

Optimizing the treatment of mood disorders in the perinatal period

Samantha Meltzer-Brody, MD, MPH; Ian Jones, MRCPsych, PhD



The perinatal period is a time of high risk for women with unipolar and bipolar mood disorders. We discuss treatment considerations for perinatal mood disorders, including unipolar and bipolar depression as well as postpartum psychosis. We further explore the unique issues faced by women and their families across the full trajectory of the perinatal period from preconception planning through pregnancy and following childbirth. Treatment of perinatal mood disorders requires a collaborative care approach between obstetrics practitioners and mental health providers, to ensure that a thoughtful risk:benefit analysis is conducted. It is vital to consider the risks of the underlying illness versus risks of medication exposure during pregnancy or lactation. When considering medication treatment, attention must be paid to prior medication trials that were most efficacious and best tolerated. Lastly, it is important to assess the impact of individual psychosocial stressors and lifestyle factors on treatment response.

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Dialogues Clin Neurosci. 2015;17:207-218.

Keywords: *perinatal mood disorder; postpartum depression; postpartum psychosis; bipolar disorder; treatment; pregnancy*

Introduction

Perinatal mood disorders (PMD) are the most common complication of childbirth and have significant repercussions, in terms of morbidity and mortality, on the mother, infant, and family.¹⁻⁹ Postpartum depression has a prevalence of 10% to 15% and is the most frequent type of PMD.^{1,7} Postpartum psychosis is a rare but severe form of PMD that can result in tragic consequences, including suicide and infanticide,^{10,11} and has been closely associated with bipolar disorder (BPD).¹² PMD-related suicide accounts for ~20% of all postpartum deaths, making PMD a leading cause of maternal perinatal mortality.^{6,13}

The effects of untreated PMD during pregnancy include delayed prenatal growth, higher rates of prematurity, and low birth weight.² Moreover, antenatal depression is one of the greatest risk factors for postpartum depression, and therefore psychiatric illness during pregnancy must be adequately treated to prevent significant postpartum adverse outcomes. PMD is also associated with reduced maternal sensitivity,¹⁴ which

Author affiliations: UNC Center for Women's Mood Disorder, Department of Psychiatry, University of North Carolina, Chapel Hill, North Carolina, USA (Samantha Meltzer-Brody); National Centre for Mental Health, MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Cardiff, UK (Ian Jones)

Address for correspondence: Samantha Meltzer-Brody, MD, MPH Campus Box #7160, Department of Psychiatry, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA (e-mail: samantha_meltzer-brody@med.unc.edu)

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can adversely affect emotional regulation and attachment.^{15,16}

Women with histories of both unipolar and bipolar mood disorders are at increased risk for exacerbation or recurrence during the vulnerable perinatal period. Therefore, in women with histories of affective illness, careful planning and monitoring by a skilled perinatal mental health specialist in collaboration with the obstetrics team should begin prior to pregnancy (preconception) and continue through the pregnancy and postpartum period. In addition, for many women, the perinatal period serves as the trigger for first onset of psychiatric illness. There are many reported risk factors for perinatal psychiatric illness, but previous histories of PMD or prior episodes of non-perinatal major depression or BPD appear to confer the greatest risks.^{4,17-19} In addition, parity status, marital conflict, perceived lack of partner support, stressful life events, unplanned pregnancy, and adverse pregnancy/birth outcomes have also been reported.²

In this paper, we will discuss treatment considerations of perinatal mood disorders, including unipolar and bipolar depression, as well as postpartum psychosis. We will explore the unique issues faced by women and their families across the full trajectory of the perinatal period from the time of preconception planning, through pregnancy, and following childbirth (Figure 1).

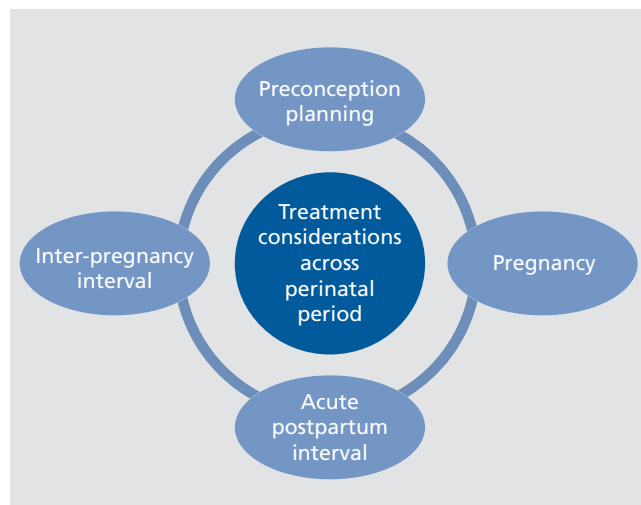


Figure 1. Conceptual model of treatment considerations across the perinatal period.

Unipolar major depression

Epidemiology, definition of the disorder, and clinical characteristics

Major depression occurring in the perinatal period is often described as antenatal depression if onset is during pregnancy, or postpartum depression if onset occurs following childbirth. However, there is some debate in the field about the diagnostic criteria based on timing of onset of PMDs. Consequently, this has led to recent changes in diagnostic criteria of postpartum depression by the *Diagnostic and Statistical Manual of Mental Disorders (DSM)-5*, resulting in an expanded definition that includes onset of symptoms during pregnancy as well as postpartum and a consequent change in terminology to “peripartum” onset.²⁰ In contrast, in the *International Classification of Diseases (ICD)-10*, postpartum onset is considered to be within 6 weeks after childbirth with no specific recognition of episodes in pregnancy.²¹

The clinical presentation of perinatal depression is often characterized by mood and anxiety symptoms that cause significant suffering to the woman and her family.²²⁻²⁴ Women with perinatal depression commonly report low mood, sadness, irritability, impaired concentration, and feeling overwhelmed.²⁵ However, anxiety or agitation is often a distinctive feature of perinatal depression and can manifest as ruminating and obsessional thoughts, often about the pregnancy or the infant.^{23,26} Importantly, most women with perinatal mood symptoms report feelings of guilt about not being able to enjoy the baby.^{27,28}

Treatment of unipolar depression in the perinatal period

Preconception

For women with a history of a unipolar depressive disorder, the primary goal of the preconception period is to achieve stability in mood and review the current treatment plan to assess safety during pregnancy. For some women, it may make sense to try to discontinue a psychotropic medication. For others, this would be a very unsafe choice and put the woman’s mental health at risk. Thoughtful and careful consideration of the risk:benefit ratio is warranted, including assessment of frequency and severity of previous unipolar episodes,

prior response to treatment, past attempts to discontinue medication treatment, and risk of exposure to psychotropic medications during pregnancy. In high-risk women, a prudent approach to the preconception period involves assembling a team of specialized perinatal providers including obstetricians, psychiatrists, psychologists, and others to support the woman through pregnancy and the postpartum period and assist in judicious decision making that will lead to the best outcomes for both mother and infant. We provide two case reports (*Box 1* and *Box 2*) to illustrate the decision-making process.

