Peripartum Administration of Synthetic Oxytocin (Pitocin) and Postpartum Mood Disorders: A Scoping Review

by

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In the United States, maternal mortality and morbidity rates are of great concern, despite advancements in medical technologies and healthcare resources. The frequency of maternal morbidities and severe birthing complications have also increased significantly in recent years. This scoping review examines risk factors, health impacts, outcomes, symptoms, and screening tools associated with administering peripartum synthetic oxytocin (pitocin) and postpartum mood disorders. The health sciences librarian searched three databases to find original research articles that addressed the peripartum administration of synthetic oxytocin (pitocin), looked at pitocin administration and postpartum mood disorders, and were written in English. A total of 364 titles and abstracts were analyzed (after removing 259 duplicates), which left seven remaining articles. Of all the full text articles reviewed, four publications met all inclusion criteria and were included in this scoping review. The author of this review conducted the data extraction, which revealed findings that the existing literature, mainly was quantitative, conducted in upper-middle to high-income countries and focused on the association of synthetic oxytocin administration and postpartum depression. Findings indicate that pregnant women who received a peripartum administration of pitocin had a range of postnatal outcomes ranging from postpartum anxiety, PPD, somatization disorders, and postpartum blues. Articles that were reviewed identified various risk factors that increase the risk of developing PPD, such as a maternal history of depression, prenatal depression and anxiety, PTSD, and a negative childbirth experience; also, one study reported no

protective factors against postpartum mood disorders or any direct association of pitocin administration with PPD.

The public health significance of the use of Pitocin during the peripartum period and its impact on maternal mood and behavior is a subject that has not received sufficient attention from the medical community and researchers, given its frequent use as a birth intervention in the United States. Therefore, future research studies should be longitudinal and conducted with more samples from the United States population. Current birthing interventions and practices should be reevaluated for their benefits, risks, and potential contribution to PPD in birthing women.

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List of Abbreviations

ACOG (American College of Obstetricians and Gynecologists)

Edinburgh Postnatal Depression Scale (EPDS)

NICU (Neonatal Intensive Care Unit)

PPD (Postpartum Depression)

PPMD (Postpartum Mood Disorders)

PTSD (Post-Traumatic Stress Disorder)

WHO (World Health Organization)

List of Definitions

Intrapartum refers to the period of labor and delivery when the mother's body undergoes changes to give birth to her baby. This period begins with the onset of labor and ends with the delivery of the baby and the placenta (American College of Obstetricians and Gynecologists, 2018)

Peripartum - the period of time that includes the weeks leading up to childbirth, the time during delivery, and the weeks immediately after delivery. During the peripartum period, the mother experiences a range of physical and emotional changes as she prepares for and recovers from the birth of her child. The term "peripartum" often refers to the postpartum period, the time after childbirth (American College of Obstetricians and Gynecologists, 2018)

Somatization Disorder - a mental illness in where individuals experience ongoing physical symptoms that cause significant distress and impair their ability to function in important areas of their life, such as work or social relationships (American College of Obstetricians and Gynecologists, 2018).

Preface

I want to start by thanking God for continually guiding my footsteps and being my firm foundation. I would like to thank my Mama for her constant support, love, and faith in who I am and my abilities. I thank my sister for being my best friend, a shoulder to lean on, and a continual inspiration. To all my friends and family who have supported me throughout my journey, I love you endlessly, and thank you. To Durga, I thank you for making this graduate school experience and thesis all worthwhile; I thank you for the endless laughs, the tears, and the motivation to be the best version of myself; I love you dearly.

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1.0 Background

1.1 Introduction

Pitocin administration during the peripartum period has become a routine birth intervention in developed countries. Synthetic oxytocin was developed in the 1950s and has played a critical role in the augmentation of labor and addressing hemorrhage risk in birthing individuals (Kroll-Desrosiers et al., 2017). According to the American College of Obstetricians and Gynecologists (ACOG), the rates of Pitocin induction doubled from 9.5% in 1990 to 23.3% in 2012 (American College of Obstetricians and Gynecologists, 2018); following the data reports from ACOG, the World Health Organization (WHO) declared that Pitocin was to be implemented as the primary agent in actively managing the third trimester of pregnancy (WHO,2012). Oxytocin is a naturally occurring chemical within the human body that facilitates contractions during childbirth. Aside from naturally progressing the body during labor, natural oxytocin contributes to mother-infant bonding and maternal mood (Karakuş & Pulatoğlu, 2019). There is limited research on how Pitocin is incorporated into the body's natural flow of oxytocin, which could be a potential explanation for the link between the peripartum administration of Pitocin and postpartum mood disorders. A systematic review was conducted on the association of synthetic oxytocin and postpartum depression, finding mixed evidence linking synthetic oxytocin administration during labor to postpartum depression (Thul et al., 2020). In addition, the existing review elected articles for review that consisted of observational studies, randomized controlled trials, and animal studies (Thul et al., 2020). This study will look specifically at original research articles with human-based

populations only. This review will also examine current literature on synthetic oxytocin administration and postpartum mood disorders like PTSD, postpartum anxiety, or postpartum psychosis.

1.2 Maternal Morbidity

Maternal morbidity is a significant problem within the United States because it is one of the few developed countries where maternal mortality rates are the highest and are continually on the rise (Ozimek & Kilpatrick, 2018). Maternal morbidity is a health problem women face during pregnancy, childbirth, or after delivery. Maternal morbidity is a severe concern in the United States, as the country has one of the highest maternal mortality rates among developed countries (Howell, 2018). In addition to maternal mortality, several other maternal morbidities can occur during or after pregnancy, including:

1. Hemorrhage: This refers to excessive bleeding during or after childbirth. It can be caused by a number of factors, including problems with the placenta, trauma during delivery, or coagulation disorders.
2. Hypertensive disorders: These are conditions such as pre-eclampsia and eclampsia that can develop during pregnancy and can lead to complications for both the mother and the baby.
3. Infection: Infections can occur during pregnancy, delivery, or after childbirth. Examples of infections that can lead to maternal morbidity include sepsis, urinary tract infections, and postpartum infections.

4. Preterm labor: Preterm labor refers to when a woman goes into labor before 37 weeks of pregnancy. This can lead to complications for the baby, such as respiratory distress syndrome, as well as for the mother, such as hemorrhage or infection.
5. Maternal mental health issues: Mental health issues can arise during or after pregnancy, including anxiety, post-traumatic stress disorder (PTSD), and, more commonly, postpartum depression (PPD).

According to data from the Centers for Disease Control and Prevention (CDC), there were 17.4 maternal deaths per 100,000 live births in the United States in 2018 (Ozimek & Kilpatrick, 2018). This is a significant increase from previous years, and the United States now has a higher maternal mortality rate than many other developed countries, especially for African American women. According to the Centers for Disease Control and Prevention (CDC), Black women are three to four times more likely to die from pregnancy-related complications than their white counterparts (Chinn et al., 2021). This alarming statistic has remained consistent for several decades, despite advances in medical technology and countless attempts to improve overall maternal health outcomes in the U.S.

The reasons that pregnant African American women are most impacted by maternal health disparities and inequities are complex and multifaceted and include factors such as:

1. Structural racism: Black women are more likely to experience discrimination and bias in healthcare settings, which can lead to lower-quality care, delayed treatment, poorer health outcomes, and death.
2. Social determinants of health: African American women are more likely to live in poverty, have limited access to healthy food and safe living environments, and experience high

levels of stress, be the sole financial contributor to their household, all of which can negatively impact maternal health and well-being.

3. Pre-existing health conditions: African American women are more likely to have pre-existing health conditions such as hypertension, diabetes, and obesity, which can increase the risk of pregnancy-related complications.
4. Implicit biases: Medical staff and physicians are taught to hold implicit biases that negatively impact the care they provide to Black women, such as assuming that Black women are less compliant with medical advice or experiences less pain than their counterparts.

   Efforts to address these disparities include:

   - Improving access to high-quality healthcare for African American women.
   - Addressing social determinants of health.
   - Increasing awareness, education, and training among healthcare providers about implicit biases.
   - Promoting policies that support maternal health and well-being for all women.

