

## *Before, Between & Beyond Pregnancy*

### **The National Preconception Curriculum and Resources Guide for Clinicians**

## **Guidance for Preconception Care of Women with Bipolar Disorders**

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Ariela Frieder, MD  
Department of Psychiatry and Behavioral Sciences  
Montefiore Medical Center  
Albert Einstein College of Medicine

**This guidance should not be considered a substitute for clinical judgment or expert consultation.**

- The prevalence of Bipolar Disorder in the general population is 1-2.4%. Bipolar disorder is a severe recurrent illness that is associated with substantial morbidity and mortality if not adequately treated (18).
- Women should be screened for bipolar disorder prior to conception by asking about current or past symptoms of depression, mania and psychosis. In addition, family history of mood disorders should be obtained. Women at risk should be referred to a psychiatrist for a formal psychiatric assessment (7).
- Women with bipolar disorder should be referred for genetic counseling prior to conception as their offspring might be at risk of developing an affective disorder. There is a strong familial pattern in bipolar disorder, with about 10% of first degree relatives, including offspring, also affected. Ideally both partners should be involved in genetic counseling, as it gives them the opportunity to discuss their reproductive decisions (19, 20)
- Bipolar disorder is associated with a higher risk of co-morbidity with other psychiatric disorders and medical illnesses such as obesity, migraines and thyroid dysfunction (1,7)
- Bipolar disorder has a high risk of relapse or recurrence during the postpartum period (20%-80%) with a prevalence of postpartum psychosis of 10%-20% (2, 9),
- Postpartum psychosis is associated with high rates of suicide and infanticide (2, 10)

- A hypomanic or manic episode may include poor insight, poor impulse control and cognitive impairment (7)
- During a hypomanic or manic episode women with bipolar disorder may engage in high-risk sexual activity with a significant risk of unintended pregnancies and sexually transmitted infections. (7)
- There is substantial evidence that discontinuing medication prior or during pregnancy can predispose to relapse (21,22)
- Women who abruptly stop their medication are at higher risk of recurrence in a short period of time while women that gradually taper medications can have a longer span to a recurrence (22)
- In a recent prospective study 70.8% of the overall population of women with bipolar disorder were found to experience at least one episode of illness during their pregnancy. Women had a recurrence risk 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. Finally, women who discontinued the mood stabilizer abruptly had a 50% risk of recurrence within two weeks versus 22 weeks in women who gradually tapered their mood stabilizer treatment. (22)
- Treatment of bipolar disorder during pregnancy is complex as there is a teratogenic risk from the medications used to control the illness. (1,2,7)
- It is highly recommended that treatment decisions and required changes in medications be done prior to conception to decrease the exposure of the fetus to multiple medications (2,7)
- Treatment should be individualized based on a risk-benefit assessment (2,7)
- Women with low risk of relapse and mild symptoms may consider tapering medications slowly over a six-week period prior to conception (2)
- Women with moderate risk of relapse and severe illness history are recommended to taper medication prior to conception and restart after the first trimester. (2)
- Women with severe risk of relapse and severe illness history are recommended to continue their medication regimen (2)
- Lithium increases the risk of cardiac malformations to levels that range 10-20 times greater than in the general population. However, the absolute risk remains low: 1:1,000 to 1:2,000 (1,2)
- A high resolution ultrasound and fetal echocardiography at 16-18 weeks is highly recommended in women exposed to lithium during the first trimester (8)

- Renal clearance of lithium increases over the pregnancy and decreases significantly during labor and delivery. It is important to monitor and adjust appropriately lithium levels both during pregnancy and postpartum. In addition, levels should be monitored closely during labor to decrease the risk of maternal and neonatal toxicity (2)
- 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 (1,2)
- In addition, valproic acid was found to have long-term cognitive effects in children exposed *in utero* across all the trimesters, therefore its use should be avoided during pregnancy. (23)
- Minimizing and avoiding the use of valproate acid and carbamazepine during pregnancy, particularly during the first trimester, is encouraged (8)
- Despite the dearth of data, supplementation with folic acid is recommended for women exposed to anticonvulsants (1,2,8)
- Vitamin K supplementation is recommended for women exposed to carbamazepine and other anticonvulsants during pregnancy to prevent hemorrhagic disease in the newborn (6)
- Recent data taken together from several pregnancy registries indicate that *in utero* exposure to lamotrigine is associated with oral cleft at an approximate rate of 4-8.9:1,000. However, compared with other mood stabilizers, lamotrigine seems to be the safest one during pregnancy. (6)
- Antipsychotics are approved and used for various phases of the treatment of bipolar disorder (1,6)
- There is substantial data about the use of typical antipsychotics during pregnancy. High potency antipsychotics (haloperidol, perphenazine, trifluoperazine) were shown to be less teratogenic than low potency ones (chlorpromazine).(6)
- Atypical antipsychotics are increasingly used in bipolar disorder. There is limited data about their use during pregnancy. They are known to increase the risk of obesity, diabetes and hypercholesterolemia. It is advisable to closely monitor these women's weight, body mass index, fasting glucose and lipid profile. (6)
- It is important to address the consumption of caffeine, drugs, alcohol, general levels of stress and sleep deprivation (7)

***Preconception recommendations of CDC select panel on preconception care clinical committee:*** (Frieder A., Dunlop A. L., Culpepper L, Bernstein P. S. The Clinical Content of Preconception Care: Women with Psychiatric Conditions.

- Women of reproductive age with bipolar disorder 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. When possible, the partner or family member should be involved in the advance planning. Women of reproductive age with bipolar disorder should be counseled regarding contraceptive options, including those that will prevent conception during bipolar episodes.

*Strength of recommendation: B; Quality of evidence: II-2*

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