Archives of Psychiatric Nursing 33 (2019) 254–266

Contents lists available at ScienceDirect

Archives of Psychiatric Nursing

journal homepage: www.elsevier.com/locate/apnu

A practical guide to the use of psychotropic medications during pregnancy and lactation

Lyons T. Hardy[a,*], Olivia L. Reichenbacker[b]

[a] Virginia Commonwealth University, School of Nursing, 1100 E Leigh St., Richmond, VA 23298, United States of America
[b] University of Virginia, 225 Jeanne Lancaster Way, Charlottesville, VA 22903, United States of America

ARTICLE INFO

Keywords:
Perinatal mental health
Perinatal psychiatry
Reproductive psychiatry

ABSTRACT

The use of psychotropic medications during the perinatal period is often met with fear and discomfort on the part of both clinicians and patients. There is a great deal of misinformation about the risks of medication use during pregnancy and lactation. The risk of untreated or undertreated mental illness during this time is an important consideration when making treatment recommendations. This paper serves as a practical guide for clinicians who may be treating patients with psychotropic medication during the perinatal period. A heuristic tool for making treatment decisions will be introduced, and coverage of specific psychiatric disorders and medication classes will be provided.

Perinatal patients are a unique population in terms of the specialized care they require across disciplines. Not only does the perinatal period represent a time of great transition and adaptation for patients and their families socially, significant hormonal and other physiologic changes make this population's needs vastly different than that of their non-pregnant peers. These changes can predispose this population to new mental health problems, and pharmacokinetic changes can cause patients who were previously stabilized on psychiatric medications to have increased risk of symptom relapse (Yonkers & Ross, 2011).

Up to 20% of women will experience a mood or anxiety disorder in the perinatal period, making perinatal mood and anxiety disorders (PMADs) the most common complication of pregnancy (O'Hara, Wisner, & Asher, 2014; Postpartum Support International, n.d.-b). While we now understand the risks of mental illness during the perinatal period, less than a half century ago the common medical knowledge was that pregnancy and postpartum were times of joy and wellness. It was not until seminal research was conducted in the 1970's that the medical community as a whole began to understand that pregnancy is not protective against mental illness (Kendell, Wainwright, Hailey, & Shannon, 1976). Despite additional research that we now have to support that original study, misconceptions still persist for some providers and patients. There are a variety of inaccurate beliefs about prescribing medication during the perinatal period; for example, many clinicians still believe that psychotropic medications should be tapered and discontinued prior to delivery. This may be the result of a 2004 Food and Drug Administration (FDA) labeling change that warned of the association between poor neonatal adaptation syndrome and third trimester exposure to antidepressants (Payne & Meltzer-Brody, 2009). Following that labeling change, a large scale retrospective study failed to show any difference in adverse neonatal outcomes between those who were exposed to SSRIs during pregnancy but not in the last 14 days of gestation (Warburton, Hertzman, & Oberlander, 2010). Nevertheless, the practice of tapering SSRIs prior to delivery persists (MGH Center for Women's Mental Health, 2017b). Media reporting raising concerns about the use of antidepressants during pregnancy has been critiqued by reproductive psychiatry experts, and there has been a call for a rational, evidence based approach to prescribing for this population (Brockington, Butterworth, & Glangeaud-Freudenthal, 2017; Rabin, 2014).

Concerns about the safety of medications during pregnancy and lactation exist for providers across disciplines and specialties, including psychiatry, and unfortunately may lead to poor access to care for perinatal patients struggling with mental illness. Approximately 86% of pregnant women with psychiatric illness never receive formal psychiatric care (Marcus, Flynn, Blow, & Barry, 2003; Muzik, Marcus, Heringhausen, & Flynn, 2009). Even among patients who are treated, many continue to experience mental health symptoms. In one study, mean dosages for most of the antidepressants fell on the low end of the dose range—e.g. fluoxetine mean dosage was 23.3 mg and sertraline mean dosage was 68.7 mg—indicating suboptimal treatment (Marcus & Flynn, 2008). This was a naturalistic, observational study that compared pregnant women who were already taking antidepressants with

* Corresponding author.
E-mail addresses: hardyl@vcu.edu (L.T. Hardy), old9b@virginia.edu (O.L. Reichenbacker).

https://doi.org/10.1016/j.apnu.2019.04.001
Received 11 September 2018; Received in revised form 4 April 2019; Accepted 8 April 2019
0883-9417/

those who were not taking antidepressants, suggesting that typical practice may involve underdosing of antidepressant medication during pregnancy. The potential risks of untreated mental illness on both the patient and the fetus are high and are not always mentioned when medication is discussed.

Medication is certainly not the only means of managing mental illness, and we also advocate for appropriate nonpharmacological treatment for patients in the perinatal period. Nonpharmacological approaches with demonstrated efficacy in the perinatal period include psychotherapy, physical exercise, yoga, bright light therapy, mindfulness, meditation, relaxation techniques, omega-3 fatty acid supplementation, and acupuncture (Brandon, Crowley, Gordon, & Girdler, 2014; Smith, Shewamene, Galbally, Schmied, & Dahlen, 2019; Tjoa, Pare, & Kim, 2010). Since medication treatment is a critical component of the treatment plan for many clients and is where discomfort typically lies for providers, the scope of this paper will be limited to pharmacologic treatment of mental illness during the perinatal period. Detailed information about assessment and diagnosis of perinatal psychiatric disorders is also beyond the scope of this paper, however we will provide an overview of prominent features of common perinatal psychiatric illnesses. In addition, we will not discuss the use of electroconvulsive therapy, although there is good evidence for the efficacy and safety of ECT during pregnancy (Rundgren et al., 2018; Thyen, Narang, Sarai, Tegin, & Lippmann, 2017). This paper will provide a practical clinical guide to the effective psychopharmacologic treatment of perinatal patients. The overarching goal is to improve clinicians' knowledge and comfort in managing mental illness in perinatal patients, and ultimately improve the access to and quality of care for this population. The research related to psychotropic medications during pregnancy in particular is constantly changing and evolving, and clinicians should stay abreast of new and updated information as it is published. Clinicians will be well served by using a systematic framework for decision making along with knowing how to access resources that can provide information relevant to individualized treatment decisions.

Overview and terminology

Perinatal will herein be defined as the timeframe from conception through one year postpartum. Though some variation exists regarding when the perinatal period begins and ends, this is the common definition utilized by groups advocating for mental healthcare of people in the perinatal period (Postpartum Support International, n.d.-a). Antepartum is defined as the period from conception to delivery, and postpartum is defined as the period from delivery to 12 months later. Perinatal patients studied in the literature are typically comprised of women aged 15 to 44 years old, although pregnancies in people younger than 15 and older than 44 can occur. Transgender clients and people not identifying as female may also become pregnant, though few data are available on these groups specifically. In addition, same gender couples may be parenting together, and the term “gestational parent” is more accurate than “mother”, since both parents may identify as mothers. Therefore, in discussing research results, the term women, girls, or other female specific words may be used, but in general, gender-neutral terminology will be favored. It is also important to note that not all patients who feed breastmilk to their infant breastfeed. Some pump their breast milk for either personal or medical reasons, and therefore the term “lactating” will be used in lieu of breastfeeding. In addition, some families may choose to feed their babies with donated breast milk from a milk bank or from individual donors.

Impact of perinatal mental illness

Perinatal mental illness costs the United States approximately $5.7 billion annually in lost income and productivity alone (Siu et al., 2016). The United Kingdom (U.K.) published a more comprehensive estimate looking at multiple cost factors including cost of care for adverse effects of perinatal mental illness as well as the cost of lost productivity and wages. Their estimates suggest that one single case of perinatal depression costs approximately £74,000. 72% of that cost is related to the negative impacts on the infant. Despite having a different type of healthcare system, the U.K. Task Force cites very similar issues to the United States of under-detection and under-treatment of perinatal mental illness (Bauer et al., 2014). The monetary cost is only a small part of the overall impact. Family units with a parent suffering from perinatal mental illness are more susceptible to separation and divorce, and there are significantly higher rates of disability and unemployment for those suffering from perinatal mental illness. More rarely, but perhaps most seriously, perinatal mental illness leads to suicide, homicide, and infanticide. In high income countries, suicide accounts for 5–20% of maternal deaths, and in low and middle income countries, it accounts for 1–5% (Khalifeh, Hunt, Appleby, & Howard, 2016). Indeed, one of the leading causes of maternal mortality in the first 12 months postpartum is perinatal suicidality, which includes completed suicides, suicide attempts, suicidal thoughts, and thoughts of self-harm (Orsolini et al., 2016).

Much like the impacts to individuals and society, impacts on the fetus or infant are vast and concerning, and this reinforces the need for better access to high quality treatment for perinatal mental illness. While the medical community has long suspected that perinatal mental illness affects the offspring, interest in research on this topic is quite recent. Over the last several years, multiple research initiatives have resulted in compounding evidence that, in fact, exposure of a fetus or infant to psychiatric illness in the gestational parent has the potential for significant and meaningful impact. Mental illness both during and after pregnancy can affect children in two ways. First, exposure of the fetus to maternal mental illness may increase levels of stress hormones, such as cortisol, alter levels of neurochemicals, or change other physiological processes, which can affect physical and neurological development (Brockington et al., 2017; Stein et al., 2014). Second, the fetus or infant may be exposed to indirect effects such as alterations in nutritional status of the mother through appetite changes, reduced breast milk supply due to stress, changes in the primary caregivers (such as through separation or divorce), increased rates of substance use, and lower rates of prenatal care, among others (Brockington et al., 2017; National Collaborating Centre for Mental Health Royal College of Psychiatrists' Research and Training, 2014). Observed consequences of perinatal mental illness on the offspring include behavioral problems, alterations in gray matter, increased levels of cortisol, alterations in sleeping and feeding patterns and quality, developmental delays (particularly in non-verbal communication), lower cognitive scores, lower birth weights, early cessation of breastfeeding, increased risk for child neglect and abuse, increased risk of psychiatric illness independent of genetic factors, and disruption of parent-infant bonding (Brockington et al., 2017; Cook, Ayers, & Horsch, 2018; Field, 2008; González et al., 2017; Judd et al., 2014; Umylny, German, & Lantiere, 2017).

The literature suggests that postpartum depression can significantly increase the risk for long term problems with mother-infant bonding (Moehler, Brunner, Wiebel, Reck, & Resch, 2006; Wan & Green, 2009). Impaired bonding between parents and infants has long been shown to have its own numerous and deleterious effects. More recently, research has identified that insecure attachments specifically resulting from maternal mental illness in the perinatal period may negatively impact child development. Children who develop insecure attachments as a result of perinatal mental illness are significantly more likely to have behavioral problems, decreased friendship and romantic relationship quality, and their own psychiatric issues. Importantly, several factors may influence the degree to which maternal mental illness affects attachment. The strongest of these is the level of mental illness in the parent, whether or not the mental health concern meets clinical criteria, and the presence of this illness throughout infancy (Wan & Green, 2009). This suggests that early intervention may lower the risk for attachment issues as a result of maternal mental illness.

These findings may seem disheartening, especially when we consider that one of the most significant current issues surrounding perinatal mental illness is the lack of appropriate treatment of perinatal psychiatric disorders. Low rates of referral and treatment for patients who screen positive for perinatal mental illness in women's healthcare settings have been observed in several studies (Goodman & Tyer-Viola, 2010; Marcus et al., 2003). Lack of comfort and knowledge about treating mental illness in the perinatal period are among the most cited reasons for not providing treatment to suffering patients. In addition, due to stigma and other personal and societal factors, people suffering from these mental health conditions may not feel comfortable seeking treatment. Systems failures must be addressed to ultimately have far reaching effects on outcomes for both gestational parents and infants, but individual practice changes can offer substantial benefits to many patients seeking care. Intervening early and appropriately can considerably reduce the risk for the negative consequences discussed above (National Collaborating Centre for Mental Health Royal College of Psychiatrists' Research and Training, 2014).

Psychiatric disorders in the perinatal period

Psychiatric illness in the perinatal period may present in two major ways. First are those patients who have pre-existing mental illness and who become pregnant. For many of these patients, pregnancy may be destabilizing, but clinicians may note anecdotally that there are also a minority of patients who have more mental stability when pregnant (Altshuler, Hendrick, & Cohen, 1998; Cohen et al., 2006; Evans, Heron, Francomb, Oke, & Golding, 2001). Since approximately 50% of pregnancies are unplanned, some of these pregnancies will occur while psychotropic medications are still being taken (Finer & Zolna, 2011). It is important to take this into consideration when prescribing any type of medication to people who have the capacity to become pregnant. For example, the European Medicine Academy, American Academy of Neurology, and American Epilepsy Society have made strong recommendations against the use of divalproex sodium/valproic acid in any women of child-bearing age due to the known teratogenic effects of the drug (Andrade, 2018; MGH Center for Women's Mental Health, 2017a). There are other patients who may be planning a future pregnancy and would be able to seek pre-conception counseling regarding psychotropic medications. They may decide to do a trial off medications or to stay on their medications while trying to conceive. If medication discontinuation is attempted, some patients who relapse will have more difficulty stabilizing on the same medications in the future. Some patients may be in remission from previous psychiatric illness at the time of conception but develop a recurrence of symptoms sometime during the perinatal period (MGH Center for Women's Mental Health, n.d.-b; National Collaborating Centre for Mental Health Royal College of Psychiatrists' Research and Training, 2014). Second are patients who develop a new onset of psychiatric illness during the perinatal period. The most common disorders to present with a new onset in the perinatal period are mood and anxiety disorders (O'Hara et al., 2014).