These life-threatening conditions can have serious health consequences for women and affect their babies' health. Several factors contribute to maternal morbidity in the United States, including inadequate access to healthcare, racial and ethnic disparities in maternal healthcare, and systemic issues within the healthcare system (Chinn et al., 2021). Addressing these issues will require a comprehensive approach that includes improving access to healthcare, increasing awareness of maternal health issues, and addressing systemic inequalities that contribute to maternal morbidity.

1.3 Postpartum Mood Disorders

Postpartum mood disorders are a group of mental health conditions that can occur after giving birth (American Psychiatric Association, 2013). These conditions are characterized by symptoms such as depression, anxiety, and mood swings and can negatively impact a mother's ability to care for herself, her baby, and her family (Werner et al., 2015). Postpartum mood disorders can include:

1. Postpartum depression (PPD): a type of depression that can occur within the first year after giving birth (American Psychiatric Association, 2013).
2. Postpartum anxiety: a condition characterized by excessive worry or fear, often about the health and safety of the baby (American Psychiatric Association, 2013).
3. Postpartum obsessive-compulsive disorder (OCD) is characterized by intrusive, repetitive thoughts and/or compulsive behaviors (American Psychiatric Association, 2013).
4. Postpartum post-traumatic stress disorder (PTSD): a condition that can occur after a traumatic birth experience, characterized by flashbacks, nightmares, and avoidance of triggers (American Psychiatric Association, 2013).
5. Postpartum psychosis: a rare but severe condition characterized by hallucinations, delusions, and disorganized thinking (American Psychiatric Association, 2013).

Postpartum mood disorders can be caused by physical, psychological, and social factors, including hormonal changes, sleep deprivation, and the stress of caring for a newborn(*Postpartum depression - Symptoms and causes - Mayo Clinic*, n.d.). Treatment for these conditions may include counseling, medication, and support from family and friends.

According to research, postpartum mood disorders are widely undiagnosed, underrated, and more commonly misdiagnosed (Werner et al., 2015). Postpartum mood disorders are

becoming increasingly common for birthing mothers, and if undiagnosed or left untreated, mood disorders can be detrimental to mothers and their infants.

Research has shown that Postpartum depression (PPD) affects approximately 19% of all mothers and is responsible for negatively impacting maternal sensitivity, mother-child bonding, child development, and parental competencies (Takács et al., 2019). Additionally, various studies have identified an association between postpartum maternal mood with a child's increased risk of decreased social development skills (Takács et al., 2019). The most common symptoms and side effects of postpartum depression are "depressed mood, decreased appetite, trouble sleeping, decreased concentration abilities, feeling worthless; and in severe cases, PPD can lead to suicidal thoughts or action, psychosis, and hallucinations or delusions to harm the infant" (Karakuş & Pulatoğlu, 2019). There are increased risks for developing PPD following childbirth, including prior diagnosis and history of prenatal anxiety, prenatal depression, and postpartum depression from previous pregnancies (Karakuş & Pulatoğlu, 2019).

Additionally, research suggests that experiencing birth trauma from the use of birthing interventions can increase the risk of developing postpartum depression (Takács et al., 2019).

Birth trauma occurs when a pregnant woman experiences physical and/or emotional injuries during childbirth. Birthing trauma can result from a variety of factors, like medical complications, unexpected events, or feelings of loss of control during the birthing process (Simpson & Catling, 2016).

There are two main types of birth trauma that are common among birthing women:

1. Physical: This refers to any injury that occurs to the mother or baby during childbirth. Physical birth trauma can include injuries to the mother's reproductive organs, such as tears,

lacerations, or pelvic floor damage, as well as injuries to the baby, such as bruises, fractures, or nerve damage (Simpson & Catling, 2016).

2. Emotional: This refers to psychological distress that can result from a difficult or traumatic childbirth experience. Emotional birth trauma can include feelings of fear, helplessness, and loss of control during childbirth, as well as feelings of guilt, shame, or inadequacy after the birth. Emotional birth trauma can also be caused by medical interventions that were unexpected or unwanted, such as a cesarean section, epidural, labor induction, labor augmentation, or the use of forceps (Simpson & Catling, 2016).

It is also critical to note that the two main types of birth trauma are not exclusive to all birthing women. Furthermore, not all birthing women will experience a traumatic birth or be diagnosed with a postpartum mood disorder, for those women that do, the effects can be chronic, impacting their overall physical and emotional well-being as well as their relationships with their family.

1.4 Birth Interventions

Birthing interventions during labor that are commonly practiced in hospital settings include labor induction, augmentation of labor, mid-wife-assisted delivery, episiotomy, and a cesarean birth (Jansen et al. 2013). Several common birthing interventions may be used during labor and delivery in the United States. Some of the most common interventions include:

1. Epidural (Epidural Anesthesia): A pain relief medication is injected into the lower back to numb the lower half of the body. It can help manage the pain of labor and delivery, but it may also increase the likelihood of other interventions, such as vacuum or forceps delivery.

2. Induction of labor: This occurs when labor is artificially started using medications such as Pitocin. Induction is often used when a pregnancy has passed its due date or if there is a medical reason that the baby needs to be birthed to save the mother and baby's life.
3. Vacuum/Forceps delivery: A *vacuum* is a soft cup attached to the baby's head to pull the baby out gently. Forceps are metal tongs that are used to grasp the baby's head and guide it out.
4. Cesarean section (C-section): This is a surgical procedure in which the baby is delivered through a cut made in the mother's abdomen and uterus. C-sections are sometimes planned if there are medical reasons why vaginal birth is not recommended, but they may also be performed in emergencies during labor.

This review will focus specifically on the labor induction and augmentation method of injecting Synthetic Oxytocin into pregnant women. However, there are several ways to induce or augment labor, including:

1. Membrane sweeping: A healthcare provider uses a gloved finger to separate the amniotic sac from the cervix to stimulate the release of prostaglandins, which can help ripen the cervix and start labor.
2. Synthetic Oxytocin (Pitocin): A synthetic form of oxytocin is administered through an IV to stimulate contractions, help the cervix dilate, and prevent postpartum hemorrhaging.
3. Foley catheter: A small tube with a balloon on end is inserted through the cervix and filled with water to help dilate the cervix and start labor.
4. Amniotomy: Also known as breaking the water, this is a procedure in which the healthcare provider uses a small instrument to break the amniotic sac, which can help stimulate labor.

5. Prostaglandin E2: A hormone medication inserted into the vagina to help ripen the cervix and start labor.

1.5 History of Pitocin

In 1953, Pitocin, a synthetic form of the hormone oxytocin, was synthesized by Sir Henry Dale, Vincent du Vigneaud, and colleagues to induce or augment labor (Zhang et al., 2018). Throughout the years, pitocin has not only been recognized by organizations such as ACOG and the Federal Drug Administration (FDA) for its aid in labor induction and augmentation, but it has also been subject to questioning by researchers and scientists regarding its risks and benefits to birthing women.

During the 1960s and 1970s, the administration of Pitocin became used more frequently among obstetricians for inducing or augmenting labor (den Hertog et al., 2001). This popularity was due to several factors, including the theory that it was safer to induce labor with Pitocin rather than to let pregnancies go past their projected due date ("ACOG Practice Bulletin No. 107: Induction of labor.," 2009). Additionally, many obstetricians appreciated the ability to control the birthing timeline and the perception that Pitocin could reduce the need for cesarean deliveries (Zhang et al., 2018). The rise in popularity of Pitocin is also credited to the general trend toward medicalizing childbirth during this timeframe (Sabetghadam et al., 2022). As a result of this medical childbirth trend, Pitocin became widely accepted and frequently utilized in obstetrics, with its usage continuing to increase throughout the 1980s and 1990s (Zhang et al., 2018).

1.6 Modern Pitocin Practices

Pitocin continues to be commonly used in obstetrics to induce or augment labor. According to a study published in Obstetrics & Gynecology in 2002, the birthing intervention of induction of labor with Pitocin increased from 9.5% to 22.3% of all births in the United States between 1992 and 2000, while the use of Pitocin for augmenting labor increased from 12.6% to 18.3% during this timeframe (Tsakiridis et al., 2020). These statistics reveal that a significant proportion of births in the United States involve using Pitocin, which may continue to increase.

