

Managing psychiatric illness during pregnancy and breastfeeding: Tools for decision making

➡ Changing drug safety ratings and conflicting information can make maintaining the mental health of the mother and the well-being of the fetus and infant complex. Here, a pharmacologic framework that allows for consistency of care.

Lucy J. Puryear, MD; Nicole R. Hall, MD; Manju Monga, MD; and Susan M. Ramin, MD

IN THIS ARTICLE

Medication vs no medication

page 31

Risks of untreated illness

page 33

Antidepressants in pregnancy and breastfeeding

page 37

Increasingly, women with psychiatric illness are undergoing pharmacologic treatment during pregnancy. In the United States, an estimated 8% of pregnant women are prescribed antidepressants, and the number of such cases has risen over the past 15 years.¹ Women with a psychiatric diagnosis were once instructed either to discontinue all medication immediately on learning they were pregnant, or to forgo motherhood because their illness might have a negative

effect on a child or because avoiding medication during pregnancy might lead to a relapse.

Fortunately, women with depression, anxiety, bipolar disorder, or schizophrenia no longer are being told that they cannot become mothers. For many women, however, stopping medication is not an option. Furthermore, psychiatric illness sometimes is diagnosed initially during pregnancy and requires treatment.



Dr. Puryear is Associate Professor and Medical Director, Center for Reproductive Psychiatry, Department of Obstetrics and Gynecology and Menninger Department of Psychiatry, Baylor College of Medicine, Texas Children's Hospital–Pavilion for Women, Houston.



Dr. Monga is Professor and Vice Chair (Clinical), Department of Obstetrics and Gynecology, Baylor College of Medicine, Texas Children's Hospital–Pavilion for Women.



At the time of this writing, Dr. Hall was Assistant Professor, Baylor College of Medicine, Texas Children's Hospital–Pavilion for Women, and is currently an obstetrician-gynecologist with Georgia Perinatal Consultants, Atlanta.



Dr. Ramin is Henry and Emma Meyer Chair in Obstetrics and Gynecology, and Professor and Vice Chair for Education, Department of Obstetrics and Gynecology, Baylor College of Medicine, Texas Children's Hospital–Pavilion for Women.

Dr. Puryear reports that she is a consultant to Sage Therapeutics. The other authors report no financial relationships relevant to this article.



Many women with psychiatric illness no longer have to choose between mental health and starting a family.

Pregnant women and their physicians need accurate information about when to taper off medication, when to start or continue, and which medications are safest. Even for clinicians with a solid knowledge base, counseling a woman who needs or may need psychotropic medication during pregnancy and breastfeeding is a daunting task. Some clinicians still recommend no drug treatment as the safest and best option, given the potential risks to the fetus.

In this review we offer a methodologic approach for decision making about pharmacologic treatment during pregnancy. As the scientific literature is constantly being updated, it is imperative to have the most current information on psychotropics and to know how to individualize that information when counseling a pregnant woman and her family. Using this framework for analyzing the risks and benefits for both mother and fetus, clinicians can avoid the unanswerable question of which medication is the “safest.”

A patient’s mental health care provider is a useful resource for information about a

woman’s mental health history and current stability, but he or she may not be expert or comfortable in recommending treatment for a pregnant patient. During pregnancy, a woman’s obstetrician often becomes the “expert” for all treatment decisions.

Analyze risks and benefits of medication versus no medication

The US Food and Drug Administration (FDA) has not approved any psychotropic medication for use during pregnancy. While a clinical study would provide more scientifically rigorous safety data, conducting a double-blinded, placebo-controlled trial in pregnant women with a psychiatric disorder is unethical. Thus, the literature consists mostly of reports on case series, retrospective chart reviews, prospective naturalistic studies, and analyses of large registry databases. Each has benefits and limitations. It is important to understand the limitations when making treatment decisions.