Pregnancy

For pregnant women with mild-to-moderate depressive illness, psychological and/or behavioral therapies are indicated as first-line treatment options.^{28,29} There exists a robust evidence base on the efficacy of a wide range

Ms T is a 32-year-old married woman with a history of BPD type I, currently stable on lithium, who presents for a preconception evaluation and states she is hoping to conceive in the next 6 months and wants to discuss medication management during the perinatal period. Ms T reports she has been stable on lithium for many years. Her first episode of mania was in her early 20s, at which time she experienced symptoms of elevated mood, grandiosity, and psychosis. She was hospitalized at that time and lithium therapy was initiated with good results. A few years later she attempted to discontinue lithium, and suffered a relapse of a manic episode with psychosis. She is fearful of discontinuing lithium during her pregnancy but is concerned about the risk of lithium exposure to the fetus. Her husband, who accompanies his wife to the appointment, is also worried about the risks to his wife and the fetus.

A careful discussion of the risks and benefits of psychotropic exposure during pregnancy versus the risk of discontinuation is discussed with the patient and her husband. Given the patient's history of suffering a relapse of mania soon after her lithium was discontinued in the past, the patient and her husband elect to continue lithium therapy during the pregnancy.

Box 1. Case report #1.

of psychological interventions including, but not limited to, interpersonal psychotherapy (IPT),³⁰⁻³³ partner-assisted IPT,³³ cognitive behavioral therapy,^{34,35} and group psychoeducation.^{36,37} It is important to tailor the type of therapeutic modality to the primary presenting symptoms of the patient. For example, women who report significant psychosocial issues may be best served by seeking IPT, which is a time-limited, problem-focused therapy that interprets depression as medical illness occurring within a social context.³⁸ In contrast, a woman who has experienced a prior negative or traumatic birth experience as a trigger for onset of symptoms will likely experience the most benefit from a psychotherapy that integrates trauma recovery work.

For more severe depressive and anxiety symptoms, pharmacotherapy is considered an appropriate and efficacious treatment option.^{29,39} Antidepressant medication (ADM) has quickly become a common treatment for perinatal depression. The current practice in many settings is that ADM is the most effective way to treat perinatal depression, and, while perhaps not as acceptable due to fetal exposure, it may be more accessible to patients than lengthy psychosocial interventions.⁴⁰ In the US, prenatal ADM use in the last 15 years has more than doubled, with approximately 13% of pregnancies in the year 2003 exposed to ADM, compared with 6%

Ms D is a 29-year-old woman with a history of anxiety and depression who presents for evaluation at 6 weeks of pregnancy. She reports she has taken an antidepressant (SSRI) at a low dose for the past 5 years with good results. She has not tried to discontinue the medication. She reports that at the time of initiation with the antidepressant, she had multiple significant stressors in her life and had ruminating thoughts, low mood, anhedonia, and insomnia. She denies ever having suicidal thoughts. Ms D now reports she is feeling well and has good psychosocial support. She is concerned about antidepressant exposure during pregnancy and states that worrying about taking the antidepressant is causing her significant anxiety. Her partner is pushing the patient to discontinue the antidepressant.

After a careful discussion of risks and benefits, Ms D decides to gradually taper off her antidepressant with careful monitoring during the pregnancy.

Box 2. Case report #2.

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in 1999.⁴¹ A new epidemiological report of ADM use in US Medicaid-eligible women (2000-2007) reported that nearly one in twelve women used an ADM during pregnancy. In Europe, the rate of prenatal ADM use has also increased, but at a lower rate compared with the US. A Danish study documents that the rate of ADM exposure increased from 0.2% in 1997 to 3.2% in 2010.⁴²

Despite the increased use of ADM in pregnancy, the literature on overall safety of ADM exposure in pregnancy based on observational studies, drug registry analyses, and case series reports is conflicting. This is largely due to the challenge of controlling for potential confounders including the underlying pathophysiology of the mood disorder and/or lifestyle factors (ie, diet, obesity, and substance use) that are more prevalent in women with mood disorders.⁴³ Accordingly, ongoing concerns about fetal drug exposure are constantly being raised, and this has been an intense area of study resulting in many published reports and papers over the past decade.⁴⁴⁻⁴⁶ The focus of this line of inquiry is on the potential associations/interactions between ADM, depression, and adverse fetal outcomes (preterm birth, primary persistent pulmonary hypertension of the newborn, risk of autism, ADHD, and cardiac effects) as well as the lack of information regarding comparative treatment efficacy. The overall result is that women and their clinicians are forced to make difficult decisions regarding treatment in the face of inconsistent literature. These controversies can discourage women from seeking antidepressant treatment, even though declining treatment may pose significant risks to the fetus and their own mental health.⁴⁷⁻⁵⁰ Moreover, many women will receive inadequate doses of ADM during pregnancy because of fear that adverse events may be dose-related.^{51,52} This practice results in the potential double exposure to both the ADM and the ongoing depressed mood.

Recently there have been a number of large systematic reviews and meta-analyses demonstrating the absolute risks associated with antidepressant exposure during pregnancy to be small, although certainly present.^{48,52,53} There is evidence for the efficacy of both newer antidepressants (selective serotonin reuptake inhibitors—SSRIs) and older tricyclic antidepressants in the treatment of perinatal depression and anxiety.^{54,55} The benzodiazepines are also commonly used for treatment of anxiety during pregnancy and lactation and are now

generally considered safe in the perinatal period if indicated.⁵⁶⁻⁶⁰ This is in contrast to the early case-control studies that reported that maternal benzodiazepine exposure increased the risk of fetal cleft lip and cleft palate, primarily with diazepam exposure.⁶¹ Multiple subsequent studies and meta-analyses have not found an association, but some concern remains and judicious use is advised.⁵⁶ In sum, the decision to treat with an antidepressant medication during pregnancy may be a difficult choice for the mother, her partner, and the physician. The literature remains conflicted, and ultimately, treatment decisions regarding how best to treat depression during pregnancy must be made on an individual basis, with thoughtful evaluation of decision risks to mother and infant.⁶²

Finally, it is important to state that the stigma associated with mental illness becomes highly exacerbated during the perinatal period. Consequently, pregnant women may be faced with significant stigma and experience shame if they decide to continue taking their antidepressant or other psychotropic medication during pregnancy in order to maintain their own mental health. This is a situation that they would likely not encounter if they were seeking treatment for a different medical illness, such as diabetes or hypertension.⁵¹

Because of the controversies surrounding antidepressant use during pregnancy, there is a need for other evidence-based treatment modalities for perinatal depression and anxiety. Examples include hormonal therapy,⁶³ such as the use of the estrogen patch in the prevention and treatment of PMD, bright-light therapy in antenatal depression,⁶⁴⁻⁶⁶ and the administration of repetitive transcranial magnetic stimulation (rTMS) during pregnancy^{67,68} and the postpartum period.^{69,70} Although these modalities are potentially interesting treatment options for the perinatal period, the evidence base is currently limited, and further work is needed to build upon initial findings.

The postpartum period

The postpartum period is one of the times of highest risk for onset of a depressive episode.⁷¹ While some women experience onset of mood symptoms during pregnancy (often in the third trimester), others will notice an acute worsening of symptoms in the first weeks postpartum. Symptoms that persist and are severe enough to impair functioning require evaluation and treatment.