Depression and anxiety

Approximately 20% of gestational parents will experience symptoms of depression or anxiety in the antepartum period. In the postpartum period, baby blues is most common, occurring in approximately 50 to 80% of patients (O'Hara et al., 2014). In DSM 5, Major Depressive Disorder (MDD) occurring in the postpartum period is diagnosed as MDD, with peripartum onset (American Psychiatric Association, 2013; Di Florio & Meltzer-Brody, 2015). We will use the terms postpartum depression and MDD, with peripartum onset interchangeably. Postpartum depression and anxiety occur in approximately 10 to 15% of patients, with onset usually in the first 2 or 3 months after delivery, but they can occur any time in the postpartum year. Postpartum depression with an onset in the first one to two months following delivery is likely to be a more hormonally driven condition than depression that occurs later in the postpartum period (Di Florio & Meltzer-Brody, 2015). For the purposes of this paper, however, we will discuss all cases of postpartum depression in the same context, since current widely available treatment options are the same regardless of timing of onset or underlying biological drivers of illness. Approximately 60% of patients diagnosed with postpartum depression actually have symptom onset of their depression before or during pregnancy. Anxiety is often the chief complaint even when depression is present, with two thirds of patients experiencing comorbid symptoms of anxiety (O'Hara et al., 2014). Insomnia is also a very common associated symptom.

Distinguishing between postpartum depression and baby blues can at times be difficult. Baby blues represents a *normal* experience related to the hormonal changes immediately following birth and resolves without treatment. There is no serious functional impairment, and suicidal ideation would not be seen (O'Hara et al., 2014). Although postpartum depression may have some similar features to baby blues, symptoms are more severe and prolonged and are an *abnormal* experience that should be identified and treated. A good rule of thumb is that in baby blues, patients tend to retain an overall positive outlook and healthy bonding with the infant, whereas with clinical depression, patients typically lose their positive outlook and experience sadness, loss of interest, or even hopelessness. Baby blues is a transient period of mood instability characterized by tearfulness, mood lability, and reactivity, typically peaking around days 3 to 5 after delivery, and lasting approximately 2 weeks (O'Hara et al., 2014). Clinical depression may be characterized by prolonged symptoms of tearfulness and mood lability and reactivity and functional impairment. Other symptoms such as sleep disturbance, appetite changes, feelings of guilt or worthlessness, suicidal thoughts, isolation, and impaired bonding with the infant may also be present (Okun, 2016).

Anxiety in the perinatal period is frequently characterized by fears of harm coming to the patient, infant, or partner. It may accompany symptoms of depression or present alone (Falah-Hassani, Shiri, & Dennis, 2017; Thorsness, Watson, & LaRusso, 2018). Symptoms of sleep disturbance, fatigue, restlessness, and excessive worry in general are typically also present. Symptoms are severe enough to cause functional impairment. Patients with insomnia related to anxiety will often report being unable to quiet their mind. In the postpartum period, patients frequently report feeling they must stay awake to listen to the baby breathe, or fear something bad happening to the infant while they sleep. They may therefore be easily awoken by the infant's noises and movements. Anxiety also commonly presents with physical complaints. These complaints may be more diffuse such as complaints of frequent headaches and gastrointestinal distress, or more acute such as occurs in a panic attack (Vythilingum, 2009). Panic disorder can also present during the perinatal period (Güler et al., 2015; Thorsness et al., 2018).

Obsessive-compulsive disorder

Postpartum obsessive-compulsive disorder (OCD) has an incidence of 3 to 5%, which is approximately twice as high as the general population (Uguz & Ayhan, 2011). Intrusive thoughts are a hallmark symptom of OCD and in the perinatal period commonly include themes of harm coming to the fetus or infant (O'Hara et al., 2014). Intrusive thoughts should not be confused with intent to harm the infant. Intrusive thoughts are typically ego dystonic in this population. An example of an intrusive thought that may be experienced by a postpartum patient would be a thought or visual image of letting the stroller roll into traffic. The patient would typically report high levels of anxiety related to this thought, likely engaging in behaviors to minimize the risk of it coming true such as clutching the stroller very tightly, performing some type of ritual that the patient believes will prevent this intrusive thought or action from occurring, or not taking the stroller out at all. Patients also frequently experience guilt and shame related to these thoughts. Intrusive thoughts may also be present in patients with other types of perinatal mental illness and are not completely limited to OCD. They are common, disturbing for the patient, and patients often

feel very scared to disclose these thoughts. Healthcare providers who have contact with perinatal patients should routinely normalize and ask about the presence of intrusive thoughts.

Post-traumatic stress disorder and other stressor related disorders

More than 12% of pregnant women and 9% of postpartum women may experience symptoms of post-traumatic stress disorder (PTSD) or a traumatic stress reaction such as hyperarousal, re-experiencing, nightmares, or isolation (Beck, Driscoll, & Watson, 2013). In addition, there are many events during pregnancy, labor, and delivery that healthcare providers may perceive as innocuous but that are experienced by patients as traumatic. These can include suffering from hyperemesis gravidarum, severe preeclampsia, emergency Caesarean birth, forceps or vacuum assisted delivery, blood loss during labor and delivery, third or fourth degree lacerations, or premature birth (Beck, 2004). Further, many patients experience any variation from a stereotypical "healthy pregnancy and delivery" as traumatic. Traumas that occur during pregnancy or labor and delivery can be associated with impaired bonding, difficulty with lactation and breastfeeding, sexual dysfunction, chronic pain, and future elective Caesarean births. While these types of events may not meet the full criteria that are required for a diagnosis of PTSD in the DSM-5 (American Psychiatric Association, 2013), they can still impact the patient in significant ways (Beck et al., 2013). Patients who have a history of sexual abuse or other traumatic experiences prior to pregnancy may also experience difficulties with intrusive memories, dissociation, and difficulty with lactation and breastfeeding (Simkin & Klaus, 2004). Even routine prenatal care and an uncomplicated labor and delivery can trigger memories of past abuse and trauma and may lead to a recurrence of trauma related psychiatric symptoms.

Bipolar disorder

Although numbers vary depending on the study, an estimated 21–54% of patients who present with postpartum depression actually have bipolar disorder (Sharma & Khan, 2010). In one study, 71% of those with an established diagnosis of bipolar disorder had a recurrence during pregnancy (Viguera et al., 2007). This study also showed that 45–52% of patients with bipolar disorder who were stable prior to pregnancy experienced relapse or exacerbation of symptoms during pregnancy, and 70% relapsed in the first six months after birth. For those who discontinued medication treatment during pregnancy, the risk of relapse was twice as high as for those who continued treatment. Other studies have shown variation in findings related to recurrence of mood symptoms during pregnancy in women with bipolar disorder, with a median range of 24% experiencing a recurrence (Salim, Sharma, & Anderson, 2018). Hormonal, neurotransmitter, and immune system changes during pregnancy and the postpartum period are thought to create a highly sensitive environment that contributes to mood instability (Jones, Chandra, Dazzan, & Howard, 2014; Yonkers & Ross, 2011). On the other hand, there are a small number of patients with bipolar disorder who experience greater mood stability during pregnancy (Grof et al., 2000).

For those who experience continuation or recurrence of symptoms during the perinatal period, symptoms are more likely to be depressive or mixed (Salim et al., 2018; Sharma, Doobay, & Baczynski, 2017). In the absence of mania, especially in patients who are poor historians, accurate diagnosis can be much more difficult. Due to the high rate of misdiagnosis of bipolar disorder and the potential consequences of inappropriate treatment, we recommend that all providers who may be called upon to treat perinatal patients familiarize themselves with the signs and symptoms of bipolar depression. We advise referral to a psychiatric provider to manage any psychiatric illness, but it is critical for non-psychiatric providers to recognize complicating factors in order to secure more timely and effective care for the patient. A depressive episode in bipolar disorder can look very similar to a depressive episode in unipolar depressive disorder, but there are some elements that more strongly indicate bipolar depression. WHIPLASHED is a pneumonic that succinctly describes some of these elements (Pies, 2007):

- Worsened symptoms or feeling wired when taking antidepressants
- History of hypomania or mood instability
- Irritability
- Psychomotor retardation
- Loaded family history (of mood disorders of any kind)
- Abrupt onset or ending of depressive episodes
- Seasonal or postpartum pattern of depression
- Hypersomnia and hyperphagia (atypical features)
- Early age at depression onset (younger than 25 years)
- Delusions, hallucinations, or other psychotic features.

Postpartum psychosis

Postpartum psychosis (PPP) represents the most serious perinatal psychiatric illness, but is also the most rare, occurring in less than 1 per 1000 births. Onset of PPP is often very quick, within the first 72 h after delivery, with almost all cases developing within 4 weeks postpartum (Sit, Rothschild, & Wisner, 2006). Though it may not be classified as true PPP outside of this short period of onset, psychosis could occur at any time postpartum either as a primary condition or as a feature of another psychiatric illness such as bipolar disorder or severe unipolar depression (Vesga-lo et al., 2008). In addition, a small number of patients may develop late onset PPP (Brockington, 2017). Patients who develop PPP have a 50–80% chance of going on to develop another psychiatric disorder, often bipolar disorder. PPP has a high morbidity and mortality rate with approximately 5% of patient committing suicide and 4% committing infanticide. It is considered a psychiatric emergency and generally requires hospitalization (Tinkelman, Hill, & Deligiannidis, 2017).

Symptoms and clinical features may include irritability, anxiety, auditory and/or visual hallucinations, delusions and abnormal thought content, confusion and disorientation, and a waxing and waning course of illness (Kamperman, Veldman-Hoek, Wesseloo, Robertson Blackmore, & Bergink, 2017). The disorder can present with primarily manic or depressive symptoms or may involve psychosis without mood features (Bergink, Rasgon, & Wisner, 2016). Thoughts of harming the infant are common and may be differentiated from perinatal OCD by their ego syntonic nature. The patient suffering from PPP may think the thoughts are reasonable and feel tempted to act on them, whereas in perinatal OCD, patients are often shocked and frightened by the thoughts they are having and do not want to carry them out (Bergink et al., 2016; Uguz & Ayhan, 2011). The mechanism of onset for PPP appears to be related to interactions between complex physiological changes after birth, including alterations in hormonal, Circadian, and immunological pathways (Bergink et al., 2016). Autoimmune thyroiditis, anti-NMDA receptor encephalitis, or infectious processes are also implicated in some cases (Davies, 2017). Thus, a comprehensive physical and neurological evaluation is indicated to rule out medical causes. 50% of patients who present with PPP have no history of previous psychiatric hospitalizations. In addition, 20–50% of patients with PPP have an isolated incident and do not have a recurrence with future pregnancies, however lithium prophylaxis after delivery in subsequent pregnancies is recommended for patients who have a history of PPP (Bergink et al., 2016; Jones et al., 2014; Sit et al., 2006; Spinelli, 2009).

Attention deficit and hyperactivity disorder

Attention deficit and hyperactivity disorder (ADHD) is not a disorder that presents in the perinatal period. However, there are a number of people who have been diagnosed with ADHD prior to pregnancy and may seek information about whether they may safely stay on their ADHD medications during pregnancy and lactation. There are no studies evaluating the natural course of ADHD in the perinatal period, and it is unclear whether pregnancy and postpartum hormonal changes have an impact on ADHD and its symptoms (Freeman, 2014).

At the time of this publication, there is one study on this topic currently underway (MGH Center for Women's Mental Health, n.d.-a). There is some evidence that hormonal changes in the perinatal period may impact neurocognitive functioning in some capacity, but the clinical significance of this is unclear. There is certainly a large amount of anecdotal discussion around the topic of "pregnancy brain" or "baby brain", but again, this has not been investigated systematically. When making decisions about whether to continue ADHD medications during pregnancy, the clinician should consider the level of functional impairment caused by the ADHD symptoms and evaluate the risk level of untreated symptoms. For example, if a patient is so disorganized and distracted when off medication that they are at high risk for car accidents, accidents at home, and the like, the benefits of medication may outweigh the risks.

