The clinical content of preconception care: women with psychiatric conditions

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For a substantial proportion of women, pregnancy can be complicated by the occurrence or reoccurrence of a psychiatric condition. Psychiatric disorders during pregnancy are associated with poor obstetric outcomes, higher risk of postpartum psychiatric illness, increased rates of substance abuse, lower participation in prenatal care, and adverse infant and family outcomes. As part of preconception care, providers should be vigilant and screen for psychiatric disorders among women of reproductive age, as the detection and appropriate management of these conditions can reduce the occurrence of adverse pregnancy and family outcomes. This manuscript reviews the treatment options and the risks and benefits of discontinuing, changing, or continuing psychotropic medications for women of reproductive age with common psychiatric disorders (depression and anxiety disorders, bipolar disorder, and schizophrenia) and offers recommendations for preconception care.

Key words: anxiety, bipolar, depression, preconception, schizophrenia

For a substantial proportion of women of reproductive age, the antenatal and postpartum periods can be complicated by the onset of a psychiatric condition or the occurrence or reoccurrence of a preexisting psychiatric condition. Psychiatric disorders during pregnancy have been associated with poor obstetric outcomes, higher risk of postpartum psychiatric illness, increased rates of substance abuse, lower participation in prenatal care, and adverse infant and family outcomes.[1] The detection and appropriate management of psychiatric conditions among women of reproductive age before or early in pregnancy is critical for preventing morbidity during and after the pregnancy for the woman and her offspring. In managing psychiatric conditions during pregnancy and among women who could become pregnant, the clinician must consider and weigh the risks and benefits of discontinuing, changing, or continuing psychotropic medications. Preconception considerations for common psychiatric disorders are discussed in this manuscript.

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Received June 17, 2008; revised Aug. 29, 2008; accepted Sept. 3, 2008.

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Conflict of Interest: Ariela Frieder, MD; Anne L. Dunlop, MD, MPH; and Peter S. Bernstein, MD, MPH have no conflict of interest including grants, honoraria, advisory board membership, or share holdings. Larry Culpepper, MD, MPH is a consultant or is on the advisory board of Forest Labs, New York, NY; Pfizer, New York, NY; Wyeth, Madison, NJ; AstraZeneca, Wilmington, DE; Lilly, Indianapolis, IN; and Cephalon, Frazer, PA. He is on a Speakers Bureau for Forest Labs, Pfizer, and Wyeth.

 • doi: 10.1016/j.ajog.2008.09.001

Depression and anxiety disorders

Burden of suffering

Mood and anxiety disorders are highly prevalent among women of reproductive age and are comorbid in over 50% of those diagnosed with either. There is evidence that the emergence of a new psychiatric illness or the relapse of a preexisting one during pregnancy is highly prevalent (10-20%).[2] Of note, while anxiety disorders tend to persist chronically following their onset, depressive disorders are usually episodic, with very high rates of recurrence (85% at 15 years). There is much evidence suggesting that depression and anxiety during pregnancy and postpartum have a severe impact on family life, the mother-infant relationship, and the future mental health of the child.[1-7] These may be mediated by environmental, neurohormonal, and genetic influences.[8,9] Depression increases the risk of tobacco, alcohol, and illicit drug use, and may contribute to inadequate prenatal care. In addition, it increases the risk of self-injurious and suicidal behavior. Several studies have found an association between depression during pregnancy and preterm delivery, lower birthweight, smaller head circumference, low Apgar scores, and postpartum depression.[2,10,11] Moreover, perinatal depression can have short- and long-term developmental, cognitive, and behavioral effects on the child.[1,2,9,12,13] Depression can lead to reduced interaction and irritability towards the child.[6]