The treatment modalities discussed earlier (antidepressant medications and psychotherapies) all demonstrate efficacy in the postpartum period. However, there are three additional relevant issues that are unique to the postpartum time interval: the first is lactation, the second is preservation of sleep, and the third is the impact of postpartum depression on fathers.

Lactation

Approximately 77% of mothers in the United States and over 80% of women in the UK initiate breastfeeding.^{72,73} Therefore, given that most women will breastfeed, a careful assessment of psychotropic use during lactation is an important discussion to have with the mother who is being treated for a mood disorder.⁷⁴ The SSRIs are generally well tolerated during lactation, but two agents in this class may be less desirable because of breast milk accumulation: (i) fluoxetine, because it has a long half-life⁷⁵; and (ii) citalopram, because of potentially high breast milk concentration.⁷⁶ In contrast, sertraline has a very favorable profile during lactation, with very little to no transmission at doses less than 100 mg.^{74,77}

Information about the safety of medications during lactation can be easily accessed by both clinicians and patients via a number of reliable resources. In general, resources maintained by academic centers or governmental agencies provide evidence-based data that is most valid. For example, LactMed®, a publicly funded database by the US National Library of Medicine, is an outstanding online resource that reviews and summarizes safety information about drugs and other chemicals to which breastfeeding mothers may be exposed.⁷⁸ It includes information on the levels of these medications or other substances in breast milk and infant blood and the potential adverse effects to the nursing infant. All data are extracted from the scientific literature, are fully referenced, and undergo a peer review process. Other excellent resources include The Breastfeeding/Human Lactation Center at the University of Rochester in Rochester, New York,⁷⁹ The Motherisk Program in Ontario, Canada⁸⁰ and The Breastfeeding Network in the United Kingdom.⁸¹

Finally, women with postpartum depression may be more likely to experience lactation difficulties.⁸² This can be a source of intense anxiety and distress to the mother and requires thoughtful guidance and modifica-

tion of routine breastfeeding recommendations to ensure best outcomes. The literature supports the relation between postpartum depression and lactation difficulties and/or failure.⁸² Postpartum depression and anxiety have been associated with reduced breastfeeding duration, and neuroendocrine mechanisms may underlie this association.⁸³ Additionally, reduced maternal sensitivity in the setting of depressive symptoms may also contribute to breastfeeding difficulties.⁸⁴

Sleep preservation

Disrupted sleep is a ubiquitous phenomenon for women in the acute postpartum period. The newborn requires frequent feedings and attention, irrespective of time of day or night. This results in most mothers feeling exhausted in the early postpartum period.⁸⁵ Women with histories of a mood disorder may be particularly vulnerable to the effects of sleep deprivation and consequently, poor postpartum sleep may serve as not only a marker of impending depression but also as a contributing cause.⁸⁶ Reports of disrupted and poor sleep during the third trimester of pregnancy are related to depressive symptoms in the postnatal period.⁸⁷ Additionally, quality of sleep in late pregnancy may also predict the timing and increase the vulnerability for recurrence of postpartum depression in women with a known history of the disorder.⁸⁸

Therefore, women with histories of perinatal mood disorders or those with new-onset postpartum depression must closely monitor their mood and attempt to preserve blocks of sleep.^{89,90} This requires the support and cooperation of the father, partner, and/or family to take shifts with infant feeding to ensure that the mother has adequate blocks of sleep. The mother must also be willing to accept that sleep preservation is a critical part of the treatment plan. Clinicians treating women with postpartum depressive symptoms should monitor subjective sleep quality in the postpartum period in addition to directly assessing mood symptoms.

Paternal/partner depression in the postpartum period

Social support, and specifically partner support, has been observed to be a moderator of depressive symptoms during pregnancy and the postpartum.⁹¹ Investigations of postpartum paternal depression report a prevalence rate of approximately 10% during the first

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year postpartum, compared with the period prevalence (12 months) rate of 3.8% reported in the general population of men.^{92,93} Although much less research has been conducted regarding the infant/child consequences of paternal depression, a growing body of evidence is suggesting that infants of depressed fathers demonstrate higher levels of distress and greater utilization of community health care resources, and that detrimental behavioral and emotional effects may persist into early childhood.⁹⁴ Therefore, it is important to engage the father in the treatment process and to inquire about paternal mood and functioning in the context of assessment and treatment of maternal postpartum psychiatric illness.

Bipolar disorder and postpartum psychosis

Epidemiology, definition of the disorder, and clinical characteristics

For any woman the transition to parenthood is a potentially difficult time. For women with BPD becoming a mother has a number of additional issues that women, their partners and the clinicians looking after them need to consider.⁹⁵ Women with BPD may experience episodes of mood disorder at any time in the perinatal period, and there is no evidence to suggest that the risk in pregnancy is any lower than at other times.⁹⁶ However, the evidence strongly suggests that the postpartum period—particularly the first few postpartum weeks—are a time of particularly high risk for bipolar women.⁹⁷

Although bipolar women may experience episodes of both high and low mood at all levels of severity across the whole perinatal period, it is the new onset of severe episodes in the immediate postpartum for which there is a dramatically increased risk. These later episodes, traditionally labelled as “postpartum” or “puerperal” psychosis (PP), are perhaps of greatest concern when managing women with BPD through pregnancy. PP most commonly takes the form of mania, severe depression, or a mixed episode with features of both high and low mood.⁹⁸ In addition to the mood component, features of psychosis such as delusions and hallucinations are common, and women may also demonstrate a marked confusion or perplexity.⁹⁸ The majority of episodes of PP have their onset within 2 weeks of delivery, with one retrospective study finding over 50% of symptom onsets occurring on postpartum days 1 to 3.⁹⁹

These episodes are characterized by sudden onset with a rapid deterioration, and the clinical picture is often constantly changing, with wide fluctuations in the intensity of symptoms.^{98,99}

Clinical and population registry studies are consistent in finding that bipolar women are at very high risk (at least 1 in 5, 20%) of suffering a severe recurrence following delivery.^{19,97,100} If episodes of nonpsychotic major depression are also included, women with BPD are at an even higher risk (approaching 1 in 2, 50%) of experiencing an episode of mood disorder in the postpartum period.¹⁹ It is worth noting, however, that the data indicating a very high risk of PP in bipolar women is based on women with the more severe, BP I form of the illness. There is much less data for women with BP II (or other forms of illness on the bipolar spectrum) and despite evidence suggesting that perinatal episodes are common in women with BP II, the risk of PP is considerably lower.¹⁹ It is clear, however, that women who have experienced a previous PP are at very high risk following subsequent pregnancies, with greater than 1 in 2 (50%) of deliveries affected.¹⁰¹ Studies have also suggested that for women with BPD, a family history of PP in first-degree relatives gives a similarly high risk in the postpartum period.^{102,103}

In considering the management of women with BPD in the perinatal period we will, as for unipolar disorder above, think about issues arising preconception, in pregnancy, and in the postpartum.

