

How to Treat Perinatal Mental Health Conditions

Learning Objectives:

1. To recognize psychiatric conditions that are specific to the perinatal population
2. To review psychopharmacologic guidelines in perinatal health
3. To appreciate special considerations when consulting for a perinatal population

Step 1: Familiarize yourself with perinatal-specific psychiatric diagnoses

- Perinatal mental health is defined as all mental health conditions during pregnancy and up to 1 year after delivery, with an additional focus on pre-conception and infertility.
- “Baby blues,” and perinatal anxiety, depression, and psychosis, are commonly encountered by CL psychiatrists (1,2,3)
 - Depression and bipolar disorder specifically have a “with peripartum onset” specifier in the DSM-5.
- Pre-existing psychiatric illnesses predispose women to obstetric complications such as gestational weight concerns, preterm labor, and pre-eclampsia; they also interfere with engagement in obstetrical care.
- Any woman with a pre-existing psychiatric disorder is at risk of relapse or deterioration during the peripartum period.
- Untreated psychiatric illness during pregnancy predisposes to post-partum deterioration

Table 1: incidence, timeline, key symptoms, and treatment of common postpartum conditions.

	Baby Blues	Postpartum Depression	Postpartum Anxiety	Postpartum Psychosis
Incidence	Up to 85%	15%	10-20%	0.1-0.2%
Timeline	Onset 2-3 days after delivery; self-limited and resolves within 10-14 days	Onset between 2 weeks-2 months, can last months to years	Onset between days after delivery to 2 months; can last months to years	Sudden onset within 2 weeks of delivery; can last weeks to months
Key symptoms	Fatigue, low mood, tearfulness, irritability	Low mood, fatigue, guilt, poor sleep/appetite, suicidal thoughts and anhedonia	Intrusions, excessive worry, feelings of dread, sleep disruption, racing thoughts, palpitations, nausea, sweating	Hallucinations, delusions (belief that child better off without her), hyper religiosity, disorganized behavior, sleep disturbance, confusion, suicidal ideation, homicidal ideation focused on infant
Treatment	• Supportive • Encourage help with infant	• Antidepressant medication • Zuranolone • Psychotherapy	• Antidepressant medication • Psychotherapy	• Lithium • Antipsychotics • Inpatient is preferred treatment setting
Notes	20% progress to postpartum depression			• 5% risk of suicide; 4.5% risk of infanticide

ACLP How To Guide: Perinatal Mental Health

				Determine location and safety of the child(ren).
--	--	--	--	--

Step 2: Psychopharmacologic Guidelines

- In general, patients can continue on most psychotropic medications which have been helpful, so long as the individual's risk-benefit assessment favors treatment.
 - This means that diagnoses should be solidified prior to starting/continuing treatment in these populations.
 - A notable exception to this includes **valproic acid**, which should be discontinued whenever pregnancy is diagnosed in favor of a safer agent.
- When considering pharmacologic treatment, always weigh risks/benefits vs that of *untreated mental illness*, rather than against controls without mental illness. This analysis should include non-pharmacologic treatment options and risk of psychotropic exposure to the fetus or breastfeeding infant.
 - It is important that psychiatric diagnoses are clarified or confirmed prior to initiating/continuing treatment to guide risk/benefit analysis

