

ABM Clinical Protocol #18: Use of Antidepressants in Breastfeeding Mothers

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A central goal of The Academy of Breastfeeding Medicine is the development of clinical protocols for managing common medical problems that may impact breastfeeding success. These protocols serve only as guidelines for the care of breastfeeding mothers and infants and do not delineate an exclusive course of treatment or serve as standards of medical care. Variations in treatment may be appropriate according to the needs of an individual patient.

Background

POSTPARTUM DEPRESSION (PPD) (SOMETIMES referred to as pregnancy-related mood disorder) is one of the most common and serious postpartum conditions, affecting 10–20% of mothers within the first year of childbirth.¹ Studies have found that up to 50% of women with PPD are undiagnosed.² Risk factors include a prior history of depression (approximately 25–30% risk of recurrence),^{3,4} including PPD, and depression during pregnancy. Other risk factors include recent stressful life events, lack of social support, unintended pregnancy,⁵ and women who are economically stressed, disadvantaged, low income, or black.⁶ Moreover, studies of economically disadvantaged families have shown that approximately 25% of women will have ongoing depressive symptoms that last well beyond the initial postpartum year.⁷

Treatment approaches include nonpharmacological therapies such as interpersonal psychotherapy or cognitive behavioral therapy, pharmacological therapies, or a combination of both. Antidepressant medications are one of the most commonly prescribed pharmacologic treatments of PPD. The mother and her provider should work together to make an individually tailored choice. Breastfeeding mothers may be concerned about continuing and/or starting medication for PPD. Some providers are reluctant to prescribe for lactating mothers due to lack of information about antidepressants and breastfeeding. The risks of untreated depression, the risks of the medication to the breastfeeding dyad, and the benefits of treatment must be fully considered when making treatment decisions.

This protocol will discuss the spectrum of disease, emphasize the importance of screening, and provide evidence-

based information recommendations for treatment of PPD in breastfeeding mothers.

Spectrum of disease

There has been controversy about whether PPD is a distinct entity. In the *Diagnostic and Statistical Manual of Mental Disorders*, 4th and 5th editions (DSM-IV and V, respectively), PPD is considered a subtype of major depression, and there is an associated specifier to denote onset in the postpartum period.⁸ The newer DSM-V expanded the definition of PPD to include onset of symptoms during pregnancy through 4 weeks postpartum.⁹ Diagnosis may be further complicated by other comorbid conditions, including anxiety and bipolar disorder. Postpartum mood disorders are common in the postpartum period but differ according to timing and severity of symptoms and encompass a wide range of disorders.^{2,8,10}

“Postpartum blues” is a condition characterized by emotional changes, insomnia, appetite loss, and feelings of being overwhelmed that can affect 30–80% of women.^{7,8} It is a transient condition that usually peaks on postpartum Day 5 and resolves by Day 10. Unlike PPD, postpartum blues does not adversely affect infant care.

“Postpartum depression” is a major depressive episode that impairs social and occupational functioning. Symptoms cause significant distress and can include suicidal ideation. If untreated, symptoms may persist beyond 14 days and can last several months to a year.¹

“Postpartum psychosis” is a psychiatric emergency and is characterized by paranoia, hallucinations, delusions, and suicidal ideation, with the potential risk of suicide and/or

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infanticide. It can occur in one to three of every 1,000 deliveries and usually has a rapid onset (within hours to a few weeks) after delivery.^{7,8} Women with postpartum psychosis may have a prior history of postpartum psychosis or bipolar disorder, but in some women there is no prior psychiatric history.^{11,12} Approximately 25–50% of women with bipolar disorder are at risk of developing postpartum psychosis.¹³

“Postpartum intrusive thoughts” and “obsessive compulsive disorder” commonly occur in women, but with a wide range of severity of symptoms they are concerns for postpartum women. Intrusive or obsessive thoughts are unwelcome and involuntary thoughts, images, or unpleasant ideas that may become obsessions. These thoughts are usually upsetting or distressing to the woman, and they can be difficult to manage or eliminate.^{14,15}

Screening for PPD

Research confirms that most mothers (80%) are comfortable with the idea of being screened for depression.¹ Internationally, guidelines and authorities recommend screening for PPD.^{16–18}

Although definitive evidence of benefit is limited, the American College of Obstetricians and Gynecologists recommends that clinicians screen patients at least once during the perinatal period for depression and anxiety symptoms using a standardized, validated tool.¹⁹ For the first time, a large U.S. multicenter study of screening and follow-up care for PPD in a family practice setting has shown improved maternal outcomes at 12 months.²⁰ (I) (Quality of evidence [levels of evidence I, II-1, II-2, II-3, and III] is based on the U.S. Preventive Services Task Force Appendix A Task Force Ratings²¹ and is noted throughout this protocol in parentheses.)

