

## REVIEW

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# Peripartum depression: Early recognition improves outcomes

## ABSTRACT

Depression is highly prevalent in women of childbearing age, especially during the postpartum period. Early recognition and treatment improve outcomes for mother, developing fetus, and infant. Caution is warranted when prescribing antidepressants to pregnant and breastfeeding mothers, but evidence is mounting that the risks of untreated maternal depression outweigh those of pharmacologic treatment for it.

## KEY POINTS

Depression occurs in up to 13% of pregnant women, a prevalence similar to that in nonpregnant women, but the incidence rises postpartum.

Depressed pregnant women are more likely to engage in behaviors that pose a risk to the fetus.

Depression in pregnancy is associated with adverse pregnancy outcomes such as preterm birth, low birth weight, gestational diabetes, and hypertensive disorders of pregnancy.

Risk factors for depression in pregnancy include past episodes of depression, poor social support, unwanted pregnancy, and domestic violence.

**C**ONTRARY TO COMMON BELIEF, pregnancy does not confer protection against depression.<sup>1,2</sup> In fact, pregnant women are just as likely as nonpregnant women to become or remain depressed, and up to 12.7% of pregnant women meet criteria for depression.<sup>1</sup>

In the postpartum period, women are particularly vulnerable to a major depressive episode, whether a first episode or a recurrence. The estimated prevalence of a depressive episode in the first 3 postpartum months is 19.2%,<sup>2</sup> making postpartum depression the most common complication of childbearing.<sup>2</sup> At the same time, peripartum depression remains largely underrecognized and undertreated.<sup>3</sup>

As evidence mounts regarding the deleterious impact of untreated mental illness on the mother, the developing fetus, and the infant, early detection and intervention for peripartum depression are paramount.<sup>3</sup>

## ■ DEPRESSION DURING PREGNANCY: SIGNIFICANT CONSEQUENCES

Although the rates of depression in pregnant and nonpregnant women are similar, depression in pregnancy carries additional significant consequences. Further, many depressed pregnant women believe their depression will lift once their baby is born, though it is well documented that depression during pregnancy is the strongest predictor of postpartum depression and that if left untreated it can be devastating for mother, infant, and family.<sup>4</sup>

Compared with nondepressed pregnant women, depressed pregnant women have poorer overall health status,<sup>5</sup> are more likely to engage in behaviors that pose risk to the developing fetus such as smoking,<sup>5</sup> alcohol con-

sumption, and substance use,<sup>6</sup> and have poor nutrition and inadequate weight gain.<sup>7,8</sup>

Pregnant women who are depressed and are also experiencing domestic violence are especially at risk for poor prenatal care as they tend to miss more prenatal appointments.<sup>9</sup> Evidence also suggests that depressed pregnant women are less attached to the fetus and more likely to have elective terminations.<sup>10,11</sup>

Depression in pregnancy is associated with higher rates of adverse pregnancy outcomes such as preterm birth, low birth weight, operative delivery, and longer predelivery hospital stay.<sup>3,12</sup> Depression and anxiety during pregnancy have been associated with prenatal hypertension,<sup>13</sup> gestational diabetes,<sup>14</sup> preeclampsia,<sup>15</sup> and HELLP syndrome (ie, hemolysis, elevated liver enzymes, and low platelet count).<sup>15</sup> Depression and anxiety during pregnancy are associated with subsequent poorer infant attachment<sup>16,17</sup> and an overall unfavorable impact on infant and child development.<sup>18</sup>

Risk factors for depression during pregnancy include past episodes of depression, current anxiety, poor social support, unintended pregnancy, life stress, being single, domestic violence, and being on Medicaid.<sup>19</sup>

Undoubtedly the most devastating consequence of severe depression during pregnancy is suicide. Rates of suicide are lower in peripartum women,<sup>20</sup> but when suicide does occur, pregnant women tend to use more violent means than nonpregnant women. Pregnant adolescents represent a particularly high-risk group.<sup>21</sup>