Treatment of bipolar disorder in the perinatal period

Preconception

Pregnancy must be a consideration in the management of childbearing-aged women with BPD at all times, not just when they present as pregnant or wish to become pregnant. For these reasons, international guidance recommends that certain medications such as valproate are best avoided where possible in *all* women with BPD in their reproductive years, and that issues around family planning and contraception are an important area of management.¹⁰⁴⁻¹⁰⁶ In addition to these more general considerations, it is important that specific preconception advice is available to women at the point they are considering starting or extending their families. The issues that need to be covered are likely to depend on each woman's individual history, but the very high

risk of a severe postpartum episode will be an important consideration. Discussions around medication will clearly feature prominently, but other pertinent issues can be addressed, such as smoking and nutrition.¹⁰⁷

The risks and benefits of medication will need to be considered, and the options set out for each individual woman. These will include continuing the current regime, stopping some or all medication, or switching to other medication if there are options with greater evidence of safety in pregnancy. In making these difficult decisions it is important to recognize that there are often no right and wrong answers, and that it is not simply a case of opting for the medication with the greatest evidence of safety in pregnancy. Rather, the individual woman's history of response to various medications and the consequences if they have previously been stopped should be a key factor in the decisions made. While it is clear that women with a history of BPD or a previous PP are at high risk of relapse in the postpartum, it is unclear whether starting prophylaxis following delivery is sufficient, or whether medication should also be taken during pregnancy. One study has suggested that the answer to this question may be different depending on whether previous episodes are limited to the postpartum or also have occurred independent of pregnancies.¹⁰⁸ Women with bipolar episodes not related to the perinatal period were at high risk in pregnancy and the postpartum, whereas in those with a history of postpartum episodes only, the risk was limited to after childbirth.

Pregnancy

Although there are few studies that have addressed the efficacy of medication in pregnancy, perhaps reflecting the ethical and practical problems of research at this time, there is direct evidence on the impact of treatment *discontinuation* on women with BPD. One study reported a doubling of risk of relapse and shorter time to relapse in women with BPD who discontinued prophylactic mood stabilisers in pregnancy, even after adjusting for confounders such as illness severity.⁹⁶ This emphasizes the potential negative impact from stopping or changing medication in those women who are stable on their current regime and highlights the need for these risks to weigh heavily in the individual risk benefit calculation.

Despite the postpartum period being a period of particularly high risk, women with BPD, particularly

those who have stopped or changed medication, may become ill during pregnancy and should be monitored closely throughout this time. Antenatal services should identify women with histories that put them at high risk, and even if currently well there is a case for them to be under the care of mental health services through pregnancy and the postpartum. If a detailed care plan has not been produced preconception, then it should be developed in pregnancy and address not only issues of medication but other relevant areas such as maintaining sleep, decreasing general levels of stress, and thinking about whether providing help with parenting may be appropriate. Other areas to address may be weight management, smoking, and domestic violence.⁹⁵

Medication is likely to be a key consideration, however, and an individualized risk:benefit analysis that lays out the options available to each woman is needed. Important areas to address include the likelihood of relapse in pregnancy and postpartum based on the woman's particular history, influenced by factors such as severity and recency of episodes. It is vital that each woman's history of response to current and past medication is obtained, and this is factored into the decisions made. In women presenting with an unplanned pregnancy it is important to appreciate that some exposure of the fetus will have already occurred and that abrupt discontinuation may not be the best option, as a relapse in pregnancy can have devastating consequences. We summarize the recommendations for treatment considerations in *Table 1*.

It is not possible in this paper to give a detailed review of the reproductive safety data for all potential medications that women with BPD may be taking. The data regarding the use of antidepressants, which are still often used in bipolar patients, has been discussed above. We will here make some general observations about the other main categories of medication used in these patients.

A number of antiepileptic medications are used as mood stabilizers, but we have little data on reproductive safety from their use in this context. There is no reason to believe, however, that the teratogenicity and adverse long-term cognitive outcomes associated with valproate use will not also apply to its use in BPD.^{104,109,110}

The atypical antipsychotics are increasingly being used in bipolar patients, and despite even less data than for antiepileptics, a systematic review¹¹¹ and the largest cohort study to date (n>750 exposures)¹¹² do not sug-

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gest that antipsychotics are major teratogens. While the traditional antipsychotics are older agents with more data available, they are less effective for mood stabilization in BPD and often have less favorable side-effect profiles.¹¹³

A medication which has been used for many decades, but for which we still have surprisingly little reproductive safety data, is lithium. Initial data from the lithium baby registry suggested a particular risk of Ebstein's anomaly, but this was subject to the biases of retrospective reporting.¹¹⁴ A recent systematic review concluded that the evidence pointing to lithium as a teratogen is weak, but the confidence intervals are wide and the upper confidence limit is consistent with a clinically significant increase in risk of congenital malformations.¹¹⁵ It therefore remains difficult to advise women on the risk of continuing this medication, which has been in use for over half a century. If lithium is continued in pregnancy, levels need to be checked more frequently and stopped at the onset of labor, being reinstated following delivery when plasma levels, and electrolyte balance, can be checked. This is critical given that lithium is primarily cleared by the kidneys and excreted in urine. Therefore, the tremendous fluctuations in fluid status that occur between onset of labor and the acute post-

partum period make it important to carefully monitor lithium levels at the time of childbirth.¹¹⁶

The postpartum period

Where possible, as discussed above, women with BPD should enter the postpartum period with a clear management plan to take them through this period of very high risk. This ideal may often not be the case, however, and, in addition, around half of postpartum psychosis episodes are the first manifestation of severe psychiatric disorder. For women who have stopped medication because of the pregnancy, consideration can be given to restarting the pre-pregnancy medication regime. Although there has not been extensive research in this area, studies provide some support for postpartum lithium prophylaxis for those women at high risk based on a previous history of BPD or postpartum psychosis.¹¹⁷⁻¹¹⁹ There are significant issues with using lithium at this time due to the fluid shifts at the time of childbirth and concerns about exposure during lactation, and therefore atypical antipsychotics are often used but without a solid evidence base for this specific indication.¹²⁰

Inpatient treatment is usually required for women presenting with postpartum psychosis or any severe

	Preconception	Pregnancy	Postpartum
Unipolar depression	Achieve stability in mood prior to conception and review the current treatment plan to assess safety during pregnancy.	There are evidence-based psychotherapies that may be a reasonable first line option. For more severe depressive and anxiety symptoms, or based on prior history of discontinuation attempts, pharmacotherapy is considered an appropriate and efficacious treatment option.	The postpartum period is one of the highest risk times for onset of a depressive episode. Close follow-up and regular monitoring is indicated. Treatment is important and considerations of medication exposure during lactation, impact of sleep deprivation and partner support should all be considered.
Bipolar disorder	Review risks and benefits and consider the options: <ul style="list-style-type: none"> • Continue the current regime • Stop some or all medications • Switch to another medication if there are options with greater evidence of safety in pregnancy. 	There is direct evidence of a potential negative impact from stopping or changing medication in bipolar women who are stable on their current regime. This highlights the need for these risks to weigh heavily in the individual risk:benefit calculation.	Women with bipolar disorder should enter the postpartum period with a clear management plan to take them through this period of very high risk. Approximately 50% of postpartum psychosis episodes are the first manifestation of severe psychiatric disorder. There is evidence for lithium prophylaxis in high risk women. ECT may also be an option to consider in bipolar women with severe postpartum episodes particularly if there is significant suicidal risk.