The rationale for using Pitocin in modern obstetrics is similar to that of the past; modern-day obstetricians choose to induce labor with Pitocin if they perceive that delivering the baby earlier than scheduled is safer than letting the pregnancy continue beyond a specific date (Tsakiridis et al., 2020) . Induction of labor with Pitocin may also be necessary for pregnancy complications requiring prompt delivery, such as preeclampsia or fetal distress. Furthermore, physicians may employ pitocin to augment labor in cases where the mother is not progressing down an optimal timeline or if the contractions are not strong enough to allow the mother to push out the baby (Tsakiridis et al., 2020).

Despite the constant utilization of Pitocin in obstetric units throughout the United States, its usage continues to be controversial. Research studies have found that using Pitocin may increase the risk of pregnant women experiencing complications, including uterine rupture, neonatal jaundice, and postpartum hemorrhage (Cheng et al., 2009). However, other studies have refuted negative associations, siding with its potential life-saving abilities. Given that Pitocin is still a prominent birthing intervention in the U.S., and the United States has the highest maternal mortality rate, healthcare professionals must carefully re-evaluate its frequent usage, benefits, and risks.

1.7 Pitocin and PPD

Recent studies suggest that there may be a positive association between the use of Pitocin during labor and the development of postpartum depression (PPD) following childbirth (Kroll-Desrosiers et al., 2017). A study published in the Journal of Women's Health in 2011 found that women who received Pitocin during labor were more likely to experience PPD symptoms within the first two postpartum weeks than women who did not receive pitocin. The study concluded that using Pitocin may alter the release of endogenous oxytocin in the body, thereby increasing the risk of PPD in birthing women.

Similarly, another study published in the Archives of Women's Mental Health in 2013 found a positive association between the use of Pitocin and PPD symptoms. The study suggested that Pitocin during labor may affect maternal mood, behavior, and mother-infant bonding, leading to an increased risk of PPD.

Despite these findings, it is crucial to note that other studies have found a negative association between Pitocin and PPD; instead suggesting it decreased the risk for pregnant women developing PPD. A study published in Obstetrics and Gynecology in 2017 concluded that using Pitocin during labor did not increase the risk of PPD (Kroll-Desrosiers et al., 2017). A systematic review published in 2019 also did not find a significant association between Pitocin administration and postpartum mood disorders.

This scoping review will specifically focus on Peripartum administration of pitocin and postpartum mood disorders including PPD, PTSD, and Postpartum anxiety. In this review, the current state of literature surrounding peripartum Pitocin administration will be analyzed as future directions for research, interventions, and policies regarding birth interventions are explored and proposed.

1.8 Rationale

The impact of peripartum Pitocin administration during labor on women's post-partum mood and behavior is largely understudied (Takács et al., 2019). Post-partum mood disorders are becoming increasingly prevalent in birthing women and currently affect approximately 20% of mothers following childbirth (Thul et al., 2020). The administration of Pitocin has become a regular protocol for individuals giving birth in some hospital settings. According to data from the Centers for Disease Control and Prevention (CDC), in 2018, Synthetic Oxytocin (pitocin) was used in approximately 59% of all births in hospitals across the United States (Bell et al. 2014). Pitocin is usually administered to induce or "augment" labor and is sometimes administered immediately following childbirth to prevent hemorrhaging (Thul et al., 2020). The administration of synthetic oxytocin is associated with the increased likelihood of a birthing person developing post-partum mood disorders, including post-partum depression and anxiety (Bell et al. 2014). In contrast, some studies validate Pitocin's usage as a protective factor against PPD, thus decreasing the likelihood of women developing PPD following childbirth (Yim et al. 2015). Post-partum depression and anxiety are linked to various adverse health outcomes for the mother and infant, including the inability to form an attachment with a newborn, decreased likelihood of breastfeeding, negative parenting behaviors, and decreased overall emotional, mental, and physical well-being of the mother. Several studies have identified Pitocin as a potential contributor to post-partum mood disorders in birthing persons following childbirth (Gu et al., 2016). By synthesizing preexisting research and knowledge surrounding Pitocin administration during the peripartum period and its association with post-partum mood disorders and determining potential, impacts risks, and contributions to maternal mood and behavior, the findings from this scoping review can

contribute to inform existing labor protocols and interventions regarding medications administered to individuals during childbirth.

1.9 Objectives

The objective of this scoping review is to synthesize existing literature on peripartum pitocin administration during childbirth and its association with postpartum mood disorders (PPMD). This scoping review has two primary aims:

Describe the relationship between synthetic oxytocin (Pitocin) and postpartum mood disorders as reported in the literature.

Describe the current state of research and literature surrounding the relationship between synthetic oxytocin (Pitocin) and postpartum mood disorders.

2.0 Methods

2.1 Author Positionality

In line with the practice of self-reflexivity, the author of this scoping review is not a physician or clinician. The author is a public health professional that has training and experience working on research concerning maternal and child health, health equity and reproductive health. Awareness of one's positionality aids in recognizing the perspective from which this work was carried out.

2.2 Search

Medline (Ovid), APA PsycInfo (Ovid), and Embase (Elsevier) were searched by a health sciences librarian with systematic review experience. The date of the last search was January 31st, 2023. Concepts that made up the searches were: Oxytocin, Anxiety, Depression, and Postpartum Period. Limiters were added for language and geographic location. The initial Medline search was developed using Medical Subject Heading (MeSH) terms, titles, abstracts, and keywords. The search was then adapted to search other databases. Duplicates were removed after the initial search using the AED method. Appendix 1 has all search strategies and data related to each search. EndNote (Clarivate) was used to store all citations found in the search process and to check for duplicates not found during the search process. Search strategies and results were tracked using an Excel workbook explicitly designed for 1-person reviews (VonVille, 2023).

2.3 Selection of Sources of Evidence

Once the initial set of sources was identified, titles, and abstracts of the articles were imported into a Microsoft Excel workbook. The author developed a screening process based on eligibility criteria. Abstracts that included one exclusion criterion were excluded from the review and recorded the exclusion in the workbook.

2.4 Eligibility Criteria

In order for an article to be considered for this review, studies met the following inclusion criteria:

1. The study had to address the peripartum administration of synthetic oxytocin (pitocin).
2. The study had to look at pitocin administration and postpartum mood disorders, or maternal mood.
3. The study had to be original research (qualitative, quantitative or mix-methods) published in a research journal.
4. The study had to be written in English.

The author excluded articles examining the association of peripartum pitocin administration and PPD with a previous medical history of postpartum mood disorders or general depression or mood disorders because mothers with prior medical diagnosis may be susceptible to contracting Postpartum mood disorders.

Based on the eligibility criteria, the author used the following logic excluding studies that:

1. Focus on Pitocin's role in childhood development through breastfeeding.

2. Focus on the body's natural oxytocin and postpartum mood disorders.
3. Focuses on mothers that have received this birth intervention but have prior history/diagnosis of depression or mood disorders, without pitocin administration.
4. Focus on pitocin that was not administered during the peripartum period.
5. Focus on pitocin and fatherhood bonding.
6. Focus on pitocin and genetics.
7. Focus on postpartum mood disorders without peripartum pitocin administration.
8. Is not published in a journal.
9. Is not original research (i.e., editorial, review)
10. Is non-human research based (I.e., animal studies)

The chosen eligibility criteria have various rationales for inclusion consideration. The author excluded articles that discussed the body's natural oxytocin and its association with postpartum mood disorders because the is no presence of the birth intervention of Pitocin to induce or augment labor; therefore, are outside the scope of this literature review. The author excluded studies if they met one of the exclusion criteria and noted the reasoning for each's study's exclusion.

2.5 Data Charting Process

The author reviewed articles chosen for inclusion to complete a data extraction form. The author expected to examine several types of studies; therefore, the data extraction form was developed based on several reporting guidelines (Vonville, 2023). One reviewer conducted the data charting process.

2.6 Data Items

The author utilized a standardized data extraction form to capture data relevant to the inclusion criteria. The form included information used to identify the article source, such as the title and abstract of the journal article, a compiled list of authors, and their corresponding publication dates. Additionally, the form used for data extraction compiled information about the study's design, the population of interest, sample population/recruitment strategies, the study aims, risk factors, measurement tools, symptoms, health impacts, and outcomes. The final portion of the form outlines study findings, gaps in research/literature analyzed, and the author's conclusions.

