

## Postpartum depression: Help patients find the right treatment



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### Accessibility of treatment, patient preference, breast- feeding help guide decisions

**P**ostpartum depression (PPD)—emergence of a major depressive episode after childbirth—has broad negative consequences for the mother, baby, and other family members. The time of onset after delivery for a depressive episode to be considered postpartum is debatable, but the DSM-IV-TR specifier states that onset within 4 weeks of childbirth is considered postpartum. PPD can impact many aspects of child development, including mother-infant attachment, cognitive development, and behavior.<sup>1-3</sup>

An estimated 10% of women who have given birth experience PPD.<sup>4,5</sup> The risk of PPD is particularly high among women who have had previous episodes of PPD or major depressive disorder (MDD). Other risk factors include stressful life events, depression and/or anxiety during pregnancy, family history of PPD, and obstetrical complications.<sup>6-8</sup> Anxiety disorders are common in postpartum women, and anxiety symptoms often are prominent in PPD.<sup>9</sup>

Despite the prevalence of PPD and its serious consequences, few studies have addressed antidepressant treatment. In this article we discuss screening and treating PPD and considerations for breast-feeding mothers. Visit this article at [CurrentPsychiatry.com](http://CurrentPsychiatry.com) for results of an open-label trial of escitalopram for PPD we conducted in which patient recruitment was challenging.

### Screening for PPD: A good start

Initiatives by state governments and health care providers have led to programs in which universal screening for PPD has been implemented. Screening provides a mechanism for early detection and intervention. The Edinburgh

Table 1

## Antidepressants for PPD: Summary of the evidence

Study	Design and size	Medication	Results
Appleby et al, 1997 <sup>20</sup>	12-week, placebo-controlled, N = 87	Fluoxetine	Patients taking fluoxetine showed greater improvement than those taking placebo
Yonkers et al, 2008 <sup>21</sup>	8-week, placebo-controlled, N = 70	Paroxetine	Both groups improved over time, but patients taking paroxetine had greater improvement in overall clinical severity
Wisner et al, 2006 <sup>22</sup>	8-week, RCT, N = 109	Sertraline vs nortriptyline	Proportion of women who responded or remitted did not differ between those taking sertraline or nortriptyline
Misri et al, 2004 <sup>23</sup>	12-week, RCT, N = 35	Paroxetine monotherapy vs paroxetine + CBT	Both groups showed significant improvement in mood and anxiety symptoms
Stowe et al, 1995 <sup>24</sup>	8-week, open-label, N = 21	Sertraline	20 patients experienced >50% reduction in SIGH-D score
Cohen et al, 1997 <sup>25</sup>	Open-label, N = 15	Venlafaxine	12 patients achieved remission
Suri et al, 2001 <sup>26</sup>	8-week, open-label, N = 6	Fluvoxamine	4 patients became euthymic, with HDRS scores ranging from 2 to 5
Nonacs et al, 2005 <sup>27</sup>	8-week, open-label, N = 8	Bupropion	6 patients had ≥50% decrease in HDRS score from baseline; 3 achieved remission

CBT: cognitive-behavioral therapy; HDRS: Hamilton Depression Rating Scale; PPD: postpartum depression; RCT: randomized controlled trial; SIGH-D: Structured Interview Guide for the Hamilton Depression Rating Scale

### Clinical Point

Use of the self-rated, 10-item Edinburgh Postnatal Depression Scale increases identification of PPD at obstetrics visits

Postnatal Depression Scale<sup>10</sup> is a self-rated, 10-item scale developed for the postpartum setting, and its use increases identification of PPD at postpartum obstetrics visits.<sup>11</sup> Other screening tools such as the Patient Health Questionnaire-9 also are commonly used. Despite the success of screening programs in attempting the feasibility of screening, it is unclear if the identification of women who may be experiencing PPD increases their engagement in treatment. Studies have demonstrated that even when depressive symptoms suggesting a PPD episode are identified in the postpartum period, many women still do not receive treatment.<sup>12,13</sup> Studies of PPD screening programs have not demonstrated that screening itself improves treatment engagement or improves outcomes.<sup>12,13</sup>

Multiple factors—including accessibility of treatment options and patient preference for specific types of treatment—determine whether mothers with PPD obtain treatment. Patients diagnosed with

depression by a primary care clinician may prefer psychotherapy to antidepressants,<sup>14</sup> and a postpartum mother's willingness to accept antidepressant treatment may be influenced by concerns about possible risks during breast-feeding.<sup>15</sup>

### Psychotherapy: An effective option

Psychotherapy is an important first-line option for PPD, particularly because of considerations of medication exposure during breast-feeding and many women are reluctant to take antidepressants while breast-feeding.<sup>16</sup> Interpersonal psychotherapy and cognitive-behavioral therapy (CBT) have been most studied for PPD, and both appear effective for prevention and acute treatment of PPD.<sup>17-20</sup> Although psychotherapy alone may be sufficient for some women, for others, medication may be an important first-line treatment, depending on symptom severity, access to psychotherapy, and personal preference.