Table 2: guidelines for use of psychotropic classes and specific agents

Class	Notes
Antidepressants	
SSRIs	- Generally safe and well-tolerated in pregnancy and lactation. (4-9) - In large recent studies, no evidence of teratogenicity or lower neurodevelopmental outcomes compared to children of non-mentally-ill mothers (note that untreated maternal mental illness has been shown to negatively affect infant neurodevelopment). - Babies have a 30%, non-dose-dependent risk of neonatal adaptation syndrome (increased infant irritability and poor feeding) for the first 3-5 days of life when exposed during late pregnancy. - Management: swaddling, skin-to-skin, and small, frequent feedings. It is not recommended to lower SSRI dose or discontinue prior to delivery to decrease risk of this - Increased risk of postpartum hemorrhage; difference in blood loss is <100mL difference, likely not clinically significant. (10) - Some, but not all studies suggest a small increased risk of persistent pulmonary HTN of the newborn with SSRI exposure in pregnancy. Risk increases from 1/1000 in general population to 2-3/1000. (11) - It is not recommended to taper off SSRIs due to concerns about neonatal adaptation syndrome or persistent pulmonary HTN of the newborn - All SSRIs have a transfer rate<10% into breastmilk; no one agent is specifically recommended above others for lactation.
SNRIs	- Less data on SNRI use than on SSRIs. However, if a patient is doing well on an SNRI, we do not have any data specifically advocating against its use in pregnancy. - There is a risk of hypertension with certain SNRIs (e.g. venlafaxine) and patients should be monitored for gestational hypertension and preeclampsia/eclampsia.
Zuranolone	- No data to support use in pregnancy, only indicated for postpartum depression. - Limited lactation data, though transfer rate is low (<1%) based on a small study (12) - Monitor infant for sedation, drowsiness, difficulty with feeding if patient breastfeeds on zuranolone
Antipsychotics	

ACLP How To Guide: Perinatal Mental Health

Atypical antipsychotics	• Rate of major malformations is similar to the general population (1.4% vs 1.1% in controls) (13) • No data to support use of one agent over another from this category. Selection should be tailored to side effect profile and tolerability. Typical lab monitoring should occur as per relevant evidence base • Transient neonatal adaptation symptoms (fussiness, tremor, feeding difficulties) have been associated with atypical antipsychotics, though exact prevalence is unknown
Typical antipsychotics	• No consistent pattern of major malformations has been associated with the use of typical antipsychotics • Pregnancy outcomes do not appear to be significantly different from controls. Use can be supported when patient is stable on this medication, or when it is needed for acute management in pregnancy. • Transient neonatal adaptation symptoms (fussiness, tremor, feeding difficulties) have been associated with typical antipsychotics, though exact prevalence is unknown
Mood stabilizers	
Lithium	• Associated with Ebstein's anomaly (a right ventricular outflow tract defect) ◦ Absolute risk of Ebstein's is very low (cardiac anomaly risk 2.41% in setting of lithium exposure in first trimester vs 1.15% in general population; RVOT anomalies specifically is 0.60% with lithium exposure vs 0.18% without). (14, 15) ◦ Therefore, pregnant patients can be maintained on lithium throughout pregnancy with minimal increased absolute risk. • Due to changes in body fluid status, lithium levels reach a trough in the second trimester, and patient's may require dose increases during pregnancy. • Fluid shifts rapidly during birth. Lithium dosing should either 1) return immediately to pre-pregnancy dose (if known) or 2) drop to 2/3 of immediate pre-delivery dose. • Doses can be split to BID dosing to minimize extremes in lithium levels. • Serum levels should be monitored monthly in pregnancy, including weekly from week 34 until 2 weeks postpartum. • Lithium levels must also be checked in infant if mother chooses to breastfeed. Further, the risk of hypothyroidism with lithium use exists in pregnancy as well, and warrants monitoring. Any signs or symptoms of thyroid derangement should be promptly assessed.
Valproic Acid	• Frequently used as a mood stabilizer □ can have adverse consequences for fetus. (16, 17) • With first trimester exposure, the rate of major malformations rises to 6.1% from the non-exposed baseline of 3%, with a specific increase in neural tube deficits. • Exposure in pregnancy during any trimester is associated with an increased risk of autism spectrum disorders and neurodevelopmental illness. • Should not be prescribed in any woman of reproductive age unless reliable long-term contraception (e.g. sterilization or IUD) is in place.
Lamotrigine	• Lamotrigine is a well-tolerated and effective mood stabilizer in pregnancy. (18) While early studies showed a possible increase in cleft lip, this has not been reproduced in larger studies. This medication is well-tolerated, with generally few side effects. • Lamotrigine clearance increases significantly in pregnancy to estrogen-induced increased glucuronidation in the liver. May require lamotrigine dose increases to 2-3x pre-pregnancy dose to maintain stability. • Can increase dose based on symptoms or can obtain lamotrigine level pre-pregnancy and repeat level PRN during pregnancy to help guide need for dose