2.7 Synthesis of Results

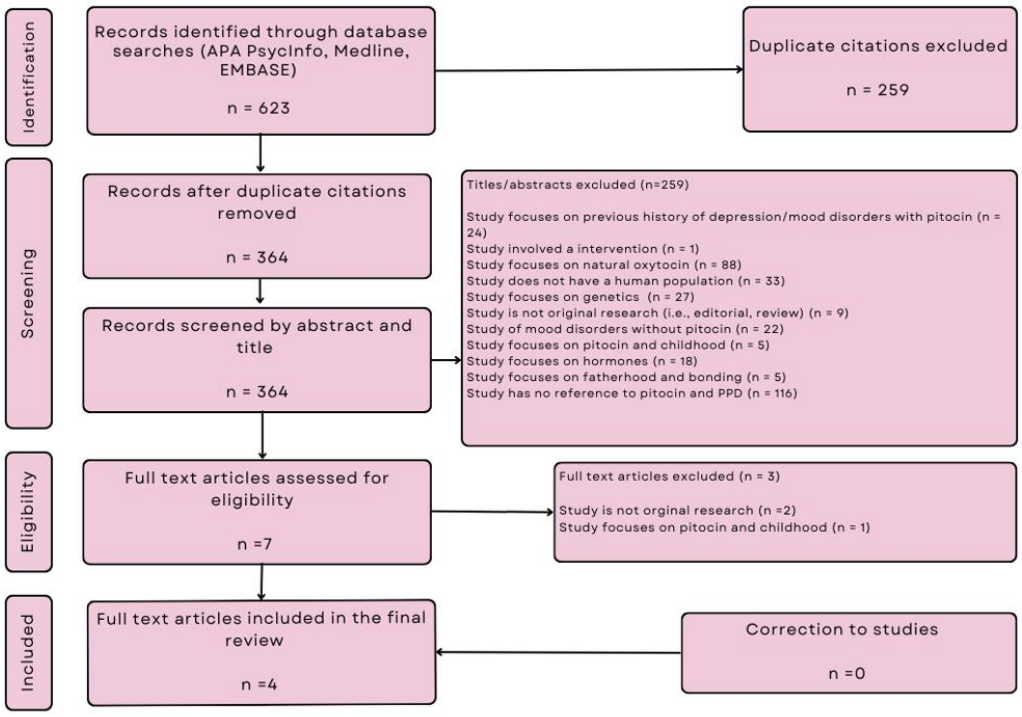
1. The studies included were grouped based on the type of study (I.e., original research) and topics addressed (i.e., risk factors, long-term complications). Where we identified a systematic review, we counted the number of studies included in the review that potentially met our inclusion criteria and noted how many studies had been missed by our search. (54) The synthesis aims to present the range of evidence identified to answer the review question or meet the objectives of the scoping review.

3.0 Results

3.1 Study Selection

The initial searches in APA PsychInfo, EMBASE, and Medline identified 623 articles; after excluding duplicate citations, 364 were screened by title and abstract. The full text of 7 articles was reviewed, and 4 publications were included in this review. The PRISMA Flowchart (Figure 1) recorded the stage at which each publication was removed from the screening process.

Figure 1 PRISMA Flowchart



3.2 Populations

The studies included pregnant women primarily in their last trimester of pregnancy who received an intravenous dosage of synthetic oxytocin in the peripartum period (OR within 48 hours of childbirth). However, one article selected their sample from the University of Massachusetts Memorial Medical Center's (UMMHC) clinical repository of patients with a prior history of pre-pregnancy depressive and anxiety disorders, which was the only U.S.-based study and did not an include analysis of outcomes by race or ethnicity. (Kroll-Desrosiers et al., 2017).

3.3 Study Location(s)

The studies reviewed were conducted in 4 different countries. All of the countries where the studies took place were developed, with two being classified as "upper-middle" or "high" income countries.

3.4 Methodology

All of the articles utilized quantitative methods in order to analyze data. The majority of the studies utilized depression screenings tools and surveys to collect data, where the primary screening tool across all studies was the Edinburgh Postnatal Depression Scale (EPDS). Additionally, the other screening tools used to collect data are 1) Beck's Depression Inventory, 2) Maternity Blues Questionnaire, 3) Generalized Anxiety Disorder 7-Item Scale, 4) Perinatal

Posttraumatic Stress Questionnaire, and 5) Somatization Subscale. One study utilized the MiCARD Query Tool from the University of Massachusetts Memorial Medical Center (UMMHC) to access a clinal repository of patients where confidential and protected health information regarding previous patients is stored according to using personal medical record numbers (Kroll-Desrosiers et al., 2017). Two of the studies were longitudinal, with one explicitly having prospective and observational design elements incorporated within the study. The quantitative study followed a retrospective study design where the study sample was taken from the data range January 5th, 2009 - April 4th, 2014. There was one study where data collected from postpartum screening tool administration was their only source of data.

3.5 Study Topics

The studies assessed were classified by the following topics: risk factors, health impacts, outcomes, symptoms, and measurements. The categories for the study topics were chosen to define and distinguish literature surrounding the peripartum administration of pitocin and postpartum mood disorders. All articles chosen to be reviewed were featured in each topic category. For more descriptive information regarding the included studies, see Table 1.

3.6 Overview of Findings

The studies analyzed in this review examined the relationship between peripartum pitocin administration and 1) postpartum symptoms of depression and anxiety, 2) postpartum blues, 3) depression, 4) postpartum depression/anxiety, and 5) somatization.

The following findings were drawn from the included studies:

1. ((Karakuş & Pulatoğlu, 2019)
    - This study aimed to investigate the association between the administration of pitocin for postpartum hemorrhage prevention, treatment, and postpartum depression (PPD) in women who gave birth at a tertiary care hospital in Istanbul, Turkey. The study comprised 204 women who had vaginal births and were administered synthetic oxytocin either for prophylaxis or treatment of postpartum hemorrhage. The study included a control group of 200 women who did not receive oxytocin. In addition, PPD was determined by using the Edinburgh Postnatal Depression Scale (EPDS) at 4-6 weeks postpartum. The study's results showed that the prevalence of postpartum depression was significantly higher in the synthetic oxytocin group compared to the control group (29.9% vs. 15.0%, p=0.001). Additionally, the authors found that the odds of developing postpartum depression were 2.44 times higher in the synthetic oxytocin group compared to the control group (OR=2.44, 95% CI: 1.44-4.13, p=0.001). The authors concluded the study by stating that "exogenous use of oxytocin" may be a pivotal contributor to postpartum symptoms/feelings of depression and/or anxiety.
2. (Gu et al., 2016)
    - This randomized controlled trial (RCT) study aimed to investigate intrapartum synthetic oxytocin's effects on maternal well-being at two months postpartum. The study included

119 women who had vaginal births. The study participants were randomly assigned to receive either intrapartum synthetic oxytocin (n=61) or no oxytocin (n=58). Maternal well-being was assessed using the Edinburgh Postnatal Depression Scale (EPDS), Generalized Anxiety Disorder 7-Item Scale, Perinatal Posttraumatic Stress Questionnaire and the Somatization Subscale at baseline, one week postpartum, and two months postpartum. The study results showed no significant differences in depressive symptom scores between the oxytocin-exposed group and the control group at any of the time points assessed. The authors found no significant association between synthetic oxytocin and perinatal posttraumatic stress symptoms. However, they noted that intranasal administration of synthetic oxytocin may play a vital role in developing depressive symptomatology in postnatal women.

3. (Kroll-Desrosiers et al., 2017)
    - This retrospective cohort study investigated the association between peripartum synthetic oxytocin administration and the risk of developing depressive and anxiety disorders within the first postpartum year. The study included a study population of 7,034 women who gave birth between 2006 and 2015 and received care at the University of Massachusetts Memorial Medical Center (UMMHC). The study population was divided into two groups based on whether or not they received peripartum synthetic oxytocin during labor and delivery. The primary outcome of this study was the incidence of depressive and anxiety disorders within the first postpartum year, which were determined by the International Classification of Diseases, Ninth Revision, and Clinical Modification (ICD-9-CM) codes stored in the hospital's electronic medical records. The study results showed no significant difference in the

incidence of depressive and anxiety disorders within the first postpartum year between the oxytocin-exposed group and the non-exposed group (11.9% vs. 12.1%, respectively, p=0.69). The authors concluded that pregnant women with peripartum exposure to synthetic oxytocin have a higher relative risk of having a clinical diagnosis of depression or anxiety disorders; however, peripartum synthetic oxytocin administration was not associated with an increased risk of developing depressive and anxiety disorders within the first postpartum year. Additionally, study participants were more likely to have received prescriptions for antidepressant/anxiolytic medications within the first postpartum year compared to women without synthetic oxytocin exposure.