See this article at  
[CurrentPsychiatry.com](https://www.currentpsychiatry.com)  
for results of an open-label trial of escitalopram for PPD



## Postpartum depression

### Clinical Point

In a randomized, double-blind study, CBT plus fluoxetine was significantly more effective than CBT plus placebo



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**Table 2**

## Considerations for antidepressant use during breast-feeding

Drug(s)	Comments
Fluoxetine	Because of long half-life, may be more likely to be detected in infant serum, especially at higher doses. Reasonable for use during breast-feeding if a woman has had a good previous response to the drug or used it during pregnancy
Sertraline	Reports of low levels of exposure. Relatively large amount of data available
Citalopram, escitalopram	Less systematic study of mother-infant pairs compared with sertraline and paroxetine. Low levels of exposure to infant via breast-feeding observed
Paroxetine	Consistent reports of low levels of exposure and has been relatively well studied without reported adverse events. Use limited by commonly experienced withdrawal symptoms; may be more sedating than other SSRIs
Bupropion	Paucity of systematic study in newborns of nursing mothers; a few case reports in older infants demonstrated low levels of exposure via breast-feeding. May help women who smoke to quit or to maintain abstinence from smoking. Reasonable to use if a woman had good previous response. One case report of possible infant seizure; no other reported adverse events
Venlafaxine, desvenlafaxine	Higher levels of desvenlafaxine than venlafaxine found in breast milk. No adverse events reported. Patients may experience withdrawal with discontinuation or missed doses
Tricyclic antidepressants	Considered reasonable for breast-feeding mothers if use is clinically warranted; few adverse effects in babies and generally low levels of exposure reported
Mirtazapine, nefazodone, MAOIs, duloxetine	Systematic human data not available for breast-feeding patients. May be reasonable if a woman previously has responded best to 1 of these; advise patients that data are not available to guide decisions

MAOIs: monoamine oxidase inhibitors; SSRIs: selective serotonin reuptake inhibitors  
**Source:** References 29-31

### Evidence for antidepressants

**Table 1 (page 15)**<sup>20-27</sup> describes clinical trials that assessed the efficacy of antidepressants for PPD. Two relatively small, double-blind, placebo-controlled trials have evaluated selective serotonin reuptake inhibitors for PPD. In a randomized, double-blind study of CBT plus fluoxetine or CBT plus placebo (N = 87), fluoxetine was significantly more effective than placebo.<sup>20</sup> In a randomized, controlled trial of paroxetine vs placebo for PPD (N = 70), both groups improved as measured by the 17-item Hamilton Rating Scale for Depression or Inventory of Depressive Symptomatology-Self-Report; those who received paroxetine did not improve significantly more than those who received placebo.<sup>21</sup> It is difficult to interpret a negative, underpowered study because placebo response rates in antidepressant trials of MDD tend to be high. Data from placebo-controlled trials in PPD are limited by the number and power of those trials.

Randomization to placebo is rare in PPD

trials. Most trials have used open-label designs because placebo arms pose ethical dilemmas considering the impact of PPD on a mother and her baby. In a randomized study of sertraline or nortriptyline for PPD, both drugs were similarly efficacious.<sup>22</sup> In another study comparing paroxetine monotherapy and paroxetine plus CBT for PPD, both groups experienced significant improvement in depression and anxiety symptoms, with no difference between groups at endpoint.<sup>23</sup> Open-label trials have suggested antidepressants' efficacy, although some studies have included small sample sizes (**Table 1, page 15**).<sup>20-27</sup>

### Breast-feeding considerations

From a nutritional standpoint, breast-feeding is optimal for a newborn. However, for some women, breast-feeding is difficult and stressful, and new mothers may experience this difficulty as failure. Some women prefer not to breast-feed, and others may prefer