Most physicians and maternal/child healthcare providers recognize the detrimental effects of PPD and agree that screening new mothers is within the scope of their practice.^{22,23} The American Academy of Pediatrics and the U.S. Surgeon General’s Office recognize and call for the early identification and treatment of mental health disorders, including PPD.^{24,25} It is important that screening for PPD be done systematically globally as detection and treatment have been shown to be beneficial in many countries.²⁶ (I)

Screening instruments

The screening instrument that has been most studied throughout the world is the Edinburgh Postnatal Depression Scale (EPDS).^{7,27} The EPDS is free, considered to be in the public domain, and available in many languages and has cross-cultural validity. It has 10 questions to be completed by the mother based on symptoms over the past 7 days and takes approximately 5 minutes to complete.²⁷ There are multiple points of contact in which screening can occur. In well-childcare visits, EPDS screening could occur during the 1-, 2-, 4-, and 6-month visits.^{7,16–18,28–30} The cesarean section incision check at 2 weeks and the postpartum visit at 4–8 weeks are also important screening opportunities. The EPDS can be readily administered and has demonstrated validity to detect postpartum mood disorders at as early as 4–8 weeks postpartum.^{30,31} (II-3) Either a score of 10 or higher or a positive response to Question 10 about suicidal thoughts is considered positive and indicates that the mother may be suffering from a depressive illness of varying severity.³² (II-3) Providers caring

for the infant must refer a mother with a positive screen for appropriate care.

Effects of PPD

In addition to the obvious adverse effects on the mother, PPD affects the child, spouse and/or partner, and other family members. It can cause family dysfunction, prevent effective mother–baby bonding, lead to early cessation of breastfeeding, and adversely affect infant growth and brain development.^{7,33–36} Rates of paternal depression are higher when the mother has PPD, which can compound the negative effects of depression on children. Infants of depressed mothers show less engagement and eye contact with their mother and are at risk for failure to thrive, attachment disorder, and development delay.²

A shared neuroendocrine mechanism among maternal mood, oxytocin levels, and maternal affect during breastfeeding has been demonstrated.³⁷ This strengthens the position that women with depression would benefit from early and sustained support with breastfeeding. Likewise, women with negative early breastfeeding experiences may be more likely to have depressive symptoms at 2 months postpartum; thus women experiencing breastfeeding difficulties should be screened for depressive symptoms.³³

Clinical Approach to Treating PPD

Once a woman is identified as being at risk for PPD, treatment choices must be considered and offered to her. For mild to moderate depression in the breastfeeding mother, psychology/cognitive behavioral therapy, if available, should be considered as first-line therapy.³⁸ (II-2)

Treatment

Nonpharmacological

Psychological therapy. Psychological therapy is effective for the treatment of major depressive disorder in the postpartum period, and different types of therapy seem equally effective.^{39–41} (I) There are three approaches to administration of psychological therapy in the postpartum period, including interpersonal therapy, cognitive behavioral therapy, and psychodynamic psychotherapy (nondirective therapy).^{39–47} Nonpharmacological treatment is not harmful to the infant and is often acceptable to mothers with PPD.