Schizophrenia

In the past, pregnancy risks for people with schizophrenia were not in the forefront of most clinicians' minds. First generation antipsychotic agents often led to infertility due to prolactin elevation as a side effect (Whitworth, 2017). In addition, perhaps due to attitudes about people with serious mental illness, levels of functional impairment, and higher rates of institutionalization in the past, pregnancy was not considered to be a viable or realistic option for many of these patients. Of course, unintended pregnancies can still occur at any point, and most clinicians will be aware of at least some number of patients with schizophrenia who have become pregnant in the past or while in their care. With the advent of second generation antipsychotics, deinstitutionalization, and consumer driven recovery movements, pregnancy rates in people with schizophrenia are increasing (Vigod et al., 2014).

The risks of untreated schizophrenia for a pregnant parent and fetus are high. Adverse pregnancy complications can include gestational hypertension, pre-eclampsia, and venous thromboembolism. There is evidence that infants born to patients with schizophrenia have higher rates of adverse neonatal outcomes such as preterm delivery, small for gestational age, and large for gestational age (Vigod et al., 2014). However as in much of the research conducted on pregnant patients, this study did not control for substance use, medication use, or body mass index. Again, most clinicians who have worked on inpatient psychiatric units will likely have a memory of an acutely psychotic pregnant patient who clearly was unable to safely care for self or obtain prenatal care. In these cases, the risks of untreated mental illness are clearly evident.

Substance use disorders

Data from the 2012 Centers for Disease Control Risk Factor Survey System suggest that 5.9% of pregnant women use illicit drugs, 8.5% drink alcohol, and 15.9% smoke cigarettes (Forray, 2016). Of pregnant women who drank alcohol, 1.4% binge drank. Polysubstance use (including nicotine) may be as high as 50%. Rates of opioid abuse have increased, and substance use disorders have a high comorbidity with other psychiatric disorders. There are several treatment guidelines for the use of medication assisted treatment (MAT) for substance use disorders during pregnancy as well as treatment protocols for infants born with a tolerance to illicit substances or to patients who have used MAT during pregnancy (McLafferty et al., 2016; Substance Abuse and Mental Health Services Administration, 2018). Substance use disorders during pregnancy are associated with poor prenatal care, poor nutrition, poverty, domestic violence, and chronic medical problems. The actual substances of abuse can also have a negative physiologic impact on the pregnant patient, fetus, and offspring (McLafferty et al., 2016).

The use of marijuana during pregnancy is increasing in prevalence among all socioeconomic groups (Brown et al., 2017). Marijuana may be perceived as a safer and more natural treatment for nausea and vomiting associated with pregnancy or as a treatment for anxiety and depressive symptoms (Metz & Stickrath, 2015). There is some early research on the effects of marijuana use on pregnancy, and findings have been mixed. One meta-analysis found an association between heavy marijuana use and both low birth weight and preterm birth, while another study found no association with small for gestational age, spontaneous preterm birth, or hypertensive disorders of pregnancy but did find an association with increased neonatal morbidity (Conner et al., 2016; Metz et al., 2017). Metabolite from marijuana has been found in breastmilk (Baker et al., 2018; Bertrand, Hanan, Honerkamp-Smith, Best, & Chambers, 2018). At this point, the recommendation is for pregnant and lactating patients to avoid the use of marijuana due to the lack of definitive research on the risks. Additionally, there are a variety of strains and varieties of marijuana and the availability of these may vary depending on the legality of marijuana in various localities, so conducting research on safety can be even more challenging.

Evaluating research on psychotropic medications during pregnancy

Interestingly, antidepressant medications are reported to be one of the most researched medication class as it relates to safety during pregnancy (Osborne, McEvoy, & Payne, 2017; Payne, 2016). Why do clinicians often feel unprepared to make treatment decisions about medications during pregnancy, and why is there so much misinformation and confusion about the safety of psychotropics during pregnancy? One possible explanation for this is the challenges that exist with conducting research in pregnant populations. Pregnant women and fetuses are considered a vulnerable population in terms of human subjects protection, and studies involving pregnant participants are required to go through additional institutional review board approval in order to progress (Brandon, Shivakumar, Lee, Inrig, & Sadler, 2009). The conditions required to conduct research involving pregnant patients are extensive (Brandon, 2011). In addition, the type of research study that clinicians are often most familiar with using to guide practice, randomized controlled trials (RCTs), cannot ethically be conducted in pregnant patients in most cases. The ideal study on the use of a psychotropic medication during pregnancy would be to prospectively compare four groups: those who have a psychiatric illness and take medication, those who have a psychiatric illness and do not take medication, those who are unaffected by psychiatric illness and do not take medication, and those who are unaffected by psychiatric illness and do take medications. Of course, this type of study would also be unethical and cannot be conducted. There are often confounding factors in people with mental illnesses that are not well controlled for in research.

Due to the limitations discussed above, research studies on the topic of psychotropic medications during pregnancy must be conducted using registries, retrospective analyses, natural history methodology, and case control design. These research methodologies are often considered "inferior" to RCTs, and clinicians may be less comfortable with evaluating their applicability to practice. Useful information can be gained from a variety of research methodologies. Triangulation, replication, controlling for confounding factors, and critically evaluating results are essential components of tracking research findings that are not as clear cut as RCTs. Unfortunately, many studies involving pregnant patients do not control for things like severity of symptoms, maternal mental illness, medication dosing, genetic history, substance abuse, prenatal care, or socioeconomic status. This makes interpretation of the results challenging. At this point, the strongest type of study involving pregnant participants is a prospective study that controls carefully for confounders. By using sophisticated statistical techniques, researchers can control for confounders and draw stronger conclusions from retrospective registry data than might have been possible in the past (Desai, Rothman, Bateman, Hernandez-Diaz, & Huybrechts, 2017; Osborne et al., 2017). There are several registries currently ongoing at Massachusetts General Hospital (MGH) which are looking at the use of antidepressants, antipsychotics, and other psychiatric medications in pregnant patients (MGH Center for Women's Mental Health, n.d.-c). These registries are enrolling pregnant participants who are and are not

taking psychotropic medications for the purposes of comparison. While animal studies are typically undertaken prior to use of a drug in humans, these models are not consistently predictive of how the drug will affect humans (Shanks, Greek, & Greek, 2009). Nevertheless, if there are data from more than two nonhuman animal species showing no increase in malformations, some experts believe we can reasonably say there is a low risk in humans as well (S. Lavigne, personal communication, September 6, 2018).

Food and Drug Administration labeling

Prior to 2015, Food and Drug Administration (FDA) labeling for drug use during pregnancy divided drugs into categories A, B, C, D, and X based on several criteria related to human and nonhuman animal data. For example, category B indicated that studies in nonhuman animals failed to demonstrate a risk to the fetus and that there were no adequate studies in pregnant humans (US Department of Health and Human Services, n.d.). The problem with this type of labeling was that clinicians often erroneously assumed that category B drugs were "safer" in humans than category C (or D) drugs and made prescribing selections accordingly (Payne, 2017). In reality, a drug could obtain a label of pregnancy category B without any reported human data at all, and there were a number of drugs that were originally marketed as category B and were later changed to other categories based on new research findings. In addition, the categories did not provide any information about the type and quality of human research available or offer decision-making support for clinicians when prescribing medications for pregnant or lactating patients (Pernia & DeMaagd, 2016). There was also no consideration of the risk of untreated illness or the trimester when the medication was used.

In June of 2015, new FDA labeling changes went into effect, titled the Pregnancy and Lactation Labeling Rule (PLLR) final rule (US Food and Drug Administration, 2014). The new system requires that information be included in the package insert for each individual medication. The information provided should review the available research in humans during pregnancy and lactation. The goal of making this change was to provide assistance and support to clinicians in evaluating risk and benefit and counseling patients effectively when prescribing the medication during pregnancy and lactation. The new guidelines also require that information about the impact of the drug on females and males of reproductive potential be shared as well. Some of the limitations of the PLLR are that it is only required for package inserts for medications approved after 2001 and that it has been rolled out in a stepwise process based on the original approval date. Another criticism is that the old category system was simpler and easier for clinicians to comprehend and that the new system requires more complex decision-making (Pernia & DeMaagd, 2016). However, more importantly, since the old system was often based on marginally relevant information from nonhuman animal studies, it can also be argued that it did not provide enough information for truly informed decision making.

Lack of information about psychotropics during lactation

Research on the use of psychotropics during lactation is even more limited than that of medication during pregnancy (Wang et al., 2017). Most information about how much of any given medication is passed in breastmilk is based on very small numbers of participants who have breastmilk samples tested, and these are most often conducted during the early infancy period. Since breastmilk composition changes and breastmilk consumption decreases as the child grows and develops, findings from early infancy studies may not be generalizable to later infancy or early childhood. Infants metabolize drugs differently from older children and adults and may respond differently as well. Research may be conducted in nonhuman animal models which are also not generalizable to humans (Anderson, 2018). Several pharmacokinetic factors are involved in the passage of medication into breastmilk. These include the lipid solubility of the drug, the molecular size of the drug, the blood level and protein binding in maternal circulation, oral bioavailability in the infant and the lactating parent, and the half-life of the drug in maternal and infant plasma (Infant Risk Center, n.d.-a; Anderson, 2018).

All drugs being considered for use during lactation should be evaluated individually and with risk/benefit and support for individual patient preferences in mind. In the past, many drugs were thought to be contraindicated in lactation. However, with more recent findings regarding safety as well as knowledge of the benefits of lactation for both the lactating parent and the breastmilk fed baby and child, recommendations to support lactation in the presence of medication use are increasing (Wang et al., 2017). Evidence based information about medications during lactation can be found through LactMed, MotherToBaby, and ReproTox. Ongoing registries and research studies are being conducted through the InfantRisk Center to obtain more information about the use of various medications during lactation (Infant Risk Center, n.d.-b).

Decision making process for psychotropics during pregnancy and lactation

In order to facilitate evidence based and patient centered decision making when prescribing psychotropic medication to pregnant or lactating patients, we recommend the use of a heuristic process involving a series of questions that can guide treatment decisions. Experienced clinicians will likely find that they quickly consider and address many of these questions internally when making treatment recommendations. Novice clinicians may find it useful to go through the steps of the process more explicitly. These questions can also be adapted to guide advice for patients who have an unplanned pregnancy or who are seeking pre-conception counseling about medication use. We also recommend the use of information available from the Reproductive Psychiatry Information Center at the MGH Center for Women's Mental Health and MotherToBaby. These are excellent resources that provide up to date, evidence based information about individual medications and medication classes.

Heuristic process for medication decision making during pregnancy

1. What is the condition being treated, and what symptoms are present?
2. How severe are the symptoms?
3. Is there any history of self-medicating with substances, self-harm or suicide attempts, or psychiatric hospitalizations?
4. How much functional impairment is present?
5. How many weeks gestation is the pregnancy?
6. Does the patient have plans to breastfeed?
7. What information and knowledge does the patient have about medications during pregnancy and lactation (from media, friends and family, other providers, etc.)? Is there a willingness to consider medication?
8. Is there a partner or other parent whose opinion may be influential to the patient?
9. What medication has been effective for the patient in the past?
   a) Do data suggest that this medication is contraindicated during pregnancy? If not, consider re-trialing.
10. Which medications that treat this disorder have the most research data about use during pregnancy?
    a) Have these medications been tried and been ineffective in the patient in the past?
       If trials have been appropriate, consider alternative choices.
    b) If these medications have not been tried, consider trial.
11. If the patient is already on medication, is there a risk of withdrawal for patient or fetus? What is the risk of relapse of psychiatric symptoms if medications are discontinued?
12. Is there a medication that could treat multiple symptom clusters?
13. Can medication doses be optimized?
14. Is there any other medication burden in this patient?
15. Does the patient have access to high risk pregnancy monitoring, NICU, etc.?
16. Are there any other risk factors for the fetus?

For pre-conception counseling, additional questions may include:

17. When does the patient desire pregnancy?
18. How long has the patient been psychiatrically stable (longer is better)?
19. Will the patient be using any assisted reproductive technology for conception?
20. What medications are working for the patient currently, and how much research is available on those?
21. Have they had other trials of medications that might be safer during pregnancy?
22. Can their current medication burden be reduced?
23. Does their condition allow for a closely monitored trial off medication?

Treatment decisions must be individualized based on the unique needs and preferences of each patient as well as on the available research on each medication class and specific drug. There are no absolutes when making these decisions. When treating psychiatric disorders during pregnancy, we cannot achieve zero risk to both patient and fetus. There are two major risks that are being balanced, the risk of exposure to untreated or undertreated mental illness and the risk of exposure to medication. Known risks of untreated mental illness can include substance abuse, low birth weight, poor fetal growth, preterm delivery, pregnancy complications, depression during adolescence in offspring, and others (Angelotta & Wisner, 2017; Gibson-Smith et al., 2015; Judd et al., 2014; Männistö et al., 2016; Rusner, Berg, & Begley, 2016; Stein et al., 2014). Potential risks of medication can include infertility, teratogenicity, neonatal complications, and long term neurobehavioral or other effects in offspring. In terms of teratogenicity, it's important to keep in mind that there is a baseline 3–5% risk of major malformation in the fetus in the general population without any exposures. Most psychotropic medications that do have established teratogenicity have an absolute risk of 1–2% or less. The majority of psychotropic medications have not been shown to have teratogenic effects (S. Lavigne, personal communication, September 6, 2018).