## ■ POSTPARTUM DEPRESSION

Postpartum depression is the most common complication of childbearing. Although the precise pathogenesis is undetermined, there is converging evidence of a subset of women particularly sensitive to dramatic fluctuations in levels of estradiol and progesterone that occur during childbirth.<sup>22,23</sup> There is also evidence that dysregulation of the hypothalamic-pituitary-adrenal axis contributes to the development of postpartum depression in certain women.<sup>24</sup> Further, women who have depression or anxiety during pregnancy are much more likely to experience postpartum depression than those who are not symptomatic during pregnancy.<sup>4</sup> A history of peripartum depression or other lifetime depres-

## The primary care management of peripartum depression

A general approach to treating peripartum depression in the primary care office setting includes the following:

- Take a thorough history, including details on the patient's social supports.
- Offer psychotherapy and alternative or complementary treatments, either alone or in combination with drug therapy.
- Discuss the risks of peripartum depression and the risks and benefits of treatment.
- Discuss any preconceptions the patient may have about medication changes during pregnancy.
- Counsel women with a history of severe depression to be alert to signs that a depressive episode is developing and to seek treatment if symptoms last for 2 weeks or longer or if there is significant impairment in functioning.
- Do not stop antidepressants abruptly; if an antidepressant must be discontinued, taper the dose.
- Prescribe the lowest effective dose.
- Advise the patient that it is unlikely that she will benefit from tapering and discontinuing medication before delivery because of the risk of recurrence postpartum.
- Advise women who are breastfeeding that the infant's exposure to the medications through breast milk is minimal, so antidepressant therapy should not be discontinued.

sive episodes, poverty, conflict with a primary partner, poor social support, stressful life events, and low self-esteem are strongly associated with postpartum depression.<sup>25</sup>

When unrecognized and untreated, postpartum depression can have profound and persistent effects on the mother and the developing infant.<sup>18,26</sup> Mothers with postpartum depression are much more likely than mothers without depression to have impaired bonding,<sup>27</sup> to be less responsive to their infant's needs,<sup>17</sup> and to be more likely to miss well-baby checkups.<sup>28</sup>

Postpartum depression's effects on maternal-infant interactions can include maternal withdrawal, disengagement, intrusion, and hostility and can lead to long-term effects on child development, including poor cognitive functioning, emotional maladjustment, and behavioral inhibition.<sup>29,30</sup> Infants and

TABLE 1

### Differentiating 'postpartum blues' from major depressive disorder

Postpartum blues	Major depressive disorder
Can occur in up to 75% of women	Occurs in up to 20% of women
Resolves by day 10 postpartum	Peaks at 3 months postpartum but can extend to up to 12 months
Typical symptoms include mood lability, tearfulness, irritability, confusion, and fatigue	Symptoms include low mood or loss of interest or pleasure in normally pleasurable activities for at least 2 weeks in addition to other diagnostic criteria for major depressive disorder
Responds well to support, reassurance, and adequate sleep	Treatment often involves both pharmacologic and nonpharmacologic therapy

children of mothers with untreated postpartum depression have been shown to exhibit a higher incidence of colic, excessive crying, sleep problems, and irritability.<sup>31,32</sup> Women with postpartum depression may be less likely to initiate or maintain breastfeeding, and depressive symptoms have been noted to precede the discontinuation of breastfeeding.<sup>33–35</sup>

#### Risk factors for postpartum depression

Characteristics to look for in the prenatal care of pregnant women include the following:

- Depression during pregnancy
- History of postpartum or other depressive episode
- Poverty
- Conflict with primary partner
- Poor social support
- Low self-esteem
- Single status.

