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SMFM Statement

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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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Pain management in pregnant and postpartum people with an opioid use disorder requires a balance among the risks associated with opioid tolerance, including withdrawal or return to opioid use, considerations around the 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 from the Society for Obstetric Anesthesia and Perinatology, the Society for Maternal-Fetal Medicine, and the American Society of Regional Anesthesia and Pain Medicine provides a framework for pain management in obstetrical patients with opioid use disorder. 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 postvaginal delivery pain management, and postcesarean delivery pain management. Topics include a discussion of nonpharmacologic and pharmacologic options for pain management, medication management for opioid use disorder (eg, buprenorphine, methadone), considerations regarding urine drug testing and other social aspects of care for maternal-infant dyads, and a review of current practices. The authors provide evidence-based recommendations to optimize pain management while reducing risks and the complications associated with opioid use disorder in the peripartum period. Ultimately, this multidisciplinary consensus statement provides practical and concise clinical guidance to optimize pain management for people with opioid use disorder in the context of pregnancy to improve maternal and perinatal outcomes.

Key words: adjuncts, analgesia, buprenorphine, cesarean delivery, medication for opioid use disorder, methadone, opioid use disorder, opioids, pain management, peripartum, prenatal, substance use disorder, urine toxicology, vaginal delivery

Introduction

Pain management in peripartum people with opioid use disorder (OUD) can be a complex and challenging issue, often with 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 that takes into consideration the patient's history of opioid use, pain management, and the potential impact on the fetus. Narrative review articles[1] and clinical guidelines for nonobstetrical perioperative opioid use and OUD in pregnancy,[2] as well as postpartum pain management,[3] 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 that is focused on peripartum pain management in people with OUD in key areas, namely (1) optimal management of medication for OUD (MOUD) in the peripartum period; (2) management

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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, namely prenatal optimization, labor analgesia and postvaginal delivery analgesia, and cesarean anesthesia and postcesarean delivery analgesia. Levels of evidence are presented with each recommendation, further highlighting specific needs for which 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), the American Society of Regional Anesthesia and Pain Medicine (ASRA), and the 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 2022.[4] 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 for this review yielded a list of 994 publications that was reduced to 84 full-text publications.[4] 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 (ie, opioid agonists, partial agonists, and antagonists), labor analgesia and postvaginal delivery analgesia, and postcesarean delivery analgesia for peripartum people with OUD were assessed in detail based on the studies identified in the recently published systematic scoping review.[4] 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 OUD.[4] These clinically relevant management questions are summarized in the Table.[4] Three smaller workgroups were assembled around the 3 phases of care in focus, namely prenatal optimization, labor analgesia and postvaginal delivery analgesia, and postcesarean delivery analgesia. These workgroups comprised expertise from anesthesiology, obstetrics, acute and chronic pain medicine, and addiction medicine. A steering committee of experts consisting of obstetrical anesthesiologists (G.L., B.C., R.L., R.B.G., and B.T.B.), obstetricians (S.O.), and addiction medicine specialists (M.T.) oversaw the activities of the 3 groups and reviewed all clinical recommendations generated for consistency. Areas of inconsistency were referred to the workgroups 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. In case evidence was lacking and the experts judged it appropriate to apply available evidence from pregnant people without OUD or from nonpregnant 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 lists specific evidence-based recommendations. The American College of Cardiology (ACC) and American Heart Association (AHA) Clinical Practice Guideline Recommendation Classification Systems[5] were used to objectively evaluate each of the element's level of evidence. The Table summarizes the 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 nonstigmatizing terminology use disorder is currently recommended and consistent with the Diagnostic and Statistical Manual of Mental Disorders 5.

Results and discussion

Prenatal optimization

1. **What medical comorbidities 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 comorbidities that may influence peripartum pain management, such as depression and anxiety.[6] One study[7] found that nearly one-third of pregnant people enrolled in an SUD treatment program screened positive for moderate to severe depression and almost half reported symptoms of postpartum depression at 6 weeks after delivery.[8] 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% met the criteria for generalized anxiety disorder, and 27.9% met the panic disorder criteria.[9] A retrospective study reported that

TABLE
Summarized consensus recommendations for key clinical questions

Prenatal optimization	Summary of recommendations
1. What medical comorbidities are associated with OUD that can affect peripartum pain management?	• Psychiatric comorbidities; may increase risk for more severe pain and analgesic requirements. • Screening for psychiatric comorbidities should occur in accordance with the ACOG recommendations. • Referral for multidisciplinary care may be needed for care plan optimization
a. How can these medical comorbidities be managed to improve peridelivery pain outcomes?	
b. What other SUDs are associated with OUD that can affect peripartum pain management?	• Other SUDs are common among people with OUD. • Screen for and discuss co-occurring SUD in accordance with the ACOG recommendations. • Offer nicotine replacement and cessation services for any SUD.
2. Prenatal anesthesiology consultation a. Should all pregnant people with OUD have a pre-delivery anesthesiology consult?	• 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. • An antenatal anesthesia consultation is recommended for the following goals: ○ coordinate care with other health professionals for pain management ○ establish a trusting relationship in a nonjudgmental environment ○ address fears, concerns, and goals regarding opioid analgesia ○ establish a clear pain management plan.
b. What should be evaluated and discussed in the anesthesia consult?	
c. What key differences between buprenorphine and methadone should anesthesia providers be aware of during anesthesia consultation and plan formulation?	• Methadone is a full mu-receptor agonist, has a long half-life (shortens in pregnancy, therefore requires titration during pregnancy, particularly in the third trimester), is associated with QTc prolongation (dose dependent), and requires prescribing and administration through a certified opioid treatment program. • Buprenorphine is a partial mu-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.
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?	• Methadone should be continued in the peridelivery period. • Higher or more frequent dosing may be needed as the pregnancy progresses, particularly in the third trimester. • Dividing the total daily dose over shorter dosing intervals (6–8 h) may maximize the analgesic benefits in the third trimester. • Rapid methadone titration is not possible. • Consider drug interactions because of dose-dependent QTc interval prolongation. • Monitoring QTc is recommended upon methadone initiation and when increasing dose above 120 mg/day.
4. Predelivery medication management: buprenorphine a. During pregnancy and in anticipation of labor and delivery, should the buprenorphine dose be split, continued, increased, reduced, or stopped?	• Buprenorphine should be continued in the peridelivery period. • Higher or more frequent dosing may be needed as the pregnancy progresses, particularly in the third trimester. • Splitting the daily dose into dosing every 6–8 h may potentially improve withdrawal symptoms, in addition to optimizing analgesic benefits.
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?	• Stop oral naltrexone at least 72 before labor and delivery or cesarean delivery. • Naltrexone depot formulations last almost 6 wk, and therefore it may not be feasible to stop naltrexone treatment before planned delivery. • Use a combination of neuraxial and regional anesthesia techniques and nonopioid analgesics to achieve adequate peridelivery pain control

Lim. Peripartum pain management for pregnant people with opioid use disorder. Am J Obstet Gynecol 2024. *(continued)*

TABLE

Summarized consensus recommendations for key clinical questions *(continued)*

Prenatal optimization	Summary of recommendations
6. Should a history of OUD impact the planned mode of delivery (cesarean vs vaginal delivery)?	• The mode of delivery should be based on obstetrical indicators and decided by a patient and their obstetrician.
Labor analgesia and postvaginal delivery analgesia	**Summary of recommendations**
1. Is there evidence for increased pain, analgesia dose requirement, or increased use of analgesia during labor in pregnant patients with OUD, treated with MOUD or untreated?	• Patients with OUD, treated or untreated, may experience a 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. • 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 the dosing as needed.
2. Neuraxial anesthesia and analgesia a. Should early neuraxial analgesia be recommended for patients with OUD?	• Early neuraxial labor analgesia for people with OUD is recommended. • Shared decisions and patient-centered planning is necessary.
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?	• Neuraxial opioid adjuncts should be routinely used in laboring patients who are 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 local epidural anesthetic solutions with lipophilic opioids for neuraxial labor analgesia. • If inadequate and if concordant with individual patient OUD treatment goals, additional epidural opioids (eg, epidural 100 μg fentanyl bolus or increasing fentanyl in epidural solution from 2 to 3 μg/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 nonopioid adjuncts can be considered in those cases. • Shared decision-making should be employed regarding the removal of neuraxial opioids, because 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?	• Initiate standard low-concentration labor epidural solutions. • If labor analgesia is inadequate, then higher concentration solutions can be used. • To minimize the potential influence of implicit bias in suboptimal pain management, use standard practice for diagnosing and treating breakthrough labor pain.
d. Should nonopioid adjuvants be added to the epidural solution (eg, clonidine, epinephrine, dexmedetomidine, neostigmine)?	• Nonopioid neuraxial adjuncts (preservative free) may be used when patients desire strict opioid avoidance or if 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 the initiation of labor analgesia (50–100 μg), for the management of breakthrough pain, or added to the epidural solution (1–2 μg/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. • Because of the potential increased risk of sedation in this patient population, sedation and respiratory depression monitoring (eg, sedation scores, respiratory rate monitoring, continuous pulse oximetry), should be applied, if not already incorporated in institutional protocols. • Combining alpha2-agonist agents (eg, epinephrine, clonidine, dexmedetomidine) is not recommended.

