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A Systematic Scoping Review of Peri-delivery Pain Management for Pregnant Women with Opioid Use Disorder: From the Society for Obstetric Anesthesia and Perinatology and Society for Maternal Fetal Medicine

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Abstract

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The prevalence of pregnant people with opioid use disorder (OUD) including those receiving medications for opioid use disorder (MOUD) is increasing. Challenges associated with pain management in people with OUD include tolerance, opioid induced hyperalgesia, and risk for return to use. Yet, there are few evidence-based recommendations for pain management in the setting of pregnancy and the postpartum period, and many peripartum pain management studies exclude people with OUD. This scoping review summarized the available literature on peri-delivery pain management in people with OUD, methodologies used, and identified specific areas of knowledge gaps. PubMed and Embase were comprehensively searched for publications in all languages on peripartum pain management, among people with OUD treated with MOUD and untreated. Potential articles were screened by title, abstract, full text. Data abstracted were descriptively analyzed to map available evidence and identify areas of limited or no evidence. 994 publications were imported for screening on title, abstracts, and full text, yielding 84 publications identified for full review: 32 (38.1%) review articles, 14 (16.7%) retrospective studies, 8 (9.5%) case reports. There were 5 randomized controlled trials. Most studies (64%) were published in perinatology (32, 38.1%) journals or anesthesiology (22, 26.2%) journals. Specific areas lacking trial or systematic review evidence include: 1) methods to optimize psychological and psychosocial co-morbidities relevant to acute pain management around delivery; 2) alternative non-opioid and non-pharmacologic analgesia methods; 3) whether or not to use opioids for severe breakthrough pain, and how best to prescribe and monitor its use after discharge; 4) monitoring for respiratory depression and sedation with co-administration of other analgesics; 5) optimal neuraxial analgesia dosing and adjuncts; 6) benefits of abdominal wall blocks after cesarean delivery. No publications discussed naloxone co-prescribing in the labor and delivery setting. We observed an increasing number of publications on peripartum pain management in pregnant people with OUD. However, existing published work are low on the pyramid of evidence (reviews, opinions, retrospective studies), with a paucity of original research articles (<6%). Opinions are conflicting on the utility and disutility of various analgesic interventions. Studies generating high quality evidence on this topic are needed to inform care for pregnant people with OUD. Specific research areas are identified including utility and disutility of short-term opioid use for postpartum pain management, role of continuous wound infiltration and truncal nerve blocks, nonpharmacologic analgesia options, and best methods to support psychosocial aspects of pain management.

INTRODUCTION

In the past decade, opioid use disorder (OUD) has increased four-fold among pregnant people.¹ Opioid use disorder increases risk for death from overdose, which is a rising leading cause of maternal deaths in the United States (CDC: <http://www.cdc.gov/reproductivehealth/opioid-use-disorder-pregnancy/index.html>). Peri-delivery pain management for pregnant patients with OUD is suboptimal because of lack of evidence-based recommendations. Research suggests that suboptimal relief of acute postoperative pain has long term sequelae including chronic pain and depression.^{2,3} This problem of pain management is further complicated in patients with OUD because of concerns about return to use triggered by pain itself, or triggered by exposure to opioids if opioids must be used for pain control.

Medication for opioid use disorder (MOUD) is the mainstay for effective treatment of OUD in pregnancy because MOUD is associated with better prenatal care adherence and birth outcomes⁴. MOUD in pregnancy typically includes opioid agonist or mixed agonist-antagonist medications (e.g., methadone, buprenorphine). Chronic use of these medications can have implications on pain management during and after labor and delivery. These medications have a strong affinity for mu opioid receptors which, in theory, may increase the likelihood of higher doses of opioids needed or consumed to control pain during labor and after delivery. In contrast, However, both opioid exposure and untreated or poorly controlled pain can lead to return to use or OUD recurrence⁵. How clinicians should optimally manage both acute pain and coexisting OUD is a source of frequent debate.

It is unclear what type of information is available in literature about pain management in patients with coexisting OUD. Systematically mapping the current research done and knowledge gaps as well as existing limitations in study methodologies will assist with planning specific directions for future research. The purpose of this scoping review is to identify and summarize the available literature on peripartum pain management in pregnant people with OUD, both treated with MOUD and untreated. The focus of this review is on three primary peripartum periods: pre-delivery pain management optimization; pain management in labor and delivery; and post-cesarean delivery pain management. The scoping review aimed to 1) characterize available evidence on how OUD affects pain management during the three peripartum periods mentioned above; and 2) identify knowledge gaps to make recommendations for future research.

METHODS

The reporting of this scoping review was guided by the Preferred Reporting Items for Systemic Reviews and Meta-Analysis extension for Scoping Review standards (PRISMA-ScR)⁶. A working group from the Society for Obstetric Anesthesia and Perinatology (SOAP) defined, by consensus, specific key questions that would be important for peripartum pain management in pregnant people with OUD treated with MOUD or untreated (Appendix 1). Questions were developed to comprehensively capture all relevant clinical decision-making points before, during, and after labor and delivery. Two investigators (G.L. and M.S.) used these questions to identify and saturate on themes of topics that are of interest to pain management in pregnant people with OUD. These questions were considered for each of the following populations: 1) Pregnant people receiving MOUD where OUD was due to an acute or chronic pain condition; 2) Pregnant people receiving MOUD where OUD not due to pain condition; 3) Pregnant people with untreated OUD; 4) Pregnant people with OUD stable in recovery not receiving MOUD.

