetric morbidity and mortality associated with OUD, the experts considered that an antenatal consult with anesthesiology service may be useful for this

population as it may allow for early identification of these potential problems and counseling on related anesthesia management.

b. What should be evaluated and discussed in the anesthesia consult?

Summary of the evidence: Prenatal anesthesia consultation can facilitate focused patient counseling, preparation, and planning for pain experiences associated with vaginal and cesarean deliveries. Evidence regarding pain experience and analgesia in these contexts suggests the possibility of worse pain and increased analgesia requirements among parturients receiving MOUD, and setting expectations and discussing options is key. A retrospective review (n=7,449, 1.1% with OUD) reported that pregnant people using chronic opioids had higher utilization rates of epidural labor analgesia (47% vs 38%) and inadequate labor analgesia (requiring more supplemental boluses) compared to controls, as well as high rates (74%) of inadequate post-cesarean analgesia.²² However, this study was limited in that the analgesia was delivered by manual boluses from an obstetric provider. Such practices may reflect clinician bias, and may not reflect modern standardized treatment strategies using infusion pump-driven programmed intermittent epidural bolus and patient-controlled epidural analgesia.

The American College of Obstetricians and Gynecologists (ACOG) recommends MOUD with methadone or buprenorphine be initiated or continued for pregnant people with OUD². Patients may be receiving methadone or buprenorphine for indications of chronic pain or OUD. Neonatal abstinence syndrome (NAS, also known as neonatal opioid withdrawal syndrome, NOWS) is an expected and treatable outcome of maternal opioid exposure with both drugs. Opioid agonist treatment with methadone or buprenorphine is preferable to medically supervised withdrawal, as withdrawal may be associated with higher rates of return to opioid use and worse outcomes.^{30, 33} In addition, MOUD with opioid agonists may improve obstetrical outcomes by improving adherence to prenatal care.³³ Methadone requires administration through an opioid treatment program (OTP) certified by the Service Abuse and Mental Health Services Administration (SAMHSA), which could be a barrier to treatment for some pregnant patients³⁴.

Pregnant people receiving methadone (n=68) experienced more pain after vaginal delivery compared with controls, using 70% more opioid analgesia postpartum.²³ Similar findings were observed in a cohort of n=63 pregnant people receiving MOUD with buprenorphine.²⁴ Notably, a retrospective cohort study comparing patients receiving MOUD with methadone versus buprenorphine, found no significant differences in post-cesarean analgesic use between the two groups.²⁵ Therefore, it appears that patients receiving MOUD may experience worse peripartum pain compared to controls, but there may be no differences in pain experience or analgesia needs among patients receiving MOUD either with buprenorphine or methadone.

Chronic exposure to opioids during pregnancy may also lead to opioid tolerance and opioid induced hyperalgesia, which in turn can make peripartum analgesia challenging.^{26, 27} There are no data or direct comparative evidence regarding differential effects of MOUD agents for pain and analgesia experiences in labor and delivery.

Pregnant people recovering from OUD who are currently abstinent, may be concerned about returning to use and may desire strictly avoiding opioids in the peripartum period. Conversely, some argue that failure to provide adequate analgesia may lead to return to opioid use behaviors, to better manage pain.²⁸

c. What key differences between buprenorphine and methadone should anesthesia providers be aware of during anesthesia consultation and plan formulation?

Summary of Evidence: Methadone is a μ -opioid and N-methyl-D-aspartate (NMDA) receptor antagonist with a slow onset of action and long elimination half-life (22-24 hours). It is associated with dose dependent QTc prolongation. Methadone has a long history of use and extensive study in pregnancy. Buprenorphine is a partial μ -opioid receptor agonist making respiratory depression less likely, is associated with less QTc interval prolongation vs. methadone and can be prescribed on an outpatient basis without daily visits²⁹⁻³¹. Limited trial data suggests that buprenorphine is associated with reduced morphine requirement, shorter hospital stay, and shorter treatment duration of neonatal opioid withdrawal syndrome (NOWS). Buprenorphine and methadone are not different with respect to absolute NOWS rates; when NOWS occurs, buprenorphine-exposed neonates have reduced severity and duration of withdrawal. A large observational study using administrative data found that pregnant people receiving buprenorphine had higher rates of psychiatric and medical co-morbidities, with higher rates of prescription fills for treatment of these conditions but did not have higher rates of opioid prescription fills during pregnancy, compared to patients receiving methadone³². Other data comparing these agents are found in Supplemental Material 1.

Clinical Recommendation: Pregnant people with OUD or receiving chronic opioid agonist therapy may experience more pain and have higher analgesic requirements during and after delivery (Level B-NR). Antenatal anesthesia consultation is recommended: to coordinate care with other health professionals as it relates to pain management; to establish a trusting, non-judgmental environment; to address fears, concerns, and goals regarding opioid analgesia; and to establish a clear pain management plan (Class I, Level C-EO).

3. Predelivery medication management: Methadone

a. During pregnancy and in anticipation of labor and delivery, should the methadone dose be split, continued, increased, reduced, or stopped?

Summary of the evidence: In non-pregnant patients, once daily dosing of methadone is usually sufficient to prevent withdrawal. However, due to physiologic and pharmacokinetic changes during pregnancy, in particular increases in CYP3A4 expression, methadone metabolism is accelerated as pregnancy progresses³⁵. In fact, one study found that the half-life of methadone in pregnancy may be as short as 8.1 h in the third trimester³⁶. Therefore, dose adjustments and more frequent dosing (e.g., every 6-8 h) may be indicated in pregnant people. However, dose adjustments should be made on an individual clinical basis (considering patient priorities and managing addiction medicine opinions), as they are not always required^{30, 37}.

For patients with chronic pain, the general goals are to avoid or minimize the use of additional opioids for pain management, highlighting alternative therapies such as nonpharmacologic and nonopioid pharmacologic options². Methadone is a potent analgesic, but the duration of analgesic action (4-8 hours) is significantly shorter than the duration of action for the suppression of opioid withdrawal symptoms (24-48 hours)^{38, 39}. Therefore, to maximize its analgesic profile for labor and delivery, it may be beneficial to administer the daily methadone dose in divided doses, e.g., every 6-8 h, in the peripartum period. No evidence is available to suggest or refute that the methadone dose or dosing interval will potentiate or impede peripartum neuraxial analgesia.

Clinical Recommendations: Methadone should be continued in the peri-delivery period (Class I, Level B-R). However, higher doses and/or more frequent dosing may be needed as pregnancy progresses, particularly in the third trimester (Class I, Level B-NR). Dose adjustments should be individualized (Class I, Level B-R). Dividing the total daily dose over shorter dosing intervals (e.g., every 6-8 h) is reasonable to maximize analgesic benefits (Class IIa, Level C-LD). If additional analgesia is required in the peripartum period, additional shorter acting opioids may be needed in addition to methadone dose adjustments because rapid methadone titration is not possible (Class IIb, Level C-LD). Because methadone is associated with dose-dependent QTc interval prolongation, drug interactions must be considered and monitored (Class I, Level C-LD). Monitoring QTc is recommended upon methadone initiation and when increasing dose above 120mg/day (Class I, Level C-LD).

4. Pre-delivery medication management: Buprenorphine

a. During pregnancy and in anticipation of labor and delivery, should the buprenorphine dose be split, continued, increased, reduced, or stopped?

Summary of the evidence: Like methadone, buprenorphine is metabolized in the liver via the CYP3A4 enzymatic pathway, and metabolism and clearance is accelerated during pregnancy, especially in the third trimester; therefore, dose adjustments are often necessary⁴⁰. Limited clinical pharmacokinetic data suggests that at doses ranging 4-12mg twice daily during pregnancy, median plasma concentrations fall below ranges required to prevent withdrawal symptoms within 4 hours of the last buprenorphine dose.^{41, 42}

Splitting the buprenorphine daily dose in three- or four-times-per-day dosing in the peripartum period may also improve pain relief. One study (n=62) gave pregnant people a choice to split their total daily dose of buprenorphine over intervals that best controlled their cravings and withdrawal symptoms, without adjusting the total daily dose. Most chose to take buprenorphine 3-4 times daily.⁴⁰ It is suggested that dosing every 6-8 hours may maximize the analgesic effect of buprenorphine,^{28, 43} however, this is based on expert opinion.

Buprenorphine has high affinity for, but low intrinsic activity at the μ -opioid receptor; buprenorphine displaces other opioids from these receptors easily, even at low doses. High doses of full μ -opioid agonists are required to displace buprenorphine from the receptors. These pharmacologic properties could make the treatment of acute peri-delivery pain

challenging. Patients receiving buprenorphine have higher peri-delivery pain scores and require more opioids after cesarean delivery, but studies have suggested that there is no significant difference between pregnant people maintained on methadone vs buprenorphine for postpartum pain outcomes (Supplemental Material 1).^{44, 25, 30}

Clinical Recommendation: Buprenorphine should be continued in the peri-delivery period (Class I, Level B-R). Buprenorphine metabolism and clearance accelerate as pregnancy progresses and higher doses and/or more frequent dosing may be needed, particularly in the third trimester (Class I, Level C-EO). Dose adjustments should be individualized considering patient priorities and managing addiction medicine opinions (Class I, Level B-NR). Splitting the daily dose to every 6-8 hours may improve withdrawal symptoms, in addition to optimizing analgesic benefits (Class IIa, Level C-EO).

5. Predelivery medication management: Naltrexone

a. During pregnancy and in anticipation of labor and delivery, should the naltrexone dose be split, continued, increased, reduced, or stopped?

Summary of the evidence: MOUD – including using a combination of behavioral counseling and opioid agonist treatment with methadone or buprenorphine – is the recommended treatment for pregnant people with OUD, although some may be receiving naltrexone.³⁰ The American Society of Addiction Medicine recommends that if a person becomes pregnant while receiving naltrexone, it may be appropriate to discontinue the medication or substitute its use with methadone or buprenorphine; however decision to continue use of naltrexone should be weighed against the lack of research on risks associated with its use in pregnancy.¹⁸¹ Naltrexone is a non-selective opioid receptor antagonist that blocks the euphoric and analgesic effects of opioids. Although the oral form is associated with low adherence, the injectable long-acting form is more effective than placebo in maintaining abstinence⁴⁵. Data on the use of naltrexone during pregnancy is limited (Supplemental Material 1). Naltrexone use may impair adequate analgesia during labor, delivery and postpartum. It is recommended to stop oral naltrexone 72 hours before planned surgical procedures⁴⁶. However, the long-acting depot form lasts approximately 6 weeks, and it is not always possible to stop naltrexone far enough in advance of planned hospitalization⁴⁷ such as labor and delivery. There are no published data on peri-delivery pain management in pregnant people receiving naltrexone, however opioid analgesia is expected to be less effective in these circumstances. Case studies in patients receiving naltrexone undergoing non-obstetric procedures, report inadequate postoperative pain control, despite high doses of opioids⁴⁸.

Clinical Recommendation: Oral naltrexone should be stopped at least 72 hours before labor and delivery or before cesarean delivery (Class IIa, Level B-NR). For naltrexone depot formulations, due to the duration of effects lasting almost 6 weeks, it may not be feasible to stop its use prior to planned delivery (Class IIa, Level B-NR). Clinicians should rely on a combination of neuraxial and regional anesthesia techniques and non-opioid analgesics to achieve adequate peri-delivery pain control. (Class IIb, Level C-EO).

6. Should a history of OUD impact planned mode of delivery (cesarean versus vaginal delivery)?

Summary of Evidence: There is no data examining whether OUD in pregnancy should impact the choice between planned cesarean delivery and a trial of labor. A joint document produced by the American College of Obstetricians and Gynecologist (ACOG), the Society for Maternal-Fetal Medicine (SMFM), and the American Society of Addiction Medicine does not comment on recommended mode of delivery.⁴⁹ In clinical practice, cesarean delivery generally is reserved for obstetric indications rather than based on the presence or absence of a patient history of OUD. Although cesarean delivery exposes patients with OUD to more opioids than vaginal delivery during the postpartum recovery period, available data from the surgical literature suggests that continuing MOUD in the postoperative period is associated with reduced opioid analgesia utilization compared to discontinuing MOUD⁵⁰.