Infant feeding considerations. Breastfeeding difficulties and perinatal depression symptoms often present together, and management of depression should include a discussion of the mother’s experience of breastfeeding. Some mothers with depression find that breastfeeding enhances bonding and improves their mood, whereas others find breastfeeding to be difficult. For dyads struggling with milk production and latch issues, efforts should be undertaken to simplify feeding plans to ensure that mother and infant have time to enjoy one another. The demands of nighttime breastfeeding can be challenging for mothers for whom interruption of sleep is a major trigger for mood symptoms. In these cases, it may be helpful to arrange for another caregiver to feed the infant once at night, allowing the mother to receive 5–6 hours of uninterrupted sleep. A caregiver may also bring the infant to the mother to feed at the breast and then assume responsibility for

settling the baby back to sleep, thereby minimizing maternal sleep disruption. (III)

Medications

If psychological/cognitive behavioral therapy is unavailable, symptoms are severe, or mothers refuse this therapy, antidepressants are an effective option. Many factors must be considered when choosing an antidepressant during breastfeeding. All antidepressants are present in human milk to some extent. Data to inform clinical decisions are derived primarily from case reports or case series. Therefore, the initial treatment choice should be based on an informed clinical approach that takes into account the patient's previous treatments for depression, especially use during the pregnancy, the targeted symptoms, family history of depression and their experiences with antidepressants, current and past medical disorders, current medications, allergies, side effects of the medications, and maternal wishes. An individualized risk–benefit analysis of the treatments must be conducted (Table 1).⁴⁸ (I)

Clinical Factors Affecting Antidepressant Choice

- Obtain a psychiatric history with a focus on previous episodes of mood and anxiety disorders and effective treatment interventions. If psychotropic medications were used, determine what treatments were effective with a tolerable side effect profile. Past treatment response is often the best predictor of future response.⁴⁸ (II-2)
- Obtain a family history of psychiatric illness and treatment response. An immediate family member's history may be indicative of the mother's treatment response.⁴⁸ (II-2)
- Consider the primary symptoms that the medication will be targeting and its potential side effect profile.
- Choose psychotropic medications with an evidence base in lactating women. Older medications with available data are preferred over newer antidepressants with limited safety information.

Choosing an Antidepressant During Lactation

When considering the use of any medication in a lactating woman, providers must consider both maternal and infant safety factors. The medication must be both efficacious for the mother and safe for the infant. Although infant serum levels of psychotropic medication are the most accurate measure of infant exposure, it is often difficult to measure infant serum levels in routine clinical practice. However, factors affecting the passage of medication into human milk must be considered, including the following:

1. Route of drug administration and pharmacokinetics⁴⁹:
 - absorption rate
 - half-life and peak serum time
 - dissociation constant
 - volume of distribution
 - molecular size
 - degree of ionization
 - pH of plasma (7.4) and milk (6.8)
 - solubility of the drug in water and in lipids
 - binding to plasma protein

2. Amount of drug received by the infant in human milk⁴⁹:
 - milk yield
 - colostrum versus mature milk
 - concentration of the drug in the milk
 - how well the breast was emptied during the previous feeding
 - the infant's ability to absorb, detoxify, and excrete the drug.

Up-to-date information about medication use during lactation is easily available from the Internet on TOXNET LACTMED (<http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm>) (available in English) and e-lactancia (<http://e-lactancia.org/>) (available in both English and Spanish).

Most antidepressant studies provide milk levels, or milk to mother's plasma ratio, that are not constant and depend on factors such as dose, frequency, duration of dosing, maternal variation in drug disposition, drug interactions, and genetic background. Few studies provide infant serum levels, although they are the best measure of infant exposure.⁴⁹

Specific Antidepressants

Data from a recent meta-analysis indicated that all antidepressants were detected in milk but that not all were found in infant serum.⁵⁰ Infant serum levels of nortriptyline, paroxetine, and sertraline were undetectable in most cases. Infant serum levels of citalopram and fluoxetine exceeded the recommended 10% maternal level in 17% and 22% of cases, respectively. Few adverse outcomes were reported for any of the antidepressants. Conclusions could not be drawn for other antidepressants due to an insufficient number of cases. There is little or no evidence that ethnic or regional "medicines" are safe or effective; thus their use by healthcare providers is strongly cautioned. (II-2) For specific antidepressant medications, see Table 1.