Lim. Peripartum pain management for pregnant people with opioid use disorder. Am J Obstet Gynecol 2024. *(continued)*

TABLE
Summarized consensus recommendations for key clinical questions *(continued)*

Labor analgesia and postvaginal delivery analgesia	Summary of recommendations
3. If the pregnant person with OUD is not a candidate for neuraxial labor analgesia, is there a role for the following: a. Nitrous oxide	• 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 (eg, sedation scores, respiratory rate monitoring, continuous pulse oximetry) if not already used in institutional standard nitrous oxide protocols.
b. IV opioid PCA	• Opioid IV PCA (eg, fentanyl, remifentanil, sufentanil) for labor analgesia in patients with OUD is an individualized decision that must be balanced against the risks for return to use and suffering from poorly managed pain. • Sufentanil may be a preferred systemic opioid supplement for acute pain in patients who are receiving buprenorphine therapy. • Should opioid IV PCA be used, given the expected higher opioid dose requirements in people with OUD, maximum opioid limits should be adjusted, and sedation and respiratory depression monitoring (eg, sedation scores, respiratory rate monitoring, continuous pulse oximetry) should be considered if not already use in standard institutional IV PCA protocols
c. Ketamine	• Usefulness and effectiveness of routine use of ketamine for labor analgesia for patients with OUD is unknown and not recommended.
d. Other adjuvants	• Nonopioid analgesia for labor analgesia in patients with OUD should follow similar indications and applications as those without OUD.
4. Treatment of postvaginal delivery pain a. Should NSAID and acetaminophen be used?	• 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.
b. If the patient has a high-order vaginal laceration, should long-acting opioids be administered epidurally? If so, what doses are recommended?	• Epidural opioids (eg, 3 mg morphine) may be considered, but there is limited data supporting its safety or efficacy. • Patients should be educated on the 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.
c. Is there a role for the routine use of oral opioids in hospital or at discharge?	• 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 postdischarge 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 (eg, 3-day supply) with short outpatient interval follow-up.
d. What is the role for other adjuvants in the treatment of postvaginal delivery pain?	• Topical local anesthetics, ice packs for perineal pain, and heating pads for uterine cramping should be used.
e. Should MOUD (methadone, buprenorphine) dose be adjusted intrapartum or postpartum for analgesic benefits?	• Ideally, beginning in the prenatal period, it may be beneficial to administer the daily methadone dose every 6–8 h or to split the daily buprenorphine dose into 6- to 8-hour doses. • These dose adjustments are not effective substitutes for neuraxial labor analgesia.

Lim. Peripartum pain management for pregnant people with opioid use disorder. Am J Obstet Gynecol 2024. *(continued)*

TABLE

Summarized consensus recommendations for key clinical questions *(continued)*

Labor analgesia and postvaginal delivery analgesia	Summary of recommendations
5. Withdrawal and toxicity (overdose) a. If a patient with OUD experiences withdrawal during labor, how should it be treated?	• Maintain usual methadone or buprenorphine regimens in the peripartum period. • Treat acute withdrawal with standard therapies employed in nonpregnant 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.
b. If a pregnant person with OUD present with opioid toxicity (overdose), how should it be treated?	• 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).
c. Can partial antagonists—for example, nalbuphine or butorphanol—be used in patients who are receiving MOUD (eg, how should opioid-induced intrapartum pruritus be managed in a laboring pregnant person receiving buprenorphine?)?	• Partial agonists or antagonists should be avoided in the patients for both the treatment of pain and opioid-induced pruritus because of 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 pharmacologic 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.
6. Monitoring a. Do pregnant people with OUD require additional monitoring during and after labor?	• 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 because of interaction with the opioids (eg, high doses of systemic opioids, benzodiazepines, magnesium, or other sedating medications), additional monitoring for respiratory depression is indicated.
Postcesarean delivery analgesia	**Summary of recommendations**
1. Is there evidence for increased pain and analgesia intake after cesarean delivery for pregnant people who are receiving MOUD, including methadone, buprenorphine, and naltrexone?	• Patients with OUD may experience increased pain and opioid needs after cesarean delivery than patients without OUD. • Multimodal analgesia care plans should integrate these considerations. • Patients should be educated on the 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
2. Anesthesia for cesarean delivery a. Should the usual dose of neuraxial opioids be increased, decreased, or should they be omitted?	• Neuraxial anesthesia is recommended over general anesthesia for cesarean delivery when possible. • Neuraxial opioids, including fentanyl or morphine, should neither be omitted, nor should the dose be reduced. • No data are available to inform routinely using neuraxial hydromorphone or increasing neuraxial fentanyl or morphine dose in patients with OUD.
b. Should nonopioid adjuvants be added to the neuraxial anesthetic, including clonidine, epinephrine, dexmedetomidine, or neostigmine?	• Limited evidence to support or refute routinely using nonopioid neuraxial adjuvants, including clonidine, epinephrine, dexmedetomidine, or neostigmine, for postcesarean delivery analgesia in patients with OUD. • If used, side effects, including respiratory depression, sedation, and nausea, must be monitored. • Intrathecal epinephrine might be proposed to increase the duration of sensory block during cesarean delivery. • Neuraxial neostigmine for postcesarean delivery analgesia remains controversial and side effects (severe nausea, vomiting) may limit its use.

Lim. Peripartum pain management for pregnant people with opioid use disorder. Am J Obstet Gynecol 2024. *(continued)*

TABLE

Summarized consensus recommendations for key clinical questions *(continued)*

Postcesarean delivery analgesia	Summary of recommendations
3. Postcesarean delivery pain management a. What is the role for continuing neuraxial analgesia into the postpartum period?	• Epidural analgesia may be continued for 12–48 h after cesarean delivery in patients with OUD. • Its use must be balanced with the 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.
b. Should NSAIDs and acetaminophen be used after cesarean delivery?	• Both the 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 postcesarean delivery pain management because of the well-established opioid sparing effects. • Ketorolac (IV) should be scheduled for 24–48 h, followed by a transition to oral ibuprofen after cesarean delivery.
c. Are changes to MOUD required to enhance analgesia after cesarean delivery?	• Maintain methadone the same as the prenatal dose throughout the postpartum period. • Buprenorphine has an analgesia ceiling effect (24–32 mg/d) beyond which greater pain control is not achieved. • Splitting the daily buprenorphine dose into 3–4 daily doses may optimize analgesia effects for the first few postcesarean delivery days. • For in-hospital patients who require high doses of systemic opioids, develop a plan early for tapering before discharge. • Short interval follow-up upon discharge may be prudent, especially when high doses of systemic opioids are used in the treatment of postcesarean delivery pain.
d. Is there a role for the routine use of oral or IV or transdermal opioids in the hospital or at discharge? Are there special considerations regarding the type, dose, and quantity?	• The need, type, dose, and quantity of other analgesics for postpartum pain in patients with OUD depends on the specific MOUD and treatment goals. • The decision to use or not to use parenteral opioids for pain must be made on an individual basis and should take into consideration individual treatment goals and ideally should be discussed before the onset of pain (refer to the section on Prenatal optimization). • If used, high doses of oral opioids may be necessary; short-term parenteral opioids may be necessary for severe pain.
e. What is the role of other oral or systemic adjuvants for postcesarean delivery analgesia?Ketamine Gabapentin Clonidine Dexamethasone	• There is limited, low-level evidence that supports the analgesic efficacy for low-dose ketamine infusion for up to 24 h after 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 after cesarean delivery for patients with OUD. • Clonidine may be proposed to patients with OUD for its enhanced analgesia and 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 who are undergoing cesarean delivery. Its use should be considered on an individual basis.
f. What is the role for regional anesthesia options such as TAP, ESP, and QLB blocks or CWI? Are any of these options more effective than others?	• 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 poscesarean delivery epidural analgesia.