Clinical Recommendation: Decisions on planned mode of delivery should be based upon obstetrical indications and decided by the pregnant person and their obstetrician (Class IIa, Level C-EO).

Labor Analgesia and Post-Vaginal Delivery Analgesia

1. Is there evidence for increased pain, analgesia dose requirement, or increased use of analgesia during labor in pregnant patients with OUD, treated or untreated with MOUD?

Summary of Evidence: MOUD may increase the perception of pain due to opioid-induced hyperalgesia and decreased production of endogenous opioid peptides.^{54, 55} These factors are suggested to contribute to an exaggerated intolerance of labor pain and inefficacy of traditional analgesic interventions. One prospective observational study (n=2,610 reporting 44,522 unique pain ratings) found that patients with OUD were more likely to experience different pain types (affective, nociceptive/neuropathic), higher pain intensity, and increased postpartum opioid consumption compared to those without OUD.⁷¹ Low-quality studies report conflicting results regarding intrapartum pain experiences, epidural labor analgesia utilization, and non-epidural analgesia utilization^{23, 24, 69, 70} (Supplemental Material 1). Notably, many of those studies are retrospective or observational and thus include the possibility of clinical provider bias around medication administration.

Clinical Recommendation: Patients with OUD, treated or untreated, may experience labor and delivery pain differently (greater intensity and different pain qualities) compared to those without OUD (Class IIa, Level B-NR). There is insufficient evidence to suggest that traditional analgesic regimens such as epidural labor analgesia are inadequate in this specific population (Class IIa, Level B-NR). Therefore, laboring people receiving MOUD should be offered analgesia consistent with practices offered to all pregnant people, and they should be frequently assessed to determine the analgesic efficacy of the currently provided treatment, with a low threshold to increase or change dosing as needed. (Class I, Level B-NR)

2. Neuraxial Anesthesia and Analgesia

a. Should early neuraxial analgesia be recommended for patients with OUD?

Summary of Evidence: One conference proceeding described expert opinions that for patients with OUD, neuraxial labor analgesia should be encouraged and received as early as possible in labor because effective neuraxial labor analgesia averts the need for supplemental systemic opioids.¹³ With OUD, higher doses of intravenous opioids may be used for labor analgesia, which may theoretically increase the risk for respiratory depression, although there are no available data to substantiate this theoretical risk. A clinical review proposed that neuraxial labor analgesia should be offered unless contraindications exist.¹⁴ There are no studies comparing early versus later or typical maternal request timing for neuraxial labor analgesia in pregnant people with OUD. Early compared to later neuraxial labor analgesia placement does not increase or negatively impact obstetric outcomes in the general population.^{52, 53}

Clinical Recommendation: Early neuraxial labor analgesia for people with OUD is recommended to minimize the need for systemic opioid analgesia (Class I, Level B-NR). Shared decisions and patient-centered planning is necessary. (Class IIa, Level C-EO)

b. Is there any evidence that the response to neuraxial opioids may be altered (less effective) with buprenorphine use? Should opioids in the epidural solution be increased, decreased, or omitted?

Summary of Evidence: Concerns are raised about the efficacy of neuraxial opioids with buprenorphine use due to its very high affinity for the mu-opioid receptor⁵⁴⁻⁵⁶, and pregnant people with OUD may desire strict avoidance of all opioids in any route of administration, depending on their treatment goals. A mixture of low concentration local anesthetic with a short-acting lipophilic opioid has become the standard for neuraxial labor analgesia formulations.⁵⁷ The addition of an opioid adjunct allows for adequate analgesia while using lower concentration of local anesthetic, resulting in less motor block, hypotension, and reduced risk for instrumented delivery that may accompany higher concentration solutions. However, the available literature on neuraxial opioid efficacy in this population is limited. One retrospective study²⁴ explored the analgesic efficacy of a local anesthetic-opioid epidural formulation (bupivacaine 0.0625% with fentanyl 2mcg/ml) in laboring patients receiving buprenorphine compared to matched controls. Median pain scores were similar between groups (buprenorphine 2 (0, 3.8); control: 1.5 (0, 4), $P=0.31$). Buprenorphine-treated patients did not receive additional epidural supplemental doses for breakthrough pain or changes to infusion rates, compared to control. This single study suggests that buprenorphine may not interfere with the efficacy of neuraxial opioids and that specific adjustments to usual standard epidural formulations may not be necessary beyond the flexibility afforded by conventional PCEA. The intentional selection of opioids with either similar affinity for the mu-opioid receptor (sufentanil, hydromorphone) or similar lipophilicity as buprenorphine (fentanyl) has been proposed as a superior option for these patients^{58, 59}. Although the pharmacokinetic advantages of these medications are theoretical, current clinical effectiveness data are lacking to conclusively recommend one full mu-opioid agonist over another. Notably, no available trials exist to guide decisions on superiority,

non-inferiority, or side effects of opioid and non-opioid adjuncts specifically among patients with complex pain and OUD who are receiving neuraxial labor analgesia. No data exist regarding this question in the context of methadone use.

There are no studies examining different opioid doses in the labor epidural solution of people with OUD.

Clinical Recommendation: Standard low-concentration local anesthetic epidural solutions with lipophilic opioids are recommended for neuraxial labor analgesia for laboring people with OUD (Class I, Level C-EO). Although current data do not exist to support the purposeful adjustment of standard epidural formulations, clinicians may choose to take advantage of the pharmacokinetic benefits offered by sufentanil, hydromorphone, or fentanyl. (Class IIb, Level C-EO). Additional opioids (e.g., epidural fentanyl 100 mcg bolus or increasing fentanyl in epidural solution from 2 to 3 mcg/ml) can be considered if epidural labor analgesia proves to be inadequate, and if concordant with individual patient OUD treatment goals; the addition of adjuvants does not preclude standard assessments of malpositioned epidural catheters requiring adjustment or replacement (Class IIa, Level C-EO). The experts agree that routinely omitting opioids from epidural solutions is not recommended unless their removal is deemed higher priority with OUD treatment goals, and other non-opioid adjuncts can be considered in those cases. (Class IIb, Level C-EO)

c. Should the concentration of the local anesthetic be increased?

Summary of Evidence: There are no studies examining different concentrations of local anesthetics in the epidural solution of laboring people with OUD. In patients without OUD, low concentrations of local anesthetics (e.g., bupivacaine < 0.1%) reduce assisted vaginal delivery, result in shorter second stage of labor, produce less motor block, increase ambulation, and cause less urinary retention, without higher pain scores compared to higher local anesthetic concentrations.^{60, 61} Pregnant people with OUD perceive and experience clinician bias in the treatment of their pain,⁶² and clinicians should be aware of these biases during pain assessments and treatments.

Clinical Recommendation: Standard, low-concentration labor epidural solution should be selected for laboring people with OUD (Class I, Level C-EO). The local anesthetic solution can subsequently be substituted for a higher concentration if labor epidural analgesia becomes inadequate (Class I, Level C-EO). To minimize the potential influence of implicit bias in suboptimal pain management, standard clinical practice for diagnosing and treating breakthrough labor pain should be followed (Class IIa, Level C-EO).

d. Should non-opioid adjuvants be added to the epidural solution (e.g., clonidine, epinephrine, dexmedetomidine, neostigmine)?

Summary of Evidence: Alternative non-opioid adjuncts may be considered, which can help minimize the local concentration requirements to reduce motor block, hypotension, and risk of assisted vaginal delivery while minimizing exposure to neuraxial opioids.^{63–68} Neuraxial clonidine or dexmedetomidine (both α_2 -agonists) provide similar analgesia compared

to neuraxial fentanyl for labor epidural analgesia infusions¹⁴ and may be an alternative to neuraxial opioids for pregnant people with OUD or patients who wish to avoid all opioids.

Clonidine, an alpha₂-agonist, is the most studied adjuvant for enhancement of neuraxial labor analgesia aside from neuraxial opioids. It carries a black box warning for obstetric use because of concerns about hemodynamic instability, so its use in this context is off label. An observational study examined the effects of epidural clonidine in seven patients receiving buprenorphine MOUD with neuraxial labor analgesia leading to spontaneous vaginal delivery.⁶⁵ In this study, combining epidural clonidine with bupivacaine effectively managed labor pain without the need for additional medication in most cases, although hypotension was a notable side effect requiring management. Sedation and maternal bradycardia were not observed.

There are no high-quality trials examining the role of systemic dexmedetomidine in laboring people with OUD. There are no available data regarding other non-opioid neuraxial adjuvants, such as epinephrine (alpha₂-agonist) or neostigmine (anticholinergic).

Clinical Recommendation: Non-opioid neuraxial adjuncts may be used when pregnant people desire strict opioid avoidance or the analgesic efficacy of neuraxial opioid is deemed insufficient and after excluding a failed or malpositioned epidural catheter (Class IIa, Level C-EO). Epidural clonidine may be given as an epidural bolus for initiation of labor analgesia (50-100mcg), for management of breakthrough pain, or added to the epidural solution (1-2mcg/mL) if epidural local anesthetic boluses and local anesthetic or opioid adjustments have failed to provide adequate analgesia (Class IIa, Level C-EO). Neuraxial dexmedetomidine for labor analgesia should follow standard clinical applications (Class IIb, Level C-EO). Due to the potential increased risk of sedation in this population, sedation, and respiratory depression monitoring (e.g., sedation scores, respiratory rate monitoring, continuous pulse oximetry), should be applied, if not already utilized in institutional protocols (Class I, Level C-EO). Combining alpha₂-agonist agents (e.g., epinephrine, clonidine, dexmedetomidine) is not recommended (Class III, Level C-EO). If used, neuraxial adjuvants should be preservative free (Class I, Level C-EO).

3. If the pregnant person with OUD is not a candidate for neuraxial labor analgesia, is there a role for any of the following adjuvants?

a. Nitrous oxide

Summary of Evidence: There are no studies examining the role of nitrous oxide in laboring people with OUD. One study suggested that nitrous oxide is an analgesic option for this population,⁷² as some people with OUD may have a history of sexual trauma and posttraumatic stress disorder that may benefit from the anxiolytic effects of nitrous oxide. However, nitrous oxide exposure may lead to maternal sedation, hypoxemic episodes, and increased risk of respiratory depression among pregnant people receiving systemic opioids or sedatives/hypnotics.^{73, 74}

Clinical Recommendation: MOUD is not an absolute contraindication to receiving nitrous oxide labor analgesia (Class I, Level C-LD). Nitrous oxide use in laboring people with OUD

should follow similar indications as patients without OUD, with consideration for sedation and respiratory depression monitoring (e.g., sedation scores, respiratory rate monitoring, continuous pulse oximetry) if not already utilized in institutional standard nitrous oxide protocols (Class I, Level C-EO).

b. Intravenous (IV) Opioid PCA

Summary of Evidence: Pregnant people with OUD are usually not included in clinical trials examining intravenous patient-controlled analgesia (IV PCA) for labor analgesia. Therefore, there are no data on IV PCA use in laboring patients with OUD. Patients receiving chronic opioid agonists (e.g., heroin or other illicit opioids, long term opioids for chronic pain), or treated with MOUD (e.g., methadone or buprenorphine, and naltrexone) may require higher than typical doses of systemic opioids (e.g., fentanyl, remifentanyl) to achieve adequate analgesia. Exposure to IV opioids for a patient with OUD may conflict with their recovery or treatment goals. For pregnant people receiving buprenorphine, sufentanil is currently the only available opioid with binding affinity higher than buprenorphine. Sufentanil also has high intrinsic efficacy (reaches maximal effect at 50% receptor occupancy; in contrast, remifentanyl has lower intrinsic efficacy and requires high fractional receptor occupancy to produce effects¹⁸⁰) and these properties make modest doses of sufentanil a potentially preferable systemic opioid supplement for acute pain in people receiving buprenorphine therapy¹.