Recommendations for Antidepressant Treatment in Lactating Women

- Current evidence suggests that untreated maternal depression can have serious and long-term effects on mothers and infants and that treatment may improve outcomes for mothers and infants. Therefore treatment is strongly preferred. (II-2)
- However, it is important not to label mothers who are only suffering from mild cases of postpartum blues as "depressed." We must make a distinction. For women with mild symptoms who are in the first 2 weeks postpartum, close follow-up, rather than initiation of antidepressant medication, is suggested. (II-2)
- When available and when symptoms are in the mild to moderate range, psychological/cognitive behavioral therapy is the first line of treatment for lactating women as it carries no known risk for the infant. Mothers must be monitored and reevaluated. If they are not improving or their symptoms are worsening, antidepressant drug treatment should be considered. (II-2)
- Both psychological/cognitive behavioral therapy and antidepressant medication are recommended for women with moderate to severe symptoms or for whom there are current stressors or interpersonal issues that psychological

TABLE 1. SPECIFIC ANTIDEPRESSANTS

<i>Class</i>	<i>Drug</i>	<i>Dosage/day</i>	<i>Indications</i>	<i>Maternal side effects</i>	<i>Infant exposure effects</i>	<i>Comments</i>
SSRIs	Citalopram ⁵²⁻⁵⁴	10-60 mg	Depressive or anxiety disorders;	Gastrointestinal distress,	All SSRIs have been detected in human milk. Paroxetine ^{71,72} and sertraline ⁷⁴⁻⁷⁸ have not exceeded the recommended 10% maternal level and are usually undetectable in infant serum. ⁷⁵ Fluoxetine ⁵⁷⁻⁶¹ and citalopram ^{52,53} have exceeded the 10% maternal level. ⁷⁹ The infant adverse events reported include uneasy sleep, colic, irritability, poor feeding, and drowsiness. ^{56,63,64,80-82} The FDA indicated that fluoxetine should not be used by nursing mothers. ⁶⁴	Sertraline is the most likely SSRI to be prescribed, low to undetectable in milk and relative safety profile in pregnancy. Long-term effects on neurobehavior and development from exposure to any SSRI during pregnancy and lactation have a limited evidence base, but more recent studies are relatively reassuring. ^{56,63,80,81}
	Escitalopram ^{55,56}	10-20 mg		headaches, sexual dysfunction, nervousness, or sedation		Sporadic case reports for these medications. ⁸²⁻⁸⁴ Limited number to report significant outcomes for nursing infants.
	Fluoxetine ⁵⁶⁻⁶⁴	10-80 mg	may be prescribed for fibromyalgia, neuropathic pain, premenstrual symptoms and disorders			Use not a reason to discontinue breastfeeding. However, another drug may be preferred.
	Fluvoxamine ⁶⁵⁻⁷⁰	50-300 mg				
	Paroxetine ^{67,71-73}	10-60 mg				
	Sertraline ^{67,74-78,a}	25-200 mg (usually a daily dose). Start at 25 mg for 5-7 days, then increase to 50 mg.				
SNRIs	Venlafaxine ^{51,83}	37.5-225 mg	Depression	Galactorrhea	Venlafaxine and its active metabolite are in milk, and its plasma of most breastfed infants, but no proven drug-related side effects. Monitor for sedation and adequate weight gain.	
	Duloxetine ⁸⁴	20-120 mg				
	Desvenlafaxine ⁸²	50-100 mg				
Other antidepressants (norepinephrine/dopamine/serotonin reuptake block)	Bupropion ⁸⁵⁻⁸⁸	150-450 mg	Depression	Dose-dependent drowsiness, dry mouth, increased appetite, weight gain, and dizziness	Very limited data, ranging from asymptomatic with undetectable infant serum levels to concerns with irritability and seizures	
	Mirtazapine ⁸⁹	15-30 mg			Limited infant data; no adverse side effects noted	
TCAs/heterocyclics	Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, maprotiline, nortriptyline, protriptyline, and trimipramine	Nortriptyline, 30-50 mg/day, in 3-4 divided doses, or the total daily dosage may be given once a day.	Depression and anxiety disorders; often used in low doses for sleep and chronic pain	Hypotension, sedation, dry mouth, urinary retention, weight gain, sexual dysfunction, and constipation. In an overdose, these medications can cause cardiac arrhythmias and death.	Only nortriptyline has a sufficient number of reported cases to comment on its use during lactation: it is generally undetectable in infant serum; no adverse events have been reported. ⁹⁰⁻⁹² Use of doxepin is often cautioned because of a case report of hypotonia, poor feeding, emesis, and sedation in a breastfed infant that resolved after discontinuation of nursing. ⁹³	One of the older classes

(continued)

TABLE 1. (CONTINUED)