Lim. Peripartum pain management for pregnant people with opioid use disorder. Am J Obstet Gynecol 2024. *(continued)*

TABLE
Summarized consensus recommendations for key clinical questions *(continued)*

Postcesarean delivery analgesia	Summary of recommendations
g. What is the role for psychotherapeutic or behavioral interventions (eg, CBT) or complementary and alternative therapies to address intra- and post-cesarean delivery pain?	• Music therapy, CBT, and supportive psychotherapy may be used as adjuncts to multimodal analgesia, especially in cases in which anxiety predominates and affects pain control.
4. Management of postoperative neuraxial opioid-induced side effects and complications in the patient receiving buprenorphine a. How should postoperative pruritus be managed?	• Mixed antagonists and agonists (eg, nalbuphine or butorphanol) or pure antagonists (eg, naloxone) for pruritus, should be completely avoided in patients who are receiving MOUD because of risks for precipitating withdrawal.
b. How should postoperative respiratory depression be managed?	• After cesarean delivery, naloxone should be included in the management of clinically significant respiratory depression in patients with OUD treated with buprenorphine or methadone. • The ideal dose for naloxone is not known but may be as high as 2 mg in the setting of buprenorphine and likely requires 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?	• Monitoring should be per the SOAP guidelines, stratified to the higher risk category after using neuraxial morphine (ie, respiratory rate and sedation assessments once per hour for the first 12 h; every 2 hours for 12−24 h thereafter, and consider additional monitoring modalities such as pulse oximetry and capnography as judged indicated)

5-HT3, 5-hydroxytryptamine 3; *ACOG*, American College of Obstetricians and Gynecologists; *CBT*, cognitive behavioral therapy; *CWI*, continuous wound infiltration; ERAC, enhanced recovery after cesarean; *ESP*, erector spinae block; *MOUD*, medication for opioid use disorder; *NSAID*, nonsteroidal anti-inflammatory drug; *OUD*, opioid use disorder; *PCA*, patient controlled analgesia; *QLB*, quadratus lumborum block; *SOAP*, Society of Obstetric Anesthesia and Perinatology; *TAP*, transversus abdominis plane; *IV*, intravenous.

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pregnant people with OUD were 2.7 times (prevalence ratio) more likely to have depression (95% confidence interval [CI], 2.5−3.2; $P<.0001$) and 2.7 times (95% CI, 2.4−3.1; $P<.0001$) more likely to have anxiety. In general, psychiatric comorbidities are predictors of more severe postoperative pain and analgesic requirements. For example, 1 study[10] found that pre-operative anxiety significantly increased the risk for more severe pain after cesarean delivery (odds ratio [OR], 1.60; 95% CI, 1.16−2.20; $P=.004$). Similarly, another study[11] found that the State Trait Anxiety Inventory, a validated questionnaire that evaluates state and trait anxiety, predicted the total analgesic needs after cesarean delivery ($R^2=0.22$; $P<.01$). 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 that reported on 48 studies.[12]

a. **How can these medical comorbidities be managed to improve peridelivery pain outcomes?**

Summary of the evidence: Although several reports have advocated for referral to psychology, for example, for cognitive behavioral treatment and psychiatry for simultaneous treatment of these psychiatric comorbidities,[13,14] there are no studies that have evaluated the outcome associated with such interventions specifically for pain outcomes.

Clinical recommendation: Pregnant people with OUD frequently have psychiatric comorbidities that may increase their risk for more severe pain and their analgesic requirements in the peripartum period (Level B-NR). Screening for psychiatric comorbidities should be performed during pregnancy in accordance with the American College for Obstetricians and Gynecologists (ACOG) recommendations for all prenatal people[15] (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 for the use of other substances, including tobacco, cannabis, and alcohol.[2,16] One study[16] compared patients with OUD who were screened for opioid agonist treatment with pregnant people without SUD and found that patients with OUD were 4 times more likely to smoke than pregnant patients without SUD (88% vs 22%; $P<.01$). In a retrospective analysis of more than 120,000 deliveries in

Maine,[8] pregnant people with OUD had a 16.8 times higher prevalence ratio (PR) for other drug abuse or dependence than pregnant people without OUD (95% CI, 13.4–20.9; $P<.0001$). Notably, the OR for cannabis use was 5.2 (95% CI, 4.6–5.9; $P<.0001$), 6 (95% CI, 5.9–6.2; $P<.0001$) for nicotine use, and 8.5 (95% CI, 5.8–12.5; $P<.0001$) for alcohol use disorder.

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 requirements.[17] A retrospective chart review that included 1899 patients without OUD who underwent cesarean delivery found that tobacco use was associated with an increased likelihood of experiencing severe postoperative pain (OR, 2.52; 95% CI, 1.17–5.44).[18] One study[19] 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 that included 9038 people who underwent vaginal delivery found that smoking increased the need for postpartum opioid analgesia (OR, 1.48; 95% CI, 1.24–1.77).[20]

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

Clinical recommendation: The 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 the ACOG recommendations[21] (Class I, Level B-NR).

2. **Prenatal anesthesiology consultation**
   a. **Should all pregnant people with opioid use disorder 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 for obstetrical morbidity and mortality associated with OUD, the experts considered that an antenatal consult with the anesthesiology department may be useful for this population, because it may enable early identification of these potential problems and counseling regarding the 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 the pain experiences associated with vaginal and cesarean deliveries. Evidence regarding the pain experience and analgesia in these contexts suggests that there is a possibility of worse pain and increased analgesia requirements among parturients who receive MOUD, and setting expectations and discussing options are key. A retrospective review (n=7449; 1.1% with OUD) reported that pregnant people who used chronic opioids had higher rates of epidural labor analgesia use (47% vs 38%) and inadequate labor analgesia (requiring more supplemental boluses) than controls, as well as high rates (74%) of inadequate postcesarean delivery analgesia.[22] However, this study was limited in that the analgesia was delivered by manual boluses from an obstetrical provider. Such practices may reflect clinician bias and may not reflect modern, standardized treatment strategies that rely on infusion pump–driven, programmed, intermittent epidural boluses and patient-controlled epidural analgesia.

The ACOG recommends that MOUD with methadone or buprenorphine should be initiated or continued for pregnant people with OUD.[2] 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, because withdrawal may be associated with higher rates of return to opioid use and worse outcomes.[23,24] In addition, MOUD with opioid agonists may improve obstetrical outcomes by improving adherence to prenatal care.[24] Methadone requires administration through an opioid treatment program (OTP) that is certified by the Service Abuse and Mental Health Services Administration, which could be a barrier to treatment for some pregnant patients.[25]

Pregnant people who received methadone (n=68) experienced more pain after vaginal delivery than controls and used 70% more opioid analgesia in the postpartum period.[26] Similar findings were observed in a cohort of 63 pregnant people who received buprenorphine as MOUD.[27] Notably, a retrospective cohort study that compared patients who received methadone as MOUD with those who received buprenorphine found no significant differences in the postcesarean delivery analgesic use between the 2 groups.[28] Therefore, it seems that patients who receive MOUD may experience worse peripartum pain than controls, but there may be no differences in the pain experienced or analgesia needs among patients who receive either buprenorphine or methadone as MOUD.

Chronic exposure to opioids during pregnancy may also lead to opioid tolerance and opioid-induced hyperalgesia, which, in turn, can make peripartum analgesia challenging.[29,30] There are no data or direct comparative evidence regarding the differential effects of MOUD agents for pain and analgesia experiences in labor and delivery.

Pregnant people who are recovering from OUD and who are currently abstinent may be concerned about returning to use and may desire to strictly avoid 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.[31]

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 an m-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 m-opioid receptor agonist, thereby making respiratory depression less likely, it is associated with less QTc interval prolongation than methadone, and can be prescribed on an outpatient basis without daily visits.[32,23,33] Limited trial data suggest that buprenorphine is associated with reduced morphine requirement, shorter hospital stay, and shorter treatment duration of NOWS. Buprenorphine and methadone are not different with respect to the absolute NOWS rates; when NOWS occurs, buprenorphine-exposed neonates have reduced severity and duration of withdrawal. A large observational study that used administrative data found that pregnant people who received buprenorphine had higher rates of psychiatric and medical comorbidities and higher rates of prescription fills for treatment of these conditions but did not have higher rates of opioid prescription fills during pregnancy when compared with patients who received methadone.[34] Additional comparison data for these agents are found in Supplemental Material 1.

