Published in final edited form as:

J Midwifery Womens Health. 2013 ; 58(6): 643–653. doi:10.1111/jmwh.12104.

Management of Postpartum Depression

Constance Guille, M.D., Roger Newman, M.D., Leah D. Fryml, B.S., Clay K. Lifton, B.S., and C. Neill Epperson, M.D.

Abstract

Postpartum depression, now termed peripartum depression by the DSM-V, is one of the most common complications in the postpartum period and has potentially significant negative consequences for mothers and their families. This article highlights common clinical challenges in the treatment of peripartum depression and reviews the evidence for currently available treatment options. Psychotherapy is the first-line treatment options for women with mild-to-moderate peripartum depression. Antidepressant medication in combination with therapy is recommended for women with moderate-to-severe depression. While pooled case reports and small controlled studies have demonstrated undetectable infant serum levels and no short-term adverse events in infants of mothers breastfeeding while taking sertraline (Zoloft) and paroxetine (Paxil), further research is needed including larger samples and long-term follow-up of infants exposed to antidepressants via breastfeeding with control for maternal depression. Pharmacological treatment recommendations in women who are lactating must include discussion with the patient regarding the benefits of breastfeeding, risks of antidepressant use during lactation and risks of untreated illness. There is a growing evidence base for non-pharmacological interventions including repetitive Transcranial Magnetic Stimulation (rTMS) which may offer an attractive option for women who wish to continue to breastfeed and are concerned about exposure of medication to their infant. Among severe cases of peripartum depression with psychosis referral to a psychiatrist or psychiatric APRN is warranted. Suicidal or homicidal ideation with a desire, intent or plan to harm oneself or anyone one else, including the infant, is a psychiatric emergency, and an evaluation by a mental health professional should be conducted immediately.

Peripartum depression treatment research is limited by small samples sizes and few controlled studies. Much work is still needed to better understand which treatments women prefer and are the most effective in ameliorating the symptoms and disease burden associated with peripartum depression.

Keywords

postpartum depression; peripartum depression; breastfeeding; psychotherapy; antidepressants; electroconvulsive therapy; repetitive transcranial stimulation

Corresponding Author: Constance Guille, M.D., Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, 67 President St. MSC861, 5 South, Charleston, SC 29425, Phone: (843) 792-6489, Fax: (843) 792-4190, guille@musc.edu.

Conflict of Interest:

Dr. Epperson receives grant support from Shire and Novartis. All other authors have no conflicts of interest to disclose.

INTRODUCTION

Postpartum depression is defined as an episode of major depression that is temporally associated with childbirth.¹ The American Psychiatric Association, in the 2013 diagnostic and statistical manual of mental disorders (DSM-V), amended the name of this condition to peripartum depression and stipulates that the onset of mood disturbance can occur in pregnancy or within four weeks of childbirth.² Peripartum depression occurs in 15–20% of childbearing women each year, resulting in approximately 600,000–800,000 cases of peripartum depression annually; it is one of the most common complications of the postpartum period.³

Peripartum depression is a potentially devastating disorder that carries significant lifetime consequences for women and their children.⁴ In addition to the suffering and impairment associated with postpartum depression, there are long-term risks associated with the illness including increased risk of recurrence of peripartum and non-peripartum depression with increased disease burden with subsequent depressive episodes.^{4–5} Further, children of mothers with peripartum depression are at increased risk for developmental delays and behavioral problems.^{6–9}

Given the prevalence and significant consequences of peripartum depression, identification and appropriate treatment of the disorder is paramount. Routine screening for depression during pregnancy and postpartum is recommended.^{10,11} Unfortunately, peripartum depression screening does not always improve treatment engagement or patient outcomes. Studies have demonstrated that even when a depressive episode is identified, many women do not receive treatment.^{12–13} This may be due to patient preferences for specific types of therapy during the postpartum period or difficulty attaining access to treatment.^{14–16}

Providing treatment options to women that are acceptable, feasible and evidence based is challenging but critical to ameliorating the symptoms and disease burden associated with peripartum depression. In this article, we will present a series of clinical case vignettes that highlight common clinical challenges in the treatment of peripartum depression and review the evidence base for currently available treatment options. Further we will highlight areas of much needed research to improve the treatment of peripartum depression.

Evaluation

Self-report assessment tools are commonly employed to screen for postpartum depression.^{10,11} A comprehensive review of these scales is beyond the scope of this review, but we refer readers to well validated screening tools that are available online (See Appendix 1). Once depressive symptoms have been identified, a comprehensive evaluation of risks and assets that influence the clinician's treatment recommendations and patient's treatment decision should be completed. This begins with evaluating the patient's current depressive symptoms. It is important to differentiate depressive symptoms from normal sequelae of childbirth (Table 1) and determine the severity of symptoms. Identifying current life stressors and how they are managed (ie, coping skills, social supports) can be helpful in understanding the impact of illness on the patient's overall well-being and level of

functioning. Comorbid anxiety symptoms commonly occur during this time and should be included in the evaluation as well.¹⁷

Next, it is important to consider the patient's past psychiatric history. Fifty percent of women with bipolar disorder will experience a mood episode (primarily depression) in the postpartum period¹⁸. Since treatment for bipolar depression differs from treatment of major depression, it is important to ask about prior episodes of mania or hypomania. A diagnosis of bipolar disorder is considered if the patient has experienced at least 4–7 days of elevated, expansive or irritable mood and 3 of the following symptoms to a significant degree: inflated self-esteem, decreased need for sleep, more talkative or pressured speech, flight of ideas or racing thoughts, distractibility, increased goal directed activity or psychomotor agitation, or excessive involvement in activities that have a high risk for negative consequences. If the mood episode is only irritable, 4 of the listed symptoms are needed to consider the diagnosis. The treatment of bipolar disorder is beyond the scope of this review and referral to a mental health professional who can manage medications is warranted.

Other important past psychiatric history includes prior outpatient or inpatient psychiatric treatment, history of suicide attempts, and psychiatric co-morbidities (ie, anxiety, substance abuse, psychosis). A medical history with careful attention to both thyroid disease and anemia, which are more common in the postnatal period,^{19–20} should be obtained; both illnesses can mimic symptoms of depression. Further, family psychiatric history and treatment should be included; mood disorders are highly heritable and treatment response among family members can guide treatment decisions. Collected information is then used to inform the discussion with the patient regarding risks and benefits including risks of untreated illness, the risks and benefits of treatment of treatment; and the benefits of breastfeeding (if applicable).