ACLP How To Guide: Perinatal Mental Health

	adjustments in pregnancy. Levels are not always needed, though can help with clinician comfort when needing to increase dose well outside usual range
Benzodiazepines	• Benzodiazepine use (particularly routine or high-dose use) is associated with preterm labor, C-section delivery, and low birth weight. • Can cause toxicity in newborns: “floppy baby syndrome,” respiratory depression, sedation. • Can be used selectively in pregnancy. (19) • Minimize to 2-3 doses PRN/week at lowest effective dose.
Stimulants	• Risk of untreated ADHD (unsafe driving, neglecting perinatal appointments, job loss, etc.) can pose true risk of harm to fetus. • Risk/benefit analysis may favor continuing treatment during pregnancy. • Patients should receive the lowest effective dose at the lowest effective frequency. Drug holidays are appropriate in this scenario when feasible. • Newer studies of appropriate clinical use demonstrate no statistically significantly increased risk of perinatal death or congenital malformations. • Risks of maternal hypertension and sleep changes exist. There is a small increase in fetal morbidity (increased NICU admissions, pre-term delivery, and CNS-related disorders).(20)

Step 3: Special Considerations

- Essential to ask all women of reproductive age routinely about their plans for pregnancy in the next 12 months to facilitate:
 - Counseling on their risks from their illness
 - Risks of prescribed medication or substance use
 - Education about contraception
 - A safe space for women to ask questions they may not feel comfortable asking elsewhere
- For patients with bipolar disorder, pharmacologic treatment is typically recommended given the strong association between untreated bipolar disorder and postpartum psychosis.
- Patients should be counseled that an infant’s requirement for frequent feeding overnight disrupts sleep and can increase the risk of mania and depression. If available, other sources of feeding support should be considered to allow the mother as much uninterrupted sleep as possible.
- Psychopharmacologic management of acute agitation in a perinatal patient is similar to nonpregnant patients. (See ACLP How To Guide: Acute Agitation for more information)
- If a pregnant patient requires restraints she should be placed in a left lateral position if feasible to avoid compression of the inferior vena cava by the gravid uterus.
 - Pregnant patients are hypercoagulable and are at higher risk for DVTs, which must be considered during restraint episodes and any resulting complications.
- For alcohol and other drugs of abuse (AODO) treatment, little changes from the management of a non-pregnant patient. (4)
 - Alcohol withdrawal is life threatening to both mother and fetus, warranting treatment to evidence-based standards.
 - Opioid withdrawal can be life-threatening to the fetus, which prompts need for further assistance with withdrawal. Both buprenorphine and methadone can be utilized to assist with withdrawal and sobriety maintenance during pregnancy.

- Buprenorphine results in fewer neonatal abstinence syndrome symptoms at delivery typically shorter infant hospitalizations.
- Whether maternal AODA constitutes “child abuse” varies by state, as do mandatory reporting guidelines in these circumstances.
- Further special considerations include infertility, pregnancy loss, termination, and care of LGBTQ+ patients. While these topics are not covered in detail in this how-to guide, please consider additional reading from the American Society for Reproductive Medicine (ASRM), the Trevor Project, or Planned Parenthood when caring for patients coping with these presentations.