Clinical Recommendation: Opioid IV PCA (e.g., fentanyl, remifentanyl, sufentanil) use for labor analgesia in patients with OUD is recommended to be an individualized decision (Class IIa, Level C-EO). Sufentanil may be a reasonable systemic opioid supplement for acute pain in patients receiving buprenorphine therapy (Class IIa, Level C-LD). Should opioid IV PCA be used, given expected higher opioid dose requirements in people with OUD, maximum opioid limits should be adjusted upward (Class I, Level C-EO). Sedation and respiratory depression monitoring (e.g., sedation scores, respiratory rate monitoring, continuous pulse oximetry) should be considered if not already utilized in standard institutional IV PCA protocols (Class I, Level C-EO). Neuraxial labor analgesia is preferred over opioid IV PCA (Class I, Level C-EO). Neuraxial labor analgesia combined with IV PCA is not recommended (Class III harm, Level C-EO). Opioid IV PCA should be considered and discussed when neuraxial block is not an option (Class I, Level C-EO).

c. Ketamine

Summary of Evidence: Clinical trials evaluating ketamine for labor analgesia or in the peripartum period are lacking. Perioperative continuous infusion of sub-anesthetic intravenous ketamine has been noted to reduce opioid requirements in patients without OUD, but lactation safety and breastmilk transfer data are currently lacking.¹⁴ There are no studies examining the role of ketamine in laboring people with OUD. There are no studies reporting potential risks for return to use after ketamine exposure with MOUD, which can co-exist with polysubstance use disorder. Under animal experimental conditions, ketamine, and other anesthetics, have been noted to exhibit neurotoxic effects in developing brains although clinical data on this topic are more difficult to interpret. The 2016 Federal Drug Administration (FDA) “Drug

Safety Communication” (www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-review-results-new-warnings-about-using-general-anesthetics-and) states that general anesthesia and sedation drugs (including but not limited to ketamine) used in children <3 years of age or in pregnant people in their third trimester who were undergoing anesthesia for more than 3 hours or repeated use of anesthetics, “may affect the development of children’s brains.” However, the present experts of this consensus statement agree that the context of exposure to these drugs in pregnancy and lactation is often under clinical circumstances of necessity and are brief, non-repetitive periods of exposure, and decisions for use or non-use must be patient-centered with appropriate individual risk and benefit considerations. Potential conditions to avoid or exert caution with ketamine use include patients with uncontrolled thyroid disease, uncontrolled cardiovascular conditions such as severe hypertension, or a history of hallucinations.

Clinical Recommendation: Given currently limited fetal-neonatal and lactation safety data on ketamine in the labor and delivery setting and considering limited available data regarding its effectiveness or side effects for labor analgesia, the usefulness/effectiveness of routine use of ketamine for labor analgesia for pregnant people with OUD is unknown (Class IIb, Level C-EO).

d. Other adjuvants

Summary of Evidence: A systematic review of pregnant people with chronic nonmalignant pain reported several descriptions of non-opioid analgesia in the peripartum period, but pointed out that comprehensive studies are lacking.⁷⁵ Such interventions include ball exercises, warm water baths, nonsteroidal anti-inflammatory drugs (NSAIDs), nitrous oxide, acupuncture, aromatherapy, music, naturopathic methods, transcutaneous electrical stimulation, and sterile water subcutaneous injections. No studies contained high-quality evidence supporting or refuting broad adoption of these pain management strategies in labor, and more high-quality studies are urged. Pudendal nerve blocks have been suggested as a possible option at the time of delivery for people who are ineligible or otherwise unable to receive neuraxial labor analgesia. Paracervical nerve blocks may be helpful for treatment of pain signals transmitted via the paracervical ganglion such as pain in the first stage of labor or pain after delivery during management of cervical lacerations. However, due to concerns about post-block fetal bradycardia¹⁸², these blocks are no longer favored for use during labor, except for delivery following known or anticipated fetal demise.

Clinical Recommendation: Non-opioid analgesia for labor analgesia with OUD should follow similar indications and applications as those without OUD (Class I, Level C-LD).

4. Treatment of post-vaginal delivery pain

a. Should non-steroidal anti-inflammatory drugs (NSAID) and acetaminophen be used?

Summary of Evidence: There are no studies dedicated to examining the use of NSAIDs following vaginal delivery with OUD. In pregnant people without OUD after cesarean delivery, a mode of delivery that is associated with higher pain scores and more pain medication requirements, NSAIDs are recommended to be used on a set schedule to

minimize additional opioid medication needs.⁷⁶ There are no studies examining the use of acetaminophen following vaginal delivery with OUD. Scheduled acetaminophen administration in hospital after vaginal delivery is warranted for patients with OUD, treated or untreated.⁷⁷

Clinical Recommendation: Absent any contraindication, NSAIDs and acetaminophen should be administered on a set schedule for analgesia following vaginal delivery with OUD (Class I, Level A). Dose adjustments or caution may be required in patients with comorbid liver disease and impaired hepatic function (Class IIa, Level C-EO). The utility of acetaminophen-opioid combination medications is uncertain, but may result in toxic acetaminophen levels if acetaminophen mono product is also consumed, or if large doses of the acetaminophen-opioid combination medications are used (Class IIa, Level C-EO).

b. If the patient has a high-order vaginal laceration, should long-acting opioids be administered epidurally? If so, what doses are recommended?

Summary of Evidence: Expected postpartum analgesic requirements in pregnant people with OUD with uncomplicated vaginal birth may be higher than patients without OUD.⁷¹ One review noted that pregnant people with OUD who have complex vaginal deliveries (e.g., high degree lacerations, vaginal hematomas) could consider the use of neuraxial morphine or hydromorphone, although the use of naltrexone may make this intervention ineffective.¹⁴ Consensus on appropriate dose for these interventions is not available in the literature. Other medications including acetaminophen and NSAIDs are universally noted to be effective, and their scheduled use with history of OUD should be done whenever possible.¹⁴ Other adjunctive medications in this setting have not been described.

Clinical Recommendation: Due to the increased pain intensity associated with vaginal deliveries complicated by high-order lacerations, epidural opioids (e.g. morphine 3mg) may be considered, but there is limited data supporting its safety or efficacy; higher doses may be associated with pruritus which may be challenging to treat given risks for withdrawal with nalbuphine (Class IIa, Level C-LD). The presence of OUD treated or untreated with MOUD has an uncertain effect on epidural opioid dose requirements. Patients with high-order vaginal lacerations should receive education on risks and benefits of opioid exposure as part of multimodal and tailored analgesic strategies (Class IIa, Level C-EO). Should short courses of opioid analgesia be required upon discharge, then short interval outpatient follow-up (e.g., 5-7 day prescription, no refills, with follow-up appointment within one week of discharge) is prudent (Class IIa, Level C-EO).

c. Is there a role for the routine use of oral opioids in hospital or at discharge?

Summary of Evidence: There are no studies examining the routine use of oral opioids in hospital or at discharge after vaginal delivery with OUD.

Clinical Recommendation: Given the risk of return to use associated with oral opioid exposure, opioid medications should not be used routinely following vaginal delivery (Class IIa, Level C-EO). The decision to use opioids for pain after vaginal delivery should be

individualized with the patient, their treatment provider, and the post-discharge primary care team who will manage pain and opioid prescribing after delivery (Class IIa, Level C-EO). Rarely, opioids may be used with caution in patients with severe pain following vaginal delivery that does not respond to NSAIDs, acetaminophen or other analgesic modalities (Class IIa, Level C-EO). When used in this manner, low-potency, non-parenteral formulations of opioids should be dispensed for a very short duration (e.g., 3-day supply) (Class IIb, Level C-EO).

d. What is the role for other adjuvants for the treatment of post-vaginal delivery pain?

Summary of Evidence: There are no studies examining the role of other adjuvants for the treatment of post-vaginal delivery pain in patients with OUD. Topical agents and temperature interventions have been reported specifically for perineal pain and uterine cramping.⁷⁷

Clinical Recommendation: Adjunct pharmacologic and non-pharmacologic approaches that should be used for post-vaginal delivery pain in patients with OUD include topical local anesthetics, ice packs for perineal pain, and heating pads for uterine cramping. (Class IIa, Level C-EO)

e. Should MOUD (methadone, buprenorphine) dose be adjusted intrapartum or postpartum for analgesic benefits?

Summary of Evidence: See “Prenatal Optimization” section for more details. In anticipation of maximizing its analgesic benefits for labor and delivery, it may be beneficial to administer the daily methadone dose in divided doses, every 6 to 8 hours, in the peripartum period. Splitting the buprenorphine daily dose in three- or four-times-per-day (every 6 to 8 hours) dosing in the peripartum period may also be beneficial for pain relief.

Clinical Recommendation: For potential analgesic benefits, and ideally beginning in the prenatal period, it may be beneficial to administer the daily methadone dose every 6-8 hours, or to split the daily buprenorphine dose to every 6-8 hours (Class IIa, Level C-EO). These dose adjustments are not effective substitutes for neuraxial labor analgesia. (Class IIa, Level C-EO)

5. Withdrawal and Toxicity (“Overdose”)

a. If a patient with OUD experiences withdrawal during labor, how should it be treated?

Summary of Evidence: There are no studies examining the treatment of opioid withdrawal during labor in patients with OUD treated or untreated with MOUD.

Clinical Recommendation: Patients receiving methadone or buprenorphine should generally be maintained on their usual regimen to prevent withdrawal or return to use (Class I, Level B-NR). For patients with OUD experiencing acute withdrawal symptoms during labor, management should follow therapies for non-pregnant patients (Class I, Level C-EO). For patients with recent illicit opioid exposure, acute withdrawal may be potentially treated with

opioids, titrated to effect, along with supportive care (Class I, Level C-EO). Ideally, however, these treatment plans should be made collaboratively with addiction medicine specialists for treatment in individual circumstances (Class I, Level C-EO).

b. If a pregnant person with OUD presents with opioid toxicity (“overdose”), how should it be treated?

Summary of Evidence: Clinically significant respiratory depression or toxicity should be treated with naloxone. Notably, pregnant people receiving buprenorphine who may subsequently require naloxone for opioid induced respiratory depression, may require higher than typical doses of naloxone. Successful reversal of buprenorphine may require very high doses of naloxone (> 2 mg).⁷⁸

Clinical Recommendation: Naloxone should be included in the management of clinically significant respiratory depression in pregnant people with OUD treated with buprenorphine or methadone (Class I, Level C-EO). The ideal dose for treatment is not known but may be as high as 2 mg in the setting of buprenorphine, and likely requires a continuous infusion (dose: two-thirds of initial effective naloxone bolus, delivered as an infusion over an hourly basis, 0.25-6.25 mg/hour) (Class IIb, Level C-LD).

c. Can partial antagonists- e.g., nalbuphine, butorphanol—be used in patients receiving MOUD (e.g., how should opioid-induced intrapartum pruritus be managed in a laboring pregnant person receiving buprenorphine?)

Summary of Evidence: There are no studies examining whether partial antagonists can be used in pregnant or postpartum people on MOUD. However, treatment with partial agonist (or antagonists) can precipitate acute withdrawal in opioid dependent people, including those receiving MOUD. One review describes removing or reducing the dose of the opioid component of the epidural medication solution and treating pruritus with other pharmacological approaches, such as 5-HT3 receptor antagonists.⁷⁹

Clinical Recommendation: Partial agonists or antagonists should not be administered in patients receiving MOUD for both the treatment of pain and opioid-induced pruritus, due to risk for precipitating acute withdrawal (Class III, Level B-R). If opioid-induced pruritus occurs during labor, consideration should be given to removing or reducing the dose of the opioid component of the epidural medication solution and treating with other pharmacological approaches, such as 5-HT3 receptor antagonists (Class I, Level C-EO). With a history of severe neuraxial opioid-induced pruritus, it is reasonable to initiate the block without neuraxial opioids. (Class IIa, Level C-EO)

6. Monitoring

a. Do pregnant people with OUD require additional monitoring during and after labor?