#### ■ DIFFERENTIATING 'POSTPARTUM BLUES' FROM MAJOR DEPRESSION

Primary care providers are often the first point of contact for depressed women. The diagnosis of major depression in pregnant and postpartum women is challenging because of changes in sleep, appetite, and energy brought on by pregnancy, complications of delivery, and demands of caring for a newborn.<sup>36</sup> Many pregnant and postpartum women are reluctant to disclose their symptoms due to a sense of shame and guilt for being depressed during a time in their life that society commonly regards as joyful, and this contributes to under-detection.

In the first few days postpartum, fatigue, emotionality, irritability, and worry over the infant's well-being affect up to 75% of women. This period, typically referred to as the "baby blues" or "postpartum blues," is not considered a disorder and responds well to support, reassurance, and adequate sleep, and it typically resolves within 2 weeks.<sup>37,38</sup> **Table 1** lists features that help distinguish postpartum blues from major depression.

#### Signs of major depressive disorder

Major depressive disorder is a serious and disabling condition. To meet criteria for major depressive disorder, women must report depressed mood and loss of interest or pleasure in normally pleasurable activities for at least 2 weeks. Completing the symptom profile, at least 5 of the following must be present: sleep disturbance (insomnia or hypersomnia), lack of energy, feelings of worthlessness or low self-esteem, guilt, difficulty concentrating, indecisiveness, psychomotor retardation or agitation, and thoughts of suicide or death.

The *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) recognizes that postpartum depression commonly begins during pregnancy, and now uses "peripartum onset" as the specifier for major depressive disorder that occurs during pregnancy, postpartum, or both.<sup>39</sup> Other hallmark symptoms with peripartum onset include a lack of interest in or attachment to the pregnancy or infant, and anxiety and worry often accompanied by intrusive, unwanted thoughts of harm befalling the infant.<sup>40</sup>

Untreated postpartum depression is associated with colic, excessive crying, sleep problems, and irritability

## Postpartum psychosis

Postpartum psychosis is a far less common presentation, occurring in 1 to 2 per 1,000 births, but it constitutes a psychiatric emergency requiring immediate referral to a psychiatric care setting. Women at highest risk are those with a personal or family history of bipolar disorder.

The clinical presentation is most commonly characterized by confusion, agitation, hallucinations, delusional beliefs, and disorientation. Suicide and infanticide, while rare, are more likely to occur in the context of a psychotic episode.<sup>41</sup>

## ■ SCREENING RECOMMENDATIONS

Screening for depression is routine in primary care settings and is no less important for peripartum women.

In 2016, the US Preventive Services Task Force issued a recommendation that all pregnant and postpartum women be screened for depression,<sup>42</sup> highlighting the need for all medical providers to be alert to the potentially serious consequences of unrecognized and untreated maternal psychiatric illness.

The American College of Obstetricians and Gynecologists (ACOG) recommends screening for depression and anxiety at least once during the peripartum period,<sup>43</sup> and the American Academy of Pediatrics recommends screening mothers for depression at the 1-, 2-, and 4-month well-baby visits.<sup>44</sup>

The peripartum period is associated with changes in sleep, appetite, and energy levels, but these are also typical of depression. Taking this into account, the Edinburgh Postnatal Depression Scale (EPDS) was developed to screen for depression specifically in this population.<sup>45</sup> The EPDS is a validated and widely used 10-item self-reporting questionnaire with a high degree of sensitivity and specificity; it is easily administered and quickly scored. A cutoff score of 13 (of a maximum of 30) is considered indicative of depressed mood and signals the need for further assessment.

ACOG, the American Academy of Pediatrics, and the US Preventive Services Task Force recommend a standardized validated tool and cite both the EPDS (<https://psychology-tools.com/epds/>) and the Patient Health Questionnaire-9 (PHQ-9) (Figure 1)

as appropriate to screen for peripartum depression.<sup>42-44</sup> Primary care providers tend to be most familiar with the PHQ-9, a highly sensitive and specific 9-item depression screen that has been validated in primary care and obstetric clinic patients.<sup>46</sup> A score on the PHQ-9 ranging from 5 to 10 indicates mild depression, 10 to 14 moderate depression, 15 to 19 moderate to severe depression, and greater than 19 severe depression.