Clinical recommendation: Pregnant people with OUD or those who are receiving chronic opioid agonist therapy may experience more pain and have higher analgesic requirements during and after delivery (Level B-NR). An antenatal anesthesia consultation is recommended to coordinate care with other health professionals as it relates to pain management to establish a trusting, nonjudgmental 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 nonpregnant patients, once daily dosing of methadone is usually sufficient to prevent withdrawal. However, because of physiologic and pharmacokinetic changes during pregnancy, in particular, increases in CYP3A4 expression, methadone metabolism is accelerated as pregnancy progresses.[35] In fact, 1 study found that the half-life of methadone in pregnancy may be as short as 8.1 hours in the third trimester.[36] Therefore, dose adjustments and more frequent dosing (eg, every 6–8 hours) may be indicated for pregnant people. However, dose adjustments should be made on an individual clinical basis (considering patient priorities and managing addiction medicine opinions), because these are not always required.[23,37]

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 options.[2] 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, for example, every 6 to 8 hours, 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 peridelivery 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 (eg, every 6–8 hours) 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 the dose above 120 mg/day (Class I, Level C-LD).

4. **Predelivery 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 necessary.[40] Limited

clinical pharmacokinetic data suggest that at doses ranging from 4 to 12 mg twice daily during pregnancy, the median plasma concentrations fall to below the ranges required to prevent withdrawal symptoms within 4 hours of the last buprenorphine dose.[41,42]

Splitting the buprenorphine daily dose into 3- or 4-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 to 4 times daily.[40] It is suggested that dosing every 6 to 8 hours may maximize the analgesic effect of buprenorphine,[31,43] however, this is based on expert opinion.

Buprenorphine has high affinity for but low intrinsic activity at the m-opioid receptor; buprenorphine displaces other opioids from these receptors easily, even at low doses. High doses of full m-opioid agonists are required to displace buprenorphine from the receptors. These pharmacologic properties could make the treatment of acute peridelivery pain challenging. Patients who are receiving buprenorphine have higher peridelivery 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 and those maintained on buprenorphine in terms of postpartum pain outcomes (Supplemental Material 1).[28,23,44]

Clinical recommendation: Buprenorphine should be continued in the peridelivery 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 and should take into consideration patient priorities and addiction medicine management opinions (Class I, Level B-NR). Splitting the daily dose to every 6 to 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.[23] 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 to substitute its use with methadone or buprenorphine; however, the decision to continue use of naltrexone should be weighed against the lack of research on the risks associated with its use in pregnancy.[45] Naltrexone is a nonselective 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 a placebo at maintaining abstinence.[46] Data on the use of naltrexone during pregnancy is limited (Supplemental Material 1). Naltrexone use may impair adequate analgesia during labor, delivery, and the postpartum period. It is recommended to stop oral naltrexone 72 hours before planned surgical procedures.[47] 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 hospitalization,[48] such as labor and delivery. There are no published data on peridelivery pain management in pregnant people who are receiving naltrexone, however, opioid analgesia is expected to be less effective in these circumstances. Case studies of patients who received naltrexone and who underwent nonobstetrical procedures reported inadequate postoperative pain control despite high doses of opioids.[49]

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, because of the duration of effects that last almost 6 weeks, it may not be feasible to stop its use before planned delivery (Class IIa, Level B-NR). Clinicians should rely on a combination of neuraxial and regional anesthesia techniques and nonopioid analgesics to achieve adequate peridelivery pain control (Class IIb, Level C-EO).

6. **Should a history of opioid use disorder impact the planned mode of delivery (cesarean vs vaginal delivery)?**

Summary of evidence: There are no data on whether OUD in pregnancy should impact the choice between planned cesarean delivery and a trial of labor. A joint document produced by the ACOG, the SMFM, and the American Society of Addiction Medicine does not comment on the recommended mode of delivery.[50] In clinical practice, a cesarean delivery is generally reserved for obstetrical indications rather than for 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 use when compared with discontinuing MOUD.[51]

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

Labor analgesia and postvaginal delivery analgesia

1. **Is there evidence for increased pain, analgesia dose requirement, or increased use of analgesia during labor in pregnant**

patients with opioid use disorder, untreated or treated with medication for opioid use disorder?

Summary of evidence: MOUD may increase the perception of pain because of opioid-induced hyperalgesia and decreased production of endogenous opioid peptides.[52,53] These factors are suggested to contribute to an exaggerated intolerance of labor pain and inefficacy of traditional analgesic interventions. One prospective observational study (n=2610 reporting 44,522 unique pain ratings) found that patients with OUD were more likely to experience different pain types (affective, nociceptive or neuropathic), higher pain intensity, and increased postpartum opioid consumption than those without OUD.[54] Low-quality studies report conflicting results on intrapartum pain experiences, epidural labor analgesia use, and nonepidural analgesia use[26,27,55,56] (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) than 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 who are receiving MOUD should be offered analgesia consistent with the 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 for increasing or changing the dosing as needed. (Class I, Level B-NR).

2. **Neuraxial anesthesia and analgesia**
   a. **Should early neuraxial analgesia be recommended for patients with opioid use disorder?**

Summary of evidence: One conference proceeding described expert opinions that stated that for patients with OUD, neuraxial labor analgesia should be encouraged and received as early as possible during 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 that compared early vs later or typical maternal request timing for neuraxial labor analgesia in pregnant people with OUD. Early compared with later neuraxial labor analgesia placement does not increase or negatively impact the obstetrical outcomes in the general population.[57–59]

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 have been raised about the efficacy of neuraxial opioids with buprenorphine use because of its very high affinity for the mu-opioid receptor,[52,53,60] 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 in neuraxial labor analgesia formulations.[57,61] The addition of an opioid adjunct allows for adequate analgesia while using lower concentrations of local anesthetic, therefore leading to less motor block, hypotension, and a 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 study[27] explored the analgesic efficacy of a local anesthetic-opioid epidural formulation (0.0625% bupivacaine with 2 μg/mL fentanyl) in laboring patients who received buprenorphine in comparison with matched controls. The median pain scores were similar between groups (buprenorphine, 2; 0–3.8; control, 1.5; 0–4; P=.31). Buprenorphine-treated patients did not receive additional epidural supplemental doses for breakthrough pain or changes to infusion rates when compared with controls. This single study suggests that buprenorphine may not interfere with the efficacy of neuraxial opioids and that specific adjustments to the standard epidural formulations may not be necessary beyond the flexibility afforded by conventional patient-controlled epidural analgesia. The intentional selection of opioids with either a similar affinity for the mu-opioid receptor (sufentanil, hydromorphone) or a similar lipophilicity as buprenorphine (fentanyl) has been proposed to be a superior option for these patients.[62,63] Although the pharmacokinetic advantages of these medications are theoretical, current clinical effectiveness data are lacking and thus one full mu-opioid agonist cannot be conclusively recommended over another. Notably, no available trials exist to guide decisions on the superiority, noninferiority, or side effects of opioid and nonopioid 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 that examined different opioid doses in the labor epidural solution for 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 (eg, 100 μg epidural fentanyl bolus or increasing fentanyl in epidural solution from 2 to 3 μg/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 that require 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 high priority for OUD treatment goals, and other nonopioid 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 that examined different concentrations of local anesthetics in the epidural solution of laboring people with OUD. In patients without OUD, low concentrations of local anesthetics (eg, $<$0.1% bupivacaine) reduced assisted vaginal delivery, led to a shorter second stage of labor, produced less motor block, increased ambulation, and caused less urinary retention without higher pain scores when compared with higher local anesthetic concentrations.[64,65] Pregnant people with OUD perceive and experience clinician bias in the treatment of their pain,[66] 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 nonopioid adjuvants be added to the epidural solution (eg, clonidine, epinephrine, dexmedetomidine, neostigmine)?**

Summary of evidence: Alternative nonopioid adjuncts may be considered, which can help to minimize the local concentration requirements to reduce motor block, hypotension, and risk for assisted vaginal delivery while minimizing exposure to neuraxial opioids.[67–72] Neuraxial clonidine or dexmedetomidine (both alpha$_2$-agonists) provide similar analgesia effects as neuraxial fentanyl for labor epidural analgesia infusions[14] and may be an alternative to neuraxial opioids for pregnant people with OUD or patients who wish to avoid all opioids.