Summary of Evidence: There are no studies explicitly examining whether pregnant people with OUD require additional monitoring during or after labor. A systematic review found that in cases where high doses of systemic opioids were used for labor or peripartum

analgesia, the combination of respiratory depression and moderate sedation were observed 2.5 times more frequently among opioid-dependent patients.⁷⁵ Despite these higher frequencies of respiratory depression, analgesia was not acceptable as evidenced by higher postoperative pain scores.

In the absence of co-administered systemic opioids beyond MOUD, there is no evidence of increased risk of respiratory depression for pregnant people with OUD receiving dilute neuraxial opioids.

Clinical Recommendation: For neuraxial labor analgesia, usual standards for and duration of monitoring is recommended to be applied (Class I, Level C-EO). However, if the patient presents with acute opioid toxicity or has received medications that may increase the risk for respiratory depression due to interaction with opioids (e.g., high doses of systemic opioids such as opioid IV PCA, benzodiazepines, magnesium, or other sedating medications), additional monitoring for respiratory depression is indicated (Class I, Level C-LD). To diminish provider biases and assist with developing informed treatment plans, providers and nurses should be educated about the potential for increased pain post vaginal delivery with high order vaginal laceration including potential risks for sedation/respiratory depression in pregnant people with OUD. (Class I, Level C-EO)

Cesarean Anesthesia and Post-Cesarean Delivery Analgesia

1. Is there evidence for increased pain and analgesia intake after cesarean for pregnant people receiving medication for OUD including methadone, buprenorphine, and naltrexone?

Summary of Evidence: Pregnant individuals receiving MOUD like methadone, buprenorphine, and naltrexone may experience heightened pain post-cesarean delivery due to comorbid chronic pain and mental health conditions^{80,81}. MOUD pharmacokinetics impact opioid effectiveness, with methadone causing tolerance, buprenorphine inducing competitive antagonism, and naltrexone acting as an antagonist⁸⁰⁻⁸³. Postoperatively, methadone and buprenorphine users typically require increased opioids compared to opioid-naïve patients, while naltrexone blocks opioid effects depending on administration timing and formulation^{23, 58, 82}. Overall, buprenorphine and methadone users may report higher pain scores and increased opioid use post-surgery, contrasting with naltrexone's blocking effects^{84, 85, 59, 86, 87}.

Although evidence indicates that patients receiving MOUD may experience increased pain and opioid use post-surgery^{16, 23, 42, 58, 59, 71, 80, 83, 84, 86-91}, it is recommended to maintain MOUD without interruption throughout the perioperative and peripartum period to prevent destabilization and potential opioid misuse⁸⁹. Buprenorphine's competitive antagonism may reduce the efficacy of other opioids for acute pain but increasing the total daily dose to 24-32mg in divided doses can optimize its analgesic effects^{92, 93}. Similarly, it is advised to continue the same daily dose of methadone, with consideration for fractionating the dose and supplementing with other opioids for analgesia as needed⁹³. For naltrexone, assessing recent dosing history and type can guide clinicians in determining the potential utility of additional opioids as naltrexone levels decline.

A retrospective study with 553 participants found that individuals on methadone or buprenorphine consumed more opioids in-hospital post-cesarean delivery compared to opioid-naïve patients, yet they were less likely to receive opioid prescriptions at discharge,⁹⁴ illustrating the potential for disparity in pain management for patients with OUD.

Clinical Recommendation: Available data suggest that pregnant people with OUD treated or untreated with MOUD may experience increased pain and opioid needs after cesarean delivery compared with pregnant people without OUD (Level C-LD). Pregnant people should be educated on risks and benefits of opioid exposure as part of multimodal and tailored analgesic strategies (Class I, Level C-EO). Encourage multimodal analgesia for peripartum care, ideally with a multidisciplinary prenatal plan involving anesthesiology, obstetricians, and addiction medicine to address MOUD management during and after discharge (Class I, Level C-EO). Discuss any dosing changes with addiction providers or outpatient prescribers to prevent relapse and ensure continuity of care, especially for new OUD diagnoses (see Part 1: Prenatal Optimization) (Class I, Level C-EO).

2. Anesthesia for Cesarean Delivery: Like patients without OUD, pregnant people with OUD who have a cesarean delivery should be given the benefits of neuraxial anesthesia (e.g., spinal or combined spinal epidural, epidural anesthesia) including improved pain recovery, enhanced participation in cesarean birth, and safety compared to general anesthesia.

a. Should the usual dose of neuraxial opioids be increased, decreased or should they be omitted?

Summary of Evidence: The goals for neuraxial anesthesia for cesarean delivery include adequate anesthesia for surgery and high-quality postoperative analgesia. Opioid use may be 2-4 times higher in patients with OUD after cesarean delivery.^{3, 95, 96}

Neuraxial lipophilic opioids enhance intraoperative block quality, while hydrophilic opioids are used for postoperative analgesia. Tailoring the dose of neuraxial opioids for cesarean delivery anesthesia is necessary considering opioid tolerance in individuals receiving MOUD^{95, 89, 97}. Continuing MOUD throughout the peripartum period is recommended and this practice may necessitate higher doses of opioids to achieve adequate analgesia post-cesarean^{98, 99, 23, 25}. However, specific dose adjustments for neuraxial opioids in this population have not been well studied. Utilizing multimodal non-opioid analgesics like NSAIDs with acetaminophen is advised to optimize pain management^{95, 89, 97}.

Clinical Recommendation: Neuraxial anesthesia is recommended over general anesthesia for cesarean delivery when possible (Class I, Level B-NR). Co-administered lipophilic and hydrophilic neuraxial opioids (e.g., fentanyl and morphine) are recommended and should neither be omitted nor dose reduced for cesarean anesthesia in pregnant people with OUD (Class I, Level B-R). No data are available to inform routinely using increased doses of neuraxial opioids for cesarean analgesia for pregnant people with OUD, and the safety and effectiveness of this practice is unknown (Class IIb, Level C-LD).

b. Should non-opioid adjuvants be added to the neuraxial anesthetic including clonidine, dexmedetomidine, epinephrine, or neostigmine?

Summary of Evidence: Pregnant people with OUD may theoretically respond differently to neuraxial morphine or other commonly used opioid analgesics, and therefore, additional adjuvant therapy may be helpful. For post-cesarean analgesia, neuraxial clonidine has been described as an adjuvant for patients with OUD. One small observational study in patients after cesarean delivery (n=7) suggested that when clonidine was added to a postoperative epidural solution, patients receiving MOUD with buprenorphine achieved good analgesia and many did not require any supplemental opioids postoperatively.⁶⁵ In that case series, patients received a post-operative epidural infusion of bupivacaine 0.1% with clonidine 1.2mcg/mL or bupivacaine 0.0625% with clonidine 2 mcg/mL and pain scores remained low (from 0 to 5/10 maximum). The average infusion time was 27 hours.

In one case report, intravenous dexmedetomidine infusion was titrated in increasing doses from 0.2 to 0.7 mcg/kg/hour for 2-3 days after cesarean delivery.¹⁰⁰ Dexmedetomidine has been reported as associated with reduced parenteral sufentanil utilization for 24h after surgery, in mono- and in multicentric studies.¹⁰¹ However, no studies have evaluated the impact of sedation side effects on breastfeeding, early ambulation, or other patient-centered goals.

Intrathecal epinephrine (100 or 200 mcg) administration is known to increase the duration of both sensory and motor blockades during and after cesarean delivery.¹⁰⁴ Its impact on postoperative analgesic requirement and pain score is debatable. There is no study on neuraxial epinephrine effectiveness among patients with OUD undergoing cesarean delivery.

In pregnant people without OUD, neostigmine has been proposed as an adjuvant for decreasing postoperative pain scores and opioid use after cesarean delivery. In one study, single-dose epidural neostigmine (75 to 300 mcg) given during cesarean delivery was associated with significant reduction in pain scores for the first 24 hours (numeric rating score 5.4 (0.2) in the saline group vs. 3.5 (0.3) in the neostigmine group); however, sedation was more frequent when 300 mcg doses were used.¹⁰² A systematic review and meta-analysis identified 16 randomized controlled trials evaluating intrathecal or epidural neostigmine, of which three evaluated neuraxial neostigmine for cesarean delivery.¹⁰³ Neuraxial neostigmine was associated with reduced postoperative pain scores and opioid use, but there was a high level of heterogeneity between studies. Moreover, intrathecal neostigmine was associated with higher risk of nausea (OR 8.99 [95% CI 4.74 to 17.05], $P < 0.001$). There are no available studies on neostigmine for pain management after cesarean delivery among people with OUD.

The use of adjuvants, especially those with sedative properties, warrants appropriate respiratory monitoring in an appropriate care unit, particularly if neuraxial or systemic opioids are co-administered.⁶⁶

Clinical Recommendation: There is limited evidence to support or refute routinely using non-opioid neuraxial adjuvants including clonidine, dexmedetomidine, epinephrine, or neostigmine, for post-cesarean delivery analgesia in patients with OUD (Level C-LD). If

used, side effects including respiratory depression, sedation, and nausea must be monitored (Class I, Level C-EO). Intrathecal epinephrine is reasonable to increase the duration of sensory block during cesarean delivery (Class IIa, Level B-NR). The benefits of neuraxial neostigmine for post-cesarean analgesia remains unclear and side effects (severe nausea, vomiting) may limit its use in pregnant people with and without OUD (Class III, Level C-LD).

3. Post-Cesarean pain management

a. What is the role for continuing neuraxial analgesia into the postpartum period?

Summary of Evidence: Continuing epidural analgesia after surgery has been proposed to potentially reduce exposure to intraoperative neuraxial opioids and postoperative supplemental opioids^{84, 96, 105, 106} but this approach may compete with Enhanced Recovery after Cesarean (ERAC)⁷⁶ goals for early ambulation. One review article suggested using epidural local anesthetics for 48-72 hours to optimize pain management and reduce systemic opioid use in pregnant people with OUD.⁶⁶ A case series (n=8) suggested that epidural analgesia (with local anesthetic or repeated doses of long-acting lipophilic opioids) after cesarean delivery provides effective post-cesarean delivery analgesia in pregnant people receiving buprenorphine MOUD.¹⁰⁷ Peripartum patients with OUD express a range of opinions and preferences regarding utility and disutility of opioids for pain management, a desire for non-opioid options.⁶²

Clinical Recommendation: Epidural analgesia may be considered to continue 12-48 hours after cesarean delivery in patients with OUD (Class IIa, Level C-EO). However, its use must be balanced with overall goals for early ambulation, newborn care, other recovery goals, and nursing support (Class I, Level C-EO). Shared decision making should be employed (Class I, Level C-EO). If abdominal wall blocks were not performed, it may be reasonable to continue epidural local anesthetics for patients with OUD after cesarean delivery. (Class IIb, Level C-EO)

b. Should NSAIDs and acetaminophen be used after cesarean delivery?