## ■ CLINICAL MANAGEMENT

### Many women prefer nondrug therapy

The gold standard treatment for moderate to severe major depressive disorder is psychotherapy plus pharmacotherapy. Yet many peripartum women voice concerns about exposure to pharmacologic treatment, and studies have shown that many women prefer nonpharmacologic intervention.<sup>47</sup>

Evidence-based psychotherapies that have demonstrated efficacy in peripartum women include cognitive behavioral therapy<sup>48</sup> and interpersonal psychotherapy when administered by a psychotherapist trained in these treatments. Pregnant and breastfeeding women often express preference for psychotherapy and complementary and alternative treatments as a means of avoiding fetal and infant exposure to antidepressants.<sup>47</sup>

For mild to moderate depression, complementary therapies such as exercise, yoga, bright light therapy, and acupuncture have shown efficacy and can be used alone or adjunctively.<sup>49</sup> Because a poor marital relationship is consistently associated with peripartum depression,<sup>25</sup> primary care physicians who routinely address social support and screen for family conflict are well positioned to detect this significant correlate and to recommend marital or family therapy as a primary or adjunctive treatment.

### When to consider drug therapy

The decision to recommend drug therapy must be individualized and based on the severity of symptoms, functional impairment, number and frequency of depressive episodes, history of response to medications, and the preferences of the patient, with the recognition that no decision is risk-free and that antidepressants enter the amniotic fluid, so fetal exposure is

**ACOG recommends screening for depression and anxiety at least once during the peripartum period**

## Patient Health Questionnaire-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1 Little interest or pleasure in doing things	0	1	2	3
2 Feeling down, depressed, or hopeless	0	1	2	3
3 Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4 Feeling tired or having little energy	0	1	2	3
5 Poor appetite or overeating	0	1	2	3
6 Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7 Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8 Moving or speaking so slowly that other people could have noticed? Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9 Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
Subtotals	0	—	—	—
Total				—
If you checked off <i>any</i> problems, how <i>difficult</i> have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult

**FIGURE 1.** Patient Health Questionnaire–9. A score ranging from 5 to 10 indicates mild depression, 10 to 14 moderate depression, 15 to 19 moderate to severe depression, and greater than 19 severe depression.

Source: Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med* 2001; 16:606–616. No permission required to reproduce, translate, display, or distribute.

unavoidable.

Table 2 lists common antidepressants. The antidepressants most commonly prescribed, especially in the primary care setting, are selective serotonin reuptake inhibitors (SSRIs), which are favored because of their effectiveness, low side-effect profile, and lack of overdose toxicity.

Serotonin syndrome is no more likely

to occur in pregnant than in nonpregnant women. Close monitoring for this condition is warranted only when patients are taking very high doses of SSRIs or SSRIs in combination with other serotonergic agonists.

Prescribing antidepressants for pregnant or breastfeeding women requires thoughtful consideration of the patient's preferences, as well as weighing the risks and benefits of fetal



TABLE 2

**Antidepressant drugs with pregnancy and lactation recommendations**

<b>Class of agent</b>	<b>Commonly prescribed agents</b>	<b>Comments</b>
<b>Tricyclics and tetracyclics</b>	Amitriptyline, nortriptyline, imipramine, desipramine	Amitriptyline and nortriptyline remain the preferred agents in this class for use in pregnancy and lactation
<b>Selective serotonin reuptake inhibitors (SSRIs)</b>	Sertraline, fluoxetine, citalopram, escitalopram, paroxetine	Sertraline is the preferred agent from this class during pregnancy and lactation Paroxetine is preferred during lactation
<b>Serotonin-norepinephrine reuptake inhibitors</b>	Venlafaxine, desvenlafaxine, duloxetine	Based on limited to fair data, venlafaxine use in pregnancy and lactation does not increase risk to fetus or neonate Some clinicians have suggested that active drug in breast milk may help to alleviate symptoms of neonatal withdrawal <sup>a</sup>
<b>Dopamine-norepinephrine reuptake inhibitors</b>	Bupropion	Published data on the safety of this agent are limited Use an SSRI or tricyclic preferably when initiating treatment in pregnancy
<b>Serotonin modulators</b>	Trazodone	Published data on the safety of this agent are limited at this time; use an SSRI or tricyclic preferably when starting treatment in pregnancy