Methodology and Sources

The databases PubMed and Embase.com were systematically searched from inception until March 31, 2020, for published journal articles. PubMed covers the healthcare literature where most peer reviewed publications are indexed. EMBASE covers European, North American, and other non-North American literature. An experienced health sciences librarian (C.B.W.) designed the PubMed search, which was then translated for use in

Embase.com by a second health sciences librarian (M.L.K.). For both databases, a search string was developed using both controlled vocabulary terms, e.g., Medical Subject Headings (MeSH) terms, and natural language informed by a subject matter expert (G.L.) to represent the concepts of opioid use disorder, peripartum pain, and pain management (Appendix 2).

The results of the database searches were downloaded to an EndNote library and duplicate records were removed by a health sciences librarian (M.L.K.) using a process developed by Bremer and colleagues⁷. Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia) was used to manage citations and track ratings.

Inclusion/Exclusion Criteria

Articles included labor and delivery pain management for vaginal, postpartum pain management for vaginal, postpartum pain management for cesarean. Articles were included if they were original research, case studies, case series, or cohort studies, letters to the editor, commentaries, white papers, published abstracts, or review articles. All languages were included, with non-English articles translated by certified medical translator services to English, the authors' primary language.

Study Selection

Article titles and abstracts were screened and included if they contained the following terms: pain, analgesia, or pain management; pregnancy, parturient, perinatal; labor and delivery, intrapartum, or cesarean delivery or postpartum; OUD with MOUD, OUD without MOUD, or substance use disorder with opioid use disorder specified in the title or abstract. Articles were excluded if pertaining to acute or chronic pain not in the peripartum period, or if non-human or animal studies. Two reviewers independently screened titles and available abstracts using the above pre-determined inclusion/exclusion criteria and key questions from Appendix 1 (A.C. and A.W.). Duplicate abstracts were removed from consideration. Discrepancies between the two abstract reviewers were resolved through discussion; for persistent discrepancies requiring a tiebreaker, a third party (G.L.) was consulted. Cohen's kappa statistic was calculated to evaluate inter-rater reliability between the two initial raters for this level of review. Full text for these studies were then located and reviewed; if duplicates were detected by full text, these were removed, as were studies that were deemed to be irrelevant and studies where full text could not be located. Two reviewers independently screened full text (A.C. and A.W.), with discrepancies resolved through discussion and persistent discrepancies resolved through third party tie breaker (G.L.).

Extraction/Charting the Results

For abstracts that met the inclusion/exclusion criteria, full text manuscripts were then reviewed. Each manuscript was then individually reviewed by G.L. using the pre-specified relevance criteria established by the key questions in Appendix 1. Each manuscript was associated with one or more codes corresponding to the relevant key questions in the three primary peripartum phases: immediate pre-delivery optimization, management of labor pain, and post-cesarean delivery pain management. Study characteristics including first author, language of original publication, year, journal, journal type (e.g., anesthesiology, pain

management, addiction medicine, obstetrics/gynecology, etc.), methodology, sample size, study objective, and salient findings were summarized (Appendix 3).

RESULTS

The database searches yielded 994 publications for review (PubMed = 473, Embase = 521). PRISMA flow diagram for study screening and eligibility assessment is shown in Figure 1. Nineteen (19) duplicate abstracts were removed, 975 titles and abstracts were screened, with 884 screened as irrelevant with 6 resolved discrepancies (moderate inter-rater reliability $\kappa=0.57$). There were 91 full text studies then reviewed and assessed for eligibility, with 7 removed (duplicates, irrelevant, or unable to locate full text). There were 2 publications originally written in non-English language, German and French. The final list included 84 full text publications for complete review.

Studies corresponding to the primary questions are shown in Table 1, and study characteristics and details are shown in Appendix 3. One article was translated from German and one article was translated from French. Only 5 randomized trials (5.9%) and 1 systematic review (1.2%) were published in the study period. Most articles ($n=32$, 38.1%) were published in obstetrics, gynecology, or perinatology journals, followed by anesthesiology ($n=22$, 26.2%) and addiction medicine journals ($n=16$, 19.0%) (Figure 2). Peer-reviewed publications on peripartum pain management in pregnant people with OUD have steadily increased in volume over time (Figure 2), with most publications encompassing narrative review articles, retrospective cohort studies, and case reports or series (Figure 3).

Publications on Pre-Delivery Pain Management Optimization

Most of the publications on pre-delivery pain management optimization for pregnant people with OUD consist of review articles, followed by retrospective chart reviews^{1,8-28}. Highlights include six case reports and series, 3 prospective observational studies, 2 guidelines, 1 randomized trial, and 1 committee opinion. Available evidence to guide medical care as it relates to pain management is notably limited.