Clonidine, an alpha$_2$-agonist, is the most studied adjuvant for enhancement of neuraxial labor analgesia aside from neuraxial opioids. It carries a black box warning for obstetrical use because of concerns for hemodynamic instability, and so its use in this context is off label. An observational study examined the effects of epidural clonidine in 7 patients who received buprenorphine as MOUD with neuraxial labor analgesia for spontaneous vaginal delivery.[69] 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 that required management. Sedation and maternal bradycardia were not observed.

There are no high-quality trials that examined the role of systemic dexmedetomidine in laboring people with OUD. There are no available data regarding other nonopioid neuraxial adjuvants, such as epinephrine (alpha$_2$-agonist) or neostigmine (anticholinergic).

Clinical recommendation: Nonopioid neuraxial adjuncts may be used when pregnant people desire strict opioid avoidance or when 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 (50–100 μg), for the management of breakthrough pain, or as additive 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). Because of the potential increased risk for sedation in this population, sedation and respiratory depression monitoring (eg, sedation scores, respiratory rate monitoring, continuous pulse oximetry), should be incorporated if not already part of institutional protocols (Class I, Level C-EO). Combining alpha$_2$-agonist agents (eg, 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 opioid use disorder 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 that examined the role of nitrous oxide in laboring people with OUD. One study suggested that nitrous oxide is an analgesic option for this population,[73] because 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 an increased

risk for respiratory depression among pregnant people who are receiving systemic opioids or sedatives/hypnotics.[74,75]

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 for patients without OUD with consideration for sedation and respiratory depression monitoring (eg, sedation scores, respiratory rate monitoring, continuous pulse oximetry) if not already part of institutional standard nitrous oxide protocols (Class I, Level C-EO).

b. **Intravenous opioid patient-controlled analgesia**

Summary of evidence: Pregnant people with OUD are usually not included in clinical trials that examine intravenous patient-controlled analgesia (IV PCA) for labor analgesia. Therefore, there are no data on IV PCA use in laboring patients with OUD. Patients who are receiving chronic opioid agonists (eg, heroin or other illicit opioids, long-term opioids for chronic pain) or who are treated with MOUD (eg, methadone or buprenorphine, and naltrexone) may require higher than typical doses of systemic opioids (eg, fentanyl, remifentanil) to achieve adequate analgesia. Exposure to IV opioids for a patient with OUD may be in conflict with their recovery or treatment goals. For pregnant people who are receiving buprenorphine, sufentanil is the only currently available opioid with a binding affinity higher than that of buprenorphine. Sufentanil also has high intrinsic efficacy (reaches maximal effect at 50% receptor occupancy; in contrast, remifentanil has lower intrinsic efficacy and requires high fractional receptor occupancy to produce effects[76]), and these properties make modest doses of sufentanil a potentially preferable systemic opioid supplement for acute pain in people who are receiving buprenorphine therapy.[1]

Clinical recommendation: Opioid IV PCA (eg, fentanyl, remifentanil, 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 who are receiving buprenorphine therapy (Class IIa, Level C-LD). Should opioid IV PCA be used because of expected higher opioid dose requirements in people with OUD, the maximum opioid limits should be adjusted upward (Class I, Level C-EO). Sedation and respiratory depression monitoring (eg, sedation scores, respiratory rate monitoring, continuous pulse oximetry) should be considered if not already part of 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 a neuraxial block is not an option (Class I, Level C-EO).

c. **Ketamine**

Summary of evidence: Clinical trials that have evaluated ketamine for labor analgesia or in the peripartum period are lacking. Perioperative continuous infusion of subanesthetic 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 that have examined the role of ketamine in laboring people with OUD. There are no studies that have reported potential risks for return to use after ketamine exposure with MOUD, which can coexist with polysubstance use disorder. Under animal experimental conditions, ketamine and other anesthetics have been noted to exhibit neurotoxic effects in developing brains, however, 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 are under anesthesia for more than 3 hours or repeated use of anesthetics "may affect the development of children's brains." However, the 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, nonrepetitive 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 in which to 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 the currently limited fetal-neonatal and lactation safety data on ketamine in the labor and delivery setting and considering the limited available data regarding its effectiveness or side effects for labor analgesia, the usefulness or 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 nonopioid analgesia in the peripartum period but pointed out that comprehensive studies are lacking.[77] 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 that supported or refuted broad adoption of these pain management strategies during 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 the 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, because of concerns for fetal bradycardia following the use of a block,[78] these blocks are no longer favored for use during labor, except for delivery in cases with known or anticipated fetal demise.

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

4. **Treatment of postvaginal delivery pain**
   a. **Should nonsteroidal anti-inflammatory drugs and acetaminophen be used?**

Summary of evidence: There are no studies dedicated to examining the use of NSAIDs following vaginal delivery among patients with OUD. In pregnant people without OUD after cesarean delivery, for 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.[79] There are no studies that examined 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.[80]

Clinical recommendation: In the absence of 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 use of acetaminophen-opioid combination medications is uncertain but may lead to 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: The expected postpartum analgesic requirements in pregnant people with OUD with uncomplicated vaginal birth may be higher than in patients without OUD.[54] One review noted that pregnant people with OUD who have complex vaginal deliveries (eg, 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 the 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 a history of OUD should be done whenever possible.[14] Other adjunctive medications in this setting have not been described.

Clinical recommendation: Because of the increased pain intensity associated with vaginal deliveries complicated by high-order lacerations, epidural opioids (eg, $\leq$3 mg morphine) may be considered, but there is limited data that support its safety or efficacy; higher doses may be associated with pruritus, which may be challenging to treat given the risks for withdrawal with nalbuphine (Class IIa, Level C-LD). The presence of OUD, untreated or treated with MOUD, has an uncertain effect on epidural opioid dose requirements. Patients with high-order vaginal lacerations should receive education on the 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 at discharge, short-interval outpatient follow-up (eg, 5- to 7-day prescription, no refills, with follow-up appointment within 1 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 that examined the routine use of oral opioids in hospital or at discharge after vaginal delivery with OUD.

Clinical recommendation: Given the risk for 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 in a shared decision-making model that includes the patient, their treatment provider, and the postdischarge 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, nonparenteral formulations of opioids should be dispensed for a very short duration (eg, 3-day supply) (Class IIb, Level C-EO).

   d. **What is the role of other adjuvants in the treatment of postvaginal delivery pain?**

Summary of evidence: There are no studies that examined the role of other adjuvants in the treatment of postvaginal delivery pain in patients with OUD. Topical agents and temperature interventions have been reported specifically for perineal pain and uterine cramping.[80]

Clinical recommendation: Adjunct pharmacologic and nonpharmacologic approaches that should be used for postvaginal 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 the dose of medication for opioid use disorder (methadone, buprenorphine) be adjusted intrapartum or postpartum for analgesic benefits?**

Summary of evidence: Refer to the section on Prenatal optimization 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 3- or 4-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, ideally beginning in the prenatal period, it may be beneficial to administer the daily methadone dose every 6 to 8 hours or to split the daily buprenorphine dose and administer it every 6 to 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 opioid use disorder experiences withdrawal during labor, how should it be treated?**

Summary of evidence: There are no studies that examined the treatment of opioid withdrawal during labor in patients with opioid use disorder, either untreated or treated with MOUD.

Clinical recommendation: Patients who are 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 who are experiencing acute withdrawal symptoms during labor, management should follow therapies for nonpregnant patients (Class I, Level C-EO). For patients with recent illicit opioid exposure, acute withdrawal potentially may be 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 opioid use disorder 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 who are receiving buprenorphine and 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).[81]

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—for example, nalbuphine and butorphanol—be used in patients who are receiving medication for opioid use disorder (for example, how should opioid-induced intrapartum pruritus be managed in a laboring pregnant person who is receiving buprenorphine?)?**

Summary of evidence: There are no studies that have examined whether partial antagonists can be used in pregnant or postpartum people on MOUD. However, treatment with partial agonists (or antagonists) can precipitate acute withdrawal in opioid-dependent people, including those who are receiving MOUD. One review describes removing or reducing the dose of the opioid component of the epidural medication solution and treating pruritus with other pharmacologic approaches, such 5-hydroxytryptamine 3 (5-HT3) receptor antagonists.[82]

Clinical recommendation: Partial agonists or antagonists should not be administered in patients who are receiving MOUD for both the treatment of pain and opioid-induced pruritus because of the 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 pharmacologic 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 opioid use disorder require additional monitoring during and after labor?**

Summary of evidence: There are no studies that have explicitly examined whether pregnant people with OUD require additional monitoring during or after labor. A systematic review found that in cases in which 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.[77] Despite these higher frequencies of respiratory depression, analgesia was not acceptable as evidenced by higher postoperative pain scores.