Neonatal complications of antidepressant use during pregnancy may include an increased risk of persistent pulmonary hypertension of the newborn (PPHN) and transient neonatal distress syndrome or poor neonatal adaptation syndrome (PNAS) (Angelotta & Wisner, 2017; Norby et al., 2016). The absolute risk for these conditions is still quite low, and research findings are inconsistent (Huybrechts et al., 2015). Data on PPHN are particularly inconsistent, with more recent studies showing a lower association than previously reported, leading to a revised FDA warning (U.S. Department of Health and Human Servi, 2011). There may be an association between antidepressant use during pregnancy and increased risk of postpartum hemorrhage (Jiang et al., 2016). When looking at long term effects in offspring, there are very little data available. There were two studies widely reported in the media that purported to show an association between prenatal antidepressant use and autism spectrum disorders in the offspring (Reuters, 2017). However those studies did not control for several important factors, including maternal mental illness. After adjusting for maternal mental illness, the risk diminishes and is mostly statistically insignificant (Andrade, 2017a, 2017b).

Making medication treatment decisions for patients who are pregnant can feel challenging and scary to many clinicians. Not only are we responsible for making the best decision for the pregnant patient, but there is also the health and safety of the fetus to consider. The golden rule of prescribing during pregnancy is to make every effort to eliminate exposure to the impact of maternal mental illness by treating to remission whenever possible. In patients who stop medications prior to pregnancy or early in pregnancy, symptom control when restarting medications can be harder to achieve. Fetal exposure to both medication and poorly treated mental illness will increase risk for complications. So for example, trying to reduce risk from medication by prescribing subtherapeutic doses actually causes exposure to both the risk of medication and the risk of untreated illness. We recommend dosing to efficacy when medications are being used. We also recommend reducing medication burden as much as possible by maximizing doses and avoiding polypharmacy if possible to do safely. As mentioned previously, augmenting medication treatment with psychosocial interventions is highly encouraged. During pregnancy, medication doses may need to be increased due to fluid volume and glomerular filtration rate increases, hormonal changes, and liver metabolism alterations (Payne, 2017). For patients who are stable, clinicians should monitor the need for dose adjustments or medication changes approximately every trimester and after delivery.

Shared decision making

Including patients in the decision-making process about medication to any extent possible is more likely to result in a successful outcome both in terms of developing and maintaining therapeutic rapport and enhancing compliance with treatment recommendations. To look at this issue beyond the utilitarian perspective, allowing pregnant and lactating patients to engage in decision making also supports their individual autonomy and agency in a meaningful way (Miller, 2009). Clinicians will observe that there is a wide range of patient presentations around this topic, from the patient who completely defers to the clinician to make medication decisions to the patient who is highly resistant to any suggestion of medication use during pregnancy and/or lactation. Additionally, patients who are experiencing severe psychotic or manic symptoms may not have the capacity to make informed treatment decisions while highly symptomatic. In part due to media reporting about psychotropic use during pregnancy that is at best incomplete and at worst sensationalist and inaccurate, many patients will have erroneous assumptions about the safety of various medications. Many clinicians of various disciplines and specialties are also poorly trained in this field and may provide misinformation. Thus, it is very important to gain an understanding of the patient's perceptions of the use of medications during pregnancy and lactation and to “meet them where they are” when discussing treatment options.

Discussion of the risks of untreated mental illness should be included in order to provide a balanced perspective. Motivational interviewing, exploring emotions and perceptions, validating emotions, and psychoeducation can all be valuable interventions. Some patients may require time to process and think about the decision of whether to use medication, and some patients may be ready to start something right away. Some may want to involve a partner, family member, or friend in the decision-making process, and some may prefer to make the decision on their own. The question of whether an extra layer of informed consent is necessary when prescribing medications for patients who are pregnant has been raised. There are different opinions about this throughout the field. As clinicians, our opinion is that a special informed consent process is not necessary in pregnant patients. Not only does this stigmatize obtaining mental health treatment during pregnancy, but it implies that pregnant patients are unable to make treatment decisions in the same way that non-pregnant patients can. If a clinician feels more comfortable obtaining informed consent from pregnant patients, we would advocate that the same informed consent process be followed for all patients.

Resources for clinicians and patients

- InfantRisk Center: infantrisk.com
- LactMed: toxnet.nlm.nih.gov/pda/lactmed.htm (app also available)
- Marce Society for Perinatal Mental Health: marcesociety.com
- MGH Center for Women's Mental Health: womensmentalhealth.org
- MotherToBaby: mothertobaby.org
- Motherisk: motherisk.org
- The PERISCOPE project: the-periscope-project.org/
- Postpartum Support International: postpartum.net (listserv for professional members available)
- Reprotox: reprotox.org

Collaboration with other disciplines and specialties

While we absolutely endorse collaboration with other disciplines and specialties who may be involved in treating pregnant patients, we also recognize that psychiatric care providers are the experts in managing psychiatric conditions. Our recommended best practice would be for psychiatric care providers to be involved in treatment of all patients who experience mental health disorders in the perinatal period. However, we are aware that referrals to psychiatric care providers can be challenging due to lack of availability, particularly in certain geographic areas. Our hope is that this paper can serve as a reference for clinicians in other disciplines and specialties to increase their awareness of resources available when working with these patients. Additionally, some psychiatric clinicians may feel uncomfortable with the idea of making medication recommendations during pregnancy and may try to defer decision making about psychotropic medications to the clinician who is managing the pregnancy (obstetrician, midwife, or other provider). This might be seen as similar to an obstetrician or midwife referring a patient to a psychiatric provider for management of the pregnancy when the patient also has a psychiatric diagnosis. Most clinicians would find this odd. We advocate for psychiatric care providers to take responsibility for informing themselves about psychotropic use during pregnancy and lactation and to serve as the psychiatric expert in this patient population.

Reproductive safety information on individual medication classes

Antidepressants

Antidepressant medications are widely used across all patient populations for a variety of concerns and problems. While there has never been consistent evidence of teratogenicity related to the use of antidepressants during pregnancy, misconceptions still exist about their safety profile. This may be due to inconsistencies in methodology across research studies as well as media reporting about certain studies without a full understanding of the data. For example, some drugs such as paroxetine have been shown in some studies to increase the risk of cardiac malformations in the fetus, but in other studies, no such finding has been observed (Huybrechts et al., 2014). As discussed previously, there may be some risk for PNAS and PPHN in neonates who were exposed to antidepressant medications in utero. Symptoms of PNAS are generally transient, resolve spontaneously typically in less than 48 h, and do not require medical intervention. Actions such as swaddling and increasing skin to skin time between parent and infant are often sufficient in managing PNAS symptoms (Kieviet, Dolman, & Honig, 2013). In the majority of cases, PNAS has not been shown to have long term consequences (Norby et al., 2016). PPHN can usually be managed with supportive measures but does have approximately a 10% mortality rate in neonates who experience it. It is estimated to occur in 0.4 to 6.8 per 1000 live births and is most often related to conditions related to prematurity and not to antidepressant use (Fuloria & Aschner, 2017). The absolute risk for PPHN in antidepressant exposed neonates appears to be quite small, approximately 23 to 36 per 10,000 births (Huybrechts et al., 2015).

A misconception related to SSRI medications is that providers should taper SSRIs two weeks prior to delivery to reduce the risk of PNAS. In response to concerns about SSRIs and this adaptation syndrome, the FDA issued a warning (now revoked) in 2004 suggesting the practice of discontinuing SSRIs in anticipation of birth (Payne & Meltzer-Brody, 2009). This practice, however, has not been empirically supported. Evidence suggests that tapering and discontinuing SSRIs does not have a significant impact on improving neonatal health (Warburton et al., 2010). Instead, it may expose the gestational parent to undue risk of symptom relapse and increase severity of postpartum mental illness (MGH Center for Women's Mental Health, 2017b). While there are data available related to the impact of antidepressant use on neonates, the long term impact of antidepressant use during pregnancy on offspring is not yet well studied. Claims that antidepressant use during pregnancy is linked to autism spectrum disorder in offspring have not been supported by high quality studies that carefully control for confounding variables, the most important of which is maternal mental illness (Andrade, 2017a, 2017b).

Generally when choosing an antidepressant to use during pregnancy, the medication that works best for the patient is the best choice. In the absence of a history of successful treatment with another agent, sertraline is often preferred due to having extensive research data supporting its safety and a lower relative dose transferred to the infant during lactation than fluoxetine, which also has extensive data. Other older agents such as fluoxetine, citalopram, escitalopram, and venlafaxine are also considered to be reasonable choices (Angelotta & Wisner, 2017; Ornoy, Weinstein-Fudim, & Ergaz, 2017; Payne, 2017; Vitale et al., 2016). Tricyclic antidepressants to include amitriptyline, imipramine, and nortriptyline have also been researched and appear to have a safe profile. There are limited data related to bupropion, but thus far the risk profile seems to be similar to that of other antidepressants (Huybrechts et al., 2014). There are a number of case reports of the use of mirtazapine for comorbid hyperemesis gravidarum and depression (Uguz, Turgut, Aydin, & Ak, 2018). Newer drugs such as vilazodone or vortioxetine have not yet been researched and would ideally be avoided during pregnancy due to lack of data. To reiterate, however, if a medication with a lack of data has been the most effective for a patient in the past, and the risk of relapse is high, clinicians should strongly consider maintaining the current regimen.

Antipsychotics

Similar to antidepressants, there is a good amount of research supporting the safety of many antipsychotics during pregnancy. Several large scale analyses of data have failed to show any association between either first generation or second generation antipsychotics and fetal malformation (Ennis & Damkier, 2015; Galbally, Snellen, & Power, 2014; Mcallister-Williams et al., 2017; Ornoy et al., 2017; Whitworth, 2017). There have been mixed findings on the question of whether second generation antipsychotics increase the risk for gestational diabetes and/or maternal weight gain (Galbally et al., 2014; Gibson-Smith et al., 2015). Some small studies have shown a risk for neonatal withdrawal after exposure to antipsychotics in utero (Galbally et al., 2014; Gibson-Smith et al., 2015). There are few studies that have followed offspring exposed to antipsychotics in utero. Some studies showed an association with prenatal exposure to second generation antipsychotics and early neurological delays, however those were no longer statistically significant at 12 months, and these studies may not have adequately controlled for confounding factors (Galbally et al., 2014; Poels et al., 2018).

The most researched choices include quetiapine, aripiprazole, ziprasidone, and olanzapine. In large scale analyses, second generation antipsychotics were not associated with an increased risk of congenital malformations. Risperidone, however, was found to have a slightly increased risk for cardiac malformations in the fetus so would not be a first line medication choice (Huybrechts et al., 2016). Haloperidol and several other first generation antipsychotics also have good research support (Gibson-Smith et al., 2015). Similar to antidepressants, older agents have the most accumulated data, and newer medications have not yet been researched and ideally should be avoided if possible. But again, the best choice is usually the medication that is most effective for the patient. Clinicians may observe a widespread perception of lurasidone as the “safest” antipsychotic medication to use during pregnancy, however this erroneous belief was based on the promotion of lurasidone as a category B medication. As discussed previously, the old category B did not indicate that there was any information about the safety of the medication in humans and did not indicate that a drug was a safer choice in humans than drugs from other categories. In fact, at present lurasidone has very little pregnancy data in humans available, and when possible, should be avoided in favor of better researched

medications.

Anticonvulsants

Some treatment guidelines for bipolar disorder during pregnancy recommend the use of anticonvulsants only if antipsychotics are ineffective (Graham, Tavella, & Parker, 2017; National Collaborating Centre for Mental Health Royal College of Psychiatrists' Research and Training, 2014). Most of the research that has been conducted on anticonvulsants during pregnancy has been in patients with seizure disorders. Of the three anticonvulsants most commonly used in psychiatric treatment (lamotrigine, valproate, and carbamazepine), lamotrigine is believed to have the best safety profile for use during pregnancy (Jones & Jones, 2017). Several large studies have shown no association between lamotrigine exposure in utero and congenital malformations in the fetus. Previous findings suggesting an association between lamotrigine exposure and cleft palate have not been replicated (Clark & Wisner, 2018). Pregnancy complications and long term impact on the offspring have not been associated with lamotrigine use during pregnancy (Clark & Wisner, 2018). Lamotrigine levels are sensitive to hormonal fluctuations, and dosing may need to be increased during pregnancy and decreased again after delivery. Some recommendations support the practice of monitoring lamotrigine levels during pregnancy to track fluctuations (Clark & Wisner, 2018).