4. (Takács et al., 2019)
    - This prospective observational study investigated the effects of intrapartum synthetic oxytocin on maternal postpartum mood. The study recruited 305 women who gave birth vaginally and received intrapartum synthetic oxytocin during labor. The study population was assessed for PPD using the Edinburgh Postnatal Depression Scale (EPDS) and the Maternity Blues Questionnaire 48 hours following childbirth, two weeks, and six weeks postpartum. The study results showed no significant difference in EPDS scores between the oxytocin-exposed group and the control group at any of the time points assessed. However, the oxytocin-exposed group had significantly higher scores on the Maternity Blues Questionnaire at 48 hours postpartum than the control group. However, there were no significant differences in the Maternity Blues scores between the two groups at two weeks and six weeks postpartum. The authors concluded that pregnant women exposed to synthetic oxytocin in the intrapartum period

may be associated with a decreased likelihood of developing postpartum mood depression. However, results found no protective factors against pregnant women developing postpartum blues.

3.7 Risk Factors and Associations

The common risk factor throughout all studies was a prior history of postpartum depression and anxiety. However, many other risk factors were examined, including perinatal or intrapartum exposure, prenatal depression, and anxiety, perinatal mental health diagnosis, posttraumatic stress disorder (PTSD), negative childbirth experience, previous or postpartum exposure to antidepressant/anxiolytic medications, and maternal history of depression. In addition, two studies identified intrapartum exposure to synthetic oxytocin as a risk for developing a postpartum mood disorder, while one study identified peripartum exposure as a risk factor.

3.8 Health Impacts

The most common health impact across all studies was symptoms of depression and anxiety in the postpartum period. Equally important, the remaining studies outlined the following health impacts for peripartum exposure to synthetic oxytocin: uterine hyperstimulation, fetal distress, poor fetal oxygenation, abnormal fetal heart rate, uterine rupture, decreased maternal mood, infant irritability, poor infant sleep, difficulty initiating/carrying out breastfeeding, failed lactation and in severe cases maternal suicide.

3.9 Outcomes

All studies found postpartum depression and anxiety as the primary outcome of exposure to pitocin in the peripartum period. Symptoms of generalized depression and anxiety disorders, somatization, and postpartum blues were also noted within these articles.

3.10 Symptoms

The articles all indicated that the most prevalent symptoms of postpartum mood disorders are the onset of feelings of depression and anxiety following childbirth. The following symptoms recorded in studies were outlined as indicators of PPD: loss of interest & energy, sleeping and eating changes, diminished ability to think or concentrate, feelings of worthlessness, recurrent suicidal ideations, anxiety, psychotic features (i.e., delusions or hallucinations) to harm infant, posttraumatic stress disorder (PTSD), somatization, avoidance, increased arousal, intrusive thoughts, bodily dysfunction, onset depressive or anxious feelings during pregnancy and diagnosis of a panic disorder.

In terms of follow-up, in order to record and determine the presence of PPD or other depressive symptomology, one study chose to follow up with their participants within 48 hours of birth, two weeks, and then at six weeks postpartum (Takács et al., 2019). Another study followed up with their study population at four to six weeks postpartum in order to assess the presence of PPD (Karakuş & Pulatoğlu, 2019). One of the studies chose to look at the effect of pitocin administration on maternal mood, specifically at two months postpartum and recorded depressive symptomology once a month following childbirth (Gu et al., 2016). The last study only looked at

primary outcomes of PPD within the postpartum year, with no clear indication of follow-up points with participants following birth (Kroll-Desrosiers et al., 2017).

3.11 Measurements

Among the articles included in this review, only one study used preexisting data from a university medical research database. On the other hand, the remaining studies utilized validated and standardized instruments to determine the presence of a mood disorder. The Edinburgh Postnatal Depression Scale (EPDS) was used across all studies to assess the symptomology of depression or anxiety disorders. The remaining surveys used within the articles are 1) Beck's Depression Inventory, 2) Somatization Subscale, 3) Generalized Anxiety Disorder 7-Item Scale, and 4) Perinatal Posttraumatic Stress Questionnaire.

Table 1 Selected Studies

Reference/ Location	N/ Sample Population	Study Design	Risk Factors	Health Impacts	Measurements/ Exposure Period	Symptoms	Outcomes
Gu et al., 2015 Canada	386 Pregnant Women (Within 48 Hours of Birth – Community Based and Quebec Clinical Subsample)	Randomized Control Trial (RCT)	Intrapartum Exposure Perinatal Mental Health Diagnosis Posttraumatic Stress Disorder (PTSD)	Abnormal Fetal Heart Rate Fetal Distress Poor Fetal Oxygenation Uterine Hyperstimulation Uterine Rupture	Edinburgh Postnatal Depression Scale (EPDS) Generalized Anxiety Disorder 7-Item Scale Perinatal Posttraumatic Stress Questionnaire Somatization Subscale	Anxiety Avoidance Bodily Dysfunction Depression Increased Arousal Intrusive Thoughts Posttraumatic Stress Somatization Disorder	Postpartum Anxiety and Depressive Disorders
Karakus & Pulatoglu 2019 Istanbul, Turkey	200 Oxytocin Users & Non-Oxytocin Users	Retrospective Cohort Study	Prenatal Anxiety Prenatal Depression Postpartum Depression	Postpartum Symptoms of Depression and Anxiety	Beck's Depression Inventory Edinburgh Postnatal Depression Scale (EPDS) for Depressive Symptomology	Anxiety Depressed Mood Diminished Ability to Think/ Concentrate Eating Changes Feelings of Worthlessness Loss of Interest & Energy Psychotic Features (Delusions/Hallucinations) to Harm Infant Recurrent Suicidal Ideations Sleep Changes	Postpartum Symptoms of Depression and Anxiety
Kroll-Desrosiers et al., 2017 United States	46,732 Women who have given birth at the University of Massachusetts Memorial Medical Center (UMMHC) with a history of Prepregnancy Depressive and Anxiety Disorders	Retrospective Cohort Study	Antidepressant /Anxiolytic Prescription within First Postpartum Year Peripartum Exposure Prepregnancy Depressive/ Anxiety Disorders	Breastfeeding Difficulty Failed Lactation Infant Irritability Maternal Suicide Poor Infant Sleep Postpartum Depressive and Anxiety Disorders	Massachusetts Integrated Clinical Academic Research Database (MiCARD) Within 2 weeks of delivery	Anxiety Disorder Onset Depression/Anxiety during Pregnancy Panic Disorder Posttraumatic Stress Disorder (PTSD)	Depression Postpartum Anxiety Postpartum Depression Somatization Disorders
Takács et al., 2019 Czech Republic	260 Community Sample of Pregnant Women in Last Trimester	Prospective Observational Study	Intrapartum Exposure Experienced Depressive Symptoms in Previous Pregnancy History of Depression Maternal History of Depression	Decreased Maternal Mood	Edinburgh Postnatal Depression Scale (EPDS) (<12 score) Maternity Blues Questionnaire	Depressive Symptoms in Third Trimester and Following Childbirth	Postpartum Blues

			Negative Childbirth Experience		During Labor		

4.0 Discussion

This scoping review included four studies representative of the literature on peripartum administration of synthetic oxytocin and postpartum mood disorders in birthing women. This review incorporated studies with quantitative methods that addressed risk factors, health impacts, outcomes, symptomology, and mood measurements for mothers who have had synthetic oxytocin administered in the peripartum and intrapartum periods. The exclusion criteria of this review were designed to add on to the standard methodology used across the majority of the scoping reviews, which looked at the role of both natural and synthetic oxytocin in the postpartum maternal mood.