<i>Class</i>	<i>Drug</i>	<i>Dosage/day</i>	<i>Indications</i>	<i>Maternal side effects</i>	<i>Infant exposure effects</i>	<i>Comments</i>
Herbal/natural	St. John's wort (<i>Hypericum perforatum</i>) contains hypericin and hyperforin as well as flavonoids such as quercetin. Omega-3 fatty acids	300 mg	Depression	One study found a slightly increased frequency of colic, drowsiness, and lethargy among breastfed infants but none required treatment. ⁹⁵ Appears to be of little risk to mothers and infants. The primary negative side effect is the "fishy smell."	Both hypericin and hyperforin are poorly excreted into human milk.	Has been used for the treatment of mild to moderate depression for many years, especially in Europe. Its use as a treatment for depression is controversial in the United States. Lack of sufficient evidence at this time to consider it a treatment for depression.
Antipsychotic	Quetiapine	Start at 25 mg, titrate. Maximum dose, 600 mg	Depression during pregnancy and the postpartum period ⁹⁴ Bipolar disorder, schizophrania	Sedation	Sedation	
Mood stabilizer	Lithium	Start at 300 mg, titrate as per LI levels. Maximum dose, 900–1,200 mg		Diarrhea, vomiting	Elevated TSH	Dosing is dictated by lithium blood levels in the mother, which need to be regularly checked.

^aBest safety profile of selective serotonin reuptake inhibitors (SSRIs) in lactation. FDA; Food and Drug Administration; LI, lithium, SNRI, serotonin–norepinephrine reuptake inhibitors; TCA, tricyclic antidepressant; TSH, thyroid-stimulating hormone.

therapy may help address. Maternal lactation status should not delay treatment. (II-2)

- Women with moderate to severe symptoms may require only antidepressant drug treatment. In the setting of moderate to severe depression, the benefits of treatment likely outweigh the risks of the medication to the mother or infant.
- There is no widely accepted algorithm for antidepressant medication treatment of depression in lactating women. An individualized risk–benefit analysis must be conducted in each situation and take into account the mother’s clinical history and response to treatment, the

risks of untreated depression, the risks and benefits of breastfeeding, the benefits of treatment, the known and unknown risks of the medication to the infant, and the mother’s wishes.

- If a mother has no history of antidepressant treatment, an antidepressant such as sertraline that has evidence of lower levels in human milk and infant serum and few side effects is an appropriate first choice. (II-2) Sertraline has the best safety profile during lactation. The recommended starting dose is 25 mg for 5–7 days to avoid side effects, which then can be increased to 50 mg/day.

TABLE 2. RESOURCES FOR WOMEN’S MENTAL HEALTH AND POSTPARTUM DEPRESSION HELP

Resource	Description	URL
Web sites		
International Marcé Society for Perinatal Mental Health	Primarily a multidisciplinary group of healthcare providers interested in promoting, facilitating, and communicating about research in all aspects of the mental health of women, their infants and partners around the time of childbirth.	www.marcesociety.com
Maternal and Child Health Bureau, U.S. Health Resources and Services Administration	Handbook entitled “ <i>Depression During and After Pregnancy: A Resource for Women, Their Families, and Friends</i> ”	www.mchb.hrsa.gov/pregnancyandbeyond/depression
National Suicide Prevention Lifeline, U.S. Substance Abuse and Mental Health Services Administration	1-800-273-TALK (8255)	www.suicidepreventionlifeline.org
Postpartum Support International	Information and resources on postpartum depression for providers, mothers, fathers, and families. Includes live chats and help for new parents. Access help according to state. PSI Warmline (weekdays only) 800-944-4PPD (4773)	www.postpartum.net
Postpartum Depression Online Support Group	A privately funded online support group that offers information, support, and assistance to those dealing with postpartum mood disorders and their families, friends, physicians, and counselors	www.ppdsupportpage.com
Mental Health America	The nonprofit Mental Health America is concerned with fathers’ mental health as well as mothers.	www.mentalhealthamerica.net/conditions/postpartum-disorders
Beyond Blue	A national initiative in Australia to raise awareness of anxiety and depression, providing resources for recovery, management and resilience	www.beyondblue.org.au
Books		
	Bennett SS, Indman P. <i>Beyond the Blues: Understanding and Treating Prenatal and Postpartum Depression & Anxiety</i> . Moodswings, San Jose, CA, 2011.	
	Cooper PJ, Murray L, eds. <i>Postpartum Depression and Child Development</i> . Guilford, New York, 1999.	
	Kendall-Tackett KA. <i>A Breastfeeding-Friendly Approach to Postpartum Depression</i> . Praeclarus Press, Amarillo, TX, 2015.	
	Kendall-Tackett KA. <i>Depression in New Mothers</i> , 2nd ed. Routledge, London, 2010.	
	Kleiman K. <i>Therapy and the Postpartum Woman: Notes on Healing Postpartum Depression for Clinicians and the Women Who Seek Their Help</i> . Routledge, Abingdon, United Kingdom, 2008.	
	Kleiman KR. <i>The Postpartum Husband: Practical Solutions for Living with Postpartum Depression</i> . Xlibris, Bloomington, IN, 2001.	
	Shields B. <i>Down Came the Rain: My Journey Through Postpartum Depression</i> . Hyperion, New York, 2006.	
	Wiegartz PS, Gyoerkoe KL, Miller LJ. <i>The Pregnancy and Postpartum Anxiety Workbook: Practical Skills to Help You Overcome Anxiety, Worry, Panic Attacks, Obsessions, and Compulsions</i> . New Harbinger Publications, Oakland, CA, 2009.	