In the absence of coadministered systemic opioids beyond MOUD, there is no evidence of an increased risk for respiratory depression among pregnant people with OUD who are receiving dilute neuraxial opioids.

Clinical recommendation: For neuraxial labor analgesia, it is recommended that the usual standards and duration of

monitoring are 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 because of the interaction with opioids (eg, 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 after vaginal delivery with high-order vaginal lacerations and about the potential risks for sedation or respiratory depression in pregnant people with OUD (Class I, Level C-EO).

Cesarean anesthesia and postcesarean delivery analgesia

1. **Is there evidence for increased pain and analgesia intake after cesarean delivery among pregnant people who are receiving medication for opioid use disorder, including methadone, buprenorphine, and naltrexone?**

Summary of evidence: Pregnant individuals who are receiving MOUD like methadone, buprenorphine, and naltrexone may experience heightened pain after a cesarean delivery because of comorbid chronic pain and mental health conditions.[83,84] The pharmacokinetics of MOUDs impact the effectiveness of opioids with methadone leading to the development of tolerance, buprenorphine inducing competitive antagonism, and naltrexone acting as an antagonist.[83–86] Postoperatively, users of methadone and buprenorphine typically require increased opioid concentrations when compared with opioid-naïve patients, whereas naltrexone blocks the opioid effects depending on the administration timing and formulation.[26,62,85] Overall, users of buprenorphine and methadone may report higher pain scores and increased opioid use after surgery, which is in contrast with naltrexone's blocking effects.[63,87–90]

Although the evidence indicates that patients who are receiving MOUD may experience increased pain and opioid use after surgery,[16,26,42,62,63,54,83,86,87,89,90,88,91–93] it is recommended that MOUD should be maintained without interruption throughout the perioperative and peripartum period to prevent destabilization and potential opioid misuse.[91] Buprenorphine's competitive antagonism may reduce the efficacy of other opioids for acute pain, but increasing the total daily dose to 24 to 32 mg in divided doses can optimize its analgesic effects.[94,95] Similarly, it is advised to continue the same daily dose of methadone with consideration for fractioning the dose and supplementing with other opioids for analgesia as needed.[95] For naltrexone, assessing the recent dosing history and type can guide clinicians in determining the potential use of additional opioids as the naltrexone levels decline.

A retrospective study with 553 participants found that individuals on methadone or buprenorphine consumed more opioids in hospital after cesarean delivery than opioid-naïve patients, however, they were less likely to receive opioid prescriptions at discharge,[96] illustrating the potential for disparity in pain management for patients with OUD.

Clinical recommendation: The available data suggest that pregnant people with OUD, untreated or treated with MOUD, may experience increased pain and opioid needs after cesarean delivery when compared with pregnant people without OUD (Level C-LD). Pregnant people should be educated on the 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 that involves anesthesiology, obstetricians, and addiction medicine specialists 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 (refer to part 1: Prenatal Optimization) (Class I, Level C-EO).

2. **Anesthesia for cesarean delivery**

Like patients without OUD, pregnant people with OUD who undergo a cesarean delivery should enjoy the benefits of neuraxial anesthesia (eg, spinal or combined spinal epidural, epidural anesthesia), including improved pain recovery, enhanced participation in cesarean delivery, and safety, over general anesthesia.

   a. **Should the usual dose of neuraxial opioids be increased, decreased, or 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 to 4 times higher among patients with OUD after cesarean delivery.[3,97,98]

Neuraxial lipophilic opioids enhance the intraoperative block quality, whereas hydrophilic opioids are used for postoperative analgesia. Tailoring the dose of neuraxial opioids for cesarean delivery anesthesia is necessary considering opioid tolerance among individuals who are receiving MOUD.[91,97,99] Continuing MOUD throughout the peripartum period is recommended, and this practice may necessitate higher doses of opioids to achieve adequate analgesia after cesarean delivery.[26,28,100,101] However, specific dose adjustments for neuraxial opioids in this population have not been well studied. Using multimodal nonopioid analgesics like NSAIDs with acetaminophen is advised to optimize pain management.[91,97,99]

Clinical recommendation: Neuraxial anesthesia is recommended over general anesthesia for cesarean delivery when possible (Class I, Level B-NR). Coadministered lipophilic and hydrophilic neuraxial opioids (eg, fentanyl and morphine) are recommended and should neither be omitted,

nor should the dose be reduced for cesarean anesthesia in pregnant people with OUD (Class I, Level B-R). No data are available to inform the routine use of increased doses of neuraxial opioids for cesarean delivery analgesia in pregnant people with OUD, and the safety and effectiveness of this practice is unknown (Class IIb, Level C-LD).

b. **Should nonopioid 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 postcesarean delivery 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 who were receiving buprenorphine as MOUD achieved good analgesia and many did not require any supplemental opioids postoperatively.[69] In that case series, patients received a postoperative epidural infusion of 0.1% bupivacaine with 1.2 μg/mL clonidine or 0.0625% bupivacaine with 2 μg/mL clonidine and pain scores remained low (from 0 to 5 of 10 maximum). The average infusion time was 27 hours.

In one case report, IV dexmedetomidine infusion was titrated in increasing doses from 0.2 to 0.7 μg/kg/hour for 2 to 3 days after cesarean delivery.[102] Dexmedetomidine has been reported to be associated with reduced parenteral sufentanil use for 24 hours after surgery in single- and multicenter studies.[103] 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 μg) administration is known to increase the duration of both sensory and motor blocks during and after cesarean delivery.[104] Its impact on postoperative analgesic requirement and pain score is debatable. There is no study on the effectiveness of neuraxial epinephrine among patients with OUD who underwent a 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, a single dose of epidural neostigmine (75 to 300 μg) given during cesarean delivery was associated with a significant reduction in the pain scores in 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 μg doses were used.[105] A systematic review and meta-analysis identified 16 randomized controlled trials that evaluated intrathecal or epidural neostigmine of which 3 evaluated neuraxial neostigmine for cesarean delivery.[106] Neuraxial neostigmine was associated with reduced postoperative pain scores and opioid use, but there was a high level of heterogeneity among studies. Moreover, intrathecal neostigmine was associated with higher risks of nausea (OR, 8.99; 95% CI, 4.74−7.05; $P<.001$). 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 coadministered.[70]

Clinical recommendation: There is limited evidence to support or refute the routine use of nonopioid neuraxial adjuvants, including clonidine, dexmedetomidine, epinephrine, or neostigmine, for postcesarean 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 the sensory block during cesarean delivery (Class IIa, Level B-NR). The benefits of neuraxial neostigmine for postcesarean delivery analgesia remain unclear and side effects (severe nausea, vomiting) may limit its use in pregnant people with and without OUD (Class III, Level C-LD).

3. **Postcesarean delivery 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,[87,98,107,108] but this approach may compete with the Enhanced Recovery after Cesarean (ERAC)[79] goals for early ambulation. One review article suggested using epidural local anesthetics for 48 to 72 hours to optimize pain management and reduce systemic opioid use in pregnant people with OUD.[70] 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 postcesarean delivery analgesia in pregnant people who are receiving buprenorphine as MOUD.[109] Peripartum patients with OUD expressed a range of opinions and preferences regarding the use and disuse of opioids for pain management and a desire for nonopioid options.[66]

Clinical recommendation: Continuation of epidural analgesia for 12 to 48 hours after cesarean delivery in patients with OUD may be considered (Class IIa, Level C-EO). However, its use must be balanced with the 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 nonsteroidal anti-inflammatories and acetaminophen be used after cesarean delivery?**

Summary of evidence: The SOAP and ACOG have recommended the use of NSAIDs as part of multimodal analgesia after cesarean delivery.[3,79] Several reviews and meta-analyses have described the benefits of perioperative NSAIDs, including a 30% to 50% opioid-sparing effect after various surgeries, such cesarean delivery, among patients with[83] and without[110–115] 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%] patients with OUD vs 4/38 [10.5%] patients without OUD; P=.006).[55] The authors suggested that clinicians should preferentially treat pain with NSAIDs instead of opioids.[55] However, another study reported that common problems expressed by patients with OUD were inadequate analgesia and their desire to increase the dosage or frequency of analgesia.[22] The opioid-sparing effects of NSAIDs in the obstetrical population are supported by a meta-analysis of 22 randomized controlled trials that compared NSAIDs (n=639) with controls (n=674) in obstetrical patients without OUD.[116] 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.[116] The availability of the parenteral NSAID formulations has made it practical for perioperative use.[117] No studies specifically in patients with OUD have compared the analgesic efficacy of different NSAID formulations.[108]