Quillivant XR™ (methylphenidate HCl) Brief Summary continued... development were observed. The no effect level for pre- and postnatal development in rats was 15 mg/kg/day (equal to the MRHD on a mg/m<sup>2</sup> basis). **Nursing Mothers** Methylphenidate is present in human milk. Long-term neurodevelopmental effects on infants from stimulant exposure are unknown. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use** The safety and effectiveness of Quillivant XR have been established in pediatric patients ages 6 to 17 years. Use of Quillivant XR in pediatric patients 6 to 12 years of age is supported by adequate and well-controlled studies. Use in 12 to 17 year olds is supported by the adequate and well-controlled studies of Quillivant XR in younger pediatric patients and additional pharmacokinetic data in adolescents, along with safety information from other methylphenidate-containing products. The long-term efficacy of methylphenidate in pediatric patients has not been established. Safety and efficacy in pediatric patients below the age of 6 years have not been established. **Long Term Suppression of Growth** Growth should be monitored during treatment with stimulants, including Quillivant XR. Children who are not growing or gaining weight as expected may need to have their treatment interrupted [see *Warnings and Precautions*]. **Juvenile Animal Data** Rats treated with methylphenidate early in the postnatal period through sexual maturation demonstrated a decrease in spontaneous locomotor activity in adulthood. A deficit in acquisition of a specific learning task was observed in females only. The doses at which these findings were observed are at least 6 times the maximum recommended human dose (MRHD) on a mg/m<sup>2</sup> basis. In the study conducted in young rats, methylphenidate was administered orally at doses of up to 100 mg/kg/day for 9 weeks, starting early in the postnatal period (postnatal day 7) and continuing through sexual maturity (postnatal week 10). When these animals were tested as adults (postnatal weeks 13-14), decreased spontaneous locomotor activity was observed in males and females previously treated with 50 mg/kg/day (approximately 6 times the maximum recommended human dose [MRHD] on a mg/m<sup>2</sup> basis) or greater, and a deficit in the acquisition of a specific learning task was observed in females exposed to the highest dose (12 times the MRHD on a mg/m<sup>2</sup> basis). The no effect level for juvenile neurobehavioral development in rats was 5 mg/kg/day (half the MRHD on a mg/m<sup>2</sup> basis). The clinical significance of the long-term behavioral effects observed in rats is unknown. **Geriatric Use** Quillivant XR has not been studied in patients over the age of 65 years.

#### DRUG ABUSE AND DEPENDENCE

**Controlled Substance** Quillivant XR contains methylphenidate, a Schedule II controlled substance.

**Abuse** Signs and symptoms of CNS stimulant abuse include increased heart rate,

respiratory rate, blood pressure, and/or sweating, dilated pupils, hyperactivity, restlessness, insomnia, decreased appetite, loss of coordination, tremors, flushed skin, vomiting, and/or abdominal pain. Anxiety, psychosis, hostility, aggression, suicidal or homicidal ideation have also been observed. Abusers of CNS stimulants may chew, snort, inject, or use other unapproved routes of administration which can result in overdose and death [see *Overdosage*]. To reduce the abuse of CNS stimulants including Quillivant XR, assess the risk of abuse prior to prescribing. After prescribing, keep careful prescription records, educate patients and their families about abuse and on proper storage and disposal of CNS stimulants, monitor for signs of abuse while on therapy, and re-evaluate the need for Quillivant XR use.

**Dependence Tolerance** Tolerance (a state of adaptation in which exposure to a drug results in a reduction of the drug's desired and/or undesired effects over time) can occur during chronic therapy with CNS stimulants including Quillivant XR. **Dependence** Physical dependence (a state of adaptation manifested by a withdrawal syndrome produced by abrupt cessation, rapid dose reduction, or administration of an antagonist) can occur in patients treated with CNS stimulants including Quillivant XR. Withdrawal symptoms after abrupt cessation following prolonged high-dosage administration of CNS stimulants include extreme fatigue and depression.

#### OVERDOSAGE

**Signs and Symptoms** Signs and symptoms of acute methylphenidate overdose, resulting principally from overstimulation of the CNS and from excessive sympathomimetic effects, may include the following: nausea, vomiting, diarrhea, restlessness, anxiety, agitation, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, hypotension, tachypnea, mydriasis, and dryness of mucous membranes.

**Management of Overdose** Consult with a Certified Poison Control Center for up-to-date guidance and advice on the management of overdose with methylphenidate (1-800-222-1222.) Provide supportive care, including close medical supervision and monitoring. Treatment should consist of those general measures employed in the management of overdose with any drug. Consider the possibility of multiple drug overdose. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. Use supportive and symptomatic measures.



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to formula feed if they require pharmacotherapy, particularly if the medication has not been well studied in breast-feeding patients. Some women may decline to take medications if they are breast-feeding out of concern for the baby's exposure via breast milk and prefer to try nonpharmacologic approaches first. Many mothers with PPD need to be reassured that stopping breast-feeding may be exactly what is needed if the experience is contributing to their PPD or making them uncomfortable accepting pharmacotherapy when indicated. Maternal mental health is more important than breast-feeding to the health and well-being of the mother-baby dyad.