Although little is known about the prevalence of anxiety disorders (social anxiety disorder, panic disorder, obsessive compulsive disorder, posttraumatic stress disorder, and generalized anxiety disorder) during and after pregnancy, anxiety disorders may be more common than depression during pregnancy.[5] Anxiety disorders during pregnancy and postpartum have been associated with poor neonatal outcome, obstetric com-

plications, childhood behavioral problems, and avoidance of the child by the mother.[2] In women with preexisting obsessive compulsive disorder (OCD), pregnancy may precipitate a worsening of symptoms. Of note, obsessions of infanticide or child harm are a common feature of postpartum OCD. Their content can include child sexual abuse.[14] Posttraumatic stress disorder (PTSD) has been described in pregnancies in women who had a previous complicated delivery. PTSD may also present in the postpartum period following a traumatic childbirth.[5,14] Postpartum PTSD may affect a woman's future childbearing decisions, her ability to breastfeed, and the relationship between mother and infant.[5,14] PTSD also frequently follows abuse and is frequently comorbid with depression and generalized anxiety disorder.[15]

How detectable is the condition?

Diagnostic and Statistical Manual of Mental Disorders-IV-TR criteria are currently used to diagnose Depressive and Anxiety disorders.[16] Available screening tools are the PHQ-9, QIDS, GAD-7, Beck Depression Inventory, and the Hamilton Rating Scale, among others. Risk factors for depression and anxiety during and after pregnancy include a history of mood or anxiety disorder, marital problems, inadequate support system, recent stressors, lower socioeconomic status, and unwanted pregnancy.[2,17]

How effective are the current treatments?

Depression and anxiety disorders can be treated effectively during pregnancy with psychotherapy, cognitive behavioral therapy, interpersonal psychotherapy, and/or medications. A review of 12 psychotherapy trials involving nonpregnant subjects in primary care settings found that psychotherapy resulted in similar outcomes to those obtained using antidepressants and better outcomes than a primary care physician's usual care.[18] In addition, electroconvulsive therapy is an effective treatment for depression, and is safe during pregnancy.[19,20]

In recent years, antidepressant use during pregnancy has increased significantly. In 1 large study, selective serotonin reuptake inhibitor use increased from 1.5% in 1996 to 6.2% in 2005.[21] All psychotropic medications diffuse across the placenta and none have yet been approved by the US Food and Drug Administration (FDA) for use during pregnancy.[2] Data accumulated over the last 30 years suggest the limited teratogenic effects of most antidepressants (including selective serotonin reuptake inhibitors [SSRIs], tricyclic antidepressants [TCAs], and venlafaxine).[2-4,22,23] However, paroxetine's FDA classification has recently been changed from C to D based upon a retrospective study that found a 1.5-2 times increased risk of congenital cardiac malformations associated with exposure to paroxetine in the first trimester. Moreover, 2 large case-control studies that found an association between SSRI use during early pregnancy—particularly paroxetine—and anencephaly, craniosynostosis, and omphalocoele[24] and right ventricular outflow abnormalities.[25] Even still, the absolute risk associated with exposure was very small. Furthermore, recent studies have linked exposure to antidepressant therapy during pregnancy with preterm delivery and/or lower birthweight. A retrospective study of depressed women treated with SSRIs or untreated found in utero exposure to SSRIs linked with earlier gestational age and lower birth rate; the exposed group also had higher rates of neonatal respiratory distress syndrome, jaundice, and feeding problems.[26,27] A particular concern was the potential adverse effect of late trimester exposure to SSRIs with 1 small study reporting pulmonary hypertension of the newborn.[28] A naturalistic study of depressed women and healthy controls found an association between preterm delivery and exposure to antidepressant therapy, while maternal depression itself was not linked with preterm delivery.[27] All of these newer studies have added an extra level of complexity in the decision-making process of the treatment of depression during pregnancy. Treatment should be the result of an individualized risk-benefit assessment.[29] Thus, in women with less severe symptoms, it may be appropriate to consider nonpharmacologic interventions such as psychotherapy.[29] However, if the symptoms are moderate to severe, if there is a history of previous postpartum depression or recurrent major depressive disorder, a combination of psychotherapy and medications is advised.[29,30]