Mild to Moderate Postpartum Depression, Currently Breastfeeding

Case A Presentation—*Ms. A presents for a follow-up appointment at 7 weeks postpartum. She is currently breastfeeding. Upon evaluation she describes a depressed mood most days over the past 3 weeks, and notes that she would prefer to 'just stay home' rather than engage in any social activities, which she used to enjoy. She describes having poor appetite, energy and concentration which make it difficult to accomplish tasks at home, but that overall she is not having a problem caring for her newborn and is able to take care of her other responsibilities. She denies any suicidal or homicidal ideation. Major stressors include tension in her relationship with her husband and recent arguments about duties around the home related to child care and managing their home. She is able to cope with this by not being so perfectionistic about the appearance of her home (ie, cleaning, laundry). Overall she and her husband get along well and she has strong social supports. She denies feeling anxious. She denies current or past symptoms of hypomania or use of substances including tobacco or alcohol. Psychiatric history is only significant for counseling in college following a difficult break-up. She has no significant past medical or family psychiatric history.*

Case A Discussion—Ms. A has mild to moderate depressive symptoms and minimal impairment in functioning as well as absence of a significant past psychiatric history. Psychotherapy is an important first line treatment recommendation for her.¹⁰ This option is particularly attractive for women who are reluctant to take medications while breastfeeding due to fear of exposing the newborn to medication.¹⁶ Psychotherapies with the largest evidence base for the acute treatment of peripartum depression include Interpersonal Psychotherapy (IPT) and Cognitive Behavioral Therapy (CBT).^{21–23} Both IPT and CBT are time-limited treatments (usually 10–12 sessions) that focus on present problems and encourage patients to regain control over their mood and functioning. With IPT, the goal is to help patients identify and modify interpersonal difficulties by better understanding themselves and their current roles and relationships with others (ie, partner, family members, friends)²⁴ In contrast, CBT helps individuals recognize the interplay between their thoughts, emotions and behaviors. Individuals are assisted in identifying maladaptive or faulty thinking patterns that result in negative emotions and behaviors. Treatment focuses on changing maladaptive thought patterns in order to improve emotional state and behavior. Individuals also work to engage in positive activities that improve mood and thought patterns.²⁵

While both IPT and CBT interventions have demonstrated significant and moderate to large reductions in depressive symptoms compared to no treatment control conditions, it is unclear if one treatment has significant advantages compared to the other. A recent meta-analysis demonstrated that therapies including an interpersonal therapy component had greater effect sizes, compared to a control condition, than interventions including a cognitive behavioral therapy component.²⁶ However, both treatments are efficacious for the treatment of depression and treatment decision can be guided by patient preference and available providers.

Women may be reluctant to see a mental health care provider for a number of reasons including concerns related to stigma, unsupportive partners, family members and health care providers, management of childcare during visits and difficulty accessing affordable care.^{14–16, 27–29} Helping women to understand the risk associated with continued depressive symptoms for her and her children^{4–9} can be helpful when discussing the barriers to treatment. Often the risks of untreated illness outweigh the barriers to treatment and can help motivate the individual to seek care. Involving supportive family members in this discussion can also be beneficial. A family member can often provide insights about the patient's behaviors that help the patient recognize the need for treatment. Further, family members are willing to help with childcare or other logistical or practical barriers that often prevent women from getting treatment.

For those with medical insurance, contacting the insurance company to determine which mental health providers are covered can help facilitate access to affordable care. Practitioners can create a list of referrals to local subsidized mental health centers for uninsured women. Postpartum Support International is an organization that provides information for women, their partners and family members about postpartum depression. In addition to education about the disorder, the organization assists women in recognizing that they are not alone and provides resources for them and their family in locating local support

groups and connecting with others that have struggled with peripartum depression (See Appendix 1).

Another common barrier to treatment among postpartum women is the requirement to leave home or fit an additional office therapy appointment into an already busy schedule. Additionally, depressed patients often feel overwhelmed and are reluctant to take on more activities, even if those activities are potentially helpful. There is a growing interest in alternative approaches to delivering evidenced based therapies to difficult to reach populations using telemedicine. Telemedicine is the delivery of health care by a health professional at a location that is different from the patient. Telemedicine can include both teletherapy and medication management, and has an expanding evidence base for the treatment of depression.³⁰ Unfortunately at this time, however the evidence base for telemedicine, or teletherapy in peripartum depression is limited to one small pilot study.³¹ In this study 20 women with mild to moderate peripartum depression received weekly therapy for 10 weeks via telephone; sessions included relaxation techniques, problem solving strategies and cognitive behavioral therapy. Only five women completed all ten teletherapy sessions. Thirteen mothers completed between two and nine sessions, while two completed only one session. Reasons for nonadherence included ‘busy with childcare and family obligations’ or ‘feeling much better’. All women completed pre and post-study depressive symptoms assessments demonstrating a 50% reduction in depressive symptoms. The study demonstrated moderate challenges with recruitment and retention but all women taking part in the program reported benefit from the therapy and had a significant reduction in depressive symptoms. The lack of control group and small sample limit application of these data. However, the program appears moderately feasible. Internet based therapies have also shown to be moderately effective for the treatment of depression and are an option for those with difficulty accessing care. Studies are currently evaluating the feasibility and efficacy of internet based CBT for the treatment of depression in pregnancy and postpartum.³²

Moderate to Severe Postpartum Depression, Not Currently Breastfeeding

Case B Presentation—*Ms. B presents for her postpartum follow-up appointment at 10 weeks postpartum. She is not currently breastfeeding. She reports feeling depressed and down most days for the past two months since giving birth. She has little interest in anything pleasurable and is concerned about her lack of interest in her newborn son. She reports having difficulty bonding with her son but still feels attached to her 18 month old daughter. She reports frequent crying spells, decreased motivation, decreased energy and becomes easily frustrated and overwhelmed. At the peak of her frustration, she reports needing to lock herself in the bathroom away from her children ‘to calm down and collect myself’. She reports sleeping more, eating all the time, and has difficulty concentrating at work. She is very concerned about these symptoms and feels that they are unlike her normal behavior or anything she experienced following the birth of her older daughter. She reports that all she wants to do is ‘stay in bed all day’ but does not because she needs to care for her children and go to work. She denies any suicidal or homicidal ideation. Current stressors include financial issue and poor social supports; her husband started nursing school and is away 4–5 days a week resulting in her being the primary income earner and caregiver for their 2 children. She denies feeling anxious. She denies current or past symptoms of hypomania or*

mania or use of substances including tobacco or alcohol. Past psychiatric history is significant for one prior episode of depression in college requiring a leave of absence. She was treated with psychotherapy which was only moderately effective. Her family history is significant for major depression in two first degree family members, but their treatment history is unknown.