Table I. Important treatment considerations across the trajectory of the perinatal period in women with unipolar depression and bipolar disorder.

postpartum episode in bipolar women, as deterioration may be rapid and the illness may soon become very severe. Medication is the mainstay of management in the acute stage, although psychological support is often required in the process of recovery. Few studies focus on pharmacological treatment of PP so the decision about treatment follows the same considerations as it would for similar episodes not related to childbirth. Factors needing to be considered include the individual symptoms experienced, the level of disturbance and previous response to medications. In addition there are specific side effects, such as excessive sedation, that may be problematic to a new mother which may impact on her ability to care for her new baby. Electroconvulsive therapy may also be an option to consider in bipolar women with severe postpartum episodes particularly if there is significant suicidal risk.¹²¹ Severe postpartum episodes can raise concern over child protection, with a number of factors influencing risk including the severity of psychiatric history, level of functioning, individual social circumstances and relationships. In addition, it is important to establish the presence of comorbid personality disorder or drug and alcohol problems.¹²² It is vital to realize, however, that the majority of women with BPD, even those who experience severe

perinatal episodes, do not have long-term problems with parenting.

The short-term prognosis for postpartum psychosis and other perinatal episodes in bipolar women is usually excellent, although one study reported one in four women to still be experiencing ongoing symptoms at 1 year.¹¹

Conclusions

The perinatal period can best be described as a time of high risk, with high stakes for women with unipolar and bipolar mood disorders. It is crucial that a thoughtful risk:benefit analysis is conducted regarding the risks of the underlying illness versus risks of medication exposure during pregnancy or lactation. The clinician providing care must carefully consider prior history of response and nonresponse to treatment. When considering medication treatment, particular attention must be paid to prior medication trials that were most efficacious and best tolerated by the woman. Considerations of psychotherapy and other treatment modalities are important to include, as is the impact of both the illness and treatment modality on patient, infant, and family. More research is needed to guide these very difficult decisions that women and their clinicians face at a vulnerable time. □

REFERENCES

1. Gaynes BN, Gavin N, Meltzer-Brody S, et al. Perinatal depression: prevalence, screening accuracy, and screening outcomes. *Evid Rep/Technol Assess (Summ)*. 2005;119:1-8.
2. O'Hara MW, McCabe JE. Postpartum depression: current status and future directions. *Annu Rev Clin Psychol*. 2013;9:379-407.
3. Stowe ZN, Hostetter AL, Newport DJ. The onset of postpartum depression: Implications for clinical screening in obstetrical and primary care. *Am J Obstet Gynecol*. 2005;192(2):522-526.
4. O'Hara MW, Swain AM. Rates and risk of postpartum depression - a meta-analysis. *Int Rev Psychiatry*. 1996;8(1):37-54.
5. O'Hara MW. Postpartum depression: what we know. *J Clinl Psychol*. 2009;65(12):1258-1269.
6. Lindahl V, Pearson JL, Colpe L. Prevalence of suicidality during pregnancy and the postpartum. *Arch Womens Ment Health*. 2005;8(2):77-87.
7. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: a systematic review of prevalence and incidence. *Obstet Gynecol*. 2005;106(5 Pt 1):1071-1083.
8. Wisner KL, Parry BL, Piontek CM. Postpartum depression. *N Engl J Med*. 2002;347(3):194-199.
9. Heron J, O'Connor TG, Evans J, Golding J, Glover V. The course of anxiety and depression through pregnancy and the postpartum in a community sample. *J Affect Disord*. 2004;80(1):65-73.
10. Sit D, Rothschild AJ, Wisner KL. A review of postpartum psychosis. *J Womens Health*. 2006;15(4):352-368.
11. Blackmore ER, Rubinow DR, O'Connor TG, et al. Reproductive outcomes and risk of subsequent illness in women diagnosed with postpartum psychosis. *Bipolar Disord*. 2013;15(4):394-404.
12. Heron J, McGuinness M, Blackmore ER, Craddock N, Jones I. Early postpartum symptoms in puerperal psychosis. *Br J Obstet Gynaecol*. 2008;115(3):348-353.
13. Chesney E, Goodwin GM, Fazel S. Risks of all-cause and suicide mortality in mental disorders: a meta-review. *World Psychiatry*. 2014;13(2):153-160.
14. Burke L. The impact of maternal depression on familial relationships. *Int Rev Psychiatry*. 2003;15(3):243-255.
15. Ashman SB, Dawson G, Panagiotides H, Yamada E, Wilkinson CW. Stress hormone levels of children of depressed mothers. *Dev Psychopathol*. 2002;14(2):333-349.
16. Field T. Postpartum depression effects on early interactions, parenting, and safety practices: a review. *Infant Behav Dev*. 2010;33(1):1-6.
17. Meltzer-Brody S, Boschloo L, Jones I, Sullivan PF, Penninx BW. The EPDS-Lifetime: assessment of lifetime prevalence and risk factors for perinatal depression in a large cohort of depressed women. *Arch Womens Ment Health*. 2013;16(6):465-473.
18. Munk-Olsen T, Laursen TM, Meltzer-Brody S, Mortensen PB, Jones I. Psychiatric disorders with postpartum onset: possible early manifestations of bipolar affective disorders. *Arch Gen Psychiatry*. 2012;69(4):428-434.
19. Di Florio A, Forty L, Gordon-Smith K, et al. Perinatal episodes across the mood disorder spectrum. *JAMA Psychiatry*. 2013;70(2):168-175.
20. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.
21. Cox J. Postnatal mental disorder: towards ICD-11. *World Psychiatry*. 2004;3(2):96-97.
22. Cooper P, Murray L. Prediction, detection, and treatment of postnatal depression. *Arch Dis Child*. 1997;77(2):97-99.

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Optimizando el tratamiento de los trastornos afectivos en el período perinatal

El período perinatal es un tiempo de alto riesgo para la mujer con trastornos afectivos unipolares o bipolares. Se discuten las consideraciones terapéuticas para los trastornos afectivos perinatales, incluyendo la depresión unipolar y bipolar como también la psicosis postparto. Además se exploran los temas específicos que enfrentan las mujeres y sus familias durante todo el período perinatal desde la planificación de la preconcepción, pasando por el embarazo y hasta el nacimiento. El tratamiento de los trastornos afectivos perinatales durante el embarazo requiere de un manejo integrado entre los obstetras y los profesionales de salud mental, para asegurar que se realice un reflexivo análisis costo beneficio. Es vital considerar los riesgos de la enfermedad subyacente versus los riesgos de la exposición a la medicación durante el embarazo o la lactancia. Cuando se considera un tratamiento medicamentoso se debe prestar atención a los ensayos con fármacos que previamente resultaron más eficaces y mejor tolerados. Por último, es importante evaluar el impacto de los estresores psicosociales individuales y los factores del estilo de vida en la respuesta al tratamiento.