- If a mother has been successfully treated with a particular selective serotonin reuptake inhibitor, tricyclic antidepressant, or serotonin–norepinephrine uptake inhibitor in the past, the data regarding this particular antidepressant should be reviewed, and it should be considered as a first-line treatment if there are no contraindications.
 - Mothers who were being treated with a selective serotonin reuptake inhibitor, tricyclic antidepressant, or serotonin–norepinephrine uptake inhibitor during pregnancy with good symptom control should continue on the same agent during breastfeeding. It is important to reassure the mother that exposure to the antidepressant in breastmilk is far less than exposure to the antidepressant during pregnancy. Moreover, ongoing treatment of the mood disorder is critical for the health of both mother and baby. Mothers should be provided information regarding the known and unknown risks and benefits of the treatment to make an informed decision.
 - Mothers should be monitored carefully in the initial stages of treatment for changes in symptoms, including worsening of symptoms. Specifically, women with histories of bipolar disorder, which may be undiagnosed, are at increased risk of developing an episode of depression, mania, or psychosis in the postpartum period. Although this situation is rare, mothers and partners should be made aware of the symptoms to watch for such as increased insomnia, delusions, hallucinations, racing thoughts, and talking/moving fast. Women experiencing such symptoms should contact their mental health provider immediately.
 - The mother's provider should communicate with the infant's provider to facilitate monitoring and follow-up. Infants should be monitored carefully by the physician/healthcare worker, including carefully following growth. Serum levels are not indicated on a regular basis without a clinical indication or concern. In addition, in most cases, the serum level would not provide helpful information unless it is a psychotropic that has a documented therapeutic window and laboratory norms (i.e., tricyclic antidepressants).
 - A strategy that may be used to decrease infant exposure based on breastfeeding pharmacokinetic reports is medication administration immediately after feedings. (III)
 - There are several Web-based and book references available for professionals and mothers to assist in gaining knowledge and help regarding these issues (Table 2).
- a. Sufficient control for level of depression
 - b. Provision of drug, information on infant serum levels, the amount detected in human milk, maternal serum levels, and the timing of sampling
 - c. Information on infant consumption in the milk
 - d. Information on infant behavioral outcomes
 - e. Evaluation of impact of continued breastfeeding on mitigating infant withdrawal symptoms for those mothers treated antenatally.
2. Study reasons mothers and clinicians elect to defer treatment in lactating mothers and follow-up behavioral outcomes of these infants.

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Conclusions and Suggestions for Future Research

Despite many publications about antidepressants and breastfeeding, the scientific literature continues to lack the depth of robust large-scale studies for clinicians and mothers to make confident decisions about individual medications. Multiple reviews of the literature broadly suggest tricyclic antidepressants and selective serotonin reuptake inhibitors are relatively safe, and all recommend individual risk–benefit assessments.⁵¹

Future research that would help guide clinical practice includes:

1. Randomized clinical trials in lactating women for any class of antidepressant that include the following:

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