The one randomized trial of 18 participants comparing pregnant people receiving methadone to those receiving buprenorphine, found that after vaginal delivery, those treated with either buprenorphine or methadone reported adequate pain control (based on pain score ratings) with opioids and ibuprofen (main effect for medication group $F(1, 19.3) = 0.01$, $P>0.9$)²⁹. The methadone group used more ibuprofen postpartum (buprenorphine group decreased average ibuprofen use from 1725mg to 1575mg on average over postpartum days 1-5, where methadone group increased ibuprofen use from 1740mg to 2040mg on average). Another study investigated differences in pain management and analgesic medication use in 40 people receiving methadone or buprenorphine during pregnancy, matched to 80 non-opioid exposed pregnant people¹². After cesarean delivery, people with MOUD received fewer opioid analgesics (day of delivery $P=0.03$, day 1 $P=0.02$), and non-steroidal anti-inflammatory drugs were administered more frequently during surgery (MOUD group: 8/19 (42.1%); comparison group: 4/38 (10.5%); $P= 0.006$) and on postpartum day 3 (MOUD group: 10/19 (52.6%), comparison group: 9/38 (23.7%); $P= 0.029$). Smoking status was an

independent predictor of altered pain experience and had a strong influence on results in the MOUD group. Many current available publications recommend continuing methadone and buprenorphine therapy throughout pregnancy and labor and delivery, rather than reducing or stopping the medication. These recommendations are primarily based on expert opinion that are focused on chronic disease management throughout pregnancy³⁰, rather than management of anticipated pain in labor and delivery. Most publications conclude that a multidisciplinary approach to patient management is necessary, with some recommending prenatal anesthesia consultation as part of that management.

Publications on Pain Management in Labor and Delivery

Articles on pain management in labor and delivery for people with OUD primarily include reviews, clinical opinions, case vignettes, and retrospective studies, and one systematic review^{5,26,31–39}. The largest study on labor pain and labor analgesia in pregnant people with OUD was a retrospective chart review of 141 cases, published in 2004, that aimed to identify obstetric and perinatal outcomes in people using opioids (n=91) or amphetamines (n=50) during pregnancy; the epidural labor analgesia rate was 77%³⁶ and pharmacologic analgesia was used more often for labor and delivery (opioids $P=0.007$, amphetamines $P=0.042$). The possibility for return to use if opioids were used for labor analgesia was postulated by the authors of a 2014 systematic review, who emphasized the need for “good” labor analgesia because inadequate analgesia can instigate postpartum addiction recurrence and return to use⁵. The authors suggested that to achieve “good” labor analgesia, neuraxial (not systemic) opioid doses need to be doubled or tripled in pregnant people with OUD⁵, although these authors acknowledge the lack of available scientific data to guide appropriate dosing. Most published papers describe higher doses of opioids, if used, during labor and postpartum, due to the distinct phenomena of opioid tolerance and opioid-induced hyperalgesia. However, published opinions are conflicting on whether to use or to avoid systemic opioids. Opinions conflict due to concerns about risk for return to substance use that can be associated with exposure to systemic opioids (used for analgesia), as well as with poor pain control (which may result from avoidance of opioids).

Most publications, including the American College of Obstetricians and Gynecologists (ACOG) committee opinion¹, do not recommend medically supervised withdrawal during pregnancy, labor, and delivery. Comprehensive, multidisciplinary, individualized care planning - including chaplains, psychosocial services, addiction medicine specialists- should be undertaken to optimize outcomes^{5,38}. Medically supervised withdrawal in pregnancy, labor, and delivery is not recommended over MOUD, due to high return to opioid use rates (59–90%), low detoxification completion rates, and limited data on maternal and neonatal outcomes beyond delivery¹. However, the lack of long-term outcomes and safe methods for medically supervised withdrawal in pregnancy or delivery, urges more research to identify appropriate cases where medically supervised withdrawal could be a non-inferior and safe option in patients wishing to avoid medication during pregnancy.

Publications on Post-Cesarean Delivery Pain Management

Articles on post-cesarean delivery pain management in pregnant people with OUD primarily include reviews, clinical opinions, letters to the editor, case series, and retrospective

studies^{32,40–47}. Studies have been conflicting on whether people receiving MOUD experience increased pain after cesarean delivery and use higher doses of pain medication. One retrospective study found that opioid-naïve patients report lower pain scores and use less morphine equivalents than pregnant people receiving MOUD with no differences between patients maintained receiving buprenorphine or methadone⁴⁷. In contrast, some studies have found evidence for increased pain and analgesia requirements after cesarean for patients receiving MOUD. Retrospective studies found patients receiving methadone and buprenorphine receive 70% and 47% more opioid medications for pain management after cesarean (respectively) compared to no opioid maintenance^{43–45}. A quality improvement project assessed adherence to a protocol for postoperative pain control in patients with MOUD, and found only 41% received the treatment protocol⁴². Efforts are needed not only to design, but also to reliably implement, systems-based solutions for pain management in patients receiving MOUD.

Available publications are conflicting with respect to use or avoidance of opioids for postpartum pain management in patients with OUD. PRO: A case series reported on continuing MOUD (buprenorphine or methadone) after cesarean delivery, adding scheduled non-steroidal anti-inflammatory drugs (NSAID) and acetaminophen after delivery, and described oral opioid use for breakthrough pain which was effective in reducing pain⁴¹. However, the authors caution on the potential need for higher than typical doses of opioids, although the data to support this conclusion were not provided. A retrospective study assessed post-cesarean opioid analgesic requirements in people with MOUD (methadone or buprenorphine) and found buprenorphine-treated people had less opioid requirements than those treated with methadone⁴⁶. CON: Papers advocating avoidance of opioids after cesarean delivery cite risk for misuse, return to use, and overdose. One retrospective study of 72 subjects found that 75% of people with OUD received opioid medications at discharge after delivery; in regression analysis, receiving opioids at discharge (β 1.35, SE 1.22, $P=0.041$) and having a cesarean delivery (β 1.27, SE 0.97, $P=0.043$) were associated with higher odds of opioid misuse within the first 30 days after delivery³². Another review article made explicit recommendations that no opioids should be used in the perioperative period, although the evidence to support this statement was not provided⁴⁰.