Optimisation du traitement des troubles de l'humeur en période périnatale

La période périnatale est un moment à haut risque de troubles de l'humeur uni- et bipolaires pour les femmes. Nous examinons le traitement des troubles de l'humeur périnataux, y compris la dépression uni- et bipolaire et la psychose du postpartum. Nous étudions ensuite les problèmes spécifiques rencontrés par les femmes et leurs familles au cours du parcours complet de la période périnatale, de la programmation de la grossesse à la gestation et à l'accouchement. Le traitement des troubles de l'humeur périnataux nécessite une collaboration entre les obstétriciens et les prestataires en santé mentale, pour s'assurer d'une analyse bénéfices/risques attentive. Il est vital de prendre en compte les risques de maladie sous-jacente versus les risques d'exposition au traitement pendant la grossesse ou l'allaitement. S'il faut un traitement médicamenteux, il est nécessaire de prendre en compte les tentatives antérieures au cours desquelles les médicaments étaient plus efficaces et mieux tolérés. Enfin, il est important d'évaluer l'impact des facteurs de stress psychosociaux individuels et les facteurs de style de vie sur la réponse au traitement.

23. Bernstein IH, Rush AJ, Yonkers K, et al. Symptom features of postpartum depression: are they distinct? *Depress Anxiety*. 2008;25(1):20-26.

24. Abramowitz JS, Meltzer-Brody S, Leserman J, et al. Obsessional thoughts and compulsive behaviors in a sample of women with postpartum mood symptoms. *Arch Womens Ment Health*. 2010;13(6):523-530.

25. Hendrick V, Altshuler L, Strouse T, Grosser S. Postpartum and nonpostpartum depression: differences in presentation and response to pharmacologic treatment. *Depress Anxiety*. 2000;11(2):66-72.

26. Abramowitz JS, Meltzer-Brody S, Leserman J, et al. Obsessional thoughts and compulsive behaviors in a sample of women with postpartum mood symptoms. *Arch Womens Ment Health*. 2010;13(6):523-530.

27. Beck CT. Postpartum depressed mothers' experiences interacting with their children. *Nurs Res*. 1996;45(2):98-104.

28. Yonkers KA, Vigod S, Ross LE. Diagnosis, pathophysiology, and management of mood disorders in pregnant and postpartum women. *Obstet Gynecol*. 2011;117(4):961-977.

29. Yonkers KA, Wisner KL, Stewart DE, et al. The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2009;114(3):703-713.

30. Stuart S, O'Hara MW. Treatment of postpartum depression with interpersonal psychotherapy. *Arch Gen Psychiatry*. 1995;52(1):75-76.

31. Grote NK, Swartz HA, Geibel SL, Zuckoff A, Houck PR, Frank E. A randomized controlled trial of culturally relevant, brief interpersonal psychotherapy for perinatal depression. *Psychiatr Serv*. 2009;60(3):313-321.

32. Zlotnick C, Miller IW, Pearlstein T, Howard M, Sweeney P. A preventive intervention for pregnant women on public assistance at risk for postpartum depression. *Am J Psychiatry*. 2006;163(8):1443-1445.

33. Brandon AR, Ceccotti N, Hynan LS, Shivakumar G, Johnson N, Jarrett RB. Proof of concept: Partner-Assisted Interpersonal Psychotherapy for perinatal depression. *Arch Womens Ment Health*. 2012;15(6):469-480.

34. Cooper PJ, Murray L, Wilson A, Romaniuk H. Controlled trial of the short- and long-term effect of psychological treatment of post-partum depression. I. Impact on maternal mood. *Br J Psychiatry*. 2003;182:412-419.

35. Chabrol H, Teissedre F, Saint-Jean M, Teisseyre N, Roge B, Mullet E. Prevention and treatment of post-partum depression: a controlled randomized study on women at risk. *Psychol Med*. 2002;32(6):1039-1047.

36. Rowe H, Sperlich M, Cameron H, Seng J. A Quasi-experimental outcomes analysis of a psychoeducation intervention for pregnant women with abuse-related posttraumatic stress. *J Obstet Gynecol Neonat Nurs*. 2014;43(3):282-293.

37. Kozinszky Z, Dudas RB, Devosa I, et al. Can a brief antepartum preventive group intervention help reduce postpartum depressive symptomatology? *Psychother Psychosomat*. 2012;81(2):98-107.

38. O'Hara MW, Stuart S, Gorman LL, Wenzel A. Efficacy of interpersonal psychotherapy for postpartum depression. *Arch Gen Psychiatry*. 2000;57(11):1039-1045.

39. Einarsen A. Antidepressants and pregnancy: complexities of producing evidence-based information. *Can Med Assoc J*. 2010;182(10):1017-1018.

40. O'Mahen HA, Flynn HA. Preferences and perceived barriers to treatment for depression during the perinatal period. *J Womens Health*. 2008;17(8):1301-1309.

41. Cooper WO, Willy ME, Pont SJ, Ray WA. Increasing use of antidepressants in pregnancy. *Am J Obstet Gynecol*. 2007;196(6):544.e541-544.e545.

42. Kjaersgaard MI, Parner ET, Vestergaard M, et al. Prenatal antidepressant exposure and risk of spontaneous abortion - a population-based study. *PLoS One*. 2013;8(8):e72095.

43. Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. Antidepressant exposure during pregnancy and congenital malformations: is there an association? A systematic review and meta-analysis of the best evidence. *J Clin Psychiatry*. 2013;74(4):e293-e308.