Case B Discussion—Given the duration and severity of Ms. B's current mood symptoms, past psychiatric history and degree to which her mood symptoms are impairing her functioning, she would benefit from antidepressant medication alone or in combination with therapy. Based on the available evidence, there is no clear first line choice of antidepressant medication for peripartum depression in women who choose not to breastfeed. There are a total of ten published clinical trials that have assessed the efficacy of antidepressants for postpartum depression.^{33–42} Only three studies have employed a double-blind placebo controlled study design. In one randomized, double-blind study of CBT + fluoxetine (Prozac) compared to CBT + placebo (n=87), fluoxetine +CBT was significantly more effective than CBT + placebo in decreasing postpartum depressive symptoms.³³ In an adequately powered randomized trial of paroxetine (Paxil) compared to placebo (n=70), depressive symptoms in both groups improved but group differences were not statistically significant.³⁴ In a third study (n=40), sertraline (Zoloft) or placebo was added to a form of psychotherapy called brief dynamic psychotherapy.³⁵ While both groups improved significantly, there were no significant differences between groups. This latter study is limited by its small sample was likely underpowered to detect differences between groups. All of these studies highlight the need for a placebo arm in evaluating the efficacy of treatments for this population.

The majority of studies have employed an open-label study design without a placebo arm. In the largest study to date (n=109), Wisner et al (2006) compared sertraline to nortriptyline (Pamelor) in a randomized open-label study of women with postpartum depression.³⁶ Both groups had a significant reduction in depressive symptoms, but no group differences were detected. Similarly, no group differences were found in an open label study of CBT + paroxetine versus paroxetine alone,³⁷ although sample size was likely too small to detect group differences (N=35). Sertraline venlafaxine (Effexor), fluvoxamine (Luvox), bupropion (Wellbutrin) and escitalopram (Lexapro)^{38–42} have all been evaluated in open-label studies of women with postpartum depression and have demonstrated a reduction in depressive symptoms, but sample sizes are small and limit interpretation of these findings. Small sample sizes are common due to the challenges of recruitment and retention of this population in clinical trials. Further work is needed to better understand what interventions are preferable and acceptable for this population.

In clinical practice, medication selection for an episode of peripartum depression in a woman who is not breastfeeding is most often determined by her prior response to an antidepressant medication.¹⁰ If a woman has a history of responding well to an antidepressant medication (ie, reduced depressive symptoms and no side effects), this is usually the best medication to use for the current episode of depression. In patients without a personal history of antidepressant use, but a family history of a good response to an antidepressant, this information can be used to guide antidepressant medication selection.

Selective serotonin re-uptake Inhibitors (SSRIs) are the first line treatment in patients without a personal or family history of prior antidepressant treatment response. A large meta-analysis of SSRIs for the acute treatment of major depression concluded that sertraline and citalopram (Celexa) are the most effective and best tolerated medications within the class of SSRIs.⁴³

Many women however, prefer not to take an antidepressant medication. While women should be informed that treatment with an SSRI is the recommendation with the greatest evidence base for the treatment of moderate to severe depression, alternatives to this treatment and patient preference should be discussed. If there is a preference for psychotherapy, this is a reasonable approach as long as symptoms are closely monitored. If symptoms continue or worsen, then antidepressant medications should be recommended again. After discussing the risks of untreated illness, not only for the patient but potentially for her family, and risks and benefits of treatment recommendations, women may choose not to engage or comply with any treatment recommendation. It is important to maintain rapport with these women and provide support. They and their family members should be encouraged to continue to monitor mood symptoms and return for follow-up in 2–3 weeks or sooner if symptoms worsen.

Moderate to Severe Depression, Currently Breastfeeding

Case C Presentation—*Ms C. presents for her postpartum follow-up appointment at 8 weeks postpartum. She is currently breastfeeding. She struggled with depression during her pregnancy and it has significantly worsened in the postpartum period. Throughout her pregnancy she continued psychotherapy 1 day a week, which she felt was very helpful. In the postpartum period however, her depressive symptoms have increased in intensity and frequency. She reports feeling sad throughout the day. Although she loves her newborn daughter she is not able to enjoy being a mother because ‘I just feel numb’ and ‘I have no interest in anything.’ She describes constant self-criticism, indecision and increased feelings of failure and guilt. These symptoms make her feel ‘paralyzed’ and unable to make a decision about anything. She denies thoughts of harming herself or anyone else, including her newborn. She describes increased anxiety including restlessness and difficulty falling back asleep following the nighttime feedings because of ‘constant worries’ about many different things. She reports constantly feeling afraid that something awful might happen to her baby or husband. She reports feeling fatigued and having little energy, but is unable to rest or sleep due to the anxious thoughts and constant worries. She denies any other anxiety symptoms (ie, panic attacks, or obsessive thoughts or images). She denies current or past symptoms of hypomania or mania, or use of substances including tobacco or alcohol. Past psychiatric history includes outpatient therapy and medication including sertraline, paroxetine and fluoxetine. Each of these antidepressants made her feel more anxious. The medications that have been most effective for her in the past include bupropion and venlafaxine. She has a family history of depression and anxiety in one first degree family member.*

Case C Discussion—Ms. C is experiencing moderate to severe depressive symptoms and pharmacological intervention is recommended. While this is similar to Ms. B’s case, it

differs in that psychotherapy as a monotherapy is clearly not effective at this time and a trial of continued therapy and symptom monitoring would not be sufficient or advised. She also is breastfeeding and experiencing co-morbid generalized anxiety disorder. Anxiety symptoms are common in this population and can often be the presenting complaint of many women with postpartum depression. Treatment needs to address both depression and anxiety in the context of breastfeeding.

The decision to continue or not continue breastfeeding must be weighted in light of the benefits of breastfeeding, a woman's preference to continue or discontinue breastfeeding, the risks of using medications during lactation as well as the risks of untreated illness. The American Academy of Pediatrics and the World Health Organization recommend the use of breast milk exclusively for the first 6 months of life with the option for adequate substitutes only for infants who cannot breastfeed.^{44–45} These recommendations are based on a multitude of short and long term health benefits for the newborn and mother. Breastfeeding facilitates mother-infant attachment and bonding.⁴⁶ Breastfed infants have less risk for infectious diseases (i.e., gastrointestinal and respiratory infections, urinary infections, sepsis, meningitis).^{44–46} The health benefits of breastfeeding have also been shown to extend into childhood and adolescence with lower rates of asthma, inflammatory bowel disease and obesity.^{44–45} Breastfeeding also provides short and long term health benefits for the mother. It has been associated with postpartum weight reduction and reduced bleeding following childbirth as well as reduced risk of ovarian and breast cancer.⁴⁶

The benefits of breastfeeding must be weighed against the risks of untreated illness as well as the potential risks and benefits associated with antidepressant treatment during lactation. Recommendations regarding the use of antidepressant medications while breastfeeding are available based on case reports, studies with small samples, as well as expert consensus and opinion.⁴⁷ In particular, three scientific commissions including the American Academy of Breastfeeding Medicine, the American College of Obstetrics and Gynecology and the National Institute of Clinical Excellence have published practical recommendations based on available albeit limited evidence to guide clinicians in the use of antidepressant medications among breastfeeding women.^{48–50} The reports are in agreement with the following recommendations.