Impact of preconception care

Identification of depression and anxiety disorders prior to pregnancy allows time to discuss treatment options and, if necessary, to change to a treatment regimen that is safer during pregnancy. The goal should be for the woman to be euthymic during pregnancy to prevent negative outcomes. Women with a history of mood or anxiety disorder should be informed about the high risk of relapse (50-75%) when discontinuing maintenance medication.[2,31] Any necessary changes in medications should be made prior to conception to decrease the exposure of the fetus to multiple medications. Such preconception medication adjustment also allows for gradual tapering of the antidepressant to minimize the risk of withdrawal symptoms. It also allows opportunity to monitor for relapse, which is most likely in the initial months following withdrawal.

Recommendations by other groups

The American College of Obstetrics and Gynecology (ACOG), in a November 2007 Practice Bulletin, recommended that paroxetine use in pregnant women and women planning a pregnancy should be avoided if possible, and that fetal echocardiography be considered for women who are exposed to paroxetine in early pregnancy. They further recommend that treatment with all SSRIs during pregnancy should be individualized, and that use of a single medication at a higher dose should be favored over the use of multiple medications.[2,4]

Recommendation. Providers should screen and be vigilant for depression and anxiety disorders among women of reproductive age, as treating or controlling these conditions prior to pregnancy may help prevent negative pregnancy and family outcomes. Women of reproductive age with depressive and anxiety disorders who are planning a pregnancy or

who could become pregnant should be informed about the potential risks of an untreated illness during pregnancy and about the risks and benefits of various treatments during pregnancy. Identifying healthy women at risk along with appropriate referral for social and psychological interventions during the preconception visit might prevent the emergence of anxiety and depressive disorders during pregnancy and postpartum. *Strength of recommendation*: B; *quality of evidence*: II-2.

Bipolar disorder

Burden of suffering

Bipolar disorder (BD) is particularly challenging during the reproductive years, as associated outcomes may include lower fertility rates, strong genetic loading, potential fetal teratogenic risk from medications to control the condition, and high risk of recurrence if treatment is discontinued abruptly.[32] There is a strong familial pattern in bipolar disorder, with about 10% of first-degree relatives, including offspring, also affected.[33] Women with BD are also at higher risk for other psychiatric disorders and medical illnesses including obesity, migraines, and thyroid dysfunction. Hypomanic and manic episodes often include high-risk sexual activity with significant risk of unintended pregnancy. Moreover, women with BD might exhibit poor insight into their condition that interferes with appropriate treatment. Some studies suggest a protective effect of BD during pregnancy.[2] More recent studies show a high risk of relapse, especially if medications are discontinued.[34] In a recent prospective study that estimated the risk of recurrence of BD during pregnancy in women who either discontinued or continued the use of a mood stabilizer, 70.8% of the overall population of women was found to experience at least 1 episode of illness during their pregnancy. Recurrence risk was 2.3 times greater after discontinuing mood stabilizer treatment. Women who discontinued the mood stabilizer spent over 40% of their pregnancy in a mood episode, compared to 8.8% of the women who continued their medication. Furthermore, women who discontinued the mood stabilizer abruptly had a 50% risk of recurrence within 2 weeks versus 22 weeks in women who gradually tapered their mood stabilizer treatment.[35] Moreover, women with BD are at high risk of relapse during the postpartum period (20-80%) and have a 10-20% prevalence of postpartum psychosis.[1,36] Postpartum psychosis is associated with high rates of suicide and infanticide.[1,4,34]

How detectable is the condition?

DSM-IV-TR criteria are currently used to diagnose BD.[16] Women should be assessed for BD at the preconception visit, at least to identify those with a history of BD but who may be functioning well, and who may not be in contact with psychiatric services. Women should be screened by asking about family history of mood disorders as well as personal history of depression, psychosis, and mania. Women at risk should receive a formal psychiatric assessment.

How effective are the current treatments?