Summary of Evidence: The Society for Obstetric Anesthesia and Perinatology (SOAP) and the American College of Obstetricians and Gynecologists (ACOG) have recommended the use of nonsteroidal anti-inflammatory drugs (NSAIDs) as part of multimodal analgesia for post-cesarean delivery^{3, 76}. Several reviews and meta-analyses have described the benefits of perioperative NSAIDs including 30-50% opioid-sparing effect after various surgeries, including after cesarean delivery among patients with⁸⁰ and without¹⁰⁸⁻¹¹³ OUD. In an observational study after cesarean delivery, patients with OUD had a higher frequency of NSAID use than those without OUD (diclofenac: 8/19 (42.1%) of subjects with OUD vs 4/38 (10.5%) of those without OUD, $P=0.006$).¹¹⁴ The authors suggested that clinicians should preferentially treat pain with NSAIDs instead of opioids.¹¹⁴ However, another study reported that common problems expressed by patients with OUD were inadequate analgesia and their desire to increase dosage or frequency of analgesia²². The opioid-sparing effects of NSAIDs in the obstetric population are supported by a meta-analysis of 22

randomized controlled trials that compared NSAIDs (n=639) to controls (n=674) in obstetric patients without OUD.¹¹⁵ They found lower reported pain scores in the NSAIDs group at 12- and 24- hours after cesarean delivery. Those in the NSAIDs group also consumed significantly fewer opioids and had less drowsiness or sedation.¹¹⁵ The availability of the parenteral NSAID formulations has made it practical for perioperative use.¹¹⁶ No studies specifically in patients with OUD have compared the analgesic efficacy of different NSAID formulations.¹⁰⁶

There are no specific data evaluating the effectiveness of acetaminophen for analgesia in pregnant people with OUD after cesarean delivery. Nonetheless, existing data on its opioid-sparing effects can be extrapolated from cohorts of patients without OUD as well as non-obstetric cohorts. Acetaminophen has an opioid-sparing effect of approximately 20%.^{108, 117} It is available in both oral (*per os*, PO) and parenteral (intravenous, IV) formulations and has minimal adverse effect profile and breast milk transfer¹¹⁸ which have encouraged its use in the perioperative period.¹¹⁹ In a retrospective cohort study, uncoupling acetaminophen from opioid administration and instead giving scheduled acetaminophen plus oxycodone as-needed resulted in patients using more acetaminophen and fewer opioids to treat their postoperative pain in the first two days after cesarean delivery, compared to patients who received as-needed combination acetaminophen-opioid medications.¹²⁰ A randomized controlled trial found a statistically significant reduction of opioid consumption in patients receiving IV acetaminophen compared to placebo, in the presence of intrathecal opioid, for the duration of the hospital stay.¹²¹ However, another randomized placebo controlled trial of 66 patients did not demonstrate the same benefits from IV acetaminophen within 24 hours postoperatively.¹²² Both of these studies excluded patients with OUD in their study and they did not compare IV acetaminophen against its oral formulation.¹²¹ A combination of acetaminophen and NSAIDs have been shown in a qualitative systematic review on the non-obstetric population to offer superior analgesia compared with either drug alone.¹²³ Evidence is lacking on this topic specifically for patients with OUD after cesarean delivery.

Clinical Recommendations: Both SOAP and ACOG recommend NSAIDs and acetaminophen as part of multimodal analgesia after cesarean delivery, in the absence of contraindications (Class I, Level B-R). It is recommended to schedule NSAIDs with acetaminophen for post-cesarean pain management due to the well-established opioid sparing effects (Class I, Level C-EO). Ketorolac (intravenous) should be scheduled for 24-48 hours followed by a transition to oral ibuprofen after cesarean delivery (Class I, Level C-EO).

c. Are changes to MOUD required to enhance analgesia after cesarean delivery?

Summary of Evidence: The American Society of Addiction Medicine recommends continuing MOUD during labor and postpartum given uncertain timing of, as well as risks for return to use when stopping MOUD.¹²⁶ Pregnant people receiving methadone generally are maintained on the same dose (consider fractionating the daily dose, see section on pre-delivery medication management) throughout the postpartum period.¹²⁴ Experts have recommended continuing predelivery buprenorphine doses or dividing the daily dose into

3-times-daily dosing to maintain adequate analgesia.^{92, 125} Because buprenorphine has a ceiling effect (24-32 mg/day) beyond which greater pain control is not achieved, increasing the buprenorphine dose solely for the purpose of analgesia may be insufficient if it exceeds the daily ceiling dose; however, splitting the daily dose may optimize analgesia effects. In the postpartum period, doses of MOUD may need to be adjusted (reduced) due to changes in weight (volume of distribution) and drug metabolism after delivery.¹⁸⁴

Clinical Recommendations: Methadone may be maintained with the same dose (consider fractionating the daily dose, see section on pre-delivery medication management) throughout the postpartum period (Class I, Level B-NR). Buprenorphine has an analgesic ceiling effect (24-32 mg per day) beyond which greater pain control is not achieved (Level C-LD). Increasing the buprenorphine dose beyond this ceiling solely for the purpose of analgesia may be ineffective (Class III, Level C-LD). However, splitting the daily buprenorphine dose to 3-4 daily doses may optimize analgesia effects for the first few post-cesarean days (Class IIa, Level C-EO). Serial evaluation of the inpatient is necessary to identify a need for high doses of systemic opioids, to determine a taper plan prior to discharge (Class I, Level B-R).

d. Is there a role for the routine use of oral or parenteral opioids in the hospital or at discharge? Are there special considerations regarding the type, dose, and quantity?

Summary of Evidence: There is limited evidence on the use of oral opioids in hospital and at discharge for post-cesarean delivery pain management in pregnant people with OUD. The type, dose, and quantity of other oral or parenteral analgesics have not been identified, but expert reviews suggest that opioids with high mu receptor affinity such as sufentanil, fentanyl, or hydromorphone should be considered, although very high doses may be necessary in this context.⁵⁸

Inpatient parenteral administration may be associated with higher abuse liability,⁸³ which risks return to opioid use and must be balanced with overall OUD treatment goals. High affinity, partial opioid agonists such as nalbuphine or butorphanol should not be used in patients receiving buprenorphine because these medications can precipitate withdrawal.¹²⁷

Finally, given that pregnant people receiving MOUD may experience opioid-induced hyperalgesia and require escalating doses of oral opioids postpartum, caution should be given to using combination opioid-acetaminophen preparations, which could increase the possibility for unintentional acetaminophen toxicity.¹²⁵

Clinical Recommendations: The need, type, dose, and quantity of other analgesics for postpartum pain in pregnant people with OUD depends on specific MOUD and treatment goals (Level C-EO). The decision to use or not use parenteral opioids for pain must be made on an individual basis in partnership with an addiction medicine practitioner, in accordance with individual treatment goals, and ideally should be discussed prior to the onset of pain (see: Prenatal Optimization) (Class I, Level C-EO). If used, high doses of oral opioids may be necessary, and short-term parenteral opioids may be necessary for severe pain; for patients requiring high systemic opioid exposure who are breastfeeding, neonatal sedation monitoring may be necessary (Class IIa, Level C-EO).

e. What is the role of other oral or systemic adjuvants for post-cesarean analgesia?

Summary of Evidence:

Ketamine: Intravenous ketamine has been reported for treatment of acute pain in non-obstetric patients with opioid use disorder or receiving chronic opioid agonist therapy¹²⁸. In routine perioperative settings, typical doses for low-dose intravenous ketamine for acute pain treatment range 0.1 to 0.3 mg/kg/hour or about 8mg/hour for 2-3 days.^{107, 129} However, the evidence around perioperative ketamine among patients with OUD is scarce and primarily case report or case series.^{107, 129} One study involving patients with OUD after cesarean delivery showed reduced milligram morphine equivalents (MME) when ketamine was offered postoperatively (90 [38-200] mg vs. 71 [15-463] mg for the first postoperative 24 hours); the median range for ketamine infusion was 14.4 (5.8-19.7) mg/hour.¹²⁹

A meta-analysis of 20 randomized controlled studies including 1737 patients undergoing cesarean delivery who received ketamine systemically (single bolus or infusion) or intrathecally (0.1mg/kg ketamine) concluded that ketamine significantly reduced pain scores (mean difference [MD] pain scores, ketamine vs. control, -1.10; 95% confidence interval [CI], -1.61, -0.59; $P < 0.0001$) and opioid consumption (MD morphine consumption, ketamine vs. control, -6.11 mg; 95% CI, -9.93, -2.29; $P = 0.002$) which was more pronounced in those who underwent spinal anesthetic compared to those who had general anesthetic.¹³⁰ It was uncertain whether intrathecal opioids played a part in these findings. However, there was significant heterogeneity amongst these included studies regarding the dose of ketamine: bolus doses ranged from 10mg to 30mg fixed dose or 0.15mg/kg to 1mg/kg weight-adjusted dose; infusion doses ranged from 2mcg/kg/min to 0.25mg/kg/hour. This meta-analysis did not report on side effects associated with ketamine exposure. The study was not specific to pregnant people with OUD. A small case series (n=26) on pregnant people receiving MOUD described results associated with low dose ketamine (n=18) infusion vs. no infusion (n=8) after cesarean delivery.¹²⁹ Most patients had spinal anesthesia and half received intrathecal morphine 100mcg. The ketamine infusion commenced between 0-20 hours post-operatively and the dose ranged from 0.1 to 0.3mg/kg/hour with a median duration of 23.9 hours (10.3-45.3 hours). They found reduced milligram morphine equivalent consumption on postoperative day 0 (morphine equivalent: 71mg; 15-463mg vs 90mg; 38-200mg) but no differences on postoperative day 1 when ketamine infusion was stopped. No major maternal adverse effects or adverse neonatal outcomes were reported in this small sample.¹²⁹ Another small case series (n=8) on patients with OUD receiving buprenorphine described using ketamine infusion at 8mg/hr for 24 hours post-cesarean delivery and reported on satisfaction and meeting goals for pain relief.¹⁰⁷

There are currently no studies on ketamine or its active metabolites in breastmilk. The minimal available data from small studies and case reports suggest that ketamine use in nursing mothers may not affect the breast-fed infant. Ketamine and other n-methyl-D-aspartate (NMDA) receptor antagonists have been found to exhibit neurotoxicity and to impair brain development in animal models in experimental conditions.^{131, 132} However, clinical exposures in humans have not demonstrated definitive risk, and dose exposures in animal models exceed those expected to reach human neonatal blood stream when

consumed orally in breastmilk. There may also be neuroprotective effects of ketamine in the presence of noxious stimuli such as pain and stress.¹³³ Ketamine is recommended to be either avoided or used in low doses with monitoring for neonatal sedation and poor feeding during breastfeeding.¹³⁴ The experts agree that brief, non-repetitive periods of exposure to these medications in lactation are permissible. Decisions for use or non-use must be patient-centered with appropriate individual risk and benefit considerations.

Clinical Recommendations: There is limited, low-level evidence supporting analgesic efficacy for low-dose ketamine infusion for up to 24 hours post-cesarean delivery for pregnant people with OUD (Level C-LD). There is currently limited data regarding ketamine safety in lactation (Level C-LD). Its use for post-cesarean analgesia with OUD may be reasonable, although individual and institutional considerations should guide decisions (Class IIb, Level C-LD).