<sup>a</sup> Koren G, Moretti M, Kapur B: Can venlafaxine in breast milk attenuate the norepinephrine and serotonin reuptake neonatal withdrawal syndrome. *J Obstet Gynaecol Can* 2006; 28:299-302.

Source: Adapted from Star J. Psychiatric disorders in pregnancy. In: Powrie RO, Greene MF, Camann W, editors. *de Sweit's Medical Disorders in Obstetrics Practice*, 5th edition. Hoboken, NJ: Wiley-Blackwell, 2010:524-552.

and infant exposure to maternal depression vs exposure to medications. Additional considerations include monotherapy, avoiding medication changes, choosing drugs that have been effective in the past, and avoiding drugs with known drug-drug interactions or teratogenic effects.<sup>50</sup>

There is increasing consensus that the short- and long-term consequences of under-treatment or nontreatment of maternal depression outweigh the risk of fetal exposure to SSRIs.<sup>3,51,52</sup> Cohen et al<sup>53</sup> have recommended that if a woman is on an antidepressant and learns she is pregnant, she should not discontinue it because of the likelihood of relapse; they found a 68% relapse rate in women who discontinued their antidepressant in the first trimester of pregnancy.<sup>53</sup>

In a comprehensive review of studies published between 1996 and 2012 that examined antidepressant use during pregnancy, Byatt et

al<sup>54</sup> found little or no evidence of increased teratogenic risk with antidepressants with the exception of paroxetine, which is associated with a small but significant increased risk of cardiac malformation during first-trimester exposure.<sup>54</sup>

These conclusions were underscored in a large cohort study in the United Kingdom.<sup>55</sup> In addition, a joint task force of the American Psychiatric Association and ACOG reviewed studies looking at the association between depression, antidepressants, and birth outcomes including miscarriage, preterm birth, cardiac abnormalities (resulting from first trimester exposure), persistent pulmonary hypertension (related to second- and third-trimester exposure), and neonatal adaptation syndrome (associated with third-trimester exposure).<sup>8</sup> They concluded that the available data neither support nor refute a link between the use of antidepressants and several of the above outcomes. No increase in risk of congenital malformations

(including cardiac abnormalities) was found. An increased risk of persistent pulmonary hypertension was noted, although the absolute risk of this disorder remained low, at 3 to 6 per 1,000 infants exposed to SSRIs in utero.<sup>8,56</sup>

## Neonatal adaptation syndrome

Neonatal adaptation syndrome is characterized by jitteriness, irritability, decreased muscle tone, and feeding difficulty in the neonate. It can occur in 15% to 30% of infants exposed to SSRIs antenatally.<sup>57,58</sup> These symptoms, however, are transient and typically resolve within 7 to 10 days after birth. A more recent study suggested that neurobehavioral symptoms for some infants extend beyond 2 weeks and that concomitant exposure to benzodiazepines results in even higher rates of this syndrome.<sup>59</sup> There is no evidence that tapering or discontinuing antidepressants near term is necessary, safe, or effective in preventing transient neonatal complications. However, this approach would increase the risk of relapse for the mother.