There is no published evidence on social support or psychotherapy for pain management post-cesarean delivery in patients with OUD. There were no identified articles on monitoring that could help answer questions on whether patients with OUD should require additional monitoring during or after cesarean delivery. No available published articles answer specific questions about pain management for patients receiving MOUD related to various pre-existing pain conditions, patients with untreated OUD, and patients with OUD who are currently abstaining from opioids. There are no published articles that address the utility of abdominal wall blocks such as continuous wound infiltration (CWI), transversus abdominis plane (TAP) or quadratus lumborum (QL) blocks after cesarean delivery in people with OUD.

DISCUSSION

Although peer reviewed publications on peripartum pain management in patients with OUD have steadily increased over the years, most of these publications are low on the hierarchy of evidence, with very few randomized trials and systematic reviews compared to available evidence on pain management in other obstetric populations. Published articles do not specify each of the four populations of OUD and MOUD that we specified, indicating a potential need to focus future work on these conditions. Future studies should focus on three key areas. First, it is important to identify heterogeneity of clinical symptoms or treatment effects among pregnant people with OUD. Next, it is critical to assess the effect of OUD or MOUD on acute pain conditions. Finally, studies should identify the influence or interaction of labor postpartum pain and the birth experience on recovery outcomes for people with OUD.

In this review, the consensus questions were considered for specific populations, namely: 1) Pregnant people with MOUD where OUD was due to pain condition; 2) Pregnant people receiving MOUD where OUD not due to pain condition; 3) Pregnant people with untreated OUD; 4) Pregnant people with OUD stable in recovery not receiving MOUD. These groups are critical to study and it is important to come to a consensus on best practices for their management in acute care settings such as labor and delivery.

Although not a part of this review, most peripartum pain management trials have actively excluded people with OUD. Future research should focus on this special population. Alternatively, studies should include them in sampling, with appropriate analyses and sample size calculations that aim to detect differences in this sub-population of interest.

The following themes in knowledge gaps and research opportunities were recognized in this review.

Opioid use for pain management in labor and delivery

The phenomenon of opioid induced hyperalgesia and opioid tolerance has shaped some published opinions that high doses of opioids will be needed for peripartum pain management in patients on opioid agonist therapies. However, exposure to parenteral opioids can also increase risk for return to opioid use. Simultaneously, poor pain control can also increase risk for return to opioid use. The available evidence highlights the need for rigorous research that will identify specific patients who may benefit from, and who may be harmed by, opioid use for peripartum pain management. Other improvements for scientific rigor include standardizing pain assessments and characterizing return to use. High-quality evidence will better guide clinicians on optimal ways to prescribe and monitor opioid use after discharge in patients with OUD.

Management of co-morbid pain and psychological conditions

The available literature shows that psychological co-morbidities are common among pregnant people with OUD. These co-morbidities include anxiety, depression, trauma history, and polysubstance use history. However, there is a lack of high-quality studies on ideal methods to optimize psychological and psychosocial co-morbidities around delivery.

Although social support strategies are essential components of multimodal pain management in non-obstetric settings, the literature related to this current review are focused on these interventions for addiction management. Effectiveness studies on social support interventions for postpartum pain management are lacking.

Notably, no publications discussed naloxone co-prescribing for addiction management, neither in the labor and delivery setting, nor as it relates to opioid prescribing for pain management. Naloxone is an important part of the public health response to the opioid crisis. Given that overdoses are one of the leading causes of maternal death in the United States, naloxone co-prescribing in pregnant and recently pregnant people, although essential, does not appear to be current standard medical management.

Optimal neuraxial analgesia dosing strategies, adjuncts, and supplemental abdominal wall blocks

Case reports, series, and retrospective reviews describe the use of neuraxial analgesia for labor and delivery and postpartum pain management, with many^{5,8,12,26,29,32–39} noting no evidence for increased medication (local anesthetic) use during labor analgesia. The harms of maintaining postpartum neuraxial analgesia is not mentioned in the literature, including potential for increasing risk for thromboembolic events as well as limiting early ambulation goals outlined by published Enhanced Recovery after Cesarean Delivery (ERAC) guidelines⁴⁸. Future research is needed on best local anesthetic dosing strategies, and on neuraxial adjuncts and their doses (e.g., clonidine, dexmedetomidine, lipophilic opioids, and others). For cesarean deliveries, there were no trials specifically addressing the potential role that supplemental abdominal wall blocks (such as continuous wound infiltration (CWI), transversus abdominis plane (TAP) or quadratus lumborum (QL) blocks) may have for optimizing pain management among people with OUD.

