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NEW YORK STATE | Office of Mental Health









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Assessment, Diagnosis and Treatment of Bipolar Disorder During the Perinatal Period

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Disclosures

Dr. Radonjic receives royalties from Routledge Press.

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Learning Objectives

- Describe the key clinical features of bipolar disorder in the perinatal period, including the high risk of postpartum relapse and postpartum psychosis.
- Apply validated screening tools and clinical strategies to tell perinatal bipolar disorder apart from unipolar perinatal depression.
- Identify best practices for managing bipolar disorder in pregnancy and postpartum, including the risks and benefits of medication and relapse-prevention planning.

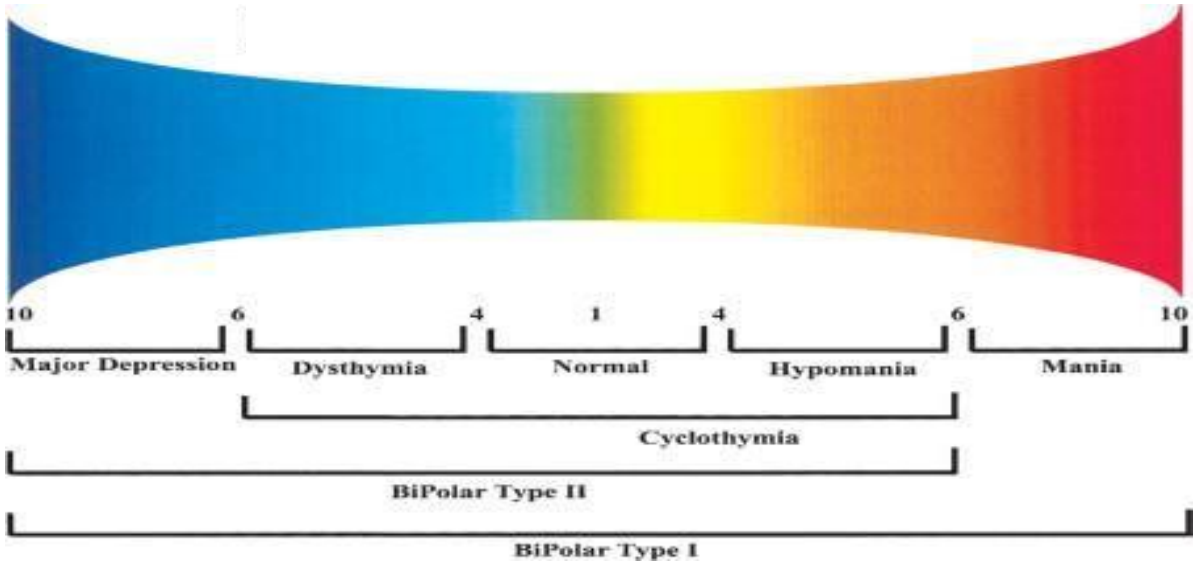
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Key Clinical Features of Bipolar Disorder in the Perinatal Period

Bipolar Disorder

- Bipolar disorder is a lifelong, complex illness with a spectrum of subtypes that vary in severity and presentation.
- BD requires active management in different stages of the disease.
- BD imposes significant morbidity on the lives of those affected.
- Medication management in women of reproductive age is challenging, given that previously stable regimens may need to be adjusted for pregnancy, and the postpartum period is an extremely high-risk period for relapse.