Summary of Evidence:

Gabapentin: The use of perioperative gabapentinoids is controversial regarding their effectiveness in postoperative analgesia, postoperative respiratory complication risk, as well as abuse potential.^{135, 136} A meta-analysis suggested benefits of gabapentin in reducing post-cesarean pain score at 24 hours, but the studies excluded patients with OUD.¹³⁷ Other studies in non-obstetric populations have suggested that gabapentin is associated with reducing acute and persistent postoperative pain and opioid consumption,^{138, 139} but contradicting data suggests only moderate or no evidence supporting the use of gabapentinoids to reduce postoperative pain and opioid consumption, at the expense of an increased adverse effects.^{140, 141} One retrospective cohort study (n=214) in pregnant people with OUD after cesarean delivery, suggested that inclusion of gabapentin in a multimodal analgesic regimen was not associated with lower opioid consumption or pain scores during the first 72 hours post-cesarean delivery.¹⁴² This study was limited by the inclusion of time periods in which opioid exposures were not actively managed, which raises questions about whether these findings could be replicated in present circumstances. Breastmilk transfer may limit the perioperative use of gabapentinoids, especially on the basis of minimal, if any, additional analgesic benefits. There is a paucity of data on neonatal side effects.^{143, 144}

Clinical Recommendations: In view of the current evidence of inconsistent and minimal benefit, at the expense of potential maternal and neonatal harm, routine use of gabapentin cannot be recommended for post-cesarean delivery for pregnant people with OUD. (Class III, Level C-EO)

Summary of Evidence:

Clonidine: Neuraxial clonidine evidence in the context of pregnant people with OUD after cesarean delivery was reviewed elsewhere in this statement.⁶⁵ Notably, a case series of seven patients observed hypotension in two of seven patients and none had bradycardia (maternal or fetal) or sedation.⁶⁵ There is no data on the use of systemic clonidine in patients with OUD. Regarding breastmilk transfer, high serum levels were found in patients taking oral clonidine although most did not have adverse effects such as sedation, dry mouth

or hypotension. Clonidine used as a single postpartum dose or infusion as analgesia adjunct has not been studied in breastfeeding people with or without OUD.¹⁴⁵

Clinical Recommendations: Currently, there is no data to support or refute the routine use of systemic clonidine after cesarean delivery in pregnant people with OUD, and the effectiveness of its use is uncertain (Class IIb, Level C-EO). Alpha-2 adrenoceptor agonists such as intravenous clonidine may be proposed to patients with OUD for enhanced analgesia opioid-sparing effects but must be balanced with individual goals for sedation avoidance, early ambulation, and dynamics with newborn care (Class IIb, Level C-EO). Side effects (sedation and respiratory depression) must be closely evaluated with appropriate monitoring. (Class IIb, Level C-EO)

Summary of Evidence:

Dexamethasone: There is no available literature on the use of intravenous dexamethasone (e.g., 4-8 mg) for analgesia for pregnant people with OUD undergoing cesarean delivery. Studies in patients without OUD in obstetric and non-obstetric settings have found conflicting results regarding the analgesic efficacy of intravenous dexamethasone for post-operative analgesia (Supplemental Material 1).^{146, 147, 148, 149, 150, 151, 152}

Clinical Recommendations: Routine use of a single dose of intravenous dexamethasone has uncertain effectiveness as part of multimodal analgesia for pregnant people with OUD undergoing cesarean delivery (Class IIb, Level C-EO). Its use should be considered on an individual basis (Class IIb, Level C-EO).

f. What is the role for regional anesthesia options such as transversus abdominis plane (TAP), erector spinae plane (ESP), and quadratus lumborum (QLB) blocks, or continuous wound infiltration (CWI)? Are any of these options more effective than others?

Summary of Evidence: ERAC recommendations are to use either abdominal wall blocks or continuous wound infusions for patients at risk for severe pain after cesarean delivery.⁷⁶ No data exists to compare single shot abdominal wall blocks with standard local anesthetic solutions, single shot abdominal wall blocks with liposomal bupivacaine, catheter-based techniques for abdominal wall blocks, wound infiltration or continuous local anesthetic wound infusion in pregnant people with OUD. Although no study has evaluated abdominal wall blocks after cesarean specifically in patients with OUD, both the quadratus lumborum block (QLB)¹⁵³⁻¹⁵⁶ and transversus abdominis plane block (TAP) have been suggested to improve post-cesarean analgesia^{76, 157, 158} in the general population and those at risk for complex pain.

The most used and studied regional anesthesia technique for cesarean delivery is the single shot bilateral transversus abdominis plane (TAP) block. Although not specific to patients with OUD, several studies on the use of ultrasound-guided TAP block perioperatively have demonstrated improved postoperative analgesia, reduced morphine consumption, and improved patient satisfaction after cesarean delivery. A small (n=40) randomized, double-blind, placebo-controlled trial¹⁵⁹ found that total morphine consumption was reduced by

more than 60% in a TAP group receiving 20 mL bupivacaine 0.25%. Another small randomized controlled trial in patients without OUD having cesarean delivery (n=47) found a statistically significant reduction in total morphine use within 24 hours after bilateral ultrasound-guided TAP blocks with 40 mL ropivacaine 0.5%.¹⁶⁰ Although these studies have small sample sizes, the data suggests that ultrasound-guided bilateral single shot TAP blocks after cesarean delivery may reduce opioid consumption as part of multimodal analgesia and especially when neuraxial morphine could not be given. These data may be extrapolated to apply to patients with OUD.

There are no studies on the single shot bilateral quadratus lumborum block (QLB) in pregnant people with OUD having cesarean delivery, but several studies in cesarean delivery among pregnant people without OUD have suggested potential benefits to reducing morphine consumption and improving analgesia in the absence of intrathecal morphine.^{161, 162, 163, 164}

Erector spinae plane (ESP) block has been described for various surgeries. There is no available data on ESP blocks in cesarean delivery specifically for pregnant people with OUD.

For local anesthetic wound infiltration (CWI) for post-cesarean analgesia, a meta-analysis included 21 studies and found that local anesthetic wound infiltration was associated with reduced postoperative opioid consumption but had minimal effect on pain scores in the first 24 hours after cesarean delivery.¹⁶⁷ The meta-analysis was limited by few studies with small sample sizes and by indirect comparisons of single injection vs. infusion performed for subgroup analysis. A meta-analysis including 42 studies with 2906 patients after cesarean delivery without intrathecal opioid, not specific to patients with OUD, found single-dose bilateral TAP block and continuous wound infiltration were associated with significantly lower 24-hour opioid consumption than inactive controls, but no significant differences between single injection wound infiltration and controls¹⁶⁸. The authors concluded that in the absence of neuraxial morphine for cesarean delivery, single-dose TAP blocks and continuous wound infiltration are both effective opioid-sparing strategies.

Local anesthetic systemic toxicity (LAST) is a rare but potentially life-threatening complication of regional anesthesia. It can manifest with symptoms ranging from central nervous system excitation to cardiovascular collapse. Prompt recognition and treatment are essential, including lipid emulsion therapy as a cornerstone of management.¹⁸³ Pregnancy increases risk for LAST due to a relatively vascular tissue plane and reduced protein binding in pregnancy, as well as increased cardiac output with increased uptake and drug distribution in pregnancy.^{165, 166} Data on risks for LAST with QLB, ESP, and CWI in cesarean delivery are currently lacking.

Clinical Recommendations: Based on available evidence, abdominal wall blocks such as TAP, ESP, QLB, and CWI blocks may offer analgesia and opioid-sparing benefits as an adjunct to the multimodal analgesia regimen for patients with OUD (Class IIb, Level C-LD) and should be performed by practitioners who are familiar with these techniques (Class

I, Level C-EO). These blocks may be considered for routine use after cesarean delivery under general anesthesia without neuraxial morphine, or in practices that do not support post-cesarean epidural analgesia (Class IIb, Level C-EO).

g. What is the role for psychotherapeutic or behavioral interventions (e.g., CBT) or complementary and alternative therapies to address intra- and post-cesarean pain?

Summary of Evidence: Pain is a personal experience that is influenced to varying degrees by individual biological, psychological, and social factors.¹⁶⁹ Postpartum patients with mood and anxiety disorders may be more likely to fill opioid prescriptions compared to patients without these conditions.¹⁷⁰ A meta-analysis of randomized trials compared complementary and alternative therapies to controls for post-cesarean pain management in patients with OUD,¹⁷¹ and found low-quality evidence on acupuncture or acupressure that precluded any conclusions. Aromatherapy as an analgesic adjunct reduced pain scores at 12 hours (mean difference -2.63 visual analogue scale (VAS) from 0 to 10, 95% CI -3.48 to -1.77) and 24 hours (mean difference -3.38 VAS, 95% CI -3.85 to -2.91).¹⁷¹ There is no evidence on music therapy or cognitive behavioral therapy specifically for people with OUD undergoing cesarean delivery.¹⁷¹ However, cognitive-behavioral techniques and supportive psychotherapy have been recommended for patients with anxiety disorders in general postpartum patients and for patients with OUD.^{172, 173}

Clinical Recommendations: There is limited data on psychotherapy or behavioral interventions in this setting, and its effectiveness is unknown (Class IIb, Level C-LD). Music therapy, aromatherapy, cognitive-behavioral therapy and supportive psychotherapy may be reasonable as adjuncts to multimodal analgesia, especially in cases where anxiety predominates and affects pain control (Class IIb, Level C-EO).

4. Management of post-operative neuraxial opioid-induced side effects and complications in the patient receiving buprenorphine

a. How should post-operative pruritus be managed?

Summary of Evidence: High level evidence suggests significantly less incidence of pruritus in patients receiving buprenorphine.⁸⁷ Compared to intravenous (IV) morphine, IV methadone (RR, 0.17 [0.03–0.90]), and IV pethidine or IV meperidine (RR, 0.47 [0.25–0.87]) had a significantly lower risk of causing pruritus.¹⁷⁴ It is important to avoid treating pregnant people receiving chronic opioid agonists with mixed antagonists and agonists (e.g., nalbuphine or butorphanol) or pure antagonists (e.g., naloxone), which are widely used for analgesia and pruritus, because these medications can precipitate withdrawal in patients with OUD treated or untreated.¹²⁵

Clinical Recommendation: Treating pregnant people with OUD treated or untreated, with mixed antagonists and agonists (e.g., nalbuphine or butorphanol) or pure antagonists (e.g., naloxone) for pruritus, should be completely avoided in pregnant people receiving MOUD due to risks for precipitating withdrawal (Class III, Level C-LD). Consider treating postoperative opioid-induced pruritus with other pharmacological approaches, such as 5-HT₃ receptor antagonists (Class I, Level C-EO).

b. How should post-operative respiratory depression be managed?

Summary of Evidence: Naloxone should be used for any patient, pregnant or not pregnant, in settings of acute life-threatening opioid toxicity.² Despite the long-standing use of naloxone to reverse symptoms of opioid toxicity, appropriate dosing remains controversial, with varying doses recommended over time and by medical specialty. The dose of naloxone should be titrated based on response to treatment and considering the duration of action of the opioid exposure, and it may require repeated doses or continuous infusion until the opioid effects have diminished. In opioid-naïve patients, naloxone has no expected harmful effects at standard doses and up to 1 mg/kg.¹⁷⁵ Although there may be a desire to prevent acute withdrawal symptoms,¹⁷⁶ these concerns should not prevent delivery of naloxone therapy: naloxone should be given per standard treatment pathways of any patient experiencing acute opioid toxicity. For the obstetric patient, based on gestational age and viability, the fetus should be monitored throughout naloxone treatment given for maternal opioid toxicity¹⁷⁶.

It was originally believed that due to buprenorphine's strong affinity for the mu-opioid receptor and the slow association and dissociation kinetics, would preclude buprenorphine reversal by naloxone, but some evidence suggests naloxone can reverse buprenorphine effects. An infusion scheme consisting of a naloxone bolus of 2 to 3 mg, followed by a continuous infusion of 4 mg/hour has been described as effective.¹⁷⁷ In one study, after buprenorphine was administered to healthy volunteers, an infusion of naloxone was required to sustain a reduction in buprenorphine-induced respiratory depression.¹⁷⁵ Successful reversal of buprenorphine may require very high doses of naloxone (> 2 mg).⁷⁸

Clinical Recommendation: Naloxone should be included in the management of clinically significant respiratory depression in pregnant people with OUD treated with buprenorphine or methadone (Class I, Level C-EO). The ideal dose for treatment is not known but may be as high as 2 mg in the setting of buprenorphine, and likely requires a continuous infusion. (Class IIb, Level C-LD)

4. Monitoring

a. Do patients with OUD require additional monitoring during or after cesarean delivery?

Summary of Evidence: Pregnant people with OUD or receiving chronic opioid agonist therapies may be at higher risk for respiratory depression when compared with opioid naive people, and therefore should be monitored appropriately with regular evaluation of sedation and oxygen saturation.⁸⁸ Pregnant people having a cesarean delivery may require opioid analgesia via any route during the perioperative period. Therefore, all pregnant people who present for cesarean delivery, irrespective of whether intrathecal morphine will be administered, should be assessed and screened for respiratory depression risk factors. For people without risk factors, aggressive monitoring for respiratory depression in the setting of low-dose neuraxial morphine may impact resource allocation and patient-centered post-cesarean delivery care without improving safety. In higher-risk people with co-morbidities (e.g., chronic opioid agonist exposure, obstructive sleep apnea, acute opioid or other sedative toxicity) that place them at higher risk of respiratory depression, it is reasonable to adjust the

frequency, duration, and modality of respiratory monitoring as guided by clinical judgment of the anesthesiologist, institutional guidelines, and the SOAP Practice Guidelines for the Prevention, Detection, and Management of Respiratory Depression Associated with Neuraxial Opioid Administration¹⁷⁸.