**Breast-feeding and antidepressants.** Any medication used during lactation should be assumed to pass into breast milk, although rigorous studies quantifying amounts of antidepressants in breast milk and infant serum generally have demonstrated low levels of exposure among the better studied antidepressants.<sup>28,29</sup> Studies that inform extent of

drug exposure during lactation have included mothers who have provided serial samples of breast milk and allowed their infant's blood levels to be checked for the drug. See *Table 2 (page 16)*<sup>29-31</sup> for details regarding specific antidepressants and breast-feeding.

Lactation exposure to paroxetine and sertraline has been most studied, and both have been nondetectable or found in low amounts in infant drug assays. Because fluoxetine has a longer half-life than other antidepressants, it may be more likely to be detected in infant blood sampling, with higher doses more likely to be detected than lower doses.<sup>32</sup> Decisions to breast-feed while taking medication must take into account unknown long-term effects of antidepressant exposure. There are a few case reports of suspected adverse events associated with antidepressant use during lactation.<sup>28,29</sup>

## The psychiatrist's role

PPD has great public health significance because it affects a large number of women



## Postpartum depression

### Clinical Point

Rigorous studies generally have found low levels of exposure to antidepressants in breast milk

### Related Resources

- American College of Obstetricians and Gynecologists. Screening for depression during and after pregnancy. [www.acog.org/Resources\\_And\\_Publications/Committee\\_Opinions/Committee\\_on\\_Obstetric\\_Practice/Screening\\_for\\_Depression\\_During\\_and\\_After\\_Pregnancy](http://www.acog.org/Resources_And_Publications/Committee_Opinions/Committee_on_Obstetric_Practice/Screening_for_Depression_During_and_After_Pregnancy).
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### Drug Brand Names

Bupropion • Wellbutrin, Zyban	Mirtazapine • Remeron
Citalopram • Celexa	Nefazodone • Serzone
Desvenlafaxine • Pristiq	Nortriptyline • Aventyl, Pamelor
Duloxetine • Cymbalta	Paroxetine • Paxil
Escitalopram • Lexapro	Sertraline • Zoloft
Fluoxetine • Prozac	Venlafaxine • Effexor
Fluvoxamine • Luvox	

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and their families. Screening during obstetrical visits or in other settings may increase identification of women who are suffering from PPD. In order for this screening to lead to meaningful changes, women must receive timely and expert evaluations for PPD and treatment that is efficacious and accessible.

Psychiatrists often are called upon to treat women with postpartum illness, and whether the mother is breast-feeding or not may influence treatment decisions. When clinically warranted, antidepressants are an important option in the context of breast-feeding, although some antidepressants have more data available than others regarding use during lactation. If a mother has had a good response to a specific antidepressant in the past, that medication

should be considered among the treatment options to avoid unnecessary medication trials and delayed response to treatment. Antidepressants with serotonergic action may be especially helpful if a woman presents with substantial postpartum anxiety. Psychotherapy is an important treatment for PPD; CBT and IPT are among the best-studied, efficacious treatments.

### Diagnosis and treatment: 4 pearls

**Verify the diagnosis.** Many women who present with postpartum depressive symptoms may have previously unrecognized bipolar disorder, and many women presenting with a primary complaint of anxiety have PPD.<sup>33,34</sup>

**Discuss breast-feeding.** This topic is important in assessing the risks and benefits of antidepressants in postpartum women, but many women also experience breast-feeding as a topic with emotional valence of its own and may need support with infant feeding.

**Meet the patient where she is.** Patient preferences strongly influence PPD treatment decisions. Women with similar clinical presentations may have strong preferences for different treatments.

**Make treatment accessible.** Postpartum women may find it challenging to engage in treatment. Treatment plans need to be feasible for women who are depressed while caring for a newborn. On-site childcare, home visits, Internet communication, and other accommodations that may facilitate treatment should be considered at a systems level.

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## Clinical Point

If a breast-feeding mother has had a good response to a specific antidepressant in the past, consider that medication

## Bottom Line

Screening for postpartum depression (PPD) may improve identification of the illness but has not been shown to improve long-term outcomes. Treatment options include antidepressants and psychotherapy. A surprisingly small evidence base exists regarding antidepressant treatment of PPD, although there is no evidence that postpartum women respond differently to antidepressants than depressed individuals who are not postpartum.