Monitoring and Alternative (Non-Opioid and Non-Pharmacologic) Methods of Analgesia

The risk for respiratory depression and moderate sedation when systemic opioids are used for in-hospital peripartum pain management in patients with OUD has been reported⁴⁸. There is an opportunity to focus research on monitoring and safety outcomes in these settings. Ketamine, nitrous oxide, and other alternative analgesia methods require further study for effectiveness and potential harms in this special population. The data are limited but the safety concerns also highlight the need for research on alternative, non-opioid, and potentially non-pharmacologic analgesic strategies in this special population.

CONCLUSIONS

Since 1975, over 80 publications on peripartum pain management in people with OUD have been primarily of low-quality, including case reports, cohort studies, and narrative review articles. Moving forward, studies and publications in this area should focus on generating high quality of evidence to guide clinical practice based on research with rigorous methodologies. Pregnant people with OUD should not be excluded from peripartum pain research; instead, studies should be adequately powered to examine sub-group analyses or should exclusively focus on this special population. Systematic and narrative review

articles and expert opinions may need to be de-emphasized until more, and higher quality evidence becomes available.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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GLOSSARY OF TERMS

ACOG	American College of Obstetricians and Gynecologists
CDC	Center for Disease Control
CWI	Continuous wound infiltration
ERAC	Enhanced Recover After Cesarean Delivery
MOUD	Medications for Opioid Use Disorder
NMDA	N-methyl-D-aspartate
NSAID	Nonsteroidal Anti-inflammatory Drug
OBGYN	Obstetrics and Gynecology
ODU	Opioid Use Disorder
PCA	Patient Controlled Analgesia
PCEA	Patient Controlled Epidural Analgesia
PRISMA	Preferred Reporting Items for Systematic Reviews
TAP	Transversus Abdominis Plane blocks
TENS	Transcutaneous Electrical Nerve Stimulation

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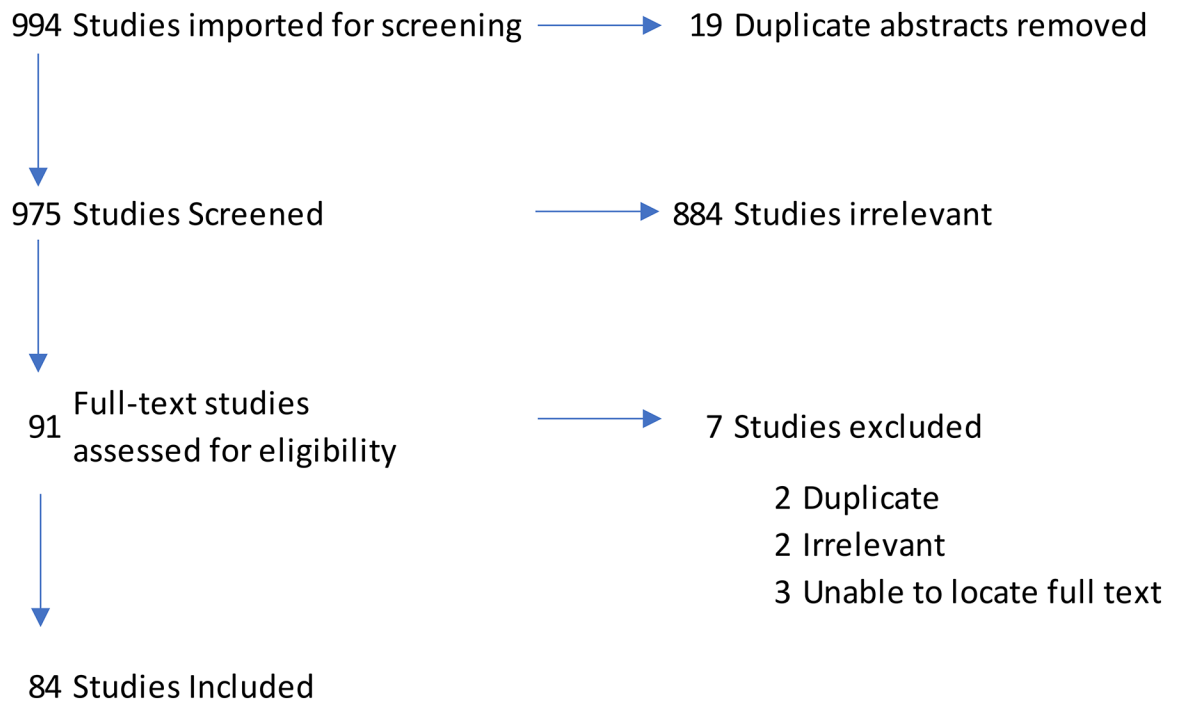


Figure 1.
PRISMA Flow Diagram.