The clinician should begin with a personalized risk-benefit analysis, which includes considerations for the risk of untreated illness for mother and baby, risks and benefits of the specific treatment and the risks and benefits of breastfeeding for mother and baby. In some instances (as seen with Ms B), trying psychotherapy first is reasonable as long as symptoms are closely monitored. However if symptoms continue and are severe, the risks associated with untreated illness are not outweighed by the benefits of breastfeeding. In cases of moderate to severe depression or in those not responding to therapy, antidepressants, alone or in combination to therapy, are recommended.

Choice of antidepressant medication is first guided by the patient's history. A first line antidepressant medication includes one with a prior favorable response (the medication has been both efficacious and well tolerated by the patient) and minimal risks for breastfeeding (Table 2). In women who have never taken an antidepressant or whose prior clinical

response to an antidepressant medication is unknown, sertraline and paroxetine are normally selected as first line treatment options. This recommendation however is based on case reports and small studies. The use of antidepressant medication during lactation should be based on up-to-date available information regarding the risks and benefits of the recommended treatment. This information, and should be provided and discussed with the patient to ensure she is making an informed decision.

Antidepressant medications should be started at a low dose and increased slowly. Monotherapy is preferable to polypharmacy. Mothers starting a medication should be asked to monitor their baby before and after starting the medication to ensure there are no behavioral changes, particularly in babies with any health problems. Routine monitoring of infant serum levels is not currently recommended.

Available data evaluating the safety of SSRIs in breastfeeding is derived from pooled case reports and small controlled studies which have demonstrated detectable antidepressant levels in breast milk for all antidepressants, but undetectable infant serum levels for sertraline and paroxetine.^{47,51–52} Further, no short-term adverse events have been reported with the use of sertraline and paroxetine.^{47,52} While, these findings are consistent across multiple laboratories and studies, studies are small and long-term effects are unknown. Further research is needed to determine the safety of these medications in breastfeeding with control for maternal depression. Paroxetine is commonly associated with sedation and withdrawal symptoms with missed doses or discontinuation of the medication¹⁰; thus sertraline is often preferred due to its more favorable side effect profile. The tricyclic antidepressants (TCAs), nortriptyline and imipramine (Tofranil), have a similar evidence base as sertraline and paroxetine, and can be considered for breastfeeding women with moderate to severe depressive symptoms.^{47,52} The main limitation of TCAs however is the poor side effect profile for the mother.¹⁰ Often TCAs are not well tolerated necessitating a switch to another medication, resulting in exposure of the infant to two antidepressant agents.

In this case of Ms C, she has a prior history of a poor response to sertraline and paroxetine; thus alternative medications need to be considered and discussed. She reports a good response to two other medications including venlafaxine, a serotonin norepinephrine re-uptake inhibitor (SNRI) and bupropion, a dopamine and norepinephrine re-uptake inhibitor and nicotinic antagonist. Given her comorbid anxiety symptoms, venlafaxine would be a better choice of antidepressant medication. In cases of depression and anxiety it is preferable to use one medication to treat both depression and anxiety (ie, an SSRI or SNRI) rather than two medications for each disorder (ie, an SSRI or SNRI + benzodiazepine). Benzodiazepine medications are not the first line treatment for generalized anxiety disorder. While the advantage of using a benzodiazepine is that its' effect is immediate, there are risks of dependence and exposure to the infant via breast milk.^{53–54} If antidepressant medication and therapy are not effective for anxiety, consultation with a mental health professional who can prescribe and manage medications is warranted.

There are very few published cases of venlafaxine and breastfeeding and only one controlled study that included breastfeeding women who were taking a variety of antidepressants

which included SSRIs and venlafaxine.^{47,52} Within this small literature, venlafaxine has been detected in some but not all infants. More commonly, the metabolite of venlafaxine, O-desmethylvenlafaxine, is detected in infant serum. While no adverse events have been associated with the medication and two cases of infants exposed to venlafaxine were found to have no developmental abnormalities at one year of age, there is too little evidence to suggest safety for the infant. Instead, the provider must discuss what is known and unknown about the risks of the medication in breastfeeding and weight these against the risks of untreated illness and benefits of breastfeeding.

If the patient had a strong preference for bupropion or if she was smoking, bupropion would be preferable to venlafaxine. Bupropion is often favored by patients as the medication is not associated with weight gain or sexual dysfunction. The medication is also effective for smoking cessation which is important for both mother and infant health. There are multiple single cases and one cohort study published in nursing mothers taking bupropion.^{47,52} In one study of 2 cases, infant serum levels of bupropion were undetected and no adverse events were reported. Similarly, in a study of bupropion for postpartum depression, two mothers were breastfeeding and no adverse events were reported. In one case, a six-month-old infant experienced a seizure after four days of the mother's treatment with bupropion, however no laboratory confirmation of mother or infant exposure to the medication was obtained. In a study of 10 healthy postpartum female volunteers, bupropion and its metabolites were measured in breast milk and infant exposure was estimated. Low levels of bupropion and its metabolites, hydroxybupropion, erythrohydrobupropion, threohydrobupropion were detected in breastmilk and infant exposure was estimated to be 2% of the standard maternal dose on a molar basis. While no adverse events were reported by the mothers in this study, there is too little evidence to suggest safety for the infant. Again, the patient and provider must weight this information against the risks of the women's untreated illness and benefits of breastfeeding.

A similar rationale for the use of other medications such as fluoxetine, citalopram and escitalopram as described above would be applied to a similar case of a breastfeeding woman with moderate to severe peripartum depression and prior poor response to sertraline or paroxetine. Comparatively, there is less systematic study of fluoxetine, citalopram and escitalopram in breastfeeding compared to sertraline or paroxetine.^{10,47,52,55} Infant serum levels of citalopram and fluoxetine have been shown to exceed the recommended 10% of maternal level in some, but not all cases.^{47,52} The use of these medications however may be warranted if a woman has a prior good response to these medications and is unable to tolerate or has not responded well to sertraline or paroxetine. Further research is needed however, including larger samples and long-term follow-up of infants exposed to these medications via breastfeeding with control for maternal depression. Other medications that have even less systematic study in breastfeeding women include mirtazapine (Remeron) and duloxetine (Cymbalta).¹⁰ Again, these medications would only be used if a woman had a prior favorable response to one of these medications and a history of poor response to a better studied medication. Patients should be advised that at this time data are not available to guide treatment decisions with these agents.

It is important to note, that many women may experience increased anxiety when starting any antidepressant medication. Thus medications should be started at a low dose and increased slowly. Some women may require a low dose benzodiazepine during the initiation of an antidepressant which can then be tapered once the medication is tolerated (~2–3 weeks).^{48–50} This can be particularly helpful for women with significant sleep disruption. Family support and/or use of a doula or night nurse if finances allow is critical at this time to allow adequate sleep.