Lamotrigine interferes with the synthesis of the bioactive form of folate (5-MTHF) as noted in the FDA package insert (GlaxoSmithKline, n.d.). While this interference has not been linked clinically to neural tube defects or other negative neonatal outcomes, some clinicians may recommend extra folic acid supplementation of 4–5 mg. daily in line with the recommendations for other anticonvulsants (Campbell et al., 2014; National Collaborating Centre for Mental Health Royal College of Psychiatrists' Research and Training, 2014). This recommendation is not, however, known through research to provide any specific benefits, although there do not appear to be risks associated with additional supplementation. In the clinical setting, the decision to recommend additional folic acid supplementation may come down to the preference of the pregnant patient after discussing the information above.

Carbamazepine use during pregnancy has been associated with an increase in congenital malformations, including neural tube defects, cleft palate, and hypospadias, in some studies (Bromley, Weston, & Marson, 2017; Clark & Wisner, 2018; National Collaborating Centre for Mental Health Royal College of Psychiatrists' Research and Training, 2014). These associations have been inconsistent, and the overall risk for malformations associated with carbamazepine varies considerably across the literature. Some studies have not replicated findings of increased risk (Campbell et al., 2014; Clark & Wisner, 2018; Hernandez-Diaz et al., 2012a; Petersen et al., 2017; Tomson et al., 2018). Some other inconsistent findings have pointed to an association between carbamazepine use during pregnancy and neurodevelopmental delay in offspring (Clark & Wisner, 2018; Jones & Jones, 2017).

Valproate use during pregnancy has been clearly associated with an increased risk for congenital malformations to include congenital heart defects and neural tube defects and neurodevelopmental delay, autism spectrum disorders, and decreased IQ in offspring (Jones & Jones, 2017). NICE guidelines recommend that valproate be avoided in people who have the capacity to become pregnant (National Collaborating Centre for Mental Health Royal College of Psychiatrists' Research and Training, 2014). Other anticonvulsants that may be used in psychiatric practice include oxcarbezapine, topiramate, and gabapentin. Data on these agents from the neurology literature are very limited but may show a higher rate of cleft palate with topiramate, higher rates of neurodevelopmental risk in offspring with oxcarbezapine (of note, this was also seen with lamotrigine in one study), and no significant risk for malformation with gabapentin (Bromley et al., 2017; Hernandez-Diaz et al., 2012b; Veroniki et al., 2017).

Lithium

Lithium has developed a reputation as a medication with an absolute contraindication for use during pregnancy. **This belief is not accurate**. It is true that in several studies lithium was shown to increase the risk of Ebstein's anomaly, a cardiac malformation in the fetus. The risk for cardiac malformation in infants who had not been exposed to lithium prenatally in one study was approximately 0.5–1%, and the risk in lithium exposed infants was approximately 2.5% (Patorno et al., 2017). So while there is an increased relative risk, the absolute risk is still low. Based on the slightly elevated risk, if possible, it is preferable to avoid lithium during fetal cardiogenesis (days 18–55 of pregnancy or 4.5–10 weeks after the last menstrual period). However, another large meta-analysis found no increased risk of cardiac malformations but did demonstrate an increased risk of other major malformations (Munk-Olsen et al., 2018). This study did not find an association between prenatal lithium use and any of the pregnancy complications or delivery outcomes studied. Some evidence suggests an increased risk of preterm birth in those taking lithium during pregnancy, but those results were not replicated elsewhere (Poels, Bijma, Galbally, & Bergink, 2018).

In many patients with bipolar disorder who are lithium responders, the risk of relapse outweighs the increased risk of fetal malformation. The decision to continue lithium during pregnancy can be well-supported. Collaboration with high risk obstetrics for increased fetal monitoring is an important component of treatment planning. Level 2 ultrasound, fetal echocardiogram, growth scans, and monitoring for polyhydramnios are recommended for routine monitoring of patients taking lithium during pregnancy (S. Lavigne, personal communication, September 6, 2018; Poels, Bijma, et al., 2018). Additionally, some experts suggest that delivery should occur in a facility that has access to advanced neonatal care in case of complications in the neonate after delivery (Poels, Bijma, et al., 2018).

Lithium levels are particularly sensitive to fluid volume changes during pregnancy due to lithium's pharmacokinetic profile. Recent recommendations suggest monitoring lithium levels closely (up to every three weeks) until week 34 of pregnancy, then weekly until delivery, and then twice a week for the first two weeks postpartum (Wesseloo et al., 2017). The authors suggest that lithium levels throughout the perinatal period should be kept as close as possible to levels that were effective pre-conception in order to protect against relapse, and twice daily dosing is recommended for consistency of blood levels. They also recommend a consideration of creatinine monitoring to track pregnancy induced changes in renal function. This study did not find a precipitous increase of lithium levels after delivery as has been suggested previously. They suggest that keeping the level greater than or equal to 0.8 mmol/L during the postpartum period would be best to prevent postpartum mood episodes. Some clinicians may prefer to closely monitor the patient's symptomatology and adjust dosing accordingly.

Other recommendations suggest that blood levels should be measured before and 24 h after delivery and that lithium blood level, thyroid-stimulating hormone, and free thyroxine should be measured in an umbilical blood sample (Poels, Bijma, et al., 2018). Lithium prophylaxis for postpartum psychosis is recommended for patients who have a history of postpartum psychosis, even if they are not taking lithium during pregnancy (Bergink et al., 2016). There are no currently accepted dosing recommendations, but some recommendations suggest starting lithium the first night after delivery and targeting a blood level of 0.8 mmol/L during the first month postpartum (Poels, Bijma, et al., 2018). The long term impact of prenatal lithium exposure on offspring has not been well-studied. Most findings thus far indicate that there are no long term neurodevelopmental consequences, but there is a lack of methodologically strong research in this area (Poels, Bijma, et al., 2018; Poels, Schrijver, et al., 2018).

Benzodiazepines, hypnotics, and other medications for anxiety and insomnia

Contrary to some beliefs, benzodiazepines do not have an absolute

contraindication for use during pregnancy. Early studies suggested an association between diazepam and cleft palate in the fetus, but those findings have not been replicated (McLafferty, Spada, & Gopalan, 2018; Thorsness et al., 2018). If possible, PRN use is better than routine use to reduce the potential for tolerance and subsequent withdrawal effects in the infant. Keeping doses as low as possible is also preferred. Recent data suggest that there may be an association between benzodiazepine use in pregnancy and higher NICU admission rates as well as smaller head circumference in the neonate (Freeman et al., 2018). Based on limited data, zolpidem does not appear to be associated with teratogenic effects, although again, PRN use is preferable (Juric, Newport, Ritchie, Galanti, & Stowe, 2009; McLafferty et al., 2018; Okun, Ebert, & Saini, 2015; Wikner & Källén, 2011). Antihistamines that may have anxiolytic and sedating effects are considered generally safe to use. Doxylamine, an over the counter antihistamine agent marketed for insomnia, is one of the ingredients in the prescription medication Diclegis™ which is FDA approved to treat pregnancy related nausea and vomiting. Diphenhydramine and hydroxyzine have also been used during pregnancy without known ill effects (Okun et al., 2015; Thorsness et al., 2018). Patients should be counseled to avoid using benzodiazepines and antihistamines on the same day, as there is a case report of a still birth with the concurrent use of temazepam and diphenhydramine (Kargas, Kargas, Bruyere, Gilbert, & Opitz, 1987). Melatonin is not recommended while planning pregnancy, during pregnancy, or during lactation since it is also an endogenous hormone, and the impact of taking exogenous melatonin on normal hormonal processes is not known (McLafferty et al., 2018; Thorsness et al., 2018). Trazodone and other sedating antidepressants including mirtazapine, doxepin, and amitriptyline have not shown an increased risk of congenital malformations or adverse outcomes (McLafferty et al., 2018; Okun et al., 2015). Finally, there are few to no human data available on buspirone use during pregnancy, so it is generally avoided (Thorsness et al., 2018).

Stimulants and non-stimulant medications for ADHD

Data related to the use of stimulants during pregnancy in nonhuman animals suggest that there may be an impact on fetal growth, particularly when stimulants are taken in the third trimester (Freeman, 2014). There has not been a clear indication that stimulant use during pregnancy increases the risk of major malformations in the human fetus. Many studies looking at the effects of stimulants during pregnancy have a number of confounding factors, including substance abuse, concomitant medications, and comorbidity. There are not enough data on any specific stimulant medication to recommend one over another in pregnancy, however one large analysis did observe a slightly increased risk of cardiac malformation in the fetus with methylphenidate but not amphetamines (Huybrechts et al., 2018). Often methylphenidate is considered the best choice for use during lactation due to low levels of transmission in breastmilk (Ornoy, 2018). The use of stimulants of abuse during pregnancy, including cocaine and methamphetamine, has been shown to increase risk for a fetal morbidity and mortality, but it is not believed that prescription stimulants carry the same level of risk (Forray, 2016; Forray & Foster, 2015).

In considering whether to continue stimulants during pregnancy, the clinician should carefully weigh the level of functional impairment and safety risk that may occur if medications are not used. The risk of untreated ADHD on pregnancy and fetal outcomes is not well understood. Some patients are able to discontinue stimulants during pregnancy or switch to PRN use instead of daily use. It may also be possible to implement psychosocial interventions and life changes (e.g. changes to work schedule or workload if feasible) to address some symptoms. One author (Freeman, 2014) recommends using the questions "(1) How have you functioned in the past at work or school without the use of medications and (2) how is your driving when not treated with medications for ADHD? Have you had a history of accidents?" to assess the value of medication for a given patient. Nonstimulant medication treatments for ADHD include clonidine, guanfacine, bupropion, and atomoxetine. Data on clonidine, guanfacine, and atomoxetine use during pregnancy and lactation are limited, and these agents are best avoided if possible. As discussed previously, bupropion appears to have a relatively safe profile (Freeman, 2014; Ornoy, 2018).

Medications during lactation

For use during lactation, each individual medication should be investigated to determine how much research information is available. The safety profile of a medication during pregnancy does not necessarily translate to use during lactation. For example, ibuprofen is not recommended for use during pregnancy but is considered safe to use during lactation. On the flip side, however, when prenatal exposure to a medication has occurred, it may be acceptable to continue the same medication during lactation. Medications that are commonly used during lactation and appear to have low transmission into breastmilk include sertraline, lorazepam, olanzapine, and quetiapine (Hatzopoulos & Albrecht, 2010; Pacchiarotti et al., 2016; Thorsness et al., 2018). Lithium was previously not recommended during lactation due to its high level of transfer into breastmilk, but more recently some clinicians have endorsed its use with close monitoring for infant restlessness or difficulty feeding (Clark & Wisner, 2018; Pacchiarotti et al., 2016). Similarly, lamotrigine does pass into breastmilk, but adverse effects in the infant have not been observed (Clark & Wisner, 2018; Pacchiarotti et al., 2016; Uguz & Sharma, 2016).

Clinicians should also consider the impact of the medication and its side effects on the lactation process. Antipsychotics can increase prolactin levels which theoretically should not have negative consequences for lactating patients. Aripiprazole, however, can decrease prolactin levels which could reduce breastmilk supply (United States National Library of Medicine, 2006). Antihistamines are also thought to decrease breastmilk supply and should be used with caution (Thorsness et al., 2018). Anticholinergic medications have been shown to negatively impact lactation in nonhuman animals (Anderson, 2018).

Conclusion

As we have reviewed, the effective treatment of psychiatric disorders during the perinatal period is of high importance due to the potential negative consequences of untreated psychiatric illness on parents, offspring, and society at large. About 15–20% of pregnant individuals will experience some type of psychiatric disorder during the perinatal period. Pharmacotherapy is an essential component of the treatment plan for many patients with these disorders. We have provided an overview and practical guide for making treatment decisions about medication use during the perinatal period. The use of a heuristic decision-making tool can guide clinicians in the selection of medications based on the individual needs and preferences of the person being treated.

Key points

1. The medication that works best for the patient is usually the best choice.
2. Weigh the risks of medication against the risks of untreated mental illness.
3. Make every effort to reduce or eliminate exposure to mental illness by treating to remission.
4. Use available resources and stay current with new research findings.

Acknowledgement

We express our gratitude to the following colleagues who provided assistance on this paper: Roy Brown, MLIS, AHIP; Sharon Voyer Lavigne, MS, LGC; My Hanh (Theresa) Nguyen, PMHNP-BC, Melinda Thiam, MD.

We also express great appreciation to the members of the Postpartum Support International professionals listserv for sharing their wisdom and knowledge.

References

Altshuler, L. L., Hendrick, V., & Cohen, L. S. (1998). Course of mood and anxiety disorders during pregnancy and the postpartum period. *The Journal of Clinical Psychiatry, 59*(Suppl. 2), 29–33.