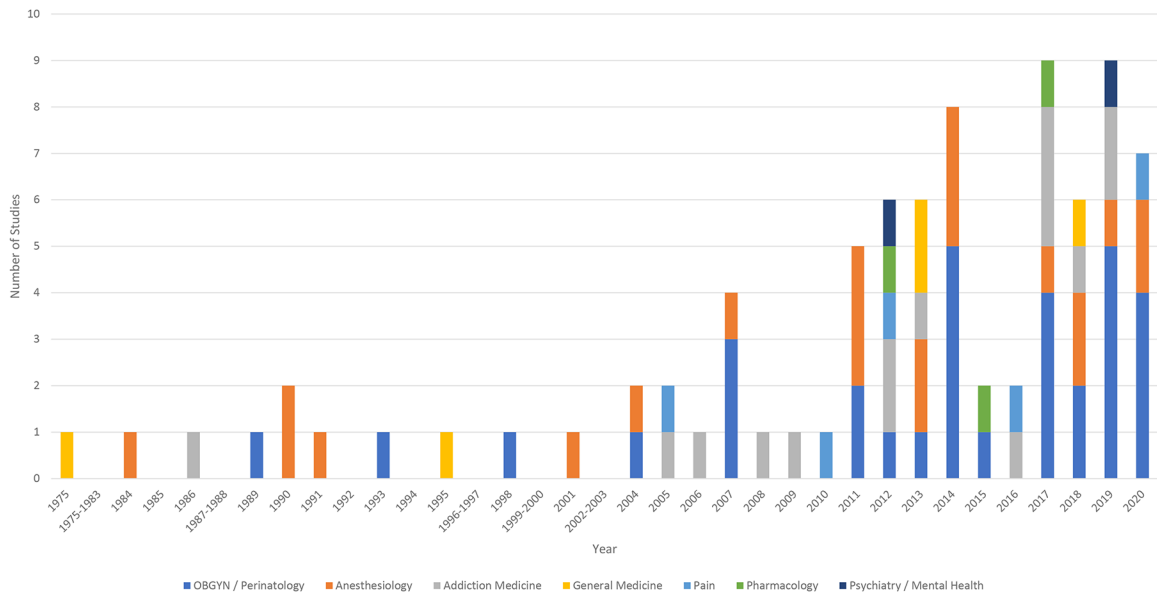


Figure 2. Publication type and counts according to journal type since 1975 indicating an increase in peer reviewed publications on peripartum pain management in people with opioid use disorder, over time.

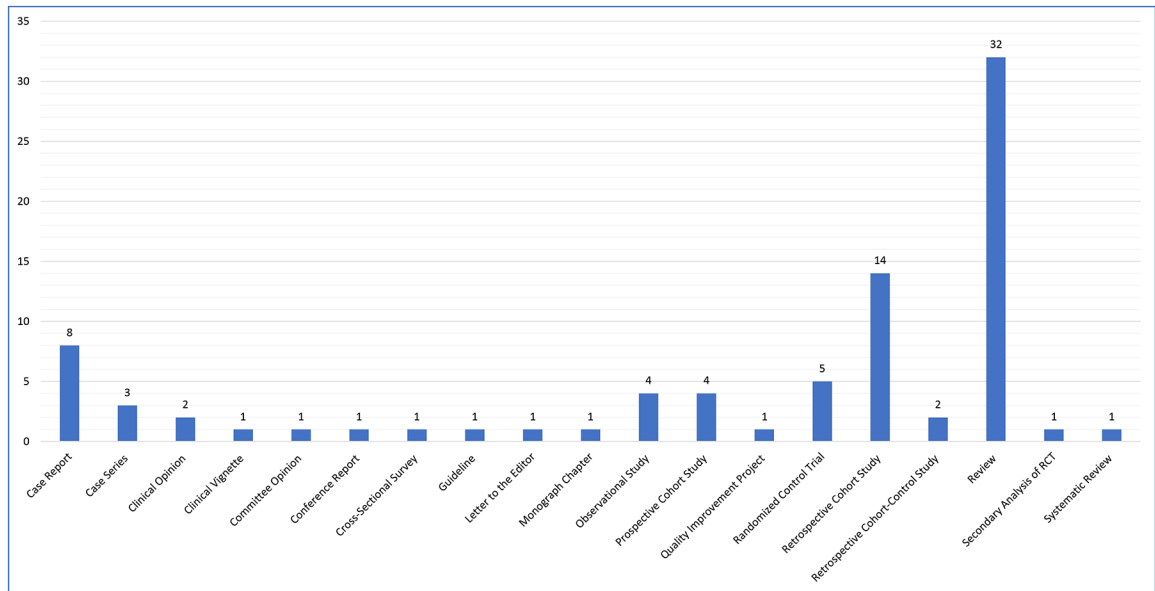


Figure 3. Study methodologies and counts within the study period 1975 to 2020. A disproportionate number of narrative review articles have been published, followed by retrospective studies and case reports. Only 1 systematic review and 5 randomized trials were published in the study period.

OBGYN, Obstetrics & Gynecology

Table 1.

Clinical questions and corresponding evidence.