## Autism spectrum disorders

The possible association between antidepressants and autism spectrum disorders in pregnancy has captured much attention in recent years. One study based on healthcare claims<sup>60</sup> and one registry-based study<sup>61</sup> associated in utero exposure to antidepressants with autism liability in children. However, a large-scale Danish registry-based study did not replicate this association.<sup>62</sup> In addition, 2 recent cohort studies, identifying children with autism spectrum disorder or attention-deficit hyperactivity disorder from electronic health records, found that neither disorder was significantly associated with prenatal antidepressant exposure in crude or adjusted models. However, both studies found a significant association with the use of antidepressants before pregnancy, indicating that the risk of autism observed with prenatal antidepressant exposure is likely confounded by the severity of maternal illness.<sup>63,64</sup>

## Concerns about drug therapy during breastfeeding

For infants of breastfeeding women, exposure to antidepressants through breast milk is minimal. Amounts in breast milk depend on the timing of the antidepressant dose, timing of

feeding, and genetically influenced metabolic activity in mother and infant. The current literature supports antidepressant use for breastfeeding mothers of healthy full-term infants.<sup>65</sup>

The 2 most widely studied antidepressants in breastfed infants are paroxetine and sertraline. It has been shown that very little can be detected in the infant's serum, with relative infant doses ranging from 0.4% to 2.8%.<sup>65</sup> While clinicians are cautioned against prescribing paroxetine for pregnant women, the drug remains a suitable alternative for breastfeeding women.

If an antidepressant is started postpartum, the recommendation is to start with a low dose and then slowly titrate upward while monitoring the infant for adverse effects.<sup>65,66</sup> Possible adverse effects in breastfeeding infants include irritability, sedation, poor weight gain, and a change in feeding patterns.<sup>67</sup> Adverse events are most likely to occur in newborns up to 8 weeks of age, and infants born prematurely or with medical problems may be particularly at risk.<sup>65,68</sup>

## Helping patients weigh risks and benefits of drug therapy

Women may hear about the risks of medications to the fetus and during breastfeeding and so may be reluctant to seek or accept intervention. Often, the information is not from a reliable, scientifically based source. Primary care physicians are well positioned to guide peripartum women in risk-benefit analysis of proper treatment of their depression vs no treatment or undertreatment. In addition, establishing referral sources—ideally with a peripartum mental health specialist—is advisable. Online resources that clinicians can refer patients to for help in managing peripartum depression include the following:

- [www.postpartum.net](http://www.postpartum.net)
- [www.womensmentalhealth.org](http://www.womensmentalhealth.org)
- [www.mothersbaby.org](http://www.mothersbaby.org) (for pharmacologic guidance).

## INCREASED AWARENESS IS KEY

Primary care physicians must remain alert to the high prevalence of depression in women of childbearing age and embrace routine screening for depression. (See the sidebar, “The primary care management of peripartum depression.”) Since half of pregnancies

Primary care physicians are positioned to guide peripartum women in the risk-benefit analysis of proper management of their depression

are unintended, awareness of the risks of undetected and untreated peripartum depression to the mother, developing fetus, and infant is essential. Untreated antepartum depression has been linked to poor pregnancy outcomes, nutritional deficits, and substance abuse. Untreated postpartum depression negatively affects mother-infant attachment, infant, and child development and maternal self care.

### Not treating depression is hazardous

Drug treatment during pregnancy and breastfeeding poses challenges for the patient and physician due to the inevitability of fetal and infant exposure, but lack of treatment can be hazardous.

To date, the evidence on the use of antidepressants in pregnant and lactating women is reassuring. Specialized peripartum psychiatric partial hospital programs<sup>69</sup> and inpatient programs<sup>70</sup> exist for women who need a higher level of care. There is also substantial evidence that psychotherapy, especially cognitive behavioral therapy and interpersonal therapy, is highly effective, and emerging data on complementary and alternative treatments are promising. Coordinated care between primary care and behavioral healthcare providers with expertise in treating peripartum depression is most likely to yield optimal outcomes. ■

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