FAST TRACK

Use a methodologic approach for decision making as a framework for analyzing the risks and benefits of pharmacologic treatment for mother and fetus

CONTINUED ON PAGE 32

Psychotropic use during pregnancy: Certain risks in offspring lower than thought, recent data show

Antidepressants. Previous studies may have overestimated the association between prenatal use of antidepressants and attention deficit/hyperactivity disorder (ADHD) in children because they did not control for shared family factors, according to investigators who say that their recent study findings raise the possibility that “confounding by indication” might partially explain the observed association.¹

In a population-based cohort study in Hong Kong, Man and colleagues analyzed the records of 190,618 maternal-child pairs.¹ A total of 1,252 children were exposed to maternal antidepressant use during pregnancy. Medications included selective serotonin reuptake inhibitors (SSRIs), non-SSRIs, and antipsychotics as monotherapy or in various combination regimens. Overall, 5,659 of the cohort children (3%) were diagnosed with or received treatment for ADHD.

When gestational medication users were compared with nongestational users, the crude hazard ratio (HR) of antidepressant use during pregnancy and ADHD was 2.26 ($P < .01$). After adjusting for potential confounding factors (such as maternal psychiatric disorders and use of other psychotropic drugs), this reduced to 1.39 (95% confidence interval [CI], 1.07–1.82; $P = .01$). Children of mothers with psychiatric disorders had a higher risk of ADHD than did children of mothers without psychiatric disorders (HR, 1.84; 95% CI, 1.54–2.18; $P < .01$), even if the mothers had never used antidepressants.

While acknowledging the potential for type 2 error in the study analysis, the investigators proposed that the results “further strengthen our hypothesis that confounding by indication may play a major role in the observed positive association between gestational use of antidepressants and ADHD in offspring.”

Lithium. Similarly, investigators of another recently published study found that the magnitude of the association between prenatal lithium use and increased

risk of cardiac malformations in infants was smaller than previously shown.² This finding may be important clinically because lithium is a first-line treatment for many US women of reproductive age with bipolar disorder.

Most earlier data were derived from a database registry, case reports, and small studies that often had conflicting results. However, Paterno and colleagues conducted a large retrospective cohort study that involved data on 1,325,563 pregnancies in women enrolled in Medicaid.² Exposure to lithium was defined as at least 1 filled prescription during the first trimester, and the primary reference group included women with no lithium or lamotrigine (another mood stabilizer not associated with congenital malformations) dispensing during the 3 months before the start of pregnancy or during the first trimester.

A total of 663 pregnancies (0.05%) were exposed to lithium and 1,945 (0.15%) were exposed to lamotrigine during the first trimester. The adjusted risk ratios for cardiac malformations among infants exposed to lithium were 1.65 (95% CI, 1.02–2.68) as compared with nonexposed infants and 2.25 (95% CI, 1.17–4.34) as compared with lamotrigine-exposed infants. Notably, all right ventricular outflow tract obstruction defects identified in the infants exposed to lithium occurred with a daily dose of more than 600 mg.

Although the study results suggest an increased risk of cardiac malformations—of approximately 1 additional case per 100 live births—associated with lithium use in early pregnancy, the magnitude of risk is much lower than originally proposed based on early lithium registry data.

—KATHY CHRISTIE, SENIOR EDITOR

References

1. Man KC, Chan EW, Ip P, et al. Prenatal antidepressant use and risk of attention-deficit/hyperactivity disorder in offspring: population based cohort study. *BMJ*. 2017;357:j2350.
2. Paterno E, Huybrechts KR, Bateman BT, et al. Lithium use in pregnancy and risk of cardiac malformations. *N Engl J Med*. 2017;376(23):2245–2254.

In 1979, the FDA developed a 5-letter system (A, B, C, D, X) for classifying the relative safety of medications used during pregnancy.² Many clinicians and pregnant women relied on this system to decide which medications were safe. Unfortunately, the information in the system was inadequate for making informed decisions. For example, although a class B medication might have appeared safer than one in class C, the studies of risk in humans might not have been

adequate to permit comparisons. Drug safety classifications were seldom changed, despite the availability of additional data.