Question	Guideline	Systematic Review	Narrative Review	Randomized Trial	Cohort Study	Case Control / Case Series / Case Reports	Opinion
Pre-Delivery Pain Management Optimization							
1. What co-morbidities are associated with opioid use disorder that can affect peripartum pain management (anxiety, depression, chronic pain)?		Jones 2008 ¹³	Kork 2011 ¹⁴ Martin 2019 ¹⁵ Park 2012 ¹⁸ Eyler 2013 ¹¹		Ordean 2013 ¹⁷ Smith 2015 ²² Towers 2019 ²⁵	Cengiz 2013 ⁴⁹ Gomar 1984 ⁵⁰	Jones 2014 ⁵¹
2. What co-morbid substance use/abuse disorders are associated with opioid use disorder that can affect peripartum pain management (smoking, benzodiazepines)?			Martin 2019 ¹⁵ Eyler 2013 ¹¹	Hoflich 2012 ¹²	Birnback 2001 ⁸ McCalla 1995 ¹⁶ Robertson 2011 ²⁰ Schulman 1993 ²¹ Ordean 2013 ¹⁷	Tabi 2019 ²⁴	
3. Should all patients with OUD have a pre-delivery anesthesia consult?	Wong 2011 ²⁸		Soens 2019 ²³ Wilder 2015 ²⁷		Cassidy 2004 ⁹ Wiegand 2014 ²⁶	Ecker 2019 ¹⁰ Reddi 2013 ¹⁹	
4. Pre-delivery medication management: Methadone a. For planned vaginal delivery should the dose be continued, increased, reduced, or stopped in anticipation of the delivery admission? b. For planned cesarean delivery should the dose be continued, increased, reduced, or stopped in anticipation of the delivery admission?	Jones 2008 ¹³ Wong 2011 ²⁸		Brown 2020 ⁴⁰ Faitot 2009 ⁵² Fultz 1975 ⁵³ Goff 2007 ⁵³ Gopman 2014 ⁵⁴ Jones 2012 ⁵⁵ Klaman 2017 ⁵⁶ Ludlow 2007 ⁵⁶ Lugo 2005 ⁵⁷ Mahoney 2019 ⁵⁸ Mozurkewich 2014 ⁵⁹ Pan 2017 ⁶⁰ Pritham 2014 ⁶¹ Raymond 2018 ⁶² Sen 2016 ⁶³ Tran 2017 ⁶⁴ Young 2014 Park 2012 ¹⁸ Soens 2019 ²³ Wilder 2015 ²⁷ Martin 2019 ¹⁵	Jones 2009 ²⁹ McNicholas 2012 ⁶⁵ / 2012 ⁶⁵ / 7	Ko 2020 ⁶⁶ Meyer 2007 ⁴³ Wendling 2020 ⁴⁷ Wiegand 2014 ²⁶ Ordean 2013 ¹⁷	Harter 2019 ⁶⁷ Klaman 1990 ⁶⁸ Ecker 2019 ¹⁰	Jones 2018 ³⁴
5. Pre-delivery medication management: Buprenorphine a. For planned vaginal delivery should the dose be continued, increased, reduced, or stopped in anticipation of the delivery admission?	Jones 2008 ¹³		Jones 2012 ⁶⁹ Safley 2017 ⁷⁰ Stanhope 2013 ⁷¹	Jones 2009 ²⁹ McNicholas 2012 ⁶⁵ / 7	Krans 2018 ⁷⁵ Tith 2018 ⁶ Wendling	Leighton 2017 ⁷⁷ Meyer 2010 ⁴⁴	ACOG Committee opinion ¹

Question	Guideline	Systematic Review	Narrative Review	Randomized Trial	Cohort Study	Case Control / Case Series / Case Reports	Opinion
admission? b. For planned cesarean delivery should the dose be continued, increased, reduced, or stopped in anticipation of the delivery admission? c. If continued, should the dose of buprenorphine be split?			Brown 2020 ⁴⁰ Fajot 2009 ⁵² Gopman 2014 ⁵⁴ Jones 2012 ⁴ Landau 2019 ⁷² Ludlow 2007 ⁷³ Mahoney 2019 ⁵⁸ Mozurkewich 2014 ⁵⁹ Pan 2017 ⁶⁰ Pritham 2014 ⁶¹ Raymond 2018 ⁶² Sen 2016 ⁶³ Tran 2017 ⁶⁴ Young 2014 ⁷⁴ Park 2012 ¹⁸ Soens 2019 ²³ Wilder 2015 ²⁷ Martin 2019 ¹⁵		2020 ⁴⁷ Wiegand 2014 ²⁶	Mittal 2017 ⁷⁸ Harter 2019 ⁶⁷ Ecker 2019 ¹⁰	
6. Pre-delivery medication management: Naltrexone a. For planned vaginal delivery should the medication be continued or stopped in anticipation of the delivery admission? b. For planned cesarean delivery should the medication be continued or stopped in anticipation of the delivery admission? c. If stopped, at what stage of pregnancy?			Stanhope 2013 ⁷¹ Tran 2017 ⁶⁴				ACOG Committee opinion ¹
Pain Management in Labor and Delivery							
1. Is there evidence for increased pain, analgesia dose requirement, or increased use of analgesia during labor for patients on OUD treatment including methadone, buprenorphine, and naltrexone?		Souzdalinski 2014 ⁵	Kuczkowski 2007 ³⁵ Wolman 1989 ³⁹ Fultz 1975 ³³		Ludlow 2004 ³⁶ Sander 2005 ³⁷ Ellis 2019 ³² Wiegand 2014 ²⁶	Thakrar 2020 ³⁸	Jones 2018 ³⁴
2. Is there any evidence that the response to neuraxial opioids may be altered (less effective) in patient on buprenorphine?			Kuczkowski 2007 ³⁵		Gupta 2013 ⁷⁹		
3. Neuraxial: a. Should early epidural analgesia be recommended for patients with OUD? b. Should opioids in the epidural solution be increased, decreased, or omitted? c. Should the concentration the local anesthetic be increased? d. Should non-opioid adjuvants be added to the epidural solution including clonidine, epinephrine, dexmedetomidine and/or neostigmine?			Pan 2017 ⁶⁰ Soens 2019 ²³	Martin 1990 ⁸⁰	Hoyt 2018 ⁸¹ Silver 1986 ⁸²	Ecker 2019 ¹⁰	
4. If the patient with OUD is not a candidate for neuraxial analgesia, is there a role for the following: a. Nitrous oxide b. IV Opioid PCA (If PCA is used, is there a particular opioid that is			Fajot 2009 ⁵² Soens 2019 ²³		Migliaccio 2017 ⁸³	Ecker 2019 ¹⁰	