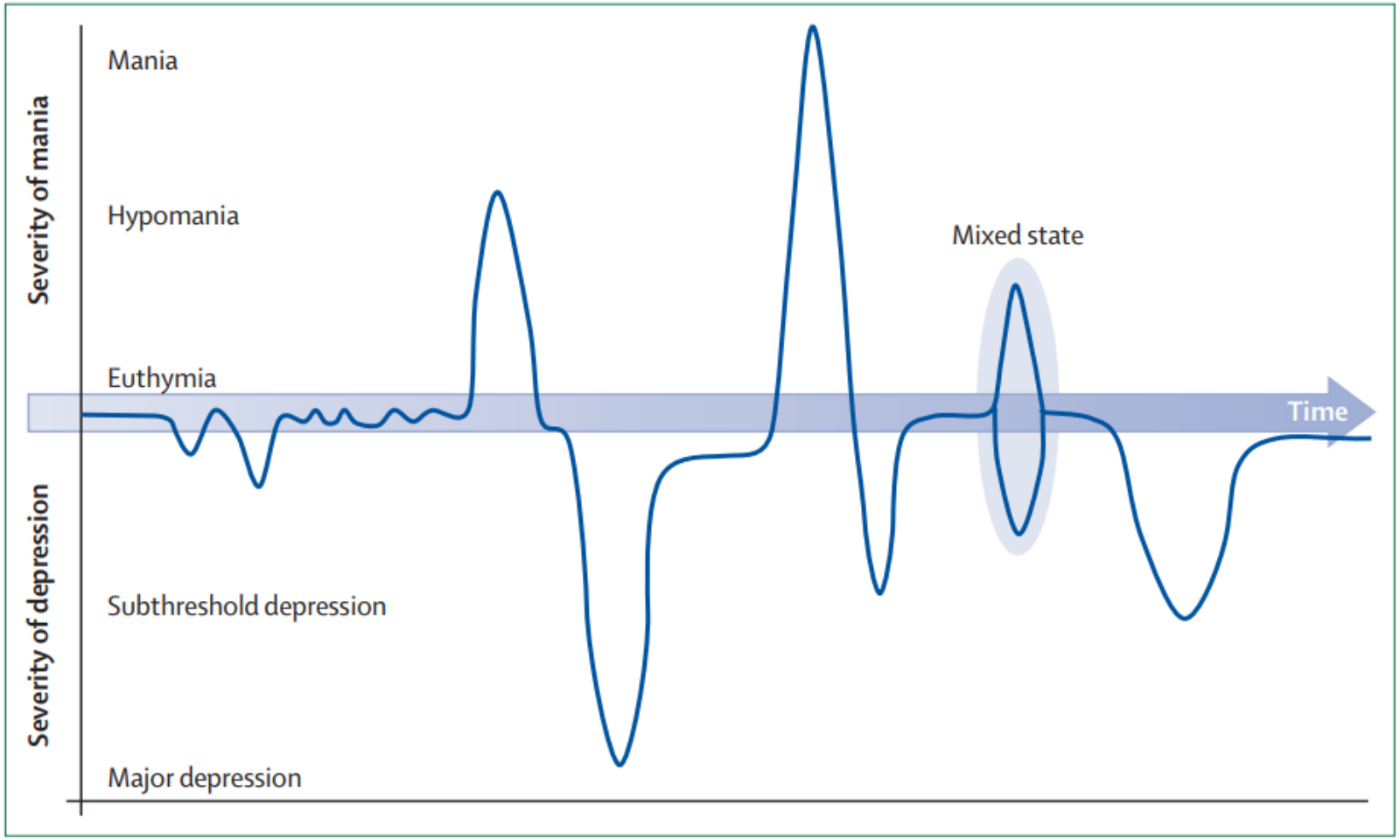
https://www.bipolarpsychologist.com.au/understanding-bipolar/



Bergink et al., 2025.

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Life chart showing the progression of bipolar disorder



Grande et al., 2018.

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Prevalence of Bipolar Disorder in Perinatal Women

- In women with no known psychiatric illness preceding the perinatal period, pooled prevalence of BD was 2.6% (95% CI, 1.2% - 4.5%) and prevalence of bipolar-spectrum mood episodes (including depressed, hypomanic/manic, mixed) during pregnancy and the postpartum period was 20.1% (95% CI, 16.0 – 24.5 %)

- In women with a prior BD diagnosis, 54.9% (95% CI, 39.2% - 70.2%) were fund to have at least one bipolar-spectrum mood episode occurrence in the perinatal period.

- Perinatal period is associated with high rates of bipolar-spectrum mood episodes; pregnant and postpartum women represent a special risk population.

Masters et al., 2022.

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Bipolar Disorder and Risks in Perinatal Period

- Multifactorial risks for increased bipolar – spectrum mood episode occurrence:
  - Overlap between peak reproductive years and onset of bipolar disorder
  - Hormonal and physiological changes accompanying pregnancy
  - Stress related to childbirth and parenting
- Bipolar disorder is a risk factor for:
  - Perinatal suicide
  - Postpartum Psychosis
  - Infanticide

Masters et al., 2022.

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Risk of Untreated Bipolar Disorder in Perinatal Period

- Higher risk of adverse pregnancy outcomes including:
  - Gestational hypertension,
  - Hemorrhage,
  - Cesarean delivery and
  - Small for gestational age infants
- Higher risk of recurrence of mood episodes
- Risk of severe psychiatric outcomes
- Risk for child protection concerns and parent –child relationship disruption due to psychiatric illness

Hasser et al. 2024

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Screening and Diagnosing Bipolar Disorder

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Which of my feelings are real? Which of the me's is me?
The wild, impulsive, chaotic, energetic, and crazy?
Or the shy, withdrawn, desperate, suicidal, doomed, and tired one?
Probably a bit of both, hopefully, much that is neither.