Another effective treatment option that may be attractive for women with moderate to severe depression who do not wish to take medications while breastfeeding include brain stimulation treatment modalities such as electroconvulsive therapy (ECT) or repetitive transcranial magnetic stimulation (rTMS).^{56,57} These modalities would only be recommended in consultation with a psychiatrist as they require specialized equipment and training. Further, ECT is normally reserved for severe cases of peripartum depression that have not responded to pharmacotherapy or in cases of postpartum psychosis.⁵⁶

In complex cases of depression with suicidal or homicidal ideation, consultation with a mental health professional is also imperative. Practitioners should inquire about suicidal and homicidal ideation in all postpartum women. Commonly employed questions include “Have you recently had thoughts about harming yourself or your baby?” or “Have you recently had thoughts that you or your baby would be better off dead?” Positive endorsement of these questions would immediately be followed by questions related to the individual’s intent, desire or plan to harm herself or her baby, access to lethal means as well as an assessment of historical and proximal risk factors for suicide and homicide. While it is very difficult to predict a suicide attempt or completion, individuals are at high risk if they have a desire, intent, or plan to end their life and have access to lethal means such as prescription medications or firearms.^{29,58} Historical risk factors include previous suicide attempts or a family history of suicide, history of impulsive behaviors, or hospitalization or violence within the last year.⁵⁸ Proximal risk factors include social isolation, current drug abuse, acute psychosis and recent family or romantic conflicts or legal problems.⁵⁸ Women at high risk should be immediately evaluated by a mental health professional or taken to an emergency room for psychiatric evaluation. Arrangements should be made for emergency transport by calling 911. Private or public transportation or walking to the emergency room are not acceptable options, due to the risk of not following through with the plan.²⁹ The woman’s partner and/or family members should also be involved immediately; this can be helpful in devising a safety plan which includes a combination of restricting access either by removing lethal means for the home and/or ensuring family members are with the patient at all times. Women should be informed that the purpose of the emergency room evaluation is to provide immediate access to psychiatric evaluation as waiting for an outpatient appointment can take weeks. Women can be reassured that being evaluated in the psychiatric emergency room does not necessarily mean they will be admitted to the hospital.

Evaluation of homicidal ideation should also begin with an understanding of the desire, intent and plan to harm anyone including the infant as well as access to lethal means.²⁹ If a woman is experiencing an intrusive, unwanted thought of harming her child that is upsetting or distressing because she has no intent or desire to harm her child, postpartum obsessive

compulsive disorder (OCD) should be considered in the differential diagnosis and a referral to a mental health professional for medication and therapy is warranted.⁵⁹ Review of OCD is beyond the scope of this article, but we refer readers to online resources related to screening and more information about OCD (See Appendix 1). If the homicidal ideation is related to the idea that their child would be better off dead (ie, living would be far more painful thus death of the child is considered a merciful act), an acute psychotic disorder is considered in the differential diagnosis and psychiatric evaluation should be obtained immediately.^{29,60} Other risk factors reported to increase the risk of mother's harming their children include younger age, little or no prenatal care, no plans for care of the infant and an underlying mental illness.^{60,61} If a mental health provider is not imminently available to evaluate the women who has a desire, intent or plan to harm the child, the patient should be taken to an emergency room for evaluation and the partner and/or family members should be involved immediately to assist with childcare and safety plan.

CONCLUSION

Women with mild-to-moderate depressive symptoms in the postpartum period should be offered psychotherapy as a first line treatment option. Therapies with the largest evidence base include IPT and CBT. Among women with moderate to severe depression, antidepressant medication and therapy are recommended. Personal history of a prior response to an antidepressant or family history can be used to guide selection of an antidepressant medication for women who are not breastfeeding. If a personal or family history is unavailable, sertraline and citalopram have been shown to be most effective and well tolerated compared to other SSRIs. While pooled case reports and small controlled studies have demonstrated undetectable infant serum levels and no short-term adverse events in infants of mothers breastfeeding while taking sertraline and paroxetine, further research is needed including larger samples and long-term follow-up of infants exposed to antidepressants via breastfeeding, making sure to control for maternal depression. Pharmacological treatment recommendations must include discussion with the patient regarding the benefits of breastfeeding, risks of antidepressants use during lactation and risk of untreated illness. Among severe cases of peripartum depression with suicidal or homicidal ideation or depression with psychosis referral to a mental health professional is warranted.

Peripartum depression is a serious health concern. Unfortunately treatment research is limited by very few controlled studies and small samples sizes. Much work is still needed to better understand which treatments are safe, preferable and most effective for the treatment of postpartum depression.

Acknowledgments

This publication was supported by the South Carolina Clinical & Translational Research Institute with an academic home at the Medical University of South Carolina CTSA, NIH/NCRR Grant Number UL1RR029882 and NIH/NCATS grant number UL1TR000062. The contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. Further support was also provided by by NIH/ORWH & NICHD (K12 HD055885) career development award, Building Interdisciplinary Research Careers in Women's Health (BIRCWH).

Biographies

Constance Guille is an Assistant Professor at the Medical University of South Carolina in the Department of Psychiatry and Behavioral Sciences.

Roger Newman is a Professor at the Medical University of South Carolina in the Department of Obstetrics and Gynecology.

Leah D. Fryml is a third year medical student at the Medical University of South Carolina.

Clay K. Lifton is a third year medical student at the Medical University of South Carolina.