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, Virginia: American Psychiatric Association.

Anderson, P. O. (2018). Drugs in lactation. *Pharmaceutical Research, 35*(3), https://doi.org/10.1007/s11095-017-2287-z.

Andrade, C. (2017a). Antidepressant exposure during pregnancy and risk of autism in the offspring, 1: Meta-review of meta-analyses. *Journal of Clinical Psychiatry, 78*(8), 9–10. https://doi.org/10.4088/JCP.17f11903.

Andrade, C. (2017b). Antidepressant exposure during pregnancy and risk of autism in the offspring, 2: Do the new studies add anything new? *Journal of Clinical Psychiatry, 78*(8), e1052–e1056. https://doi.org/10.4088/JCP.17f11916.

Andrade, C. (2018). Valproate in pregnancy: Recent research and regulatory responses. *Journal of Clinical Psychiatry, 79*(3), 13–16. https://doi.org/10.4088/JCP.18f12351.

Angelotta, C., & Wisner, K. L. (2017). Treating depression during pregnancy: Are we asking the right questions? *Birth Defects Research, 109*(12), 879–887. https://doi.org/10.1002/bdr2.1074.

Baker, T., Datta, P., Rewers-Felkins, K., Thompson, H., Kallem, R. R., & Hale, T. W. (2018). Transfer of inhaled cannabis into human breast milk. *Obstetrics & Gynecology, 131*(5), 1. https://doi.org/10.1097/AOG.0000000000002575.

Bauer, A., Parsonage, M., Knapp, M., Iemmi, V., Adelaja, B., & Hogg, S. (2014). *The costs of perinatal mental health problems.* Centre for Mental Healthhttps://doi.org/10.13140/2.1.4731.6169.

Beck, C. T. (2004). Birth trauma: In the eye of the beholder. *Nursing Research, 53*(1).

Beck, C. T., Driscoll, J. W., & Watson, S. (2013). *Traumatic childbirth.* New York, NY: Rountledge.

Bergink, V., Rasgon, N., & Wisner, K. L. (2016). Postpartum psychosis: Madness, mania, and melancholia in motherhood. *American Journal of Psychiatry, 173*(12), 1179–1188. https://doi.org/10.1176/appi.ajp.2016.16040454.

Bertrand, K. A., Hanan, N. J., Honerkamp-Smith, G., Best, B. M., & Chambers, C. D. (2018). Marijuana use by breastfeeding mothers and cannabinoid concentrations in breast milk. *Pediatrics, 142*(3), e20181076. https://doi.org/10.1542/peds.2018-1076.

Brandon, A. R. (2011). Ethical barriers to perinatal mental health research and evidence-based treatment: An empirical study. *AJOB Primary Research, 2*(1), 2–12. https://doi.org/10.1080/21507716.2011.561517.

Brandon, A. R., Crowley, S. K., Gordon, J. L., & Girdler, S. S. (2014). Nonpharmacologic treatments for depression related to reproductive events. *Current Psychiatry Reports, 16*(12), https://doi.org/10.1007/s11920-014-0526-0.

Brandon, A. R., Shivakumar, G., Lee, S. C., Inrig, S. J., & Sadler, J. Z. (2009). Ethical issues in perinatal mental health research. *Current Opinion in Psychiatry, 22*(6), 601–606. https://doi.org/10.1097/YCO.0b013e3283318e6f.

Brockington, I. (2017). Late onset postpartum psychoses. *Archives of Women's Mental Health, 20*(1), 87–92. https://doi.org/10.1007/s00737-016-0680-y.

Brockington, I., Butterworth, R., & Glangeaud-Freudenthal, N. (2017). An international position paper on mother-infant (perinatal) mental health, with guidelines for clinical practice. *Archives of Women's Mental Health, 20*(1), 113–120. https://doi.org/10.1007/s00737-016-0684-7.

Bromley, R. L., Weston, J., & Marson, A. G. (2017). Maternal use of antiepileptic agents during pregnancy and major congenital malformations in children. *JAMA - Journal of the American Medical Association, 318*(17), 1700–1701. https://doi.org/10.1001/jama.2017.14485.

Brown, Q. L., Sarvet, A. L., Shmulewitz, D., Martins, S. S., Wall, M. M., & Hasin, D. S. (2017). Trends in marijuana use among pregnant and nonpregnant reproductive-aged women, 2002–2014. *JAMA - Journal of the American Medical Association, 317*(2), 207–209. https://doi.org/10.1001/jama.2016.17383.

Campbell, E., Kennedy, F., Russell, A., Smithson, W. H., Parsons, L., Morrison, P. J., ... Morrow, J. (2014). Malformation risks of antiepileptic drug monotherapies in pregnancy: Updated results from the UK and Ireland epilepsy and pregnancy registers. *Journal of Neurology, Neurosurgery and Psychiatry, 85*(9), 1029–1034. https://doi.org/10.1136/jnnp-2013-306318.

Clark, C. T., & Wisner, K. L. (2018). Treatment of peripartum Bipolar Disorder. *Obstetrics and Gynecology Clinics of North America, 45*(3), 403–417. https://doi.org/10.1016/j.ogc.2018.05.002.

Cohen, L. S., Altshuler, L. L., Harlow, B. L., Nonacs, R., Newport, D. J., Viguera, A. C., ... Stowe, Z. N. (2006). Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. *JAMA, 295*(5), 499–507. https://doi.org/10.1001/jama.295.5.499.

Conner, S. N., Bedell, V., Lipsey, K., Macones, G. A., Cahill, A. G., & Tuuli, M. G. (2016). Maternal marijuana use and adverse neonatal outcomes: A systematic review and meta-analysis. *Obstetrics and Gynecology, 128*(4), 713–723. https://doi.org/10.1097/AOG.0000000000001649.

Cook, N., Ayers, S., & Horsch, A. (2018). Maternal posttraumatic stress disorder during the perinatal period and child outcomes: A systematic review. *Journal of Affective Disorders, 225*(June 2017), 18–31. https://doi.org/10.1016/j.jad.2017.07.045.

Davies, W. (2017). Understanding the pathophysiology of postpartum psychosis: Challenges and new approaches. *World Journal of Psychiatry, 7*(2), 77. https://doi.org/10.5498/wjp.v7.i2.77.

Desai, R. J., Rothman, K. J., Bateman, B. T., Hernandez-Diaz, S., & Huybrechts, K. F. (2017). A propensity-score-based fine stratification approach for confounding adjustment when exposure is infrequent. *Epidemiology, 28*(2), 249–257. https://doi.org/10.1097/EDE.0000000000000595.

Di Florio, A., & Meltzer-Brody, S. (2015). Is postpartum depression a distinct disorder? *Current Psychiatry Reports, 17*(10), 1–6. https://doi.org/10.1007/s11920-015-0617-6.

Ennis, Z. N., & Damkier, P. (2015). Pregnancy exposure to olanzapine, quetiapine, risperidone, aripiprazole and risk of congenital malformations. A systematic review. *Basic and Clinical Pharmacology and Toxicology, 116*(4), 315–320. https://doi.org/10.1111/bcpt.12372.

Evans, J., Heron, J., Francomb, H., Oke, S., & Golding, J. (2001). Cohort study of depressed mood during pregnancy and after childbirth. *BMJ (Clinical Research Ed.), 323*(7307), 257–260.

Falah-Hassani, K., Shiri, R., & Dennis, C. L. (2017). The prevalence of antenatal and postnatal co-morbid anxiety and depression: A meta-analysis. *Psychological Medicine, 47*(12), 2041–2053. https://doi.org/10.1017/S0033291717000617.

Field, T. (2008). Infants of depressed mothers. *Development and Psychopathology, 4*(01), 49. https://doi.org/10.1017/S0954579400005551.

Finer, L. B., & Zolna, M. R. (2011, November). Unintended pregnancy in the United States: Incidence and disparities, 2006. *Contraception*. https://doi.org/10.1016/j.contraception.2011.07.013.

Forray, A. (2016). Substance use during pregnancy. *F1000Research, 5*(May), 887. https://doi.org/10.12688/f1000research.7645.1.

Forray, A., & Foster, D. (2015). Substance use in the perinatal period. *Current Psychiatry Reports, 17*(11), https://doi.org/10.1007/s11920-015-0626-5.

Freeman, M. P. (2014). ADHD and pregnancy. *American Journal of Psychiatry, 171*(7), 723–728. https://doi.org/10.1176/appi.ajp.2013.13050680.

Freeman, M. P., Góez-Mogollón, L., McInerney, K. A., Davies, A. C., Church, T. R., Sosinsky, A. Z., ... Cohen, L. S. (2018). Obstetrical and neonatal outcomes after benzodiazepine exposure during pregnancy: Results from a prospective registry of women with psychiatric disorders. *General Hospital Psychiatry, 53*, 73–79. https://doi.org/10.1016/J.GENHOSPPSYCH.2018.05.010.

Fuloria, M., & Aschner, J. L. (2017). Persistent pulmonary hypertension of the newborn. *Seminars in Fetal and Neonatal Medicine, 22*(4), 220–226. https://doi.org/10.1016/j.siny.2017.03.004.

Galbally, M., Snellen, M., & Power, J. (2014). Antipsychotic drugs in pregnancy: A review of their maternal and fetal effects. *Therapeutic Advances in Drug Safety, 5*(2), 100–109. https://doi.org/10.1177/2042098614522682.

Gibson-Smith, D., Bot, M., Milaneschi, Y., Twisk, J. W., Visser, M., Brouwer, I.a., & Penninx, B. W. J. H. (2015). A systemized review of atypical antipsychotics in pregnant women: Balanding between risks of untreated illness and risks of drug-related adverse effects. *Journal of Clinical Psychiatry, 77*(September), 22–27. https://doi.org/10.4088/JCP.14m09658.

GlaxoSmithKline. (n.d.). Lamictal prescribing information. Retrieved from https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020241s037s038,020764s030s031lbl.pdf.

González, G., Moraes, M., Sosa, C., Umpierrez, E., Duarte, M., Cal, J., & Ghione, A. (2017). Depresión materna postnatal y su repercusión en el neurodesarrollo infantil: Estudio de cohorte. *Revista Chilena de Pediatria, 88*(3), 360–366. https://doi.org/10.4067/S0370-41062017000300008.

Goodman, J. H., & Tyer-Viola, L. (2010). Detection, treatment, and referral of perinatal depression and anxiety by obstetrical providers. *Journal of Women's Health, 19*(3), 477–490. https://doi.org/10.1089/jwh.2008.1352.

Graham, R. K., Tavella, G., & Parker, G. B. (2017). Is there consensus across international evidence-based guidelines for the psychotropic drug management of bipolar disorder during the perinatal period. *Journal of Affective Disorders, 228*, 216–221. https://doi.org/10.1016/j.jad.2017.12.022.

Grof, P., Robbins, W., Alda, M., Berghoefer, A., Vojtechovsky, M., Nilsson, A., & Robertson, C. (2000). Protective effect of pregnancy in women with lithium-responsive bipolar disorder. *Journal of Affective Disorders, 61*(1–2), 31–39. https://doi.org/10.1016/S0165-0327(99)00197-4.

Güler, Ö., Kaya, V., Gezginç, K., Kayhan, F., Çiçek, E., Sönmez, Ö., & Uğuz, F. (2015). Pregnancy-onset panic disorder: Incidence, comorbidity and associated factors. *Noropsikiyatri Arsivi, 52*(3), 216–220. https://doi.org/10.5152/npa.2015.7565.

Hatzopoulos, F. K., & Albrecht, L. M. (2010). Antidepressant use during breastfeeding. *Journal of Human Lactation, 12*(2), 139–141. https://doi.org/10.1177/089033449601200219.

Hernandez-Diaz, S., Smith, C. R., Shen, A., Mittendorf, R., Hauser, W. A., Yerby, M., & Holmes, L. B. (2012a). Comparative safety of antiepileptic drugs during pregnancy. *Neurology, 78*(21), 1692–1699. https://doi.org/10.1212/WNL.0b013e3182574f39.

Hernandez-Diaz, S., Smith, C. R., Shen, A., Mittendorf, R., Hauser, W. A., Yerby, M., & Holmes, L. B. (2012b). Comparative safety of antiepileptic drugs during pregnancy for the North American. *Neurology, 78*, 1692–1699. https://doi.org/10.1212/WNL.0b013e3182574f39.

Huybrechts, K. F., Bateman, B. T., Palmsten, K., Desai, R. J., Patorno, E., Gopalakrishnan, C., ... Hernandez-Diaz, S. (2015). Antidepressant use late in pregnancy and risk of persistent pulmonary hypertension of the newborn. *JAMA - Journal of the American Medical Association, 313*(21), 2142–2151. https://doi.org/10.1001/jama.2015.5605.