4.1 Findings of the Scoping Review

The included studies do not provide sufficient evidence to make conclusions or clear associations between peripartum synthetic oxytocin administration and postpartum mood disorders. Studies look at various risk factors like prenatal depression/anxiety, negative childbirth experience, and maternal history of depression. Studies also identified a range of health impacts of peripartum pitocin administration like, decreased maternal mood, breastfeeding, lactation difficulty, uterine rupture, or fetal distress. The outcomes of synthetic oxytocin exposure across studies were postpartum mood disorders, depression, somatization, and postpartum blues. Additionally, this review identified various symptoms associated with peripartum pitocin exposure, such as delusions/hallucinations, loss of energy/sleep, decreased thinking/concentration abilities, and recurrent suicidal thoughts. The measurements used across the studies were primarily

using quantitative data which included: The Edinburgh Postnatal Depression Scale (EPDS), Beck's Depression Inventory, Somatization Subscale, Generalized Anxiety Disorder 7-Item Scale, and the Perinatal Posttraumatic Stress Questionnaire.

One of the studies suggested that using synthetic oxytocin to prevent hemorrhaging in childbirth may contribute to symptoms of depression and anxiety in birthing women postpartum(Karakuş & Pulatoğlu, 2019). Another study noted that their results were an extension of previous studies that evaluated whether intranasal synthetic oxytocin was a contributing factor to symptoms of depression in postnatal women (Gu et al., 2016). In addition, this article proposed the idea that synthetic oxytocin may be an "index" for traumatic or stressful birth experiences, which worsens postpartum mental health in birthing women (Gu et al., 2016). Although researchers could not identify a clear association, peripartum administration of synthetic oxytocin critically influences postpartum maternal mood through the dysregulated oxytocin system (Gu et al., 2016).

The study that chose not to use postpartum screening tools as their measurement indicated that birthing women who had been exposed to peripartum synthetic oxytocin had a greater relative risk of being diagnosed with mood disorders or having been prescribed antidepressant/anxiolytic medications within the first postpartum year compared to birthing women without the exposure (Kroll-Desrosiers et al., 2017). That study also was the only United States-based study, and it did not explore potential racial disparities among those exposed to peripartum synthetic oxytocin.

However, one study observed a decreased likelihood of a postpartum mood disorder diagnosis with intrapartum exposure to synthetic oxytocin. However, the authors noted that although they found a decreased likelihood, their results yielded no protective factor against postpartum blues, which is a mild mood disorder that affects many women after giving birth. It

was further suggested that the effects of synthetic oxytocin exposure might not be immediate, coming weeks into the postpartum period (Takács et al., 2019).

4.2 Gaps in Literature and Future Study Recommendations

Within the data extraction phase, the reviewer noted and recorded gaps in the literature and future study recommendations outlined in the articles. One of the gaps in the literature identified within one of the studies was that the researchers could not measure blood oxytocin levels in the study sample, which indicates mood and correlates depression to the level of oxytocin in the body (Karakuş & Pulatoğlu, 2019). One of the studies that used an observational design in their study noted that their results be interpreted with caution due to observation needing to be about to determine causality.

All of the studies suggested that further research must be conducted to determine associations. It is recommended that future studies focus on the longitudinal role of synthetic oxytocin and maternal mood and conduct more research on the safety and long-term health implications (Karakuş & Pulatoğlu, 2019). Similarly, another study suggested that before clinical recommendations are made, it is vital to reinforce the existing literature on peripartum synthetic oxytocin and postpartum mood disorders (Takács et al., 2019).

On the other hand, one study emphasized the underdiagnosis and the lack of documentation on maternal mood disorders, the absence of patient data from Medicaid (representative of high-risk pregnancy populations), and varying timeframes in which synthetic oxytocin was administered to the birthing woman (Kroll-Desrosiers et al., 2017). It was also noted that future studies should focus on being able to control for certain factors like prenatal mental

health, oxytocin level before synthetic oxytocin administration, and prevalence of common mood disorders symptoms (Gu et al., 2016). However, as noted earlier, that study did not explore potential racial disparities among those exposed to peripartum synthetic oxytocin.

4.3 Policy Recommendations

All studies assessed within this review did not provide any future recommendation for policy surrounding the administration of pitocin to induce or augment labor and prevent postpartum hemorrhage. Generating policy surrounding the development of alternative forms of birthing interventions to prevent postpartum hemorrhage is essential to navigating the potential mental health risks that synthetic oxytocin may pose to birthing mothers in the postpartum period.

4.4 Limitations

It is essential to note that the review has several limitations. Studies were only included if they were published in English, which may introduce bias and skew the results by excluding findings from studies not written in English. In addition, studies that were only published in research journals were included, which may have led to missing out on any relevant findings in research conference abstracts or doctoral dissertations. The study search was limited to three databases, which could have ruled out relevant information in studies located in other research or medical databases. Three studies were excluded because they must meet all eligibility criteria for the final study selection. Furthermore, this scoping review utilizes one reviewer, potentially adding

bias due to their potential interpretation of the selected eligibility criteria. With the addition of a second reviewer, there is more leeway in discussing the conflicting interpretations, which inversely minimizes bias.

5.0 Conclusion

All findings indicate that there needs to be more longitudinal research developed surrounding the effect of peripartum administration of synthetic oxytocin on postpartum maternal mood. Future longitudinal research should also focus on understanding the long-term relationship and effects of Pitocin administration during labor and the increased likelihood of developing PPD. Studies also suggest that there needs to be more research that looks at the safety of repetitive pitocin exposure during pregnancy and dosage effects (high vs. low). Most of the literature surrounding the peripartum effects of synthetic oxytocin and PPD has conflicting results regarding the association. Some studies suggest no direct association, and others suggest that the association is not definite but rather is a significant influence on maternal mood. Synthetic oxytocin administration is becoming a routine intervention for clinical practice, which should prompt more research to determine its acute and chronic effects on birthing women in the United States. Also, there is limited research surrounding the long-term impacts of having one or multiple birthing interventions on maternal mood and maternal-infant bonding; therefore, the medical and research community needs to explore further the long-term implications of birth intervention on maternal health and wellbeing.

All articles reviewed for this study did not indicate a standardized dosage, time of administering, or proper follow-up timeframe for exposure to pitocin during childbirth. Being there is a lack of standards and timelines for pitocin administration and depressive symptoms screening, another recommendation is that future policy and practice is aimed towards identifying the best time to administer pitocin, determine the proper dosage for birthing women, and establish the

proper timeframe to follow-up with women in order to identify presence of postpartum mood disorders following administration of pitocin at childbirth.

It is also important to note that since there was only one United States-based study on this topic included in this review, which did not touch on the issues of racial disparities within maternal mortality outcomes for African American women who are more likely to suffer adverse pregnancy or birthing outcomes. Future research should evaluate whether pregnant African American women are more likely to receive pitocin administration and have higher prevalence rates of postpartum mood disorders after childbirth.