There are no specific data on 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 from nonobstetrical cohorts. Acetaminophen has an opioid-sparing effect of approximately 20%.[110,118] It is available in both oral and parenteral (IV) formulations and has minimal adverse effects and breast milk transfer,[119] which have encouraged its use in the perioperative period.[120] In a retrospective cohort study, uncoupling acetaminophen from opioid administration and instead giving scheduled acetaminophen plus oxycodone as needed led to patients using more acetaminophen and fewer opioids to treat their postoperative pain in the first 2 days after cesarean delivery when compared with patients who received an as-needed combination of acetaminophen-opioid medications.[121] A randomized controlled trial found a statistically significant reduction in opioid consumption among patients who were receiving IV acetaminophen when compared with those who were receiving a placebo in the presence of intrathecal opioids for the duration of the hospital stay.[122] However, another randomized, placebo-controlled trial of 66 patients did not demonstrate the same benefits for IV acetaminophen within 24 hours postoperatively.[123] Both of these studies excluded patients with OUD, and they did not compare IV acetaminophen against its oral formulation.[122] A combination of acetaminophen and NSAIDs have been shown in a qualitative systematic review in the nonobstetrical population to offer superior analgesia when compared with either drug alone.[124] Evidence is lacking on this topic specifically for patients with OUD after cesarean delivery.

Clinical recommendations: Both the 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 postcesarean delivery pain management because of the well-established opioid sparing effects (Class I, Level C-EO). Ketorolac (IV) should be scheduled for 24 to 48 hours, followed by a transition to oral ibuprofen after cesarean delivery (Class I, Level C-EO).

c. **Are changes to medication for opioid use disorder required to enhance analgesia after cesarean delivery?**

Summary of evidence: The American Society of Addiction Medicine recommends continuing MOUD during labor and the postpartum period given the uncertain timing of and risks for return to use when MOUD is stopped.[125] Pregnant people who are receiving methadone are generally maintained on the same dose (consider fractionating the daily dose; refer to section on predelivery medication management) throughout the postpartum period.[126] Experts have recommended continuing predelivery buprenorphine doses or dividing the daily dose into 3-times-daily dosing to maintain adequate analgesia.[94,127] 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 the analgesia effects. In the postpartum period, doses of MOUD may need to be adjusted (reduced) because of changes in weight (volume of distribution) and drug metabolism after delivery.[45]

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 into 3 to 4 daily doses may optimize the analgesia effects for the first few days after cesarean delivery (Class IIa, Level C-EO). Serial evaluation of the patient during hospital stay is necessary to identify a need for high doses of systemic opioids and to determine a taper plan before 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 postcesarean 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.[62]

Inpatient parenteral administration may be associated with higher abuse liability,[86] which risks return to opioid use and must be balanced with the overall OUD treatment goals. High-affinity partial opioid agonists, such as nalbuphine or butorphanol, should not be used in patients who are receiving buprenorphine because these medications can precipitate withdrawal.[128]

Finally, given that pregnant people who are receiving MOUD may experience opioid-induced hyperalgesia and require escalating doses of oral opioids in the postpartum period, caution should be exercised in using combination opioid-acetaminophen preparations, which could increase the possibility for unintentional acetaminophen toxicity.[127]

Clinical recommendations: The need, type, dose, and quantity of other analgesics for postpartum pain in pregnant people with OUD depends on the specific MOUD and treatment goals (Level C-EO). The decision to use or not to use parenteral opioids for pain must be made on an individual basis in partnership with an addiction medicine practitioner-and in accordance with individual treatment goals and ideally should be discussed before the onset of pain (refer to the section on Prenatal 0ptimization) (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 who require high systemic opioid exposure and 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 postcesarean delivery analgesia?**

Summary of evidence: ketamine

IV ketamine has been reported for the treatment of acute pain in nonobstetrical patients with OUD or in those who are receiving chronic opioid agonist therapy.[129] In routine perioperative settings, typical doses for low-dose IV ketamine for acute pain treatment range from 0.1 to 0.3 mg/kg/hour or about 8 mg/hour for 2 to 3 days.[109,130] However, the evidence around perioperative ketamine among patients with OUD is scarce and primarily limited to case reports or case series.[109,130] 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 24 hour after operation); the median range for ketamine infusion was 14.4 (5.8–19.7) mg/hour.[130]

A meta-analysis of 20 randomized controlled studies, including 1737 patients who underwent cesarean delivery and who received ketamine systemically (single bolus or infusion) or intrathecally (0.1 mg/kg ketamine), concluded that ketamine significantly reduced the pain scores (mean difference [MD] pain scores for ketamine vs control, −1.10; 95% CI, −1.61 to −0.59; $P<.0001$) and opioid consumption (MD morphine consumption for ketamine vs control, −6.11 mg; 95% CI, −9.93 to −2.29; $P=.002$), which was more pronounced in those who underwent spinal anesthetic than in those who had general anesthetic.[131] It was uncertain whether intrathecal opioids played a part in these findings. However, there was significant heterogeneity among the included studies in terms of the dose of ketamine; bolus doses ranged from 10 mg to 30 mg fixed dose or 0.15 mg/kg to 1 mg/kg weight-adjusted dose; infusion doses ranged from 2 μg/kg/min to 0.25 mg/kg/hour. This meta-analysis did not report on the 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 who were receiving MOUD described the results associated with low-dose ketamine (n=18) infusion vs no infusion (n=8) after cesarean delivery.[130] Most patients had spinal anesthesia and half received 100 μg morphine intrathecally. The ketamine infusion commenced between 0 and 20 hours after operation, and the dose ranged from 0.1 to 0.3 mg/kg/hour with a median duration of 23.9 hours (10.3–45.3 hours). They found reduced MME consumption on postoperative day 0 (morphine equivalent: 71 mg; 15–463 mg vs 90 mg; 38–200 mg) 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.[130] Another small case series (n=8) on patients with OUD who were receiving buprenorphine described using ketamine infusion at 8 mg/h for 24 hours after cesarean delivery and reported on satisfaction and meeting the goals for pain relief.[109]

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 breastfed infant. Ketamine and other NMDA receptor antagonists have been found to exhibit neurotoxicity and to impair brain development in animal models under experimental conditions.[132,133] However, clinical exposures in humans have not demonstrated definitive risk, and dose exposures in animal models exceed those expected to reach the 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.[134] Ketamine is recommended to be either avoided or used in low doses with monitoring for neonatal sedation and poor

feeding during breastfeeding.[135] The experts agree that brief, nonrepetitive periods of exposure to these medications in lactation are permissible. Decisions for use or nonuse must be patient-centered with appropriate individual risk and benefit considerations.

Clinical recommendations: There is limited, low-level evidence that support the analgesic efficacy of low-dose ketamine infusion for up to 24 hours after 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 postcesarean delivery 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 in terms of their effectiveness in postoperative analgesia, the postoperative respiratory complication risk, and abuse potential.[136,137] A meta-analysis suggested that gabapentin has benefits in reducing postcesarean delivery pain score at 24 hours, but the studies excluded patients with OUD.[138] Other studies in nonobstetrical populations have suggested that gabapentin is associated with a reduction in acute and persistent postoperative pain and opioid consumption,[139,140] but contradicting data suggest that only moderate-level evidence or no evidence supports the use of gabapentinoids in the reduction of postoperative pain and opioid consumption at the expense of increased adverse effects.[141,142] One retrospective cohort study (n=214) in pregnant people with OUD after cesarean delivery suggested that the inclusion of gabapentin in a multimodal analgesic regimen was not associated with lower opioid consumption or pain scores during the first 72 hours after cesarean delivery.[143] 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 contemporary 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 the neonatal side effects.[144,145]

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 postcesarean delivery analgesia for pregnant people with OUD. (Class III, Level C-EO)