44. Wisner KL, Appelbaum PS, Uhl K, Goldkind SF. Pharmacotherapy for depressed pregnant women: overcoming obstacles to gathering essential data. *Clinical Pharmacol Therapeut*. 2009;86(4):362-365.
45. Oberlander TF, Gingrich JA, Ansorge MS. Sustained neurobehavioral effects of exposure to SSRI antidepressants during development: molecular to clinical evidence. *Clinical Pharmacol Therapeut*. 2009;86(6):672-677.
46. Warburton W HC, Oberlander TF. A register study of the impact of stopping third trimester selective serotonin reuptake inhibitor exposure on neonatal health. *Acta Psychiatr Scand*. 2010;121(6):471-479.
47. Huybrechts KF, Palmsten K, Avorn J, et al. Antidepressant use in pregnancy and the risk of cardiac defects. *N Engl J Med*. 2014;370(25):2397-2407.
48. Ross LE, Grigoriadis S. Selected pregnancy and delivery outcomes after exposure to antidepressant medication. *JAMA Psychiatry*. 2014;71(6):716-717.
49. Clements CC, Castro VM, Blumenthal SR, et al. Prenatal antidepressant exposure is associated with risk for attention-deficit hyperactivity disorder but not autism spectrum disorder in a large health system. *Mol Psychiatry*. 2015;20(6):727-734.
50. Croen LA, Grether JK, Yoshida CK, Odouli R, Hendrick V. Antidepressant use during pregnancy and childhood autism spectrum disorders. *Arch Gen Psychiatry*. 2011;68(11):1104-1112.
51. Meltzer-Brody S. Treating perinatal depression: risks and stigma. *Obstet Gynecol*. 2014;124(4):653-654.
52. Andersen JT, Andersen NL, Horwitz H, Poulsen HE, Jimenez-Solem E. Exposure to selective serotonin reuptake inhibitors in early pregnancy and the risk of miscarriage. *Obstet Gynecol*. 2014;124(4):655-661.
53. Suri R, Lin AS, Cohen LS, Altshuler LL. Acute and long-term behavioral outcome of infants and children exposed in utero to either maternal depression or antidepressants: a review of the literature. *J Clin Psychiatry*. 2014;75(10):e1142-1152.
54. Wisner KL, Hanusa BH, Perel JM, et al. Postpartum depression: a randomized trial of sertraline versus nortriptyline. *J Clin Psychopharmacol*. 2006;26(4):353-360.
55. Newport DJ, Hostetter A, Arnold A, Stowe ZN. The treatment of postpartum depression: minimizing infant exposures. *J Clin Psychiatry*. 2002;63(suppl 7):31-44.
56. Wikner BN, Stiller CO, Bergman U, Asker C, Kallen B. Use of benzodiazepines and benzodiazepine receptor agonists during pregnancy: neonatal outcome and congenital malformations. *Pharmacoepidemiol Drug Saf*. 2007;16(11):1203-1210.
57. Burt VK, Suri R, Altshuler L, Stowe Z, Hendrick VC, Muntean E. The use of psychotropic medications during breast-feeding. *Am J Psychiatry*. 2001;158(7):1001-1009.
58. Buist A, Norman TR, Dennerstein L. Breastfeeding and the use of psychotropic medication: a review. *J Affect Disord*. 1990;19(3):197-206.
59. Kelly LE, Poon S, Madadi P, Koren G. Neonatal benzodiazepines exposure during breastfeeding. *J Pediatr*. 2012;161(3):448-451.
60. Dolovich LR, Addis A, Vaillancourt JM, Power JD, Koren G, Einarson TR. Benzodiazepine use in pregnancy and major malformations or oral cleft: meta-analysis of cohort and case-control studies. *BMJ*. 1998;317(7162):839-843.
61. Saxen I, Saxen L. Letter: Association between maternal intake of diazepam and oral clefts. *Lancet*. 1975;2(7933):498.
62. Jones I, McDonald L. Living with uncertainty: antidepressants and pregnancy. *Br J Psychiatry*. 2014;205(2):103-104.
63. Moses-Kolko EL, Berga SL, Kalro B, Sit DK, Wisner KL. Transdermal estradiol for postpartum depression: a promising treatment option. *Clin Obstet Gynecol*. 2009;52(3):516-529.
64. Wirz-Justice A, Bader A, Frisch U, et al. A randomized, double-blind, placebo-controlled study of light therapy for antepartum depression. *J Clin Psychiatry*. 2011;72(7):986-993.
65. Epperson CN, Terman M, Terman JS, et al. Randomized clinical trial of bright light therapy for antepartum depression: preliminary findings. *J Clin Psychiatry*. 2004;65(3):421-425.
66. Oren DA, Wisner KL, Spinelli M, et al. An open trial of morning light therapy for treatment of antepartum depression. *Am J Psychiatry*. 2002;159(4):666-669.
67. Kim DR, Sockol L, Barber JP, et al. A survey of patient acceptability of repetitive transcranial magnetic stimulation (TMS) during pregnancy. *J Affect Disord*. 2011;129(1-3):385-390.
68. Zhang X, Liu K, Sun J, Zheng Z. Safety and feasibility of repetitive transcranial magnetic stimulation (rTMS) as a treatment for major depression during pregnancy. *Arch Womens Ment Health*. 2010;13(4):369-370.
69. Garcia KS, Flynn P, Pierce KJ, Caudle M. Repetitive transcranial magnetic stimulation treats postpartum depression. *Brain Stimul*. 2010;3(1):36-41.
70. Myczkowski ML, Dias AM, Luvisotto T, et al. Effects of repetitive transcranial magnetic stimulation on clinical, social, and cognitive performance in postpartum depression. *Neuropsychiatr Dis Treat*. 2012;8:491-500.
71. Gaynes BN, Gavin N, Meltzer-Brody S, et al. Perinatal depression: prevalence, screening accuracy, and screening outcomes. *Evid Rep Technol Assess (Summ)*. 2005(119):1-8.
72. Prevention CfDca. Breastfeeding among U.S. children born 2000-2010, CDC National Immunization Survey. Available at: http://www.cdc.gov/breastfeeding/data/nis_data/ - any-exclusive-bf-rates. Accessed March 2015.
73. Unicef UK. UK Baby friendly breastfeeding initiative. Available at: <http://www.unicef.org.uk/BabyFriendly/About-Baby-Friendly/Breastfeeding-in-the-UK/UK-Breastfeeding-rates/>. Accessed March 2015.
74. Payne JL. Antidepressant use in the postpartum period: practical considerations. *Am J Psychiatry*. 2007;164(9):1329-1332.
75. Kristensen JH, Ilett KF, Hackett LP, Yapp P, Paech M, Begg EJ. Distribution and excretion of fluoxetine and norfluoxetine in human milk. *Br J Clin Pharmacol*. 1999;48(4):521-527.
76. Rampono J, Kristensen JH, Hackett LP, Paech M, Kohan R, Ilett KF. Citalopram and demethylcitalopram in human milk; distribution, excretion and effects in breast fed infants. *Br J Clin Pharmacol*. 2000;50(3):263-268.
77. Eberhard-Gran M, Eskild A, Opjordsmoen S. Use of psychotropic medications in treating mood disorders during lactation: practical recommendations. *CNS Drugs*. 2006;20(3):187-198.
78. US National Library of Medicine. LactMed: a TOXNET database. Available at: <http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm>. Accessed March 2015.
79. University of Rochester Medical Center. Breastfeeding/Human Lactation Center. Available at: <http://www.urmc.rochester.edu/childrens-hospital/neonatology/lactation.aspx>. Accessed March 2015.
80. Motherisk. Available at: <http://www.motherisk.org/index.jsp>. Accessed March 2015.
81. The Breastfeeding Network. Drugs in breastmilk: is it safe? Available at: <http://www.breastfeedingnetwork.org.uk/detailed-information/drugs-in-breastmilk/>. Accessed March 2015.
82. Stuebe AM, Grewen K, Pedersen CA, Propper C, Meltzer-Brody S. Failed lactation and perinatal depression: common problems with shared neuroendocrine mechanisms? *J Womens Health*. 2012;21(3):264-272.
83. Stuebe AM, Horton BJ, Chetwynd E, Watkins S, Grewen K, Meltzer-Brody S. Prevalence and risk factors for early, undesired weaning attributed to lactation dysfunction. *J Womens Health*. 2014;23(5):404-412.
84. Feldman R, Granat A, Pariente C, Kanety H, Kuint J, Gilboa-Schechtman E. Maternal depression and anxiety across the postpartum year and infant social engagement, fear regulation, and stress reactivity. *J Am Acad Child Adolesc Psychiatry*. 2009;48(9):919-927.
85. Hunter LP, Rychnovsky JD, Yount SM. A selective review of maternal sleep characteristics in the postpartum period. *J Obstet Gynecol Neonat Nurs*. 2009;38(1):60-68.
86. Ross LE, Murray BJ, Steiner M. Sleep and perinatal mood disorders: a critical review. *J Psychiatry Neurosci*. 2005;30(4):247-256.
87. Okun ML, Hanusa BH, Hall M, Wisner KL. Sleep complaints in late pregnancy and the recurrence of postpartum depression. *Behav Sleep Med*. 2009;7(2):106-117.
88. Okun ML, Luther J, Prather AA, Perel JM, Wisniewski S, Wisner KL. Changes in sleep quality, but not hormones predict time to postpartum depression recurrence. *J Affect Disord*. 2011;130(3):378-384.
89. Park EM, Meltzer-Brody S, Stickgold R. Poor sleep maintenance and subjective sleep quality are associated with postpartum maternal depression symptom severity. *Arch Womens Ment Health*. 2013;16(6):539-547.