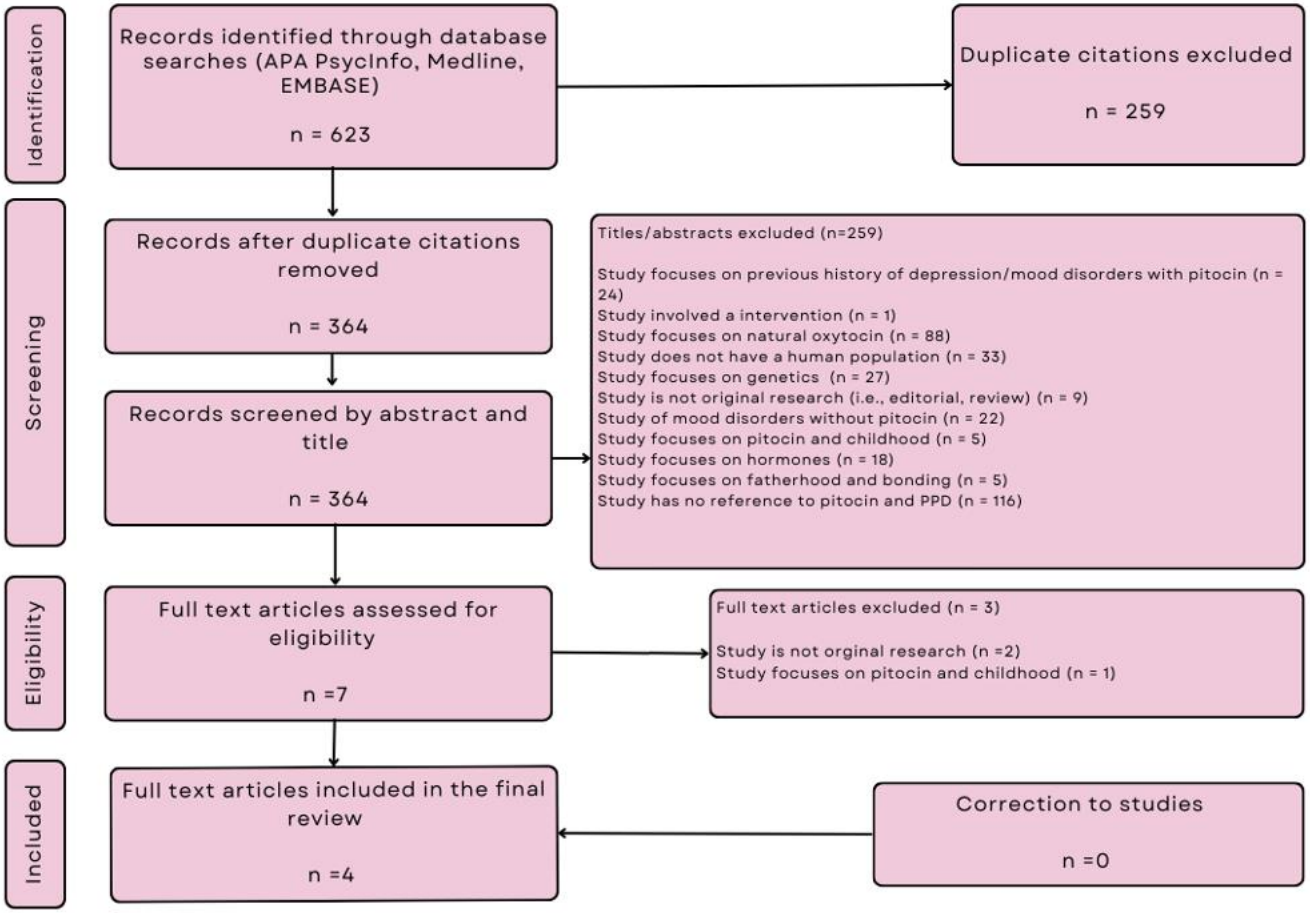
The review's findings will benefit public health practitioners and physicians to develop more original research surrounding this topic, building upon existing research and developing new interventions to prevent hemorrhaging following childbirth.

Appendix A Summary of Literature Databases

Appendix Table 1

Table	Vendor/ Interface	Database	Date searched	Database update	Searcher(s)
1b	Ovid	Medline	31 January 2023	1946 to January 30, 2023	Helena M. VonVille; Jaelyn A. Murphy
1b	Ovid	APA PsycInfo ®	31 January 2023	1806 to January Week 4 2023	Helena M. VonVille
1c	Elsevier	EMBASE®	31 January 2023	31 January 2023	Helena M. VonVille

Appendix B PRISMA Flowchart



Appendix Figure 1 PRISMA Flowchart

Appendix C Preliminary Search Strategy for Ovid Medline

Provider/Interface	Ovid
Database	Medline®
Date searched	January 31, 2023
Database update	1946 to January 30, 2023
Search developer(s)	Helena M. Vonville; Jaelyn A. Murphy
Limit to English	Yes
Date Range	No limit by date
Publication Types	No limit by publication type
Search filter source	No search filter used

1	Oxytocin/
2	(Duratocin or ocytocin or oxytocin or pitocin or syntocinon). ti,ab,kf,rn.
3	1 or 2
4	Anxiety/ or Anxiety Disorders/
5	Depression/
6	Depressive Disorder/
7	(anxiety or depression or depressive). ti,ab,kf.
8	maternal behavior/ or object attachment/
9	(attachment or bonding). ti,ab,kf.
10	4 or 5 or 6 or 7 or 8 or 9
11	postpartum period/
12	((post adj1 (natal or partum)) or postnatal or postpartum). ti,ab,kf.
13	11 or 12
14	10 and 13
15	Depression, Postpartum/
16	14 or 15
17	3 and 16
18	(17 and english.la.) not (exp "Animals"/ not "Humans"/)

Appendix D Preliminary Search Strategy for Ovid *APA PsycInfo*

Provider/Interface	Ovid
Database	APA PsycInfo
Date searched	January 31, 2023
Database update	1806 to January Week 4 2023
Search developer(s)	Helena M. VonVille
Limit to English	Yes
Date Range	No limit by date
Publication Types	Journals only
Search filter source	No search filter used

1	oxytocin/
2	(Duratocin or ocytocin or oxytocin or pitocin or syntocinon). ti,ab,id.
3	1 or 2
4	anxiety/ or anxiety disorders/
5	major depression/ or "depression (emotion)"/
6	(anxiety or depression or depressive). ti,ab,id.
7	Mother Child Relations/ or Attachment Behavior/
8	(attachment or bonding). ti,ab,id.
9	4 or 5 or 6 or 7 or 8
10	postnatal period/
11	((post adj1 (natal or partum)) or postnatal or postpartum). ti,ab,id.
12	10 or 11
13	9 and 12
14	Postpartum Depression/
15	13 or 14
16	3 and 15
17	16 not ((albanian or arabic or bulgarian or catalan or chinese or croatian or czech or danish or dutch or estonian or farsi iranian or finnish or french or georgian or german or greek or hebrew or hindi or hungarian or italian or japanese or korean or lithuanian or malaysian or nonenglish or norwegian or polish or portuguese or romanian or russian or serbian or serbo croatian or slovak or slovene or spanish or swedish or turkish or ukrainian or urdu) not English). lg.
18	limit 17 to all journals
19	18 not (animal not human).po.
20	19 not ("361330" or "879183" or "2782950" or "6829731" or "7618451" or "7981471" or "9439163" or "9575469" or "9584534" or "10074992" or "10643833" or "11264623" or "11573030" or "11589124" or "11600543" or "11694638" or

	"12614602" or "12954433" or "15364035" or "15730889" or "15982459" or "15996533" or "16019595" or "16835035" or "16879936" or "17355401" or "17513013" or "17604088" or "17956324" or "17958710" or "17974588" or "18040595" or "18406738" or "18715415" or "18726143" or "19826497" or "20153585" or "20359699" or "20399783" or "20493795" or "20888383" or "21250892" or "21252405" or "21562482" or "21629841" or "22285934" or "22306668" or "22580735" or "22795645" or "22942878" or "23012383" or "23039942" or "23085508" or "23181531" or "23249130" or "23325323" or "23333868" or "23450994" or "23541877" or "23586800" or "23608126" or "23637833" or "23695233" or "23846912" or "23941164" or "24084810" or "24239932" or "24376405" or "24462937" or "24472136" or "24523054" or "24704390" or "24956026" or "24995584" or "25074620" or "25147513" or "25229827" or "25287533" or "25449701" or "25562711" or "25768266" or "25862151" or "25902327" or "25941501" or "25956962" or "25988992" or "25997760" or "26112436" or "26130435" or "26232032" or "26236256" or "26257770" or "26268151" or "26554749" or "26574573" or "26634176" or "26735320" or "26834435" or "26857197" or "26887958" or "26957508" or "27052823" or "27100724" or "27107296" or "27108164" or "27184829" or "27187722" or "27295067" or "27320943" or "27347899" or "27366554" or "27513806" or "27538784" or "27589498" or "27617302" or "27620964" or "27870443" or "28027955" or "28050900" or "28103103" or "28133901" or "28161387" or "28193868" or "28431269" or "28435979" or "28594092" or "28683833" or "28749705" or "28812269" or "28918249" or "28950923" or "29168023" or "29317891" or "29390992" or "29405799" or "29407512" or "29423334" or "29460795" or "29483344" or "29484271" or "29544195" or "29596076" or "29674170" or "29705572" or "29769663" or "29781504" or "29843655" or "29908404" or "29957480" or "29968131" or "29981523" or "30000550" or "30191332" or "30306269" or "30522458" or "30554286" or "30593425" or "30684507" or "30690225" or "30690935" or "30858011" or "30893095" or "30928624" or "31065789" or "31118457" or "31150502" or "31233509" or "31315861" or "31347150" or "31385103" or "31401811" or "31406740" or "31440401" or "31479475" or "31520440" or "31555107" or "31626779" or "31755553" or "31780957" or "31782341" or "31911347" or "31927723" or "31944828" or "32010366" or "32066670" or "32088172" or "32394561" or "32407376" or "32463265" or "32505925" or "32584616" or "32683141" or "32722725" or "32756565" or "32854075" or "32937192" or "32982827" or "33008536" or "33088973" or "33163384" or "33192370" or "33304247" or "33324730" or "33346016" or "33426200" or "33487439" or "33633538" or "33635103" or "33757778" or "33860940" or "33899582" or "34077815" or "34166764" or "34174336" or "34182251" or "34210188" or "34266612" or "34389972" or "34398584" or "34539776" or "34540120" or "34545656" or "34585111" or "34614012" or "34650456" or "34687351" or "34745566" or "34745566" or "34745566" or "34777247" or "34795176" or "34816221" or "34843839" or "34937662" or "34963414" or "35065634" or "35112090" or "35198245" or "35242106" or "35288124" or "35312059" or "35365803" or "35390436" or "35462200" or "35721318" or "35819947" or

	"35858105" or "35917937" or "35967921" or "36087759" or "36098825" or "36115939" or "36359022" or "36516698" or "36590100" or "36592494" or "36682156").pm.