C. Neill Epperson is an Associate Professor at the University of Pennsylvania.

REFERENCES

1. Epperson CN. Postpartum major depression: Detection and treatment. *American Family Physician*. 1999; 59(8):2247–2254. [PubMed: 10221309]
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed.. Washington, DC: Author; 2013. text rev
3. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression FA systematic review of prevalence and incidence. *Obstetr Gynecol*. 2005; 106:1071–1083.
4. Logsdon MC, Wisner KL, Pinto-Foltz MD. The impact of peripartum depression on mothering. *J Obst, Gyn, and Neo Nurs*. 2006; 35:652–658.
5. Logsdon MC, Usui W. Psychosocial predictors of peripartum depression in diverse groups of women. *Western Jnl of Nurs Res*. 2001; 23:563–574.
6. Beck CT. The effects of peripartum depression on child development: A meta-analysis. *Arch Psych Nursing*. 1998; 12:12–20.
7. Hay DF, Pawlby S, Angold A, Harold GT, Sharp D. Pathways to violence in the children of mothers who were depressed postpartum. *Develop Psych*. 2003; 39:1083–1094.
8. Murray L, Fiori-Cowley A, Hooper R, et al. The impact of postnatal depression and associated adversity on early mother-infant interactions and later infant outcome. *Child Dev*. 1996; 67(5): 2512–2526. [PubMed: 9022253]
9. Nulman I, Koren G, Rovet J, et al. Exposure to Venlafaxine, Selective Serotonin Reuptake Inhibitors, or Untreated Maternal Depression. *American Journal of Psychiatry*. 2012; 169(11):1165–1174. [PubMed: 23128923]
10. Freeman MP, Joffe H, Cohen LS. Postpartum depression: Help patients find the right treatment. *Current psychiatry*. 2012; 11(11):14–21.
11. Evins GG, Theofrastous JP, Galvin SL. Postpartum depression: a comparison of screening and routine clinical evaluation. *Am J Obstet Gynecol*. 2000; 182(5):1080–1082. [PubMed: 10819833]
12. Flynn HA, O'Mahen HA, Massey L, et al. The impact of a brief obstetrics clinic-based intervention on treatment use for perinatal depression. *J Women's Health*. 2006; 15(10):1195–1204.
13. Yonkers KA, Smith MV, Lin H, et al. Depression screening of perinatal women: an evaluation of the healthy start depression initiative. *Psychiatr Serv*. 2009; 60(3):322–328. [PubMed: 19252044]
14. Van Schaik DJ, Klijn AF, van Hout HP, et al. Patients' preferences in the treatment of depressive disorder in primary care. *Gen Hosp Psychiatry*. 2004; 26(3):184–189. [PubMed: 15121346]
15. Boath E, Bradley E, Henshaw C. Women's views of antidepressants in the treatment of postnatal depression. *J Psychosom Obstet Gynaecol*. 2004; 25(3–4):221–233. [PubMed: 15715021]
16. Pearlstein TB, Zlotnick C, Battle CL, et al. Patient choice of treatment for postpartum depression: a pilot study. *Arch Women's Ment Health*. 2006; 9(6):303–308. [PubMed: 16932988]

17. Austin MP, Hadzi-Pavlovic D, Priest SR, et al. Depressive and anxiety disorders in the postpartum period: how prevalent are they and can we improve their detection? *Arch Women's Ment Health*. 2010; 13(5):395–401. [PubMed: 20232218]
18. Viguera AC, Tondo L, Koukopoulos AE, Reginaldi D, Lepri B, Baldessarini RJ. Episodes of Mood Disorders in 2,252 Pregnancies and Postpartum Periods. *Am J Psychiatry*. 2011; 168(11):1179–1185. [PubMed: 21799064]
19. De Groot L, Abalovich M, Alexander EK, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2012; 97(8):2543–2565. [PubMed: 22869843]
20. Beard JL, Hendricks MK, Perez EM, Murray-Kolb L, Berg A, Vernon-Feagans L, Irlam J, Isaacs W, Sive A, Tomlinson. Maternal Iron Deficiency Anemia Affects Postpartum Emotions and Cognition. *J Nutr*. 2005; 135(2):267–272. [PubMed: 15671224]
21. Zlotnick C, Johnson SL, Miller IW, et al. Peripartum depression in women receiving public assistance: pilot study of an interpersonal-therapy-oriented group intervention. *Am J Psychiatry*. 2001; 158(4):638–640. [PubMed: 11282702]
22. Klier CM, Muzik M, Rosenblum KL, et al. Interpersonal psychotherapy adapted for the group setting in the treatment of postpartum depression. *J Psychother Pract Res*. 2001; 10(2):124–131. [PubMed: 11264336]
23. Stuart S, O'Hara MW, Gorman LL. The prevention and psychotherapeutic treatment of postpartum depression. *Arch Women's Ment Health*. 2003; 6(suppl 2):S57–S69. [PubMed: 14615924]
24. Markowitz JC, Weissman MM. Interpersonal psychotherapy: Principles and applications. *World Psychiatry*. 2004; 3(3):136–139. [PubMed: 16633477]
25. Beck AT. The past and future of cognitive therapy. *J Psychother Pract Res*. 1997; 6(4):276–284. [PubMed: 9292441]
26. Sockol LE, Epperson CN, Barber JP. A Meta-Analysis of Treatments for Perinatal Depression. *Clinical Psychology Review*. 2011; 31:839–849. [PubMed: 21545782]
27. Dennis CL, Chung-Lee L. Peripartum depression help-seeking barriers and maternal treatment preferences: a qualitative systematic review. *Birth*. 2006; 33(4):323–331. [PubMed: 17150072]
28. Gjerdingen DK, Yawn BP. Peripartum depression screening: importance, methods, barriers, and recommendations for practice. *J Am Board Fam Med*. 2007; 20(3):280–288. [PubMed: 17478661]
29. Hackley B, Sharma C, Kedzior A, Sreenivasan S. Managing mental health conditions in primary care settings. *J Midwifery Women's Health*. 2010; 55(1):9–19. [PubMed: 20129225]
30. Ruskin PE, Silver-Aylaian M, Kling M, et al. Treatment Outcomes in Depression: Comparison of Remote Treatment Through Telepsychiatry to In-Person Treatment. *Am J Psychiatry*. 2004; 161:1471–1476. [PubMed: 15285975]
31. Ugarriza DN, Schmidt L. Telecare for women with postpartum depression. *Journal of Psychosocial Nursing and Mental Health*. 2006; 44(1):37–45.
32. Maloni JA, Przeworski A, Damato EG. Web recruitment and internet use and preferences reported by women with peripartum depression after pregnancy complications. *Arch Psychiatr Nurs*. 2013; 27(2):90–95. [PubMed: 23540519]
33. Appleby L, Warner R, Whitton A, et al. A controlled study of fluoxetine and cognitive-behavioral counseling in the treatment of postnatal depression. *BMJ*. 1997; 314(7085):932–936. [PubMed: 9099116]
34. Yonkers KA, Lin H, Howell HB, et al. Pharmacologic treatment of postpartum women with new-onset major depressive disorder: a randomized controlled trial with paroxetine. *J Clin Psychiatry*. 2008; 69(4):659–665. [PubMed: 18363420]
35. Bloch M, Meiboom H, Lorberblatt M, Bluvstein I, Aharonov I, Schreiber S. The effect of sertraline add-on to brief dynamic psychotherapy for the treatment of postpartum depression: a randomized, double-blind, placebo-controlled study. *J Clin Psychiatry*. 2012; 73(2):235–241. [PubMed: 22401479]
36. 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. [PubMed: 16855451]