References

1. Brockington I. Suicide and filicide in postpartum psychosis. *Arch Womens Ment Health*. 2017;20:63-69.
2. Viguera AC, Tondo L, Koukopoulos AE, Reginaldi D, Lepri B, Baldessarini RJ. Episodes of Mood disorders in 2,252 Pregnancies and Postpartum Periods. *Am J Psychiatry*. 168:1179–1185.
3. Dunkel Schetter C, Tanner L. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. *Curr Opin Psychiatry*. 2012;25(2):141-148. doi:10.1097/YCO.0b013e3283503680
4. Forray A. Substance use during pregnancy. *F1000Research*. 2016;5(887):1-9. doi:10.12688/f1000research.7645.1
5. Sachs HC, Committee on Drugs. The Transfer of Drugs and Therapeutics Into Human Breast Milk: An Update on Selected Topics. *Pediatrics*. 2013;132(3):e796-e809. doi:10.1542/peds.2013-1985
6. Chad L, Pupco A, Bozzo P. Update on antidepressant use during breastfeeding. *Can Fam Physician*. 2013;59:633-634.
7. Huybrechts KF, Cohen LS, Mogun H, Setoguchi S. Antidepressant Use in Pregnancy and the Risk of Cardiac Defects. *N Engl J Med*. 2014;370(25):2397-2407.
8. Ross L, Grigoriadis S, Mamisashvili L, et al. Selected Pregnancy and Delivery Outcomes After Exposure to Antidepressant Medication: A Systematic Review and Meta-analysis. *JAMA Psych*. 2013;70(4):436-443.
9. Stephansson O, Kieler H, Haglund B, et al. Selective Serotonin Reuptake Inhibitors During Pregnancy and Risk of Stillbirth and Infant Mortality. *JAMA Psych*. 2013;309(1):48-54.
10. Palmsten K, Hernandez-Diaz S, Huybrechts KF, et al. Use of antidepressants near delivery and risk of postpartum hemorrhage: cohort study of low income women in the United States. *BMJ*. 2013;347:1-15. doi:10.1136/bmj.f4877
11. Occhiogrosso M, Omran SS, Altemus M. Persistent pulmonary hypertension of the newborn and selective serotonin reuptake inhibitors: lessons from clinical and translational studies. *Am J Psychiatry*. 2012;169(2):134-140
12. Deligiannidis KM, Bullock A, Nandy I, Dunbar J, Lasser R, Witte M, Leclair B, Wald J. Zuranolone Concentrations in the Breast Milk of Healthy, Lactating Individuals: Results From a Phase 1 Open-Label Study. *J Clin Psychopharmacol*. 2024 Jul-Aug 01;44(4):337-344.
13. Cohen LS, Viguera A, McInerney K, et al. Reproductive Safety of Second-Generation Antipsychotics: Current Data From the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics. *Am J Psychiatry*. 2016;173(3):263-270.
14. Paterno E, Huybrechts KF, Bateman BT, et al. Lithium Use in Pregnancy and the Risk of Cardiac Malformations. *N Engl J Med*. 2017;376(23):2245-2254. doi:10.1056/NEJMoa1612222
15. Wesseloo R, Wierdsma A, van Kamp I, et al. Lithium dosing strategies during pregnancy and the postpartum period. *Br J Psychiatry*. 2017;211:31-36.
16. Angus-Leppan H, Liu RSN. Weighing the risks of valproate in women who could become pregnant. *BMJ*. 2018;361:1-8. doi:10.1136/bmj.k1596
17. Christensen J, Gronborg TK, Sorensen MJ, et al. Prenatal Valproate Exposure and Risk of Autism Spectrum Disorders and Childhood Autism. *JAMA*. 2013;309(16):1696-1703.
18. Dolk H, Wang H, Loane M, et al. Lamotrigine use in pregnancy and risk of orofacial cleft and other congenital anomalies. *Neurology*. 2016;86(18):1716-1725. doi:10.1212/WNL.0000000000002540

ACLP How To Guide: Perinatal Mental Health

19. Shyken JM, Babbar S, Babbar S, Forinash A. Benzodiazepines in Pregnancy: *Clin Obstet Gynecol*. 2019;62(1):156-167. doi:10.1097/GRF.0000000000000417
20. Norby U, Winbladh B, Kallen K. Perinatal Outcomes After Treatment with ADHD Medication During Pregnancy. *Pediatrics*. 2017;140(6). <https://doi.org/10.1542/peds.2017-0747>