In June 2015, the FDA changed the requirements for the Pregnancy and Lactation subsections of the labeling for human prescription drugs and biologic products. Drug manufacturers must now include in each subsection a risk summary, clinical considerations supporting patient care decisions and counseling, and detailed data. These

CONTINUED ON PAGE 33

TABLE 1 When to taper off, or start or continue, psychotropic medication during pregnancy and the postpartum period

Taper off	Start or continue
<ul style="list-style-type: none"> • First episode of illness • Symptom stability for 6 months to 1 year with medication • History of symptom stability for 1 year or more after medication is stopped • Mild symptoms • Patient preference 	<ul style="list-style-type: none"> • Chronic psychiatric illness • Relapse of illness within weeks to months after medication is stopped • History of severe symptoms without medication: inability to function (activities of daily living), suicidal, psychotic, manic • History of psychiatric hospitalization • Diagnosis of psychotic disorder: bipolar disorder or schizophrenia • Several medication trials with difficulty stabilizing symptoms

subsections provide information on available human and animal studies, known or potential maternal or fetal adverse reactions, and dose adjustments needed during pregnancy and the postpartum period. In addition, the FDA added a subsection: Females and Males of Reproductive Potential.³

These changes acknowledge there is no list of “safe” medications. The safest medication generally is the one that works for a particular patient at the lowest effective dose. As each woman’s history of illness and effective treatment is different, the best medication may differ as well, even among women with the same illness. Therefore, medication should be individualized to the patient. A risk-benefit analysis comparing psychotropic medication treatment with no medication treatment must be performed for each patient according to her personal history and the best available data.

What is the risk of untreated illness during pregnancy?

During pregnancy, women are treated for many medical disorders, including psychiatric illness. One general guideline is that, if a pregnant woman does not need a medication—whether it be for an allergy, hypertension, or another disorder—she should not take it. Conversely, if a medication is required for a patient’s well-being, her physician should continue it or switch to a safer one. This general guideline is the same for women with depression, anxiety, or a psychotic disorder.

Managing hypertension during pregnancy is an example of choosing treatment when the risk of the illness to the mother and the infant outweighs the likely small risk associated with taking a medication. Blood pressure is monitored, and, when it reaches a threshold, an antihypertensive is started promptly to avoid morbidity and mortality.

Psychiatric illness carries risks for both mother and fetus as well, but no data show a clear threshold for initiating pharmacologic treatment. Therefore, in prescribing medication the most important steps are to take a complete history and perform a thorough evaluation. Important information includes the number and severity of previous episodes, prior history of hospitalization or suicidal thoughts or attempts, and any history of psychotic or manic status.

Whether to continue or discontinue medication is often decided after inquiring about other times a medication was discontinued. A patient who in the past stayed well for several years after stopping a medication may be able to taper off a medication and conceive during a window of wellness. Some women who have experienced only one episode of illness and have been stable for at least a year may be able to taper off a medication before conceiving (TABLE 1).

In the risk-benefit analysis, assess the need for pharmacologic treatment by considering the risk that untreated illness poses for both mother and fetus, the benefits of treatment for both, and the risk of medication exposure for the fetus.⁴



Assess the need for pharmacologic treatment by considering the risk of untreated illness for mother and fetus, benefits of treatment for both, and risk of drug exposure for the fetus

CONTINUED ON PAGE 34

Mother: Risk of untreated illness versus benefit of treatment

A complete history and a current symptom evaluation are needed to assess the risk that nonpharmacologic treatment poses for the mother. Women with functional impairment, including inability to work, to perform activities of daily living, or to take care of other children, likely require treatment. Studies have found that women who discontinue treatment for a psychiatric illness around the time of conception are likely to experience a recurrence of illness during pregnancy, often in the first trimester, and must restart medication.^{5,6} For some diagnoses, particularly bipolar disorder, symptoms during a relapse can be more severe and more difficult to treat, and they carry a risk for both mother and fetus.⁷ A longitudinal study of pregnant women who stopped medication for bipolar disorder found a 71% rate of relapse.⁷ In cases in which there is a history of hospitalization, suicide attempt, or psychosis, discontinuing treatment is not an option; instead, the physician must determine which medication is safest for the particular patient.