Appendix E Preliminary Search Strategy for EMBASE

Provider/Interface
Database EMBASE
Date searched
Database update
Search developer(s)
Limit to English Yes
Date Range
Publication Types
Search filter source

#1	'oxytocin'/de OR 'oxytocin derivative'/exp
#2	(Duratocin:ti,ab,kw OR ocytocin:ti,ab,kw OR oxytocin:ti,ab,kw OR pitocin:ti,ab,kw OR syntocinon:ti,ab,kw)
#3	#1 OR #2
#4	'anxiety'/de OR 'depression'/de OR 'major depression'/de
#5	(anxiety:ti,ab,kw OR depression:ti,ab,kw OR depressive:ti,ab,kw)
#6	'emotional attachment'/de OR 'maternal behavior'/de
#7	(attachment:ti,ab,kw OR bonding:ti,ab,kw)
#8	#4 OR #5 OR #6 OR #7
#9	'perinatal period'/de OR 'post natal':ti,ab,kw OR 'post partum':ti,ab,kw OR postnatal:ti,ab,kw OR postpartum:ti,ab,kw
#10	#8 AND #9
#11	'postnatal depression'/de
#12	#10 OR #11
#13	#3 AND #12
#14	#13 AND ([article]/lim OR [article in press]/lim OR [preprint]/lim)
#15	#14 NOT (([animal cell]/lim OR [animal experiment]/lim OR [animal model]/lim OR [animal tissue]/lim) NOT 'human'/de)
#16	#15 AND [english]/lim
#17	#16 NOT (361330:ui OR 879183:ui OR 2782950:ui OR 6829731:ui OR 7618451:ui OR 7981471:ui OR 9439163:ui OR 9575469:ui OR 9584534:ui OR 10074992:ui OR 10643833:ui OR 11264623:ui OR 11573030:ui OR 11589124:ui OR 11600543:ui OR 11694638:ui OR 12614602:ui OR 12954433:ui OR 15364035:ui OR 15730889:ui OR 15982459:ui OR 15996533:ui OR 16019595:ui OR 16835035:ui OR 16879936:ui OR 17355401:ui OR 17513013:ui OR 17604088:ui OR 17956324:ui OR 17958710:ui OR 17974588:ui OR 18040595:ui OR 18406738:ui OR 18715415:ui OR 18726143:ui OR 19826497:ui OR 20153585:ui OR 20359699:ui OR 20399783:ui OR 20493795:ui OR 20888383:ui OR 21250892:ui OR 21252405:ui OR 21562482:ui OR 21629841:ui OR

	22285934:ui OR 22306668:ui OR 22580735:ui OR 22795645:ui OR 22942878:ui OR 23012383:ui OR 23039942:ui OR 23085508:ui OR 23181531:ui OR 23249130:ui OR 23325323:ui OR 23333868:ui OR 23450994:ui OR 23541877:ui OR 23586800:ui OR 23608126:ui OR 23637833:ui OR 23695233:ui OR 23846912:ui OR 23941164:ui OR 24084810:ui OR 24239932:ui OR 24376405:ui OR 24462937:ui OR 24472136:ui OR 24523054:ui OR 24704390:ui OR 24956026:ui OR 24995584:ui OR 25074620:ui OR 25147513:ui OR 25229827:ui OR 25287533:ui OR 25449701:ui OR 25562711:ui OR 25768266:ui OR 25862151:ui OR 25902327:ui OR 25941501:ui OR 25956962:ui OR 25988992:ui OR 25997760:ui OR 26112436:ui OR 26130435:ui OR 26232032:ui OR 26236256:ui OR 26257770:ui OR 26268151:ui OR 26554749:ui OR 26574573:ui OR 26634176:ui OR 26735320:ui OR 26834435:ui OR 26857197:ui OR 26887958:ui OR 26957508:ui OR 27052823:ui OR 27100724:ui OR 27107296:ui OR 27108164:ui OR 27184829:ui OR 27187722:ui OR 27295067:ui OR 27320943:ui OR 27347899:ui OR 27366554:ui OR 27513806:ui OR 27538784:ui OR 27589498:ui OR 27617302:ui OR 27620964:ui OR 27870443:ui OR 28027955:ui OR 28050900:ui OR 28103103:ui OR 28133901:ui OR 28161387:ui OR 28193868:ui OR 28431269:ui OR 28435979:ui OR 28594092:ui OR 28683833:ui OR 28749705:ui OR 28812269:ui OR 28918249:ui OR 28950923:ui OR 29168023:ui OR 29317891:ui OR 29390992:ui OR 29405799:ui OR 29407512:ui OR 29423334:ui OR 29460795:ui OR 29483344:ui OR 29484271:ui OR 29544195:ui OR 29596076:ui OR 29674170:ui OR 29705572:ui OR 29769663:ui OR 29781504:ui OR 29843655:ui OR 29908404:ui OR 29957480:ui OR 29968131:ui OR 29981523:ui OR 30000550:ui OR 30191332:ui OR 30306269:ui OR 30522458:ui OR 30554286:ui OR 30593425:ui OR 30684507:ui OR 30690225:ui OR 30690935:ui OR 30858011:ui OR 30893095:ui OR 30928624:ui OR 31065789:ui OR 31118457:ui OR 31150502:ui OR 31233509:ui OR 31315861:ui OR 31347150:ui OR 31385103:ui OR 31401811:ui OR 31406740:ui OR 31440401:ui OR 31479475:ui OR 31520440:ui OR 31555107:ui OR 31626779:ui OR 31755553:ui OR 31780957:ui OR 31782341:ui OR 31911347:ui OR 31927723:ui OR 31944828:ui OR 32010366:ui OR 32066670:ui OR 32088172:ui OR 32394561:ui OR 32407376:ui OR 32463265:ui OR 32505925:ui OR 32584616:ui OR 32683141:ui OR 32722725:ui OR 32756565:ui OR 32854075:ui OR 32937192:ui OR 32982827:ui OR 33008536:ui OR 33088973:ui OR 33163384:ui OR 33192370:ui OR 33304247:ui OR 33324730:ui OR 33346016:ui OR 33426200:ui OR 33487439:ui OR 33633538:ui OR 33635103:ui OR 33757778:ui OR 33860940:ui OR 33899582:ui OR 34077815:ui OR 34166764:ui OR 34174336:ui OR 34182251:ui OR 34210188:ui OR 34266612:ui OR 34389972:ui OR 34398584:ui OR 34539776:ui OR 34540120:ui OR 34545656:ui OR 34585111:ui OR 34614012:ui OR 34650456:ui OR 34687351:ui OR 34745566:ui OR 34777247:ui OR 34795176:ui OR 34816221:ui OR 34843839:ui OR 34937662:ui OR 34963414:ui OR 35065634:ui OR 35112090:ui OR 35198245:ui OR 35242106:ui OR 35288124:ui OR 35312059:ui OR 35365803:ui OR 35390436:ui OR 35462200:ui OR 35721318:ui OR 35819947:ui OR 35858105:ui OR 35917937:ui OR 35967921:ui OR 36087759:ui OR 36098825:ui OR 36115939:ui OR 36359022:ui OR 36516698:ui OR 36590100:ui OR 36592494:ui OR 36682156:ui)

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