BD is a severe recurrent illness that is associated with high rates of morbidity and mortality in the absence of adequate treatment. Identifying and treating women prior to pregnancy might prevent negative outcomes. Medications used to treat BD (including lithium and anticonvulsants) are associated with increased risk of fetal anomalies. First-trimester exposure to lithium increases the risk of cardiac malformations to levels that range 10-20 times greater than in the general population. Still the absolute risk remains low, 1:1000-1:2000. Compared with lithium, anticonvulsants such as carbamazepine and valproic acid may confer even greater risks of malformations (1-7%), including neural tube defects, craniofacial anomalies, and microcephaly. Moreover, valproic acid was found to have long term neurobehavioral effects in children exposed in utero across all the trimesters.[37] Of note, most of the data regarding use of lamotrigine as monotherapy have not shown an increase in risk of major malformations. However, a recent report of the North American Antiepiletic Drug Registry has suggested an increase risk of oral clefts associated to first-trimester exposure to lamotrigine monotherapy. More data are still necessary to corroborate these findings.[34,38,39] Atypical antipsychotics are widely used in the treatment of BD; however, there are limited data about their use during pregnancy. It is highly recommended that required changes in medications be done prior to conception to decrease the exposure of the fetus to multiple medications. Illness history and reproductive safety of medications are the most important factors to consider when planning treatment. A risk assessment should include the patient's: 1) prior response to medications; 2) illness severity; 3) duration of euthymia; 4) time to relapse after discontinuing medications; and 5) time to recover with reintroduction of medications.[34] Thus, in women with low risk of relapse, medication should be tapered slowly over the course of 6 weeks. High potency antipsychotics could be used if needed. Women with more severe risk of relapse are recommended to continue medications.[40] Despite the dearth of data, folic acid supplementation (4 mg daily) is recommended to prevent neural tube defects for patients being treated with anticonvulsants.[34] It is also important to address the consumption of caffeine, nicotine, illicit drugs, and alcohol, as well as poor nutrition and the general level of stress and sleep deprivation.

Impact of preconception care

Identification of bipolar disorder prior to pregnancy allows time to discuss treatment options and, if necessary, to switch to a medication that is safer during pregnancy. The goal should be for the woman to be euthymic during pregnancy to prevent negative outcomes. Women with a history of BD should be informed about the high risk of relapse when discontinuing maintenance medication.[2] Any necessary changes in medications should be made prior to conception to decrease the exposure of the fetus to multiple medications.[41] Women with BD often have limited social supports, and preconception assessment can provide an opportunity to help such women mobilize these. When possible, the partner or family should be involved in the

advance planning of relapse prevention and management strategies. This can be particularly helpful to improve outcome in women with poor insight, poor impulse control, and cognitive impairment. The preconception visit also provides for the opportunity to educate women regarding the importance of planning for pregnancy and of available long-acting contraceptive methods that can provide protection during bipolar relapses.

Recommendations by other groups

The ACOG, in an April 2008 Practice Bulletin, recommend that the use of valproate and carbamazepine during pregnancy should be avoided, when possible, particularly during the first trimester. They further recommend that a fetal echocardiogram should be considered in women exposed to lithium during the first trimester.

Recommendation. Women of reproductive age with BD should be counseled that pregnancy is a time of substantial risk of relapse, particularly following discontinuation of ongoing mood stabilizing maintenance treatment. A relapse prevention and management strategy for bipolar disorder should be outlined before the patient attempts conception.[42] When possible, the partner or family member should be involved in the advance planning. Women of reproductive age with BD should be counseled regarding contraceptive options, including those that will prevent conception during bipolar episodes. *Strength of recommendation*: B; *quality of evidence*: II-2.

Schizophrenia

Burden of suffering

Women with schizophrenia are probably among the most vulnerable to psychiatric complications of pregnancy. They have a high risk of malformations and fetal demise. They are at high risk for relapse while not taking their medications, placing prenatal care and their own well-being in jeopardy. Psychosis during pregnancy can lead to fetal abuse, neonaticide, and inability to recognize signs or symptoms of labor. In addition, they have a higher risk of unwanted and unplanned pregnancies, and are more likely to be unmarried and have limited social support.[2,43] Women with schizophrenia are more prone to exhibit poor insight into their condition and cognitive impairment that might interfere with their ability to participate in treatment.