Fetus: Risk of untreated illness versus benefit of treatment

Mothers with untreated psychiatric illness are at higher risk for poor prenatal care, substance abuse, and inadequate nutrition, all of which increase the risk of negative obstetric and neonatal outcomes.⁸ Evidence indicates that untreated maternal depression increases the risk of preterm delivery and low birth weight.⁹ Children born to mothers with depression have more behavioral problems, more psychiatric illness, more visits to pediatricians, lower IQ scores, and attachment issues.¹⁰ Some of the long-term negative effects of intrauterine stress, which include hypertension, coronary heart disease, and autoimmune disorders, persist into adulthood.¹¹

Fetus: Risk of medication exposure

With any pharmacologic treatment, the timing of fetal exposure affects resultant risks and therefore must be considered in the management plan.

Before conception. Is there any effect on ovulation or fertilization?

Implantation. Does the exposure impair the blastocyst's ability to implant in the uterine lining?

First trimester. This is the period of organogenesis. Regardless of drug exposure, there is a 2% to 4% baseline risk of a major malformation during any pregnancy. The risk of a particular malformation must be weighed against this baseline risk.

According to limited data, selective serotonin reuptake inhibitors (SSRIs) may increase the risk of early miscarriage.¹² SSRIs also have been implicated in increasing the risk of cardiovascular malformations, although the data are conflicting.^{13,14}

Antiepileptics such as valproate and carbamazepine are used as mood stabilizers in the treatment of bipolar disorder.¹⁵ Extensive data have shown an association with teratogenicity. Pregnant women who require either of these medications also should be prescribed folic acid 4 or 5 mg/day. Given the high risk of birth defects and cognitive delay, valproate no longer is recommended for women of reproductive potential.¹⁶

Lithium, one of the safest medications used in the treatment of bipolar disorder, is associated with a very small risk of Ebstein anomaly.¹⁷

Lamotrigine is used to treat bipolar depression and appears to have a good safety profile, along with a possible small increased risk of oral clefts.^{18,19}

Atypical antipsychotics (such as aripiprazole, olanzapine, quetiapine, and risperidone) are often used first-line in the treatment of psychotic disorders and bipolar disorder in women who are not pregnant. Although the safety data on use of these drugs during pregnancy are limited, a recent analysis of pregnant Medicaid enrollees found no increased risk of birth defects after controlling for potential confounding factors.²⁰ Common practice is to avoid these newer agents, given their limited data and the time needed for rare malformations to emerge (adequate numbers require many exposures during pregnancy).



Women with functional impairment—inability to work, perform activities of daily living, take care of other children—likely require treatment

Second trimester. This is a period of growth and neural development. A 2006 study suggested that SSRI exposure after pregnancy week 20 increases the risk of persistent pulmonary hypertension of the newborn (PPHN).²¹ In 2011, however, the FDA removed the PPHN warning label for SSRIs, citing inconsistent data. Whether the PPHN risk is increased with SSRI use is unclear, but the risk is presumed to be smaller than previously suggested.²² Stopping SSRIs before week 20 puts the mother at risk for relapse during pregnancy and increases her risk of developing postpartum depression. If we follow the recommendation to prescribe medication only for women who need it most, then stopping the medication at any time during pregnancy is not an option.

Third trimester. This is a period of continued growth and lung maturation.

Delivery. Is there a potential for impairment in parturition?

Neonatal adaptation. Newborns are active mainly in adapting to extrauterine life: They regulate their temperature and muscle tone and learn to coordinate sucking, swallowing, and breathing. Does medication exposure impair adaptation, or are signs or symptoms of withdrawal or toxicity present? The evidence that in utero SSRI exposure increases the risk of neonatal adaptation syndrome is consistent, but symptoms are mild and self-limited.²³ Tapering off SSRIs before delivery currently is not recommended, as doing so increases the mother's risk for postpartum depression and, according to one study, does not prevent symptoms of neonatal adaptation syndrome from developing.²⁴

Behavioral teratogenicity. What are the long-term developmental outcomes for the child? Are there any differences in IQ, speech and language, or psychiatric illness? One study found an increased risk of autism with in utero exposure to sertraline, but the study had many methodologic flaws and its findings have not been replicated.²⁵ Most studies have not found consistent differences in speech, IQ, or behavior between infants exposed and infants not exposed to antidepressants.^{26,27} By contrast, in utero exposure

to anticonvulsants, particularly valproate, has led to significant developmental problems in children.²⁸ The data on atypical antipsychotics are limited.