Huybrechts, K. F., Bröms, G., Christensen, L. B., Einarsdóttir, K., Engeland, A., Furu, K., ... Bateman, B. T. (2018). Association between methylphenidate and amphetamine use in pregnancy and risk of congenital malformations: A cohort study from the international pregnancy safety study consortium. *JAMA Psychiatry, 75*(2), 167–175. https://doi.org/10.1001/jamapsychiatry.2017.3644.

Huybrechts, K. F., Hernández-Díaz, S., Patorno, E., Desai, R. J., Mogun, H., Dejene, S. Z., ... Bateman, B. T. (2016). Antipsychotic use in pregnancy and the risk for congenital

malformations. *JAMA Psychiatry, 73*(9), 938–946. https://doi.org/10.1001/jamapsychiatry.2016.1520.
Huybrechts, K. F., Palmsten, K., Avorn, J., Cohen, L. S., Holmes, L. B., Franklin, J. M., ... Hernández-Díaz, S. (2014). Antidepressant use in pregnancy and the risk of cardiac defects. *New England Journal of Medicine, 370*(25), 2397–2407. https://doi.org/10.1056/NEJMoa1312828.
Infant Risk Center. Drug entry into human milk. (2016). Retrieved September 9, 2018, from https://www.infantrisk.com/content/drug-entry-human-milk (n.d.-a).
Infant Risk Center. Help the Infant Risk Center study drugs in human milk. (2016). Retrieved September 9, 2018, from https://www.infantrisk.com/research (n.d.-b).
Jiang, H.y., Xu, L.l., Li, Y.c., Deng, M., Peng, C.t., & Ruan, B. (2016). Antidepressant use during pregnancy and risk of postpartum hemorrhage: A systematic review and meta-analysis. *Journal of Psychiatric Research, 83*(2016), 160–167. https://doi.org/10.1016/j.jpsychires.2016.09.001.
Jones, I., Chandra, P. S., Dazzan, P., & Howard, L. M. (2014). Bipolar disorder, affective psychosis, and schizophrenia in pregnancy and the post-partum period. *The Lancet, 384*(9956), 1789–1799. https://doi.org/10.1016/S0140-6736(14)61278-2.
Jones, S. C., & Jones, I. (2017). Pharmacological management of bipolar disorder in pregnancy. *CNS Drugs, 31*(9), 737–745. https://doi.org/10.1007/s40263-017-0452-x.
Judd, F., Komiti, A., Sheehan, P., Newman, L., Castle, D., & Everall, I. (2014). Adverse obstetric and neonatal outcomes in women with severe mental illness: To what extent can they be prevented? *Schizophrenia Research, 157*(1–3), 305–309. https://doi.org/10.1016/j.schres.2014.05.030.
Juric, S., Newport, D. J., Ritchie, J. C., Galanti, M., & Stowe, Z. N. (2009). Zolpidem (Ambien®) in pregnancy: Placental passage and outcome. *Archives of Women's Mental Health, 12*(6), 441–446. https://doi.org/10.1007/s00737-009-0100-7.
Kamperman, A. M., Veldman-Hoek, M. J., Wesseloo, R., Robertson Blackmore, E., & Bergink, V. (2017). Phenotypical characteristics of postpartum psychosis: A clinical cohort study. *Bipolar Disorders, February*, 450–457. https://doi.org/10.1111/bdi.12523.
Kargas, G. A., Kargas, S. A., Bruyere, H. J., Gilbert, E., & Opitz, J. M. (1987). Perinatal mortality due to interaction of diphenhydramine and temazepam. *New England Journal of Medicine, 317*(4), 185–191.
Kendell, R. E., Wainwright, S., Hailey, A., & Shannon, B. (1976). The influence of childbirth on psychiatric morbidity. *Psychological Medicine, 6*(2), 297–302.
Khalifeh, H., Hunt, I. M., Appleby, L., & Howard, L. M. (2016). Suicide in perinatal and non-perinatal women in contact with psychiatric services: 15 year findings from a UK national inquiry. *The Lancet Psychiatry, 3*(3), 233–242. https://doi.org/10.1016/S2215-0366(16)00003-1.
Kieviet, N., Dolman, K. M., & Honig, A. (2013). The use of psychotropic medication during pregnancy: How about the newborn? *Neuropsychiatric Disease and Treatment, 9*, 1257–1266. https://doi.org/10.2147/NDT.S36394.
Männistö, T., Mendola, P., Kiely, M., O'Loughlin, J., Werder, E., Chen, Z., ... Grantz, K. L. (2016). Maternal psychiatric disorders and risk of preterm birth. *Annals of Epidemiology, 26*(1), 14–20. https://doi.org/10.1016/j.annepidem.2015.09.009.
Marcus, S. M., & Flynn, H. A. (2008). Depression, antidepressant medication, and functioning outcomes among pregnant women. *International Journal of Gynecology & Obstetrics, 100*(3), 248–251. https://doi.org/10.1016/j.ijgo.2007.09.016.
Marcus, S. M., Flynn, H. A., Blow, F. C., & Barry, K. L. (2003). Depressive symptoms among pregnant women screened in obstetrics settings. *Journal of Women's Health, 12*(4), 373–380. https://doi.org/10.1089/154099903765448880.
Mcallister-Williams, R. H., Baldwin, D. S., Cantwell, R., Easter, A., Gilvarry, E., Glover, V., ... Young, A. H. (2017). British Association for Psychopharmacology consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum. *Journal of Psychopharmacology, 31*(5), 519–552. https://doi.org/10.1177/0269881117699361.
McLafferty, L. P., Becker, M., Dresner, N., Meltzer-Brody, S., Gopalan, P., Glance, J., ... Worley, L. L. M. (2016). Guidelines for the management of pregnant women with substance use disorders. *Psychosomatics, 57*(2), 115–130. https://doi.org/10.1016/j.psym.2015.12.001.
McLafferty, L. P., Spada, M., & Gopalan, P. (2018). Pharmacologic treatment of sleep disorders in pregnancy. *Sleep Medicine Clinics, 13*(2), 243–250. https://doi.org/10.1016/j.jsmc.2018.02.004.
Metz, T. D., Allshouse, A. A., Hogue, C. J., Goldenberg, R. L., Dudley, D. J., Varner, M. W., ... Silver, R. M. (2017). Maternal marijuana use, adverse pregnancy outcomes, and neonatal morbidity. *American Journal of Obstetrics and Gynecology, 217*(4), 478.e1–478.e8. https://doi.org/10.1016/j.ajog.2017.05.050.
Metz, T. D., & Stickrath, E. H. (2015). Marijuana use in pregnancy and lactation: A review of the evidence. *American Journal of Obstetrics and Gynecology, 213*(6), 761–778. https://doi.org/10.1016/j.ajog.2015.05.025.
MGH Center for Women's Mental Health (2017a). Why are we still using valproic acid in women of childbearing age? Retrieved September 8, 2018, from https://womensmentalhealth.org/posts/why_valproic_acid_depakote_women_childbearing_age/.
MGH Center for Women's Mental Health (2017b). Why do many continue to recommend tapering SSRI antidepressants during the third trimester? Retrieved September 7, 2018, from https://womensmentalhealth.org/posts/many-continue-recommend-tapering-ssri-antidepressants-third-trimester/.
MGH Center for Women's Mental Health. Course of ADHD in pregnancy and the postpartum. (2009). Retrieved September 8, 2018, from https://womensmentalhealth.org/research/course-adhd-pregnancy-postpartum/ (n.d.-a).
MGH Center for Women's Mental Health. Psychiatric disorders during pregnancy. Retrieved September 8, 2018, from. (2009). https://womensmentalhealth.org/specialty-clinics/psychiatric-disorders-during-pregnancy/ (n.d.-b).
MGH Center for Women's Mental Health. Research program. (2009). Retrieved September 8, 2018, from https://womensmentalhealth.org/research/ (n.d.-c).
Miller, L. J. (2009). Ethical issues in perinatal mental health. *Psychiatric Clinics of North America, 32*(2), 259–270. https://doi.org/10.1016/j.psc.2009.02.002.
Moehler, E., Brunner, R., Wiebel, A., Reck, C., & Resch, F. (2006). Maternal depressive symptoms in the postnatal period are associated with long-term impairment of mother–child bonding. *Archives of Women's Mental Health, 9*(5), 273–278. https://doi.org/10.1007/s00737-006-0149-5.
Munk-Olsen, T., Liu, X., Viktorin, A., Brown, H. K., Di Florio, A., D'Onofrio, B. M., ... Bergink, V. (2018). Maternal and infant outcomes associated with lithium use in pregnancy: An international collaborative meta-analysis of six cohort studies. *The Lancet Psychiatry, 5*(8), 644–652. https://doi.org/10.1016/S2215-0366(18)30180-9.
Muzik, M., Marcus, S. M., Heringhausen, J. E., & Flynn, H. (2009). When depression complicates childbearing: Guidelines for screening and treatment during antenatal and postpartum obstetric care. *Obstetrics and Gynecology Clinics of North America, 36*(4), 771–788. https://doi.org/10.1016/j.ogc.2009.10.006.
National Collaborating Centre for Mental Health Royal College of Psychiatrists' Research and Training. (2014). *Antenatal and postnatal mental health: The NICE guideline on clinical management.* The British Psychological Society and The Royal College of Psychiatrists1–922. Retrieved from http://www.nice.org.uk/guidance/index.jsp?action=bypublichealth&PUBLICHEALTH=Mental+health#/search/?reload.
Norby, U., Forsberg, L., Wide, K., Sjo rs, G., Winbladh, B., & Ka llen, K. (2016). Neonatal morbidity after maternal use of antidepressant drugs during pregnancy. *Pediatrics, 138*(5), e20160181–e20160181. https://doi.org/10.1542/peds.2016-0181.
O'Hara, M. W. O., Wisner, K. L., & Asher, H. (2014). Perinatal mental illness: Definition, description, and aetiology. *Best Practice & Research Clinical Obstetrics & Gynaecology, 28*(1), 3–12. https://doi.org/10.1016/j.bpobgyn.2013.09.002.
Okun, M. L. (2016). Disturbed sleep and postpartum depression. *Current Psychiatry Reports, 18*(7), 1–7. https://doi.org/10.1007/s11920-016-0705-2.
Okun, M. L., Ebert, R., & Saini, B. (2015). A review of sleep-promoting medications used in pregnancy. *American Journal of Obstetrics and Gynecology, 212*(4), 428–441. https://doi.org/10.1016/j.ajog.2014.10.1106.
Ornoy, A. (2018). Pharmacological treatment of Attention Deficit Hyperactivity Disorder during pregnancy and lactation. *Pharmaceutical Research, 35*(3), https://doi.org/10.1007/s11095-017-2323-z.
Ornoy, A., Weinstein-Fudim, L., & Ergaz, Z. (2017). Antidepressants, antipsychotics, and mood stabilizers in pregnancy: What do we know and how should we treat pregnant women with depression. *Birth Defects Research, 109*(12), 933–956. https://doi.org/10.1002/bdr2.1079.
Orsolini, L., Valchera, A., Vecchiotti, R., Tomasetti, C., Iasevoli, F., Fornaro, M., ... Bellantuono, C. (2016). Suicide during perinatal period: Epidemiology, risk factors, and clinical correlates. *Frontiers in Psychiatry, 7*(AUG), 1–6. https://doi.org/10.3389/fpsyt.2016.00138.
Osborne, L. M., McEvoy, K., & Payne, J. L. (2017, April 29). Antidepressants in pregnancy: Balancing needs and risks in clinical practice. Retrieved from Psychiatric Timeshttps://www.psychiatrictimes.com/antidepressants-pregnancy-balancing-needs-and-risks-clinical-practice.
Pacchiarotti, I., León-Caballero, J., Murru, A., Verdolini, N., Furio, M. A., Pancheri, C., ... Vieta, E. (2016). Mood stabilizers and antipsychotics during breastfeeding: Focus on bipolar disorder. *European Neuropsychopharmacology, 26*(10), 1562–1578. https://doi.org/10.1016/j.euroneuro.2016.08.008.
Patorno, E., Huybrechts, K. F., Bateman, B. T., Cohen, J. M., Desai, R. J., Mogun, H., ... Hernandez-Diaz, S. (2017). Lithium use in pregnancy and the risk of cardiac malformations. *New England Journal of Medicine, 376*(23), 2245–2254. https://doi.org/10.1056/NEJMoa1612222.
Payne, J. L. (2016, February 19). Yes or no: Prescribing antidepressants to pregnant patients. *Psychiatric news*. Retrieved from https://psychnews.psychiatryonline.org/doi/full/10.1176/appi.pn.2016.PP2b6.
Payne, J. L. (2017). Psychopharmacology in pregnancy and breastfeeding. *Psychiatric Clinics of North America, 40*(2), 217–238. https://doi.org/10.1016/j.psc.2017.01.001.
Payne, J. L., & Meltzer-Brody, S. (2009). Antidepressant use during pregnancy: Current controversies and treatment strategies. *Clinical Obstetrics and Gynecology, 52*(3), 469–482. https://doi.org/10.1097/GRF.0b013e3181b52e20.
Pernia, S., & DeMaagd, G. (2016). The new pregnancy and lactation labeling rule. *P & T: A Peer-Reviewed Journal for Managed Care and Formulary Management Decision-Makers, 41*(11), 713–715.
Petersen, I., Collings, S. L., McCrea, R. L., Nazareth, I., Osborn, D. P., Cowen, P. J., & Sammon, C. J. (2017). Antiepileptic drugs prescribed in pregnancy and prevalence of major congenital malformations: Comparative prevalence studies. *Clinical Epidemiology, 9*, 95–103. https://doi.org/10.2147/CLEP.S118336.
Pies, R. (2007). WHIPLASHED: A mnemonic for recognizing bipolar depression. *Psychiatric Times, 24*.
Poels, E. M. P., Bijma, H. H., Galbally, M., & Bergink, V. (2018). Lithium during pregnancy and after delivery: A review. *International Journal of Bipolar Disorders, 6*(1), https://doi.org/10.1186/s40345-018-0135-7.
Poels, E. M. P., Schrijver, L., Kamperman, A. M., Hillegers, M. H. J., Hoogendijk, W. J. G., Kushner, S. A., & Roza, S. J. (2018). Long-term neurodevelopmental consequences of intrauterine exposure to lithium and antipsychotics: A systematic review and meta-analysis. *European Child and Adolescent Psychiatry, 27*(9), 1209–1230. https://doi.org/10.1007/s00787-018-1177-1.
Postpartum Support International. Frequently asked questions. (2014, September 1). Retrieved September 8, 2018, from http://www.postpartum.net/learn-more/frequently-asked-questions/ (n.d.-a).
Postpartum Support International. Pregnancy and postpartum mental health. (2014, September 1). Retrieved from http://www.postpartum.net/learn-more/pregnancy-postpartum-mental-health/ (n.d.-b).
Rabin, R. C. (2014, September 1). *Are antidepressants safe during pregnancy?* New York