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90. Coo S, Milgrom J, Trinder J. Mood and objective and subjective measures of sleep during late pregnancy and the postpartum period. *Behav Sleep Med*. 2014;12(4):317-330.
91. Ritter C, Hobfoll SE, Lavin J, Cameron RP, Hulsizer MR. Stress, psychosocial resources, and depressive symptomatology during pregnancy in low-income, inner-city women. *Health Psychol*. 2000;19(6):576-585.
92. Paulson JF, Bazemore SD. Prenatal and postpartum depression in fathers and its association with maternal depression: a meta-analysis. *JAMA*. 2010;303(19):1961-1969.
93. Blazer DG, Kessler RC, McGonagle KA, Swartz MS. The prevalence and distribution of major depression in a national community sample: the National Comorbidity Survey. *Am J Psychiatry*. 1994;151(7):979-986.
94. Edoka IP, Petrou S, Ramchandani PG. Healthcare costs of paternal depression in the postnatal period. *J Affect Disord*. 2011;133(1-2):356-360.
95. Jones I, Chandra PS, Dazzan P, Howard LM. Bipolar disorder, affective psychosis, and schizophrenia in pregnancy and the post-partum period. *Lancet*. 2014;384(9956):1789-1799.
96. Viguera AC, Whitfield T, Baldessarini RJ, et al. Risk of recurrence in women with bipolar disorder during pregnancy: prospective study of mood stabilizer discontinuation. *Am J Psychiatry*. 2007;164(12):1817-1824; quiz 1923.
97. Jones I, Craddock N. Bipolar disorder and childbirth: the importance of recognising risk. *Br J Psychiatry*. 2005;186:453-454.
98. Jones IHJ, Robertson Blackmore E. In: Cohen, ed. *Puerperal psychosis*. In: *The Oxford Textbook of Women's Mental Health*. Oxford, UK: Oxford University Press; 2010.
99. Heron J, McGuinness M, Blackmore ER, Craddock N, Jones I. Early postpartum symptoms in puerperal psychosis. *Br J Obstet Gynaecol*. 2008;115(3):348-353.
100. Munk-Olsen T, Laursen TM, Mendelson T, Pedersen CB, Mors O, Mortensen PB. Risks and predictors of readmission for a mental disorder during the postpartum period. *Arch Gen Psychiatry*. 2009;66(2):189-195.
101. Robertson E, Jones I, Haque S, Holder R, Craddock N. Risk of puerperal and non-puerperal recurrence of illness following bipolar affective puerperal (post-partum) psychosis. *Br J Psychiatry*. 2005;186:258-259.
102. Jones I, Craddock N. Familiality of the puerperal trigger in bipolar disorder: results of a family study. *Am J Psychiatry*. 2001;158(6):913-917.
103. Munk-Olsen T, Laursen TM, Pedersen CB, Mors O, Mortensen PB. Family and partner psychopathology and the risk of postpartum mental disorders. *J Clin Psychiatry*. 2007;68(12):1947-1953.
104. National Collaborating Centre for Mental Health. *Antenatal and Postnatal Mental Health. NICE Guidelines No 45*. London, UK: British Psychological Society and the Royal College of Psychiatrists; 2007.
105. Scottish Intercollegiate Guidelines Network. *Management of Perinatal Mood Disorders*. Edinburgh, UK: Scottish Intercollegiate Guidelines Network; 2012.
106. BeyondBlue. *Perinatal Depression and Anxiety. A Guideline for Primary Care Health Professionals*. Hawthorn, Australia: BeyondBlue; 2011.
107. Howard LM, Bekele D, Rowe M, Demilew J, Bewley S, Marteau TM. Smoking cessation in pregnant women with mental disorders: a cohort and nested qualitative study. *Br J Obstet Gynaecol*. 2013;120(3):362-370.
108. Bergink V, Bouvy PF, Vervoort JS, Koorengel KM, Steegers EA, Kushner SA. Prevention of postpartum psychosis and mania in women at high risk. *Am J Psychiatry*. 2012;169(6):609-615.
109. Meador K, Reynolds MW, Crean S, Fahrback K, Probst C. Pregnancy outcomes in women with epilepsy: a systematic review and meta-analysis of published pregnancy registries and cohorts. *Epilepsy Res*. 2008;81(1):1-13.
110. Meador KJ, Baker GA, Browning N, et al. Fetal antiepileptic drug exposure and cognitive outcomes at age 6 years (NEAD study): a prospective observational study. *Lancet Neurology*. 2013;12(3):244-252.
111. Gentile S. Antipsychotic therapy during early and late pregnancy. A systematic review. *Schizophr Bull*. 2010;36(3):518-544.
112. Habermann F, Fritzsche J, Fuhlbruck F, et al. Atypical antipsychotic drugs and pregnancy outcome: a prospective, cohort study. *J Clin Psychopharmacol*. 2013;33(4):453-462.
113. Chengappa KN, Suppes T, Berk M. Treatment of bipolar mania with atypical antipsychotics. *Expert Rev Neurother*. 2004;4(6 suppl 2):S17-25.
114. Weinstein M. Lithium treatment of women during pregnancy and in the postdelivery period. In: Johnson F, ed. *Handbook of Lithium Therapy*. Lancaster, UK: MTP Ltd; 1980.
115. McKnight RF, Adida M, Budge K, Stockton S, Goodwin GM, Geddes JR. Lithium toxicity profile: a systematic review and meta-analysis. *Lancet*. 2012;379(9817):721-728.
116. Deligiannidis KM, Byatt N, Freeman MP. Pharmacotherapy for mood disorders in pregnancy: a review of pharmacokinetic changes and clinical recommendations for therapeutic drug monitoring. *J Clin Psychopharmacol*. 2014;34(2):244-255.
117. Stewart DE, Klompenhouwer JL, Kendell RE, van Hulst AM. Prophylactic lithium in puerperal psychosis. The experience of three centres. *Br J Psychiatry*. 1991;158:393-397.
118. Austin MP. Puerperal affective psychosis: is there a case for lithium prophylaxis? *Br J Psychiatry*. 1992;161:692-694.
119. Bergink V, Bouvy PF, Vervoort JS, Koorengel KM, Steegers EA, Kushner SA. Prevention of postpartum psychosis and mania in women at high risk. *Am J Psychiatry*. 2012;169(6):609-615.
120. Sharma V, Smith A, Mazmanian D. Olanzapine in the prevention of postpartum psychosis and mood episodes in bipolar disorder. *Bipolar Disord*. 2006;8(4):400-404.
121. Babu GN, Thippeswamy H, Chandra PS. Use of electroconvulsive therapy (ECT) in postpartum psychosis--a naturalistic prospective study. *Arch Womens Ment Health*. 2013;16(3):247-251.
122. Howard LM, Goss C, Leese M, Appleby L, Thornicroft G. The psychosocial outcome of pregnancy in women with psychotic disorders. *Schizophr Res*. 2004;71(1):49-60.