None of the medications used to treat depression, bipolar disorder, anxiety, or schizophrenia is considered first-line or safest therapy for the pregnant woman. For any woman who is doing well on a certain medication, but particularly for a pregnant woman, there is no compelling, data-supported reason to switch to another agent. For depression, options include all of the SSRIs, with the possible exception of paroxetine (**TABLE 2**). In conflicting studies, paroxetine was no different from any other SSRI in not being associated with cardiovascular defects.²⁹

One goal in treatment is to use a medication that previously was effective in the remission of symptoms and to use it at the lowest dose possible. Treating simply to maintain a low dose of drug, however, and not to effect symptom remission, exposes the fetus to both the drug and the illness. Again, the lowest *effective* dose is the best choice.

Treatment during breastfeeding

Women are encouraged to breastfeed for physical and psychological health benefits, for both themselves and their babies. Many medications are compatible with breastfeeding.³⁰ The amount of drug an infant receives through breast milk is considerably less than the amount received during the mother's pregnancy. Breastfeeding generally is allowed if the calculated infant dose is less than 10% of the weight-adjusted maternal dose.³¹

The amount of drug transferred from maternal plasma into milk is highest for drugs with low protein binding and high lipid solubility.³² Drug clearance in infants must be considered as well. Renal clearance is decreased in newborns and does not reach adult levels until 5 or 6 months of age. In addition, liver metabolism is impaired in neonates and even more so in premature infants.³³ Drugs that require extensive first-pass metabolism may have higher bioavailability, and this factor should be considered.



One goal in treatment is to use a medication that previously was effective in symptom remission at the lowest dose possible

Some clinicians recommend pumping and discarding breast milk when the drug in it is at its peak level; although the drug is not eliminated, the infant ingests less of it.³⁴ Most women who are anxious about breastfeeding while on medication “pump and dump” until they are more comfortable nursing and the

infants are doing well. Except in cases of mother preference, most physicians with expertise in reproductive mental health generally recommend against pumping and discarding milk.

Through breast milk, infants ingest drugs in varying amounts. The amount depends on the qualities of the medication, the timing and

TABLE 2 Oral antidepressants commonly used during pregnancy and breastfeeding, with dose ranges

Class	Medication	When to use	Dose range
SSRI	Sertraline	<ul style="list-style-type: none"> • Often first choice for depression and anxiety • Well tolerated • Abundant data on safety during pregnancy and breastfeeding • Higher doses for obsessive-compulsive disorder 	<ul style="list-style-type: none"> • Start at 25 mg for 1 week • Increase to 50 to 200 mg • Monitor clinical response every 2 to 3 weeks, before increasing dose
	Citalopram	<ul style="list-style-type: none"> • Good choice for depression and anxiety • Abundant data on safety during pregnancy and breastfeeding • Higher doses associated with prolonged QT interval 	<ul style="list-style-type: none"> • Start at 5 to 10 mg for 1 week • Increase to 20 to 40 mg
	Escitalopram	<ul style="list-style-type: none"> • Compared with citalopram, this S enantiomer of citalopram has fewer data on safety during pregnancy and breastfeeding • May have fewer adverse effects 	<ul style="list-style-type: none"> • Start at 5 mg for 1 week • Increase to 10 mg • Dose range: 10–20 mg
	Fluoxetine	<ul style="list-style-type: none"> • Of SSRIs, has most data available • Possible small increased risk of cardiac defect • Conflicting data • Useful for depression and anxiety • Long half-life • No withdrawal effects in adults 	<ul style="list-style-type: none"> • Start at 10 mg for 1 week • Increase to 20 mg (usually effective) • Dose range: 20–80 mg • Higher doses for obsessive-compulsive disorder
	Paroxetine	<ul style="list-style-type: none"> • Possible small increased risk of cardiac defect • Missed doses lead to significant withdrawal symptoms • Compared with other SSRIs, may be more effective for anxiety 	<ul style="list-style-type: none"> • Start at 10 mg for 1 week • Increase to 20 mg • Dose range: 20–40 mg
NDRI	Bupropion	<ul style="list-style-type: none"> • Not useful for anxiety symptoms, may exacerbate anxiety • Compared with SSRIs, has fewer safety data • Good antidepressant for complaints related to attention and focus • No weight gain or sexual dysfunction 	<ul style="list-style-type: none"> • Start at 150 mg for 1 week • Increase to 300 mg • Dose range: 150–450 mg
SNRI	Venlafaxine	<ul style="list-style-type: none"> • May be related to hypertension during pregnancy • In many patients, missed doses lead to significant withdrawal symptoms • Limited data on safety during pregnancy • Useful for treatment-resistant depression 	<ul style="list-style-type: none"> • Start at 37.5 mg • Increase every week to 150 mg • Dose range: 75–300 mg