How detectable is the condition?

DSM-IV-TR criteria are currently used to diagnose schizophrenia.[16,43] Women should be screened by asking about family history of psychotic and affective disorders, as well as personal history of psychosis. Women at risk should receive a formal psychiatric assessment.

How effective are the current treatments?

Schizophrenia is a chronic and debilitating illness. Treatment of schizophrenia with antipsychotics has been shown to decrease psychotic symptoms and improve functioning. When possible, antipsychotics should be avoided during the first trimester.[1] However, women with severe symptoms, including the inability to care for oneself or cooperate in prenatal care; impairment of reality testing, with potential danger to self or others; and disorganized thought, perception, and behavior, should receive pharmacotherapy.[4] There are more data about the use of typical than atypical antipsychotics. High-potency typical antipsychotics (haloperidol, perphenazine, trifluoperazine) were shown to be less teratogenic than low-potency typical antipsychotics (chlorpromazine).[4,44] Currently, many women with schizophrenia are using atypical antipsychotics; however, there are limited data about their use during pregnancy. Recommendations call for their use during pregnancy if the woman has a history of nonresponse to the better-studied antipsychotics, or is at significant risk of relapse should the medication be discontinued.[43,44] Atypical antipsychotics increase the risk for obesity, diabetes, and hypertension. It is advisable to closely monitor weight gain, blood pressure, and blood glucose. It is also recommended to address avoidable factors such as the use of caffeine, nicotine, illicit drugs, and alcohol, as well as poor nutrition, general level of stress, and sleep deprivation.

Impact of preconception care

Although the course of schizophrenia during pregnancy is not well defined, these pregnancies should be considered high risk. Psychosis itself poses a substantial risk for both mother and fetus. Women with schizophrenia tend to have poor nutrition and a high prevalence of tobacco, alcohol, and illicit drug use. Identification and treatment of women prior to pregnancy might improve outcomes for both mother and baby. Any necessary changes in medications should be done prior to conception to decrease the exposure of the fetus to multiple medications.[4] Preconception care also provides the opportunity to offer contraceptive methods to prevent unintended pregnancy.

Recommendations by other groups

None identified.

Recommendation. Women of reproductive age with schizophrenia should be counseled, together with a partner or family member whenever possible, about the risks of pregnancy on their condition and the risk of their condition on pregnancy-related outcomes. They should be counseled about the importance of prenatal care, and a relapse prevention and management strategy of the illness should be outlined before the patient attempts conception. When possible, the partner or family member should be involved in the advance planning. Appropriate contraception should be offered to women who do not desire a pregnancy. *Strength of recommendation*: B; *quality of evidence*: II-2.

Conclusion

As part of preconception care, providers should be vigilant and screen for psychiatric disorders among women of reproductive age, particularly those who are planning a pregnancy or who could become pregnant, as treating and controlling these conditions prior to pregnancy may reduce the occurrence of adverse pregnancy and family outcomes. In making treatment decisions for women of reproductive age with psychiatric disorders, the clinician, together with the

patient, must consider both the risks of the condition during pregnancy and postpartum as well as the risk and benefits of the medications used to control these disorders. ■

REFERENCES

1. Burt VK, Hendrick VC. Clinical manual of women's mental health. In: Wyszynski AA, Wyszynski B, eds, Manual of psychiatric care for the medically ill. Arlington, VA: American Psychiatric Publishing, Inc; 2005.

2. Cohen LS, Nonacs RM. Mood and anxiety disorders during pregnancy and postpartum. Review of psychiatry, volume 24. In: Wyszynski AA, Wyszynski B, eds, Manual of psychiatric care for the medically ill. Arlington, VA: American Psychiatric Publishing, Inc; 2005.