- Kay Redfield Jamison

Author of "An Unquiet Mind"

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Presenting symptoms
Step 1 · clinical interview

- Mania/hypomania: elevated or irritable mood, ↑ energy, ↓ need for sleep, racing thoughts
- Depression: low mood, anhedonia; note mixed or psychotic features

↓

Psychiatric history
Step 2 · past episodes

- Prior depressive episodes (early onset, recurrent); missed past highs; suicide attempts
- Antidepressant-induced switch; family history; substance use; collateral from family

↓

Screening tools
Step 3 · MDQ or RMS

- MDQ: ≥7 of 13 items, occurring together, with moderate or serious impairment
- RMS: 6 yes/no items, under 2 min, positive if ≥4 yes (screens are not diagnostic)

↓

Rule out other causes
Step 4 · medical workup

- Substances/meds (stimulants, steroids); thyroid disease, TBI, MS; labs: TSH, CBC, tox
- Differentials: MDD, ADHD, borderline personality disorder, schizoaffective disorder

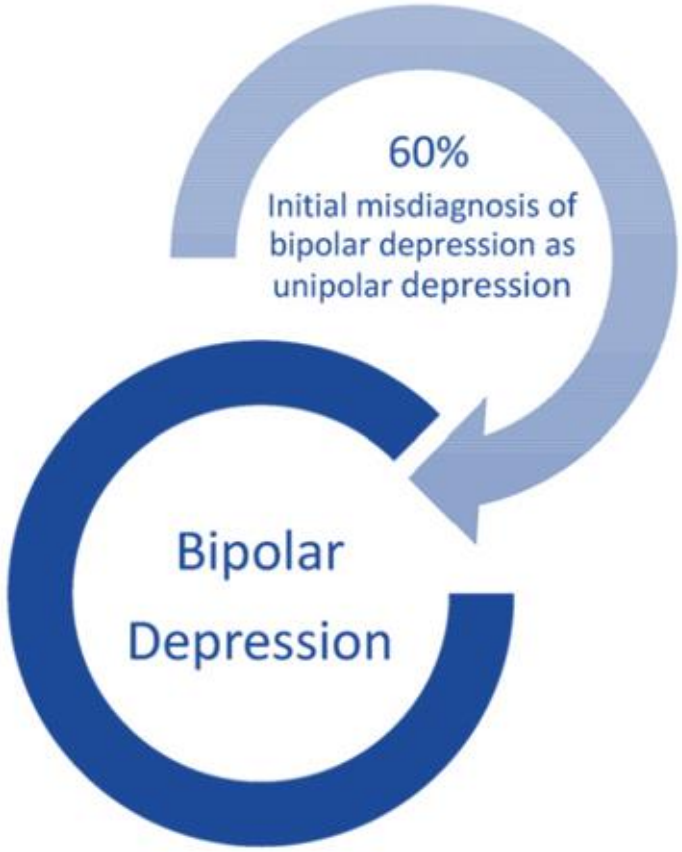
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Confirm diagnosis
Step 5 · DSM-5-TR criteria

- Bipolar I: ≥1 manic episode · Bipolar II: hypomania (≥4 days) + major depression
- Cyclothymia: ≥2 years subthreshold cycling · Specifiers: rapid cycling, mixed, psychotic

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Importance of Differentiating Between Unipolar and Bipolar depression



Reasons for misdiagnosis:

- Incomplete understanding of bipolar disorder by healthcare professionals
- Overlooked or no history of mania
- Failure to differentiate symptoms that can help identify unipolar and bipolar depression

Consequences of misdiagnosis:

- Inappropriate use of antidepressant agents
- Increased acute risk of switch from depression to mania/hypomania with antidepressant use
- Delay of proper treatment

McIntyre and Calabrese, 2019.