Abbreviations: NDRI, norepinephrine-dopamine reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

CONTINUED ON PAGE 38

duration of breastfeeding, and the characteristics of the infant. Few psychotropic drugs have significant effects on breastfed infants. Even lithium, previously contraindicated, is successfully used, with infant monitoring, during breastfeeding.³⁵ Given breastfeeding's benefits for both mother and child, many more women on psychotropic medications are choosing to breastfeed.

Balance the pros and cons

Deciding to use medication during pregnancy and breastfeeding involves considering the risk of untreated illness versus the

benefit of treatment for both mother and fetus, and the risk of medication exposure for the fetus. Mother and fetus are inseparable, and neither can be isolated from the other in treatment decisions. Avoiding psychotropic medication during pregnancy is not always the safest option for mother or fetus. The patient and her clinician and support system must make an informed decision that is based on the best available data and that takes into account the mother's history of illness and effective treatment. Many women with psychiatric illness no longer have to choose between mental health and starting a family, and their babies will be healthy. 

References

- Andrade SE, Raebel MA, Brown J, et al. Use of antidepressant medications during pregnancy: a multisite study. *Am J Obstet Gynecol*. 2008;198(2):194.e1–e5.
- Hecht A. Drug safety labeling for doctors. *FDA Consum*. 1979;13(8):12–13.
- Ramoz LL, Patel-Shori NM. Recent changes in pregnancy and lactation labeling: retirement of risk categories. *Pharmacotherapy*. 2014;34(4):389–395.
- Yonkers KA, Wisner KL, Stewart DE, et al. The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists. *Gen Hosp Psychiatry*. 2009;31(5):403–413.
- Cohen LS, Altshuler LL, Harlow BL, et al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. *JAMA*. 2006;295(5):499–507.
- O'Brien L, Laporte A, Koren G. Estimating the economic costs of antidepressant discontinuation during pregnancy. *Can J Psychiatry*. 2009;54(6):399–408.
- Viguera AC, Whitfield T, Baldessarini RJ, et al. Risk of recurrence in women with bipolar disorder during pregnancy: prospective study of mood stabilizer discontinuation. *Am J Psychiatry*. 2007;164(12):1817–1824.
- Bonari L, Pinto N, Ahn E, Einarson A, Steiner M, Koren G. Perinatal risks of untreated depression during pregnancy. *Can J Psychiatry*. 2004;49(11):726–735.
- Straub H, Adams M, Kim JJ, Silver RK. Antenatal depressive symptoms increase the likelihood of preterm birth. *Am J Obstet Gynecol*. 2012;207(4):329.e1–e4.
- Hayes LJ, Goodman SH, Carlson E. Maternal antenatal depression and infant disorganized attachment at 12 months. *Attach Hum Dev*. 2013;15(2):133–153.
- Field T. Prenatal depression effects on early development: a review. *Infant Behav Dev*. 2011;34(1):1–14.
- Kjaersgaard MI, Parner ET, Vestergaard M, et al. Prenatal antidepressant exposure and risk of spontaneous abortion—a population-based study. *PLoS One*. 2013;8(8):e72095.
- Nordeng H, van Gelder MM, Spigset O, Koren G, Einarson A, Eberhard-Gran M. Pregnancy outcome after exposure to antidepressants and the role of maternal depression: results from the Norwegian Mother and Child Cohort Study. *J Clin Psychopharmacol*. 2012;32(2):186–194.