Times.
Reuters (2017). Study finds slight autism risk link to antidepressants in pregnancy. Retrieved September 9, 2018, from https://www.reuters.com/article/us-health-autism-antidepressants-idUSKBN1A42NN.
Rundgren, S., Brus, O., Bave, U., Landen, M., Lundberg, J., Nordanskog, P., & Nordenskjold, A. (2018). Improvement of postpartum depression and psychosis after electroconvulsive therapy: A population-based study with a matched comparison group. *Journal of Affective Disorders, 235*, 258–264. https://doi.org/10.1016/j.jad.2018.04.043.
Rusner, M., Berg, M., & Begley, C. (2016). Bipolar disorder in pregnancy and childbirth: A systematic review of outcomes. *BMC Pregnancy and Childbirth, 16*(1), https://doi.org/10.1186/s12884-016-1127-1.
Salim, M., Sharma, V., & Anderson, K. K. (2018). Recurrence of bipolar disorder during pregnancy: A systematic review. *Archives of Women's Mental Health,* 475–479. https://doi.org/10.1007/s00737-018-0831-4.
Shanks, N., Greek, R., & Greek, J. (2009). Are animal models predictive for humans? *Philosophy, Ethics, and Humanities in Medicine, 4*(1), 1–20. https://doi.org/10.1186/1747-5341-4-2.
Sharma, V., Doobay, M., & Baczynski, C. (2017). Bipolar postpartum depression: An update and recommendations. *Journal of Affective Disorders, 219*(April 2017), 105–111. https://doi.org/10.1016/j.jad.2017.05.014.
Sharma, V., & Khan, M. (2010). Identification of bipolar disorder in women with postpartum depression. *Bipolar Disorders, 12*(3), 335–340. https://doi.org/10.1111/j.1399-5618.2010.00809.x.
Simkin, P., & Klaus, P. H. (2004). When survivors give birth: Understanding and healing the effects of early sexual abuse on childbearing women. Seattle, Wash: Classic Day.
Sit, D., Rothschild, A. J., & Wisner, K. L. (2006). A review of postpartum psychosis. *Journal of Women's Health (2002), 15*(4), 352–368. https://doi.org/10.1089/jwh.2006.15.352.
Siu, A. L., Bibbins-Domingo, K., Grossman, D. C., Baumann, L. C., Davidson, K. W., Ebell, M., ... Pignone, M. P. (2016). Screening for depression in adults. *JAMA, 315*(4), 380. https://doi.org/10.1001/jama.2015.18392.
Smith, C. A., Shewamene, Z., Galbally, M., Schmied, V., & Dahlen, H. (2019). The effect of complementary medicines and therapies on maternal anxiety and depression in pregnancy: A systematic review and meta-analysis. *Journal of Affective Disorders, 245*(November 2018), 428–439. https://doi.org/10.1016/j.jad.2018.11.054.
Spinelli, M. G. (2009). Postpartum psychosis: Detection of risk and management. *American Journal of Psychiatry, 166*(4), 405–408. https://doi.org/10.1176/appi.ajp.2008.08121899.
Stein, A., Pearson, R. M., Goodman, S. H., Rapa, E., Rahman, A., McCallum, M., ... Pariante, C. M. (2014). Effects of perinatal mental disorders on the fetus and child. *The Lancet, 384*(9956), 1800–1819. https://doi.org/10.1016/S0140-6736(14)61277-0.
Substance Abuse and Mental Health Services Administration (2018). *Clinical guidance for treating pregnant and parenting women with opioid use disorder and their infants* (HHS Public)Rockville, MD: Substance Abuse and Mental Health Services Administration.
Thorsness, K. R., Watson, C., & LaRusso, E. M. (2018). Perinatal anxiety: Approach to diagnosis and management in the obstetric setting. *American Journal of Obstetrics and Gynecology*. https://doi.org/10.1016/j.ajog.2018.05.017.
Thyen, A., Narang, P., Sarai, S., Tegin, G., & Lippmann, S. (2017). Electroconvulsive therapy during pregnancy. *The Primary Care Companion for CNS Disorders, 19*(4), https://doi.org/10.4088/PCC.17br02096.
Tinkelman, A., Hill, E. A., & Deligiannidis, K. M. (2017). Management of new onset psychosis in the postpartum period. *Journal of Clinical Psychiatry, 78*(9), 1423–1424. https://doi.org/10.4088/JCP.17ac11880.
Tjoa, C., Pare, E., & Kim, D. R. (2010). Unipolar depression during pregnancy: Nonpharmacologic treatment options. *Women's Health, 6*(4), 565–576. https://doi.org/10.2217/whe.10.27.
Tomson, T., Battino, D., Bonizzoni, E., Craig, J., Lindhout, D., Perucca, E., ... Zarifi-Oskoie, M. (2018). Comparative risk of major congenital malformations with eight different antiepileptic drugs: A prospective cohort study of the EURAP registry. *The Lancet Neurology, 17*(6), 530–538. https://doi.org/10.1016/S1474-4422(18)30107-8.
U.S. Department of Health and Human Servi (2011). Selective serotonin reuptake inhibitor (SSRI) antidepressant use during pregnancy and reports of a rare heart and lung condition in newborn babies. Retrieved February 16, 2019, from https://www.fda.gov/Drugs/DrugSafety/ucm283375.htm.
Uguz, F., & Ayhan, M. (2011). Epidemiology and clinical features of obsessive-compulsive disorder during pregnancy and postpartum period: A review. *Journal of Mood Disorders, 1*(4), 178. https://doi.org/10.5455/jmood.20111219111846.
Uguz, F., & Sharma, V. (2016). Mood stabilizers during breastfeeding: A systematic review of the recent literature. *Bipolar Disorders, 18*(4), 325–333. https://doi.org/10.1111/bdi.12398.
Uguz, F., Turgut, K., Aydin, A., & Ak, M. (2018). Low-dose mirtazapine in major depression developed after hyperemesis gravidarum: A case series. American Journal of Therapeutics, 0, 1–2.
Umylny, P., German, M., & Lantiere, A. (2017). Treating postpartum mood and anxiety disorders in primary care pediatrics. *Current Problems in Pediatric and Adolescent Health Care, 47*(10), 254–266. https://doi.org/10.1016/j.cppeds.2017.08.003.
United States National Library of Medicine (2006). Aripiprazole. *Drugs and lactation database*. Bethesda (MD). Retrieved from https://toxnet.nlm.nih.gov/cgi-bin/sis/search2.
US Department of Health and Human Services. (n.d.). FDA pregnancy categories. Retrieved September 8, 2018, from https://chemm.nlm.nih.gov/pregnancycategories.htm.
US Food and Drug Administration (2014). Pregnancy and lactation labeling final rule. Retrieved September 8, 2018, from https://www.fda.gov/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/actsrulesregulations/ucm445102.htm.
Veroniki, A. A., Rios, P., Cogo, E., Straus, S. E., Finkelstein, Y., Kealey, R., ... Tricco, A. C. (2017). Comparative safety of antiepileptic drugs for neurological development in children exposed during pregnancy and breast feeding: A systematic review and network meta-analysis. *BMJ Open, 7*(7), 1–11. https://doi.org/10.1136/bmjopen-2017-017248.
Vesga-lo, O., Blanco, C., Keyes, K., Olfson, M., Grant, B. F., & Hasin, D. S. (2008). Psychiatric disorders in pregnant and postpartum women in the United States. *Archives of General Psychiatry, 65*(7), 805–815. https://doi.org/10.1001/archpsyc.65.7.805.
Vigod, S. N., Kurdyak, P. A., Dennis, C. L., Gruneir, A., Newman, A., Seeman, M. V., ... Ray, J. G. (2014). Maternal and newborn outcomes among women with schizophrenia: A retrospective population-based cohort study. *BJOG: An International Journal of Obstetrics and Gynaecology, 121*(5), 566–574. https://doi.org/10.1111/1471-0528.12567.
Viguera, A. C., Whitfield, T., Baldessarini, R., Newport, D., Stowe, Z. N., Reminick, A. M., ... Cohen, L. S. (2007). Risk of recurrence in women with bipolar disorder during pregnancy: Prospective study of mood stabilizer discontinuation. *American Journal of PsychiatryViguera, 164*(12), 1817–1923. https://doi.org/10.1176/appi.ajp.2007.06101639.
Vitale, S. G., Laganà, A. S., Muscatello, M. R. A., La Rosa, V. L., Currò, V., Pandolfo, G., ... Bruno, A. (2016). Psychopharmacotherapy in pregnancy and breastfeeding. *Obstetrical and Gynecological Survey, 71*(12), 721–733. https://doi.org/10.1097/OGX.0000000000000369.
Vythilingum, B. (2009). Anxiety disorders in pregnancy and the postnatal period. *Continuing Medical Education, 27*(10), 450–452. Retrieved from https://www.ajol.info/index.php/cme/article/view/50326.
Wan, M. W., & Green, J. (2009). The impact of maternal psychopathology on child-mother attachment. *Archives of Women's Mental Health, 12*(3), 123–134. https://doi.org/10.1007/s00737-009-0066-5.
Wang, J., Johnson, T., Sahin, L., Tassinari, M. S., Anderson, P. O., Baker, T. E., ... Yao, L. P. (2017). Evaluation of the safety of drugs and biological products used during lactation: Workshop summary. *Clinical Pharmacology and Therapeutics, 101*(6), 736–744. https://doi.org/10.1002/cpt.676.
Warburton, W., Hertzman, C., & Oberlander, T. F. (2010). A register study of the impact of stopping third trimester selective serotonin reuptake inhibitor exposure on neonatal health. *Acta Psychiatrica Scandinavica, 121*(6), 471–479. https://doi.org/10.1111/j.1600-0447.2009.01490.x.
Wesseloo, R., Wierdsma, A. I., Van Kamp, I. L., Munk-Olsen, T., Hoogendijk, W. J. G., Kushner, S. A., & Bergink, V. (2017). Lithium dosing strategies during pregnancy and the postpartum period. *British Journal of Psychiatry, 211*(1), 31–36. https://doi.org/10.1192/bjp.bp.116.192799.
Whitworth, A. B. (2017). Psychopharmacological treatment of schizophrenia during pregnancy and lactation. *Current Opinion in Psychiatry, 30*(3), 184–190. https://doi.org/10.1097/YCO.0000000000000329.
Wikner, B. N., & Källén, B. (2011). Are hypnotic benzodiazepine receptor agonists teratogenic in humans? *Journal of Clinical Psychopharmacology, 31*(3), 356–359. https://doi.org/10.1097/JCP.0b013e3182197055.
Yonkers, K. A., & Ross, L. E. (2011). Management of mood disorders in pregnant and postpartum women. *117*(4), 961–977. https://doi.org/10.1097/AOG.0b013e31821187a7.