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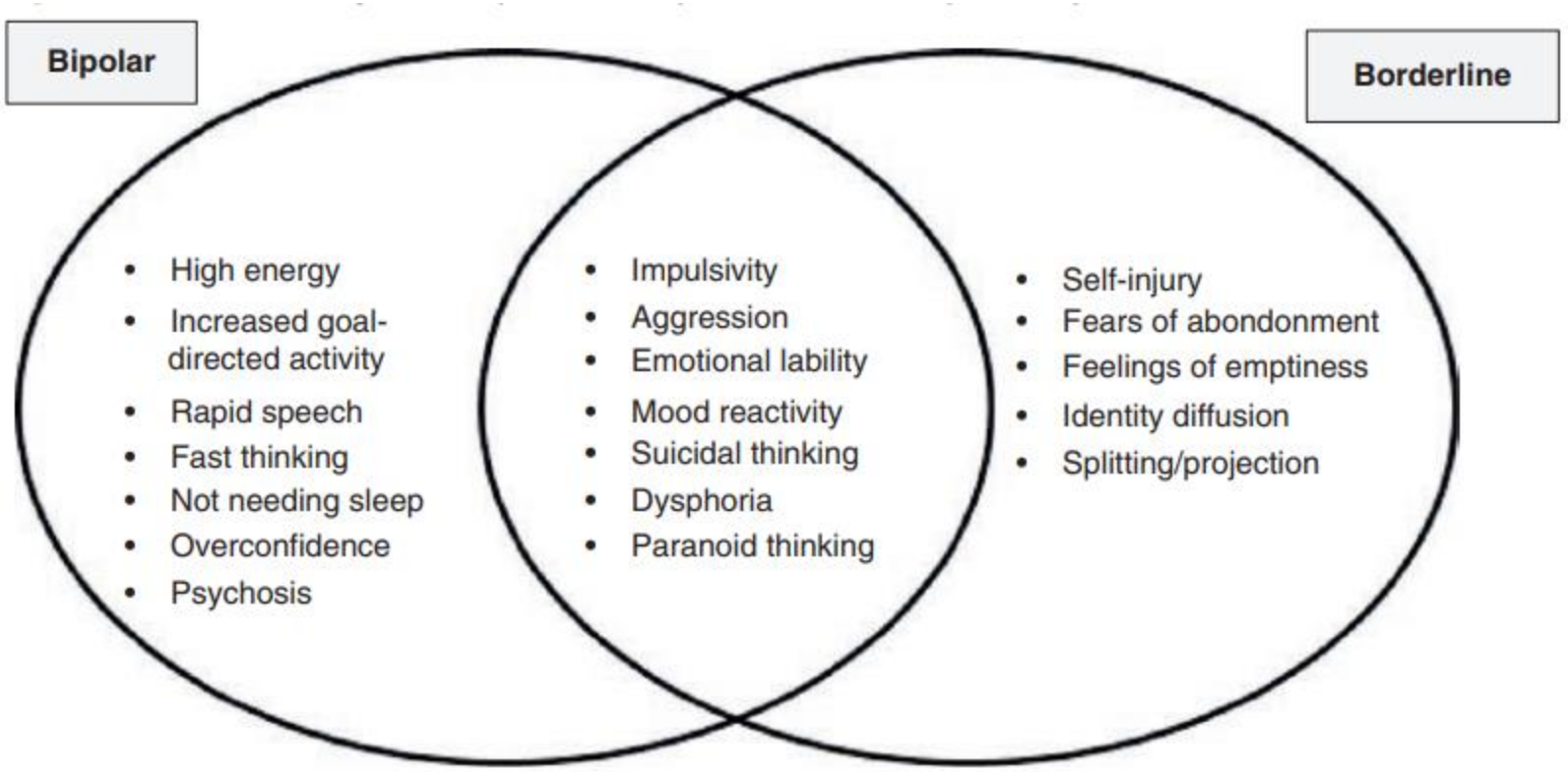
Bipolar Disorder vs. Major Depressive Disorder

Bipolar Disorder		MDD
Earlier (< 25 y)	Age at onset	Later
More frequent	Family history of psychiatric disorders	Less frequent
Yes	Hypomania	No
More likely	Atypical depressive features	Less likely
Higher	Episode recurrence	Lower
More likely	Antidepressant treatment failure	Less likely

Culpepper, 2014.

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Bipolar Disorder vs. Borderline Personality Disorder



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Management of Bipolar Disorder

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Bipolar Disorder in Perinatal Period

- Medication management of bipolar disorder in women of reproductive age is challenging.
- Previously stable regimens may need to be adjusted for pregnancy, and the postpartum period is an extremely high-risk period for relapse.
- Pharmacologic management is central to the care of patients with bipolar disorder, and medication decisions during pregnancy and the postpartum period require careful, individualized consideration.
- During pregnancy, the primary goal is maintaining maternal mood stability — reducing the substantial risks of untreated illness — while carefully minimizing medication-related harms, including teratogenicity, neurodevelopmental effects, and perinatal complications.

Bergink et al., 2025.

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Bipolar Disorder in Perinatal Period



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Bipolar Disorder – Preconception Considerations

- Preconception care is a key opportunity to review and streamline pharmacologic regimens, weighing the risks of undertreated illness against potential fetal exposure.
- Reducing polypharmacy while preserving euthymia should be the guiding principle.
- Dose reduction is appropriate when a patient has documented stability at a lower dose or has never been exposed to one.
- Dose changes are contraindicated when they have previously precipitated relapse.
- Proactive education about physiological changes in drug metabolism during pregnancy and the high postpartum relapse risk is essential.

Bergink et al., 2025

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Bipolar Disorder – How to Choose the Medication