- Källén BA, Otterblad Olausson P. Maternal use of selective serotonin re-uptake inhibitors in early pregnancy and infant congenital malformations. *Birth Defects Res A Clin Mol Teratol*. 2007;79(4):301–308.
- Tomson T, Battino D. Teratogenic effects of antiepileptic drugs. *Lancet Neurol*. 2012;11(9):803–813.
- Balon R, Riba M. Should women of childbearing potential be prescribed valproate? A call to action. *J Clin Psychiatry*. 2016;77(4):525–526.
- Giles JJ, Bannigan JG. Teratogenic and developmental effects of lithium. *Curr Pharm Design*. 2006;12(12):1531–1541.
- Nguyen HT, Sharma V, McIntyre RS. Teratogenesis associated with antipolar agents. *Adv Ther*. 2009;26(3):281–294.
- Campbell E, Kennedy F, Irwin B, et al. Malformation risks of antiepileptic drug monotherapies in pregnancy. *J Neurol Neurosurg Psychiatry*. 2013;84(11):e2.
- Huybrechts KE, Hernández-Díaz S, Paterno E, et al. Antipsychotic use in pregnancy and the risk for congenital malformations. *JAMA Psychiatry*. 2016;73(9):938–946.
- Chambers CD, Hernández-Díaz S, Van Marter LJ, et al. Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. *N Engl J Med*. 2006;354(6):579–587.
- 't Jong GW, Einarson T, Koren G, Einarson A. Antidepressant use in pregnancy and persistent pulmonary hypertension of the newborn (PPHN): a systematic review. *Reprod Toxicol*. 2012;34(3):293–297.
- Oberlander TF, Misri S, Fitzgerald CE, Kostaras X, Rurak D, Riggs W. Pharmacologic factors associated with transient neonatal symptoms following prenatal psychotropic medication exposure. *J Clin Psychiatry*. 2004;65(2):230–237.
- Warburton W, Hertzman C, Oberlander TF. A register study of the impact of stopping third trimester selective serotonin reuptake inhibitor exposure on neonatal health. *Acta Psychiatr Scand*. 2010;121(6):471–479.
- Croen LA, Grether JK, Yoshida CK, Odouli R, Hendrick V. Antidepressant use during pregnancy and childhood autism spectrum disorders. *Arch Gen Psychiatry*. 2011;68(11):1104–1112.
- Batton B, Batton E, Weigler K, Aylward G, Batton D. In utero antidepressant exposure and neurodevelopment in preterm infants. *Am J Perinatol*. 2013;30(4):297–301.
- Austin MP, Karatas JC, Mishra P, Christl B, Kennedy D, Oei J. Infant neurodevelopment following in utero exposure to antidepressant medication. *Acta Paediatr*. 2013;102(11):1054–1059.
- Bromley RL, Mawer GE, Briggs M, et al. The prevalence of neurodevelopmental disorders in children prenatally exposed to antiepileptic drugs. *J Neurol Neurosurg Psychiatry*. 2013;84(6):637–643.
- Einarson A, Pistelli A, DeSantis M, et al. Evaluation of the risk of congenital cardiovascular defects associated with use of paroxetine during pregnancy. *Am J Psychiatry*. 2008;165(6):749–752.
- Davanzo R, Copertino M, De Cunto A, Minen F, Amadeo A. Antidepressant drugs and breastfeeding: a review of the literature. *Breastfeed Med*. 2011;6(2):89–98.
- Ito S. Drug therapy for breast-feeding women. *N Engl J Med*. 2000;343(2):118–126.
- Suri RA, Altshuler LL, Burt VK, Hendrick VC. Managing psychiatric medications in the breast-feeding woman. *Medscape Womens Health*. 1998;3(1):1.
- Milsap RL, Jusko WJ. Pharmacokinetics in the infant. *Environ Health Perspect*. 1994;102(suppl 1):107–110.
- Newport DJ, Hostetter A, Arnold A, Stowe ZN. The treatment of postpartum depression: minimizing infant exposures. *J Clin Psychiatry*. 2002;63(suppl 7):31–44.
- Viguera AC, Newport DJ, Ritchie J, et al. Lithium in breast milk and nursing infants: clinical implications. *Am J Psychiatry*. 2007;164(2):342–345.