37. Misri S, Reebye P, Corral M, et al. The use of paroxetine and cognitive-behavioral therapy in peripartum depression and anxiety: a randomized controlled trial. *J Clin Psychiatry*. 2004; 65(9): 1236–1241. [PubMed: 15367052]
38. Stowe ZN, Casarella J, Landry J, et al. Sertraline in the treatment of women with postpartum major depression. *Depression*. 1995; 3(1–2):49–55.
39. Cohen LS, Viguera AC, Bouffard SM, et al. Venlafaxine in the treatment of postpartum depression. *J Clin Psychiatry*. 2001; 62(8):592–596. [PubMed: 11561929]
40. Suri R, Burt VK, Altshuler LL, et al. Fluvoxamine for postpartum depression. *Am J Psychiatry*. 2001; 158(10):1739–1740. [PubMed: 11579021]
41. Nonacs RM, Soares CN, Viguera AC, et al. Bupropion SR for the treatment of postpartum depression: a pilot study. *Int J Neuropsychopharmacol*. 2005; 8(3):445–449. [PubMed: 15817137]
42. Freeman MP, Joffe H, Cohen LS. An open-label trial of escitalopram for postpartum depression: considerations for research. *Current Psychiatry*. 2012; 11:E4–E5.
43. Cipriani A, Santilli C, Furukawa TA, et al. Escitalopram versus other antidepressive agents for depression. *Cochrane Database Syst Rev*. 2009; 15(2) CD006532.
44. World Health Organization. *Infant and Young Child Feeding*. Geneva, Switzerland: World Health Organization; 2003. Available at: <http://www.who.int/en/> [Accessed on: January 26, 2009]
45. Gartner LM, Morton J, Lawrence RA, et al. American Academy of Pediatrics Policy statement: breastfeeding and the use of human milk. *Pediatrics*. 2005; 115:496–506. [PubMed: 15687461]
46. Goldman AS, Hopkinson JM, Rassin DK. Benefits and risks of breastfeeding. *Adv Pediatr*. 2007; 25:275–304. [PubMed: 17918475]
47. Di Scalea TL, Wisner KL. Antidepressant Medication Use During Breastfeeding. *Clinical Obstetrics and Gynecology*. 2009; 52(3):483–497. [PubMed: 19661763]
48. Chaudron LH, Giannandrea SAM. The Academy of Breastfeeding Medicine Protocol Committee. ABM Clinical Protocol #18: Use of antidepressants in nursing mothers. *BreastfeedMed*. 2008; 3:44–52.
49. ACOG Practice Bulletin Clinical Management Guidelines for Obstetrician–Gynecologists: Use of psychiatric medications during pregnancy and lactation. *Obstet Gynecol*. 2008; 111(92):1001–1020. [PubMed: 18378767]
50. Tomson D, Pilling S, Blake F, et al. National Institute for Clinical Excellence: Antenatal and Postnatal Mental Health: Clinical Management and Service Guidance, Clinical Guideline No. 47.
51. Epperson CN, Ward-O'Brien D, Czarkowski KA, Weiss E, Jatlow P, Anderson GA. Maternal sertraline treatment and serotonin transport in breast-feeding mother-infant pairs. *American Journal of Psychiatry*. 2001; 158(10):1631–1637. [PubMed: 11578995]
52. Weissman AM, Levy BT, Hartz AJ, et al. Pooled analysis of antidepressant levels in lactating mothers, breast milk, and nursing infants. *Am J Psychiatry*. 2004; 161:1066–1078. [PubMed: 15169695]
53. Kelly LE, Poon S, Madadi P, et al. Neonatal benzodiazepines exposure during breastfeeding. *J Pediatr*. 2012; 161(3):448–451. [PubMed: 22504099]
54. Birnbaum CS, Cohen LS, Bailey JW, et al. Serum concentrations of antidepressants and benzodiazepines in nursing infants: A case series. *Pediatrics*. 1999; 104(1):e11. [PubMed: 10390297]
55. Epperson CN, Jatlow P, Czarkowski KA, Anderson G. Maternal fluoxetine treatment in the postpartum period: Effects on platelet serotonin and plasma drug levels in breastfeeding mother-infant pairs. *Pediatrics*. 2003; 112(5):e425–e429. [PubMed: 14595087]
56. Focht A, Kellner C. Electroconvulsive therapy in the treatment of postpartum psychosis. *Journal of ECT*. 2012; 28(1):31–33. [PubMed: 22330704]
57. 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. [PubMed: 23118543]
58. Nock M, Borges G, Bromet E, Cha C, Kessler R, Lee S. Suicide and suicidal behavior. *Epidemiol Rev*. 2008; 30:133–154. [PubMed: 18653727]

59. Hudak R, Wisner K. Diagnosis and the treatment of postpartum obsessions and Compulsions that involve infant harm. *Am J Psychiatry*. 2012; 169:360–363. [PubMed: 22476676]
60. Friedman S, Hrouda D, Holden C, Noffsinger S, Resnick P. Filicide-suicide: Common factors in parents who kill their children and themselves. *J Am Acad Psychiatry Law*. 2005; 33:496–504. [PubMed: 16394226]
61. Borget D, Grace J, Whitehurst L. A review of maternal and paternal filicide. *J Am Acad Psychiatry Law*. 2007; 35:74–82. [PubMed: 17389348]
62. Gentile S. Use of contemporary antidepressants during breastfeeding: a proposal for a specific safety index. *Drug Saf*. 2007; 30:107–121. [PubMed: 17253877]
63. Sie SD, Wennink JMB, Van Driel JJ, et al. Maternal use of SSRIs, SNRIs and NaSSAs: practical recommendations during pregnancy and lactation. *Arch Dis Child Fetal Neonatal Ed*. 2012; 97:F472–F476. [PubMed: 23080479]
64. Lee A, Woo J, Ito S. Frequency of infant adverse events that are associated with citalopram use during breastfeeding. *Am J Obstet Gynecol*. 2004; 190:218–221. [PubMed: 14749663]
65. Franssen EJF, Meijs V, Ettaher F, et al. Citalopram serum and milk levels in mother and infant during lactation. *Ther Drug Monit*. 2006; 28:2–4. [PubMed: 16418683]
66. Schmidt K, Olesen O, Jensen P. Citalopram and breast-feeding: serum concentration and side effects in the infant. *Biol Psychiatry*. 2000; 47:164–165. [PubMed: 10664835]
67. Potts AL, Young KL, Carter BS, et al. Necrotizing enterocolitis associated with in utero and breast milk exposure to the selective serotonin reuptake inhibitor, escitalopram. *J Perinatol*. 2007; 27:120–122. [PubMed: 17262045]
68. Hendrick V, Stowe ZN, Altshuler LL, Mintz J, Hwang S, Hostetter A, Suri R, Leight K, Fukuchi A. Fluoxetine and norfluoxetine concentrations in nursing infants and breast milk. *Biol Psychiatry*. 2001; 50:775–782. [PubMed: 11720696]
69. Chaudron LH, Schoenecker CJ. Bupropion and breastfeeding: a case of a possible infant seizure. *J Clin Psychiatry*. 2004; 65:881–882. [PubMed: 15291673]

Appendix 1

Resource	Description	Link
The Macarthur Initiative on Depression and Primary Care	This site contains a depression toolkit intended to help primary care clinicians recognize and manage depression	http://www.depression-primarycare.org
Edinburgh Postnatal Depression Scale	This is a commonly employed Screening tool for postpartum depression.	http://www.fresno.ucsf.edu/pediatrics/downloads/edinburghscale
International OCD Foundation	This site contains Information about Postpartum OCD	www.ocfoundation.org/EO_Postpartum.aspx
OCD rating scales	This site contains a commonly employed	http://www.mssm.edu/research/centers/center-of-excellence-for-ocd