3. Brockington I. Motherhood and mental health. New York, NY: Oxford University Press; 1996.

4. Wyszynski AA, Lusskin S. The obstetric patient. In: Wyszynski AA, Wyszynski B, eds, Manual of psychiatric care for the medically ill. Arlington, VA: American Psychiatric Publishing, Inc; 2005.

5. Ross LE, McLean LM. Anxiety disorders during pregnancy and the postpartum period: a systematic review. J Clin Psychiatry 2006;67:8.

6. Halbreich U. The association between pregnancy processes, preterm delivery, low birth weight and postpartum depression—the need for interdisciplinary integration. Am J Obstet Gynecol 2005;193:1312-22.

7. Brockington I. Postpartum psychiatric disorders. Lancet 2004;363:303-10.

8. Davis EP, Glynn LM, Schetter CD, Hobel C, Chicz-Demet A, Sandman CA. Prenatal exposure to maternal depression and cortisol influences infant temperament. J Am Acad Child Adolesc Psychiatry 2007;46:737-46.

9. Talge NM, Neal C, Glover V. Early Stress, Translational Research and Prevention Science Network: fetal and Neonatal Experience on child and Adolescent Mental Health. Antenatal maternal stress and long term effects on child neurodevelopment: how and why? J Child Psychol Psychiatry 2007;48:245-61.

10. Bloch M, Rotenberg N, Koren D, Klein E. Risk factors for early postpartum depressive symptoms. Gen Hosp Psychiatry 2006;28:1-2.

11. Robertson E, Grace S, Wallington T, Stewart DE. Antenatal risk factors for postpartum depression: a synthesis of recent literature. Gen Hosp Psychiatry 2004;26:289-95.

12. Monk C. Stress and mood disorders during pregnancy: implications for child development. Psychiatric Quarterly 2001;72:347-357.

13. Davis EP, Snidman N, Wadhwa PD, Glynn LM, Schetter CD, Sandman CA. Prenatal maternal anxiety and depression predict negative behavioral reactivity in infancy. Infancy 2004;6:319-31.

14. Brockington IF, Macdonald E, Wainscott G. Anxiety, obsessions and morbid preoccupations in pregnancy and the puerperium. Arch Womens Ment Health 2006;9:253-63.

15. Loveland Cook CA, Flick LH, Homan SM, Campbell C, McSweeney M, Gallagher ME. Posttraumatic stress disorder in pregnancy: prevalence, risk factors, and treatment. Obstet Gynecol 2004;103:710-17.

16. Diagnostic and statistical manual of mental disorders. Text revision. Fourth edition. Arlington, VA: American Psychiatric Association; 2000.

17. Robertson E, Grace S, Wallington T, Stewart DE. Antenatal risk factors for postpartum depression: a synthesis of recent literature. Gen Hosp Psychiatry 2004;26:289-95.

18. Schulberg HC, Raue PJ, Rollman BL. The effectiveness of psychotherapy in treating depressive disorders in primary care practice: clinical and cost perspectives. Gen Hosp Psychiatry 2002;24:203-12.

19. Miller LJ. Use of electroconvulsive therapy during pregnancy. Hosp Community Psychiatry 1994;45:444-50 (Level III).

20. Rabheru K. The use of elelctroconvulsive therapy in special patient populations. Can J Psychiatry 2001;46:710-19 (Level III).

21. Andrade SE, Raebel MA, Brown J, et al. Use of antidepressant medications during pregnancy: a multisite study. Am J Obstet Gynecol 2008;198:191.e1-e5.

22. Altshuler LL, Cohen LS, Szuba MP, Burt VK, Fitlin M, Mintz J. Pharmacologic management of psychiatric illness during pregnancy: dilemmas and guidelines. Am J Psychiatry 1996;153:392-606.

23. Wisner KL, Gelenberg AJ, Leonard H, Zarin D, Frank E. Pharmacologic treatment of depression during pregnancy. JAMA 1999;282:1264-9.