Summary of evidence: clonidine

Evidence for the use of neuraxial clonidine in the context of pregnant people with OUD after cesarean delivery was reviewed elsewhere in this statement.[69] Notably, a case series of 7 patients observed hypotension in 2 of the 7 patients and none had bradycardia (maternal or fetal) or sedation.[69] There is no data on the use of systemic clonidine in patients with OUD. Regarding breastmilk transfer, high serum levels were found in patients who were 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.[146]

Clinical recommendations: Currently, there are 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 for use in patients with OUD for enhanced analgesia and 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 (eg, 4–8 mg) for analgesia for pregnant people with OUD who are undergoing cesarean delivery. Studies in patients without OUD in obstetrical and nonobstetrical settings have found conflicting results regarding the analgesic efficacy of intravenous dexamethasone for postoperative analgesia (Supplemental Material 1).[147–153]

Clinical recommendations: Routine use of a single dose of IV dexamethasone has uncertain effectiveness as part of multimodal analgesia in pregnant people with OUD who are 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 of regional anesthesia options such as transversus abdominus plane, erector spinae plane, and quadratus lumborum blocks or continuous wound infiltration? Are any of these options more effective than others?**

Summary of evidence: The ERAC recommendations are to use either abdominal wall blocks or continuous wound infusions for patients at risk for severe pain after cesarean delivery.[79] There are no studies that compared 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 delivery specifically in patients with OUD, both the quadratus lumborum (QLB) block[154–157] and transversus abdominis plane (TAP) block have been suggested to improve postcesarean delivery analgesia[79,158,159] in the general population and in those at risk for complex pain.

The most used and studied regional anesthesia technique for cesarean delivery is the single-shot bilateral 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 trial[160] found that the total morphine consumption was reduced by more than 60% in a TAP group that received 20 mL of 0.25% bupivacaine. Another small randomized controlled trial in patients without OUD who underwent cesarean delivery (n=47) found a statistically significant reduction in the total morphine use within 24 hours after bilateral ultrasound-guided TAP blocks with 40 mL of 0.5% ropivacaine.[161] Although these studies have small sample sizes, the data suggest that ultrasound-guided, bilateral, single-shot TAP blocks after cesarean delivery as part of multimodal analgesia may reduce opioid consumption, 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 QLB block in pregnant people with OUD who underwent cesarean delivery, but several studies on cesarean delivery among pregnant people without OUD have suggested potential benefits in reducing morphine consumption and improving analgesia in the absence of intrathecal morphine.[162–165]

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

For local anesthetic continuous wound infiltration (CWI) for postcesarean delivery analgesia, a meta-analysis that included 21 studies found that local anesthetic CWI was associated with reduced postoperative opioid consumption, but it had minimal effect on the pain scores in the first 24 hours after cesarean delivery.[166] The meta-analysis was limited by a few studies with small sample sizes and by indirect comparisons between single injection and infusion performed as a subgroup analysis. A meta-analysis that included 42 studies with 2906 patients after cesarean delivery without intrathecal opioid administration, not specific to patients with OUD, found that single-dose bilateral TAP block and CWI were associated with significantly lower 24-hour opioid consumption than inactive controls, but there were no significant differences between single injection wound infiltration and controls.[167] The authors concluded that, in the absence of neuraxial morphine for cesarean delivery, single-dose TAP blocks and CWI 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.[168] Pregnancy increases the risk for LAST because of a relatively vascular tissue plane and reduced protein binding in pregnancy and because of increased cardiac output with increased uptake and drug distribution in pregnancy.[169,170] Data on the risks for LAST with QLB, ESP, and CWI in cesarean delivery are currently lacking.

Clinical recommendations: Based on the 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 postcesarean delivery epidural analgesia (Class IIb, Level C-EO).

g. **What is the role for psychotherapeutic or behavioral interventions (eg, cognitive behavioral therapy) or complementary and alternative therapies to address intra- and postcesarean delivery pain?**

Summary of evidence: Pain is a personal experience that is influenced to varying degrees by individual biologic, psychological, and social factors.[171] Postpartum patients with mood and anxiety disorders may be more likely to fill opioid prescriptions than patients without these conditions.[172] A meta-analysis of randomized trials compared complementary and alternative therapies with controls for postcesarean delivery pain management in patients with OUD[173] and found low-quality evidence for acupuncture or acupressure that precluded any conclusions. Aromatherapy as an analgesic adjunct reduced pain scores at 12 hours (MD, −2.63 based on visual analogue scale [VAS] scores from 0 to 10; 95% CI, −3.48 to −1.77) and 24 hours (MD, −3.38 VAS; 95% CI, −3.85 to −2.91).[173] There is no evidence for music therapy or cognitive behavioral therapy specifically for people with OUD who are undergoing cesarean delivery.[173] However, cognitive behavioral techniques and supportive psychotherapy have been recommended for patients with anxiety disorders for general postpartum patients and for patients with OUD.[174,175]

Clinical recommendations: There are 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 in which anxiety predominates and affects pain control (Class IIb, Level C-EO).

4. **Management of postoperative neuraxial opioid-induced side effects and complications in the patient receiving buprenorphine**
   a. **How should postoperative pruritus be managed?**

Summary of evidence: High level evidence suggests a significantly lower incidence of pruritus among patients who

are receiving buprenorphine.[90] When compared with IV morphine, IV methadone (relative risk [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 for causing pruritus.[176] It is important to avoid treating pregnant people who are receiving chronic opioid agonists with mixed antagonists and agonists (eg, nalbuphine or butorphanol) or pure antagonists (eg, naloxone), which are widely used for analgesia and pruritus, because these medications can precipitate withdrawal in patients with OUD that is treated or untreated.[127]

Clinical recommendation: Treating pregnant people with OUD, treated or untreated, with mixed antagonists and agonists (eg, nalbuphine or butorphanol) or pure antagonists (eg, naloxone) for pruritus should be completely avoided in pregnant people receiving MOUD because of 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 the 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 with consideration for 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.[177] Although there may be a desire to prevent acute withdrawal symptoms,[178] these concerns should not prevent the delivery of naloxone therapy; naloxone should be given per standard treatment pathways to any patient who is experiencing acute opioid toxicity. For the obstetrical patient, based on gestational age and viability, the fetus should be monitored throughout naloxone treatment given for maternal opioid toxicity.[178]

It was originally believed that because of buprenorphine's strong affinity for the mu-opioid receptor and the slow association and dissociation kinetics it 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.[179] 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.[177] Successful reversal of buprenorphine may require very high doses of naloxone (>2 mg).[81]

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 opioid use disorder require additional monitoring during or after cesarean delivery?**

Summary of evidence: Pregnant people with OUD or those who are receiving chronic opioid agonist therapies may be at higher risk for respiratory depression than opioid-naïve people and therefore should be monitored appropriately with regular evaluation of sedation and oxygen saturation.[84] Pregnant people who are undergoing 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 comorbidities (eg, chronic opioid agonist exposure, obstructive sleep apnea, acute opioid, or other sedative toxicity) that place them at higher risk for 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 Administration.[180]

Clinical recommendation: Pregnant people with OUD, untreated or treated with MOUD, should be monitored per the SOAP respiratory monitoring guidelines, stratified to the higher risk category (ie, respiratory rate and sedation assessments every hour for the first 12 hours and every 2 hours for 12 to 24 hours thereafter with consideration for additional monitoring modalities such as pulse oximetry and capnography as 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 obstetrical, 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 (eg, systemic, neuraxial, etc.) can potentially lead to unexpected positive urine

toxicology results, sometimes unbeknown to the patient. Such a turn of events can cause stress and challenges for patients with OUD, may increase the difficulty of accessing medications, and could breed mistrust in the medical system. Therefore, we consider that it is critically important for patients to be aware of what medications are being used during labor and delivery, and a frank and open discussion with the patient should 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 according to clinical care standards. This discussion is also relevant for patients who may require or desire short courses of postoperative opioid analgesia at discharge but who may feel limited by their treatment programs or other circumstances that involve 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 or family services must be educated regarding the expected positive urine toxicology results and accurate interpretation of these results.

Conclusion

This consensus statement provides clinical recommendations for the optimization of pain management during pregnancy, labor and delivery, and the postpartum period for people with OUD. We emphasize the importance of early antenatal evaluations by anesthesia providers and a comprehensive and individualized approach to pain management that takes into consideration a history of opioid use, pain management, and the potential impact on obstetrical management. This consensus statement provides healthcare providers with practical and concise information to optimize pain management and reduce the risk for OUD during pregnancy. Further research, especially when evidence has been rated as weak or when 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.

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