Resource	Description	Link
	screening tool for OCD	
Postpartum Support International	This site Contains Educational Information About Peripartum Depression and referral information to support groups	http://www.postpartum.net/

Abbreviations: OCD: obsessive-compulsive disorder

Quick Points

- Psychotherapy is the first line treatment option for women with mild to moderate peripartum depression.
- Psychotherapy and antidepressant medication are the first line treatment option for women with moderate to severe peripartum depression. The benefits of breastfeeding, the risks of untreated illness and the risks and benefits of antidepressant medication use during breastfeeding need to be carefully weighted.
- Comorbid anxiety symptoms and/or disorders commonly occur during the postpartum period. Treatment of both depression and anxiety are critical to improving mental health.
- 50% of women with Bipolar Disorder will experience a mood episode (primarily depression) in the postpartum period; thus it is important to ask about prior episodes of mania or hypomania as treatment for Bipolar Depression differs from treatment of Major Depression.
- Peripartum depression with suicidal or homicidal intent or plan as well as peripartum depression with psychotic features is a psychiatric emergency. Immediate evaluation by a mental health professional is warranted.

Table 1

Considerations for the Diagnosis of Major Depression with Postpartum Onset

DSM-V Diagnosis of Major Depression: 5 or more symptoms (below) with at least 1 symptom being #1 or #2, present for most of the day, nearly every day for at least 2 weeks.	Occurrence in the Postpartum Period	Suggestive of Postpartum Depression
1) Depressed Mood	Common in 'baby blues': typically peaks four to five days after delivery, may last hours to days and resolve by 2 weeks	Sad or depressed mood that persists daily for at least 2 weeks
2) Lack of Pleasure or Interest in Activities	Uncommon after childbirth	Inability to derive pleasure from experiences or lack of interest in things that are normally enjoyable.
3) Sleep Disturbance	Common due to newborn care	Inability to rest or sleep when baby is sleeping or inability to care for baby because of hypersomnia.
4) Loss of Energy	Common due to sleep deprivation	Continues despite adequate sleep or napping.
5) Agitation or Retardation	Uncommon after childbirth	Moving or speaking so slowly that others have noticed or being so fidgety or restless that one is unable to sit still.
6) Excessive feelings of guilt or worthlessness	Uncommon after childbirth	Feeling badly about ones' self- feeling like a failure or have let self or family down.
7) Diminished concentration, or indecisiveness	Common due to sleep deprivation	Frequently losing train of thought or inability to make decisions
8) Frequent thoughts of death or suicide	Uncommon after childbirth	Thoughts of 'I wish I would not wake up' or 'my baby would be better off without me' or intent, desire or plans to end ones' life.

Table 2**Considerations for Antidepressant Use During Breastfeeding**

Medication	Suggested Use
Sertraline (Zoloft)	Approximate number of mother/infants evaluated is 146 with low to undetectable levels in infants and no reports of short-term adverse events. ^{42, 47, 62–63} The literature consistently cites a preference for using this medication during lactation compared to other SSRIs. ^{42, 47, 62–63}
Paroxetine (Paxil)	Approximate number of mother/infants evaluated is 131 and low to undetectable levels in infants and no reports of short-term adverse events. ^{42, 47, 62–63} The literature consistently cites a preference for using this medication during lactation compared to other SSRIs. ^{42, 47, 62–63}
Fluvoxamine (Luvox)	Approximate number of mother/infants evaluated is 14 with low to undetectable levels in infants and no reports of short-term adverse events. ^{42, 47, 62–63} Given the paucity of data, this medication can be considered in moderate to severe depression or OCD, if unable to use other SSRIs or patient has a history of a good response to the medication. ^{10, 59, 63}
Citalopram (Celexa)	Approximate number of mother/infants evaluated is 76. 1 case report of an infant with 'uneasy sleep' which resolved with cutting the dose in half ⁶⁴ ; 1 case report of an infant with irregular breathing, hypotonia and sleep disruption ⁶⁵ ; 1 cohort study with 2 infants with decreased feeding, colic and irritability. ⁶⁶ Low levels of exposure have been observed. Given the adverse effects associated with this medication, use can be considered in moderate to severe depression if unable to use other SSRIs and patient has a history of a good response to the medication. ^{10, 42, 47, 63}
Escitalopram (Lexapro)	Approximate number of mother/infants evaluated is 12. 1 case report of an infant with necrotizing enterocolitis on postnatal day 5. ⁶⁷ Low levels of exposure have been observed. Given the paucity of data and adverse outcome, this medication can be considered in moderate to severe depression if unable to use other SSRIs and patient has a history of a good response to the medication. ^{10, 42, 47, 63}
Fluoxetine (Prozac)	Approximate number of mother/infants evaluated is 200. Caution should be taken with fluoxetine (Prozac) as infant levels are higher than other SSRIs. ^{10, 42, 47, 62–63} Cohort study identified possible seizure in 1 infant which occurred twice after drug was stopped and uncontrolled crying, irritability and poor feeding in 2 infants. ⁶⁸ Given the higher infant drug levels and adverse effects, this medication can be considered in moderate to severe depression if unable to use other SSRIs and patient has a history of a good response to the medication. ^{10, 42, 47, 63}
Venlafaxine (Effexor)	Approximate number of mother/infants evaluated is 15. Low levels of metabolite, desvenlafaxine, are often detected in infant serum and no adverse effects have been reported. ^{42, 47, 62–63} Given the paucity of data, this medication can be considered in moderate to severe depression if unable to use other SSRIs and patient has a history of a good response to the medication. ¹⁰
Bupropion (Wellbutrin)	Approximate number of mother/infants evaluated is 16. Low levels of bupropion and its metabolites, hydroxybupropion, erythrohydrobupropion, threohydrobupropion, are detected in breastmilk and infant. 1 case report of possible infant seizure ⁶⁹ but no other adverse events reported. ^{42, 47, 62–63} Given the paucity of data and adverse outcome, this medication can be considered in moderate to severe depression, especially if smoking, if unable to use other SSRIs and patient has a history of a good response to the medication. ¹⁰
Mirtazapine (Remeron)	Approximate number of mother/infants evaluated is 10. This medication can be considered in moderate-to-severe depression and prior favorable response, but patient's need to be advised that data are unavailable to guide decision. ^{10, 42, 47}
Duloxetine (Cymbalta)	Approximate number of mother/infants evaluated is 6. This medication can be considered in moderate-to-severe depression and prior favorable response, but patient's need to be advised that data are unavailable to guide decision. ^{10, 42, 47}

Abbreviations: SSRIs: selective serotonin reuptake inhibitors; OCD: obsessive-compulsive disorder