Clinical Recommendation: Pregnant people with OUD treated or untreated with MOUD should be monitored per the SOAP respiratory monitoring guidelines, stratified to the higher risk category (i.e., respiratory rate and sedation assessments q1h for the first 12h; q2h for 12-24h thereafter, and consider additional monitoring modalities such as pulse oximetry, capnography as judged indicated). (Class I, Level C-EO)

Special Consideration: Opioid Medications, Disclosure and Shared Decisions, and Urine Toxicology

The experts note that patients with OUD who are receiving obstetric, labor, and delivery care may experience punitive treatment for positive urine toxicology results from a variety of stakeholders, including the criminal justice system, child protective services, and outpatient MOUD providers. Exposure to opioid medications (e.g., systemic, neuraxial, etc.) can potentially lead to unexpected positive urine toxicology results, sometimes unbeknownst to the patient. Such a turn of events can cause stress and challenges for patients with OUD, may increase difficulty accessing medications, and could breed mistrust in the medical system. Therefore, we consider that it is critically important that patients be aware of what medications are being used during labor and delivery, and a frank and open discussion with the patient be had such that patients can decline any opioid if so desired, or conversely, that planned opioid medications be used if desired by the patient and as indicated for effective analgesia by clinical care standards. This discussion is also relevant for patients who may require or desire short courses of postoperative opioid analgesia on discharge but may feel limited by their treatment programs or other circumstances involving state social services. Documentation of these discussions in the medical record, along with communication and coordination with the primary obstetrician, primary care, and primary prescribing teams are paramount. Hospital systems and child/family services must be educated regarding expected positive urine toxicology results and accurate interpretation of these results.

CONCLUSIONS

This consensus statement provides clinical recommendations for optimization of pain management during pregnancy, labor and delivery, and postpartum for people with OUD. We emphasize the importance of early antenatal evaluations by anesthesia providers and a comprehensive and individualized approach to pain management, taking into consideration a history of opioid use, pain management, and the potential impact on obstetric management. This consensus statement provides healthcare providers with practical and concise information to optimize pain management and reduce the risk of OUD during pregnancy. Further research, especially where evidence has been rated weak or primarily based on expert opinion, is necessary to better understand the best practices for pain management in this special population and to address gaps in current evidence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Summarized consensus recommendations for key clinical questions.

Prenatal Optimization	Summary of Recommendations
<p>1. What medical co-morbidities are associated with opioid use disorder that can affect peripartum pain management?</p> <p>a. How can these medical co-morbidities be managed to improve peri-delivery pain outcomes?</p>	<ul style="list-style-type: none"> • Psychiatric comorbidities; may increase risk for more severe pain and analgesic requirements • Screening for psychiatric comorbidities should occur in accordance with ACOG recommendations • Referral for multidisciplinary care may be needed for care plan optimization
<p>b. What other substance use disorders are associated with opioid use disorder that can affect peripartum pain management?</p>	<ul style="list-style-type: none"> • Other substance use disorder is common among people with opioid use disorder • Screen and discuss co-occurring substance use disorder in accordance with ACOG recommendations • Offer nicotine replacement and cessation services for any substance use disorder
<p>2. Prenatal Anesthesiology Consultation</p> <p>a. Should all pregnant people with OUD have a pre-delivery anesthesiology consult?</p>	<ul style="list-style-type: none"> • OUD in pregnancy is associated with increased maternal morbidity and mortality • Patients with OUD may experience more pain and have higher analgesic requirements during and after delivery • Antenatal anesthesia consultation is recommended for the following goals: <ul style="list-style-type: none"> • coordinate care with other health professionals for pain management • establish a trusting relationship in non-judgmental environment • address fears, concerns, and goals regarding opioid analgesia • establish a clear pain management plan.
<p>b. What should be evaluated and discussed in the anesthesia consult?</p>	<ul style="list-style-type: none"> • Methadone is a full μ-receptor agonist, has a long half-life (shortens in pregnancy, therefore requires titration during pregnancy particularly third trimester), is associated with QTc prolongation (dose dependent), and requires prescribing and administration through a certified Opioid Treatment Program • Buprenorphine is a partial μ-receptor agonist, associated with less QTc prolongation than methadone, can be prescribed on an outpatient basis and taken at home, and is associated with shorter treatment durations of neonatal abstinence syndrome
<p>c. What key differences between buprenorphine and methadone should anesthesia providers be aware of during anesthesia consultation and plan formulation?</p>	<ul style="list-style-type: none"> • Methadone should be continued in the peri-delivery period • Higher or more frequent dosing may be needed as pregnancy progresses, particularly in the third trimester • Dividing the total daily dose over shorter dosing intervals (6-8 hours) may maximize analgesic benefits in the third trimester • Rapid methadone titration is not possible • Consider drug interactions due to dose-dependent QTc interval prolongation • Monitoring QTc is recommended upon methadone initiation and when increasing dose above 120mg/day
<p>3. Pre-delivery medication management: Methadone</p> <p>a. During pregnancy and in anticipation of labor and delivery, should the methadone dose be split, continued, increased, reduced, or stopped?</p>	<ul style="list-style-type: none"> • Buprenorphine should be continued in the peri-delivery period • Higher or more frequent dosing may be needed as pregnancy progresses, particularly in the third trimester • Splitting the daily dose to every 6-8 hours may potentially improve withdrawal symptoms, in addition to optimizing analgesic benefits
<p>4. Pre-delivery medication management: Buprenorphine</p> <p>a. During pregnancy and in anticipation of labor and delivery, should the buprenorphine dose be split, continued, increased, reduced, or stopped?</p>	<ul style="list-style-type: none"> • Stop oral naltrexone at least 72 hours before labor and delivery or cesarean delivery • Naltrexone depot formulations last almost 6 weeks, and therefore it may not be feasible to stop naltrexone treatment prior to planned delivery • Use a combination of neuraxial and regional anesthesia techniques and non-opioid analgesics to achieve adequate peri-delivery pain control • Mode of delivery should be based on obstetrical indicators and decided by a patient and their obstetrician
<p>5. Pre-delivery medication management: Naltrexone</p> <p>a. During pregnancy and in anticipation of labor and delivery, should the naltrexone dose be split, continued, increased, reduced, or stopped?</p>	<ul style="list-style-type: none"> • Mode of delivery should be based on obstetrical indicators and decided by a patient and their obstetrician
<p>6. Should a history of OUD impact planned mode of delivery (cesarean versus vaginal delivery)?</p>	<ul style="list-style-type: none"> • Mode of delivery should be based on obstetrical indicators and decided by a patient and their obstetrician
<p>Labor Analgesia and Post-Vaginal Delivery Analgesia</p>	<p>Summary of Recommendations</p>
<p>1. Is there evidence for increased pain, analgesia dose requirement, or increased use of analgesia during</p>	<ul style="list-style-type: none"> • Patients with OUD, treated or untreated, may experience greater pain intensity and different pain qualities during labor and delivery • No evidence suggests that traditional analgesic regimens such as epidural labor analgesia are inadequate in this specific population

Prenatal Optimization	Summary of Recommendations
labor in pregnant patients with OUD, treated or untreated with MOUD?	<ul style="list-style-type: none"> Offer analgesia consistent with practices offered to all patients, and assess frequently to determine the analgesic efficacy, with a low threshold to increase or change dosing as needed Early neuraxial labor analgesia for people with OUD is recommended Shared decisions and patient-centered planning is necessary
2. Neuraxial Anesthesia and Analgesia a. Should early neuraxial analgesia be recommended for patients with OUD?	<ul style="list-style-type: none"> Neuraxial opioid adjuncts should be routinely used in laboring patients receiving buprenorphine, consistent with standard practice Data do not exist to support the purposeful adjustment of standard epidural formulations, but clinicians may elect to take advantage of the pharmacokinetic benefits offered by sufentanil, hydromorphone, or fentanyl Initiate standard low-concentration epidural local anesthetic solutions, with lipophilic opioids, for neuraxial labor analgesia If inadequate and if concordant with individual patient OUD treatment goals, additional epidural opioids (e.g., epidural fentanyl 100 mcg bolus or increasing fentanyl in epidural solution from 2 to 3 mcg/mL) can be used Routinely omitting opioids from epidural solutions is not recommended unless removal is deemed higher priority within an individual patient's OUD treatment goals Other non-opioid adjuncts can be considered in those cases Shared decision making should be employed regarding removal of neuraxial opioids, as epidural opioid exposure may have implications for postpartum care in some cases (see section on Urine Toxicology testing)
c. Should the concentration of the local anesthetic be increased?	<ul style="list-style-type: none"> Initiate standard low-concentration labor epidural solutions If labor analgesia inadequate, then higher concentration solutions can be substituted To minimize the potential influence of implicit bias in suboptimal pain management, use standard practice for diagnosing and treating breakthrough labor pain
d. Should non-opioid adjuncts be added to the epidural solution (e.g., clonidine, epinephrine, dexmedetomidine, neostigmine)?	<ul style="list-style-type: none"> Non-opioid neuraxial adjuncts (preservative free) may be used when patients desire strict opioid avoidance or the analgesic efficacy of neuraxial opioid is deemed insufficient, and after excluding failed epidural catheter Epidural clonidine may be given as an epidural bolus for initiation of labor analgesia (50-100mcg), for management of breakthrough pain, or added to the epidural solution (1-2mcg/mL) if epidural local anesthetic boluses and local anesthetic or opioid adjustments have failed to provide adequate analgesia Neuraxial dexmedetomidine should follow typical clinical applications Due to the potential increased risk of sedation in this patient population, sedation and respiratory depression monitoring (e.g., sedation scores, respiratory rate monitoring, continuous pulse oximetry), should be applied, if not already utilized in institutional protocols Combining alpha2-agonist agents (e.g., epinephrine, clonidine, dexmedetomidine) is not recommended
3. If the pregnant person with OUD is not a candidate for neuraxial labor analgesia, is there a role for the following:	<ul style="list-style-type: none"> OUD is not an absolute contraindication to receiving nitrous oxide labor analgesia Follow similar indications as patients without OUD Use sedation and respiratory depression monitoring (e.g., sedation scores, respiratory rate monitoring, continuous pulse oximetry) if not already utilized in institutional standard nitrous oxide protocols
b. Intravenous (IV) Opioid PCA	<ul style="list-style-type: none"> Opioid IV PCA (e.g., fentanyl, remifentanyl, sufentanil) for labor analgesia in patients with OUD is an individualized decision that must be balanced against risks for return to use vs. suffering from poorly managed pain Sufentanil may be a preferred systemic opioid supplement for acute pain in patients receiving buprenorphine therapy Should opioid IV PCA be used, given expected higher opioid dose requirements in people with OUD, maximum opioid limits should be adjusted, and sedation and respiratory depression monitoring (e.g., sedation scores, respiratory rate monitoring, continuous pulse oximetry) should be considered if not already utilized in standard institutional IV PCA protocols
c. Ketamine	<ul style="list-style-type: none"> Usefulness and effectiveness of routine use of ketamine for labor analgesia for patients with OUD is unknown and not recommended
d. Other adjuncts	<ul style="list-style-type: none"> Non-opioid analgesia for labor analgesia in patients with OUD should follow similar indications and applications as those without OUD
4. Treatment of post-vaginal delivery pain a. Should non-steroidal anti-inflammatory drugs (NSAID) and acetaminophen be used?	<ul style="list-style-type: none"> Absent any contraindication, NSAIDs and acetaminophen should be administered on a set schedule for analgesia following vaginal delivery Acetaminophen dose adjustments or caution may be required in patients with comorbid liver disease and impaired hepatic function Acetaminophen-opioid combination medications should be avoided to reduce risk for hepatotoxicity with additional acetaminophen dosing