Question	Guideline	Systematic Review	Narrative Review	Randomized Trial	Cohort Study	Case Control / Case Series / Case Reports	Opinion
<p>optimal?)</p> <p>c. Ketamine</p> <p>d. Dexmedetomidine</p> <p>e. Other adjuvants?</p> <p>f. How do narcotic analgesic alternatives interact with MOUD management goals?</p>							
<p>5. Treatment of post-vaginal delivery pain</p> <p>a. If the patient has a high-order vaginal laceration, should long-acting opioids be administered through an indwelling epidural catheter? If so, what doses are recommended?</p> <p>b. Should NSAIDs be used?</p> <p>c. Should acetaminophen be used?</p> <p>d. Is there a role for the routine use of oral opioids in-hospital or at discharge?</p> <p>e. What is the role for other adjuvants for the treatment of post-vaginal delivery pain?</p>							
<p>6. Withdrawal</p> <p>a. If a patient with OUD experiences withdrawal during labor, how should it be treated?</p> <p>b. What are the potential interactions between MOUD and partial antagonists; e.g., nalbuphine, butorphanol (How should opioid-induced intrapartum itching be managed in a patient on buprenorphine?)</p>			Wolman 1989 ³⁹				
<p>7. Monitoring</p> <p>a. Do patients with OUD require additional monitoring during or after labor?</p>							
Post-Cesarean Delivery Pain Management							
<p>1. Should history of OUD impact on the planned mode of delivery (cesarean versus vaginal delivery)?</p>			Eyler 2013 ¹¹			Jones 2006 ⁴¹	Jones 2008 ¹³
<p>2. Is there evidence for increased pain and analgesia intake after cesarean for patient on OUD treatment including methadone, buprenorphine, and naltrexone?</p>			Eyler 2013 ¹¹ Shankar 2012 ⁴⁵		Ellis 2019 ³² Parad 2020 ⁸⁴ Vilkins 2017 ⁸⁵ Meyer 2010 ⁴⁴ Meyer 2007 ⁴³ Wendling 2020 ⁴⁷		
<p>3. Neuraxial anesthesia</p> <p>a. Should the usual dose of neuraxial opioids be increased, decreased or should they be omitted?</p> <p>b. Should non-opioid adjuvants be added to the neuraxial anesthetic including clonidine, epinephrine, dexmedetomidine and/or neostigmine?</p> <p>c. Is there any evidence to suggest superiority of any specific non-opioid neuraxial adjuvant?</p>							

Question	Guideline	Systematic Review	Narrative Review	Randomized Trial	Cohort Study	Case Control / Case Series / Case Reports	Opinion
<p>4. Post-cesarean pain management</p> <ul style="list-style-type: none"> a. What is the role for continuing neuraxial analgesia into the postpartum period? b. Should NSAIDs be used? c. Should acetaminophen be used? d. Is there a role for the routine use of oral opioids in hospital? i. Are there special considerations regarding the type, dose, and quantity? e. Is there a role for the routine use of oral opioids at discharge? <ul style="list-style-type: none"> i. Are there special considerations regarding the type, dose, and quantity? ii. What type of follow-up should be provided? f. What is the role for other adjuvants for the treatment of post-cesarean pain? g. What is the role for regional anesthesia options such as transversus abdominis plane (TAP), erector spinae plane (ESP) and quadratus lumborum (QLB) blocks, or continuous wound infiltration? If so, is any option more effective? h. What is the role for psychotherapeutic or behavioral interventions (e.g., cognitive behavioral therapy) to address post-cesarean pain? <p>5. Management of neuraxial opioid-induced side effects and complications in the patient on buprenorphine</p> <ul style="list-style-type: none"> a. How should itching be managed (Nalbuphine? Dose?) b. How should respiratory depression be managed (Naloxone? Dose?) c. Is morphine-induced hypothermia more common in patients on buprenorphine? How should it be managed <p>6. Monitoring</p> <ul style="list-style-type: none"> a. Do patients with OUD require additional monitoring during or after cesarean delivery? 			Brown 2020 ⁴⁰	Duzyj 2020 ⁸⁶	Kunycky 2018 ⁴² Wilkins 2016 ⁴⁶	Stanislaus 2020 ⁸⁷ Jones 2006 ⁴¹ Leighton 2017 ⁷⁷	Wasiluk 2011 ⁸⁸

Opium, opioid use disorder

IV, intravenous

PCA, patient controlled analgesia

MOUD, medications for opioid use disorder

NSAID, non-steroidal anti-inflammatory drug

TAP, transversus abdominis plane block

ESP, erector spinae plane block

QLB, quadratus lumborum block

⁷ second