24. Alwan S, Reefhuis J, Rasmussen SA, Olney RS, Friedman JM. Use of selective serotonin-reuptake inhibitors in pregnancy and the risk of birth defects. N Engl J Med 2007;356:2684-92.

25. Louik C, Lin AE, Werler MM, Hernández-Díaz S, Mitchell AA. First-trimester use of selective serotonin reuptake inhibitors and the risk of birth defects. N Engl J Med 2007;356:2675-83.

26. Oberlander TF, Warburton W, Misri S, Aghajanian J, Hertzman C. Neonatal outcomes after prenatal exposure to selective serotonin reuptake inhibitor antidepressants and maternal depression using population-based linked health data. Arch Gen Psychiatry 2006;64:898-906.

27. Suri R, Altshuler L, Hellemann G, Burt VK, Aquino A, Mintz J. Effects of antenatal depression and antidepressant treatment on gestational age at birth and risk of preterm birth. Am J Psychiatry 2007;164:1206-13.

28. Chambers CD, Hernandez-Diaz S, VanMarter LJ, et al. Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. N Engl J Med 2006;354:579-87.

29. Kahn D. Moline ML, Ross RW, Cohen LS, Altshuler LL. Major depression during conception and pregnancy: a guide for patients and families. Expert Consensus Guideline Series. March 2001.

30. Freeman MP. Antenatal depression: navigating the treatment dilemmas. Am J Psychiatry 2007;164:1162-5.

31. Cohen LS, Nanacs RM, Bailey JW, et al. Relapse of depression during pregnancy following antidepressant discontinuation: a preliminary prospective study. Arch Womens Ment Health 2004;7:217-21.

32. Viguera AC, Cohen LS, Bouffard S, Whitfield TH, Baldessarini RJ. Reproductive decisions by women with bipolar disorder after pre pregnancy psychiatric consultation. Am J Psychiatry 2002;159:2102-4.

33. Merikangas KR, Low NC. The epidemiology of mood disorders. Curr Psychiatry Rep 2004;6:411-21.

34. Yonkers KA, Wisner KL, Stowe Z, et al. Management of bipolar disorder during pregnancy and the postpartum period. Am J Psychiatry 2004;161:608-20.

35. 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;164:1817-24.

36. Stewart DE, Klompenhouwer JL, Kendell RE, Van Hulst AM. Prophylactic lithium in puerperal psychosis. The experience of three centers. Br J Psychiatry 1991;158:393-7.

37. Cohen LS. Treatment of bipolar disorder during pregnancy. J Clin Psychiatry 2007;68(suppl 9):4-9.

38. Shor S, Koren G, Nulman I. Teratogenicity of lamotrigine. Can Fam Physician 2007;53:1007-9.

39. Viguera AC, Koukopoulos A, Muzina DJ, Baldessarini RJ. Teratogenicity and anticonvulsants: lessons from neurology to psychiatry. J Clin Psychiatry 2007;68(suppl 9):29-33.

40. Jones I, Craddock N. Bipolar disorder and childbirth: the importance of recognizing risk. Br J Psychiatry 2005;186:453-4.

41. Viguera AC, Cohen LS, Baldessarini RJ, Nonacs R. Managing bipolar disorder during pregnancy: weighing the risks and benefits. Can J Psychiatry 2002;47:426-36.

42. Gentil S. Prophylactic treatment of bipolar disorder in pregnancy and breastfeeding: focus on emerging mood stabilizers. Bipolar Disorders 2006;8:207-20.

43. Yaeger D, Smith HG, Altshuler LL. Atypical antipsychotics in the treatment of schizophrenia during pregnancy and postpartum. Am J Psychiatry 2006;163:2064-70.

44. Patton SW, Misri S, Corral MR. Antipsychotic medication during pregnancy and lactation in women with schizophrenia: evaluating the risk. Can J Psychiatry 2002;47:959-65.