Prenatal Optimization	Summary of Recommendations
<p>b. If the patient has a high-order vaginal laceration, should long-acting opioids be administered epidurally? If so, what doses are recommended?</p> <p>c. Is there a role for the routine use of oral opioids in hospital or at discharge?</p>	<ul style="list-style-type: none"> • Epidural opioids (e.g. morphine 3mg) may be considered, but there is limited data supporting its safety or efficacy • Patients should be educated on risks and benefits of opioid exposure as part of multimodal and tailored analgesic strategies • Should short courses of opioid analgesia be required upon discharge, then short interval outpatient follow-up is prudent
<p>d. What is the role for other adjuvants for the treatment of post-vaginal delivery pain?</p>	<ul style="list-style-type: none"> • Oral opioids should not be used routinely following vaginal delivery • The decision to use opioids for pain after vaginal delivery must be individualized with the patient, their treatment provider, and post-discharge primary care team • Rarely, opioids may be used with caution in patients with severe pain following vaginal delivery that does not respond to NSAIDs, acetaminophen or other analgesic modalities • If used, low-potency, non-parenteral formulations of opioids should be dispensed for a very short duration (e.g., 3-day supply) with short outpatient interval follow-up
<p>e. Should MOUD (methadone, buprenorphine) dose be adjusted intrapartum or postpartum for analgesic benefits?</p>	<ul style="list-style-type: none"> • Topical local anesthetics, ice packs for perineal pain, and heating pads for uterine cramping should be used
<p>5. Withdrawal and Toxicity (“Overdose”)</p> <p>a. If a patient with OUD experiences withdrawal during labor, how should it be treated?</p>	<ul style="list-style-type: none"> • Ideally beginning in the prenatal period, it may be beneficial to administer the daily methadone dose every 6-8 hours, or to split the daily buprenorphine dose to every 6-8 hours • These dose adjustments are not effective substitutes for neuraxial labor analgesia
<p>b. If a pregnant person with OUD present with opioid toxicity (“overdose”), how should it be treated?</p>	<ul style="list-style-type: none"> • Maintain usual methadone or buprenorphine regimens in the peri-partum period • Treat acute withdrawal with standard therapies employed in non-pregnant patients • For patients with recent illicit opioid exposure, acute withdrawal may be potentially treated with opioids, titrated to effect, along with supportive care therapies • Collaborative with addiction medicine specialists for treatment in individual circumstances
<p>c. Can partial antagonists- e.g., nalbuphine, butorphanol—be used in patients receiving MOUD (e.g., how should opioid-induced intrapartum pruritus be managed in a laboring pregnant person receiving buprenorphine?)</p>	<ul style="list-style-type: none"> • Naloxone should be included in the management of clinically significant respiratory depression • The ideal dose for naloxone treatment is not known but may be as high as 2 mg in the setting of buprenorphine, and likely requires a continuous infusion (dose: two-thirds of initial effective naloxone bolus on an hourly basis, 0.25-6.25 mg/hour) • Partial agonists or antagonists should be avoided in the patients for both the treatment of pain and opioid-induced pruritus, due to risk for precipitating acute withdrawal • If opioid-induced pruritus occurs during labor, consider removing or reducing the dose of the opioid component of the epidural medication solution and treating with other pharmacological approaches, such as 5-HT₃ receptor antagonists • For patients with a history of severe neuraxial opioid-induced pruritus, consider initiating the block without neuraxial opioids
<p>6. Monitoring</p> <p>a. Do pregnant people with OUD require additional monitoring during and after labor?</p>	<ul style="list-style-type: none"> • Usual standards for and duration of monitoring can be applied • If the patient presents with acute opioid toxicity or has received medications that may increase the risk for respiratory depression due to interaction with opioids (e.g., high doses of systemic opioids, benzodiazepines, magnesium, or other sedating medications), additional monitoring for respiratory depression is indicated
<p>Post-Cesarean Delivery Analgesia</p> <p>1. Is there evidence for increased pain and analgesia intake after cesarean for pregnant people receiving medication for OUD including methadone, buprenorphine, and naltrexone?</p>	<p>Summary of Recommendations</p> <ul style="list-style-type: none"> • Patients with OUD may experience increased pain and opioid needs after cesarean delivery compared with patients without OUD • Multimodal analgesia care plans should integrate these considerations • Patients should be educated on risks and benefits of opioid exposure as part of multimodal and tailored analgesic strategies • Should short courses of opioid analgesia be required upon discharge, then short interval outpatient follow-up is prudent
<p>2. Anesthesia for Cesarean Delivery</p> <p>a. Should the usual dose of neuraxial opioids be increased, decreased or should they be omitted?</p>	<ul style="list-style-type: none"> • Neuraxial anesthesia is recommended over general anesthesia for cesarean delivery when possible • Neuraxial opioids (including fentanyl) or morphine should neither be omitted nor dose reduced • No data are available to inform routinely using neuraxial hydromorphone or increasing neuraxial fentanyl or morphine dose in patients with OUD
<p>b. Should non-opioid adjuvants be added to the neuraxial anesthetic including clonidine, epinephrine, dexmedetomidine or neostigmine?</p>	<ul style="list-style-type: none"> • Limited evidence to support or refute routinely using non-opioid neuraxial adjuvants including clonidine, epinephrine, dexmedetomidine, or neostigmine, for post-cesarean delivery analgesia in patients with OUD • If used, side effects including respiratory depression, sedation, and nausea must be monitored

Prenatal Optimization	Summary of Recommendations
<p>3. Post-Cesarean pain management</p> <p>a. What is the role for continuing neuraxial analgesia into the postpartum period?</p>	<ul style="list-style-type: none"> • Intrathecal epinephrine might be proposed to increase the duration of sensory block during cesarean delivery • Neuraxial neostigmine for post-cesarean analgesia remains controversial and side effects (severe nausea, vomiting) may limit its use • Epidural analgesia may be continued 12-48 hours after cesarean delivery in patients with OUD • Its use must be balanced with overall goals for opioid avoidance, early ambulation, newborn care, other ERAC goals, and appropriate nursing support • Use shared decision making • If abdominal wall blocks were not performed, it may be reasonable to continue epidural local anesthetics for patients with OUD after cesarean delivery
<p>b. Should NSAIDs and acetaminophen be used after cesarean delivery?</p>	<ul style="list-style-type: none"> • Both SOAP and ACOG recommend NSAIDs and acetaminophen as part of multimodal analgesia after cesarean delivery, in the absence of contraindications • Use scheduled NSAIDs with acetaminophen for post-cesarean pain management due to the well-established opioid sparing effects • Ketorolac (intravenous) should be scheduled for 24-48 hours followed by a transition to oral ibuprofen after cesarean delivery
<p>c. Are changes to MOUD required to enhance analgesia after cesarean delivery?</p>	<ul style="list-style-type: none"> • Maintain methadone the same prenatal dose throughout the postpartum period • Buprenorphine has an analgesia ceiling effect (24-32 mg/day) beyond which greater pain control is not achieved • Splitting the daily buprenorphine dose to 3-4 daily doses may optimize analgesia effects for the first few post-cesarean days • For inpatients requiring high doses of systemic opioids, develop a plan early for tapering prior to discharge • Short interval follow-up upon discharge may be prudent, especially when high doses of systemic opioids are used in the treatment of post-cesarean pain
<p>d. Is there a role for the routine use of oral or intravenous, or transdermal opioids in the hospital or at discharge? Are there special considerations regarding the type, dose, and quantity?</p>	<ul style="list-style-type: none"> • The need, type, dose, and quantity of other analgesics for postpartum pain in patients with OUD depends on specific MOUD and treatment goals • The decision to use or not use parenteral opioids for pain must be made on an individual basis and consider individual treatment goals, and ideally should be discussed prior to the onset of pain (see: Prenatal Optimization). • If used, high doses of oral opioids may be necessary, short-term parenteral opioids may be necessary for severe pain.
<p>e. What is the role of other oral or systemic adjuvants for post-cesarean analgesia?</p> <p><i>Ketamine</i></p> <p><i>Gabapentin</i></p> <p><i>Clonidine</i></p> <p><i>Dexamethasone</i></p>	<ul style="list-style-type: none"> • There is limited, low-level evidence supporting analgesic efficacy for low-dose ketamine infusion for up to 24 hours post-cesarean delivery for patients with OUD. There is currently limited data regarding ketamine safety in lactation. Individual and institutional considerations should guide decisions. • Routine use of gabapentin is not recommended for post-cesarean delivery for patients with OUD. • Clonidine may be proposed to patients with OUD for enhanced analgesia opioid-sparing effects but must be balanced with individual goals for sedation avoidance, early ambulation, and dynamics with newborn care. If used, monitor side effects, respiratory depression, and sedation. • Routine use of a single dose of intravenous dexamethasone is not recommended as part of multimodal analgesia for patients with OUD undergoing cesarean delivery. Its use should be considered on an individual basis.
<p>f. What is the role for regional anesthesia options such as transversus abdominis plane (TAP), erector spinae plane (ESP), and quadratus lumborum (QLB) blocks, or continuous wound infiltration (CWI)? Are any of these options more effective than others?</p>	<ul style="list-style-type: none"> • Abdominal wall blocks may offer analgesia and opioid-sparing benefits for patients with OUD • Should be performed by practitioners familiar with these techniques • These blocks can be routinely used in practices that do not support post-cesarean epidural analgesia
<p>g. What is the role for psychotherapeutic or behavioral interventions (e.g., CBT) or complementary and alternative therapies to address intra- and post-cesarean pain?</p>	<ul style="list-style-type: none"> • Music therapy, cognitive-behavioral therapy and supportive psychotherapy may be used as adjuncts to multimodal analgesia, especially in cases where anxiety predominates and affects pain control
<p>4. Management of post-operative neuraxial opioid-induced side effects and complications in the patient receiving buprenorphine</p> <p>a. How should post-operative pruritus be managed?</p>	<ul style="list-style-type: none"> • Mixed antagonists and agonists (e.g., nalbuphine or butorphanol) or pure antagonists (e.g., naloxone) for pruritus, should be completely avoided in patients receiving MOUD due to risks for precipitating withdrawal
<p>b. How should post-operative respiratory depression be managed?</p>	<ul style="list-style-type: none"> • After cesarean delivery, naloxone should be included in the management of clinically significant respiratory depression in patients with OUD treated with buprenorphine or methadone

<i>Prenatal Optimization</i>	Summary of Recommendations
	<ul style="list-style-type: none"> • Ideal dose for naloxone is not known but may be as high as 2 mg in the setting of buprenorphine, and likely requires a continuous infusion (dose: two-thirds of initial effective naloxone bolus on an hourly basis, 0.25-6.25 mg/hour)
4. Monitoring a. Do patients with OUD require additional monitoring during or after cesarean delivery?	<ul style="list-style-type: none"> • Monitoring should be per the SOAP guidelines, stratified to the higher risk category after using neuraxial morphine (i.e., respiratory rate and sedation assessments q1h for the first 12h; q2h for 12-24h thereafter, and consider additional monitoring modalities such as pulse oximetry, capnography as judged indicated)

OUD, opioid use disorder; MOUD, medication for opioid use disorder; ACOG, American College of Obstetricians and Gynecologists; mcg, micrograms; mg, milligrams; mL, milliliters; IV, intravenous; PCA, patient controlled analgesia; NSAID, nonsteroidal anti-inflammatory drug; ERAC, enhanced recovery after cesarean; SOAP, Society of Obstetric Anesthesia and Perinatology; TAP, transversus abdominis plane; QLB, quadratus lumborum block; ESP, erector spinae block; CWI, continuous wound infiltration; CBT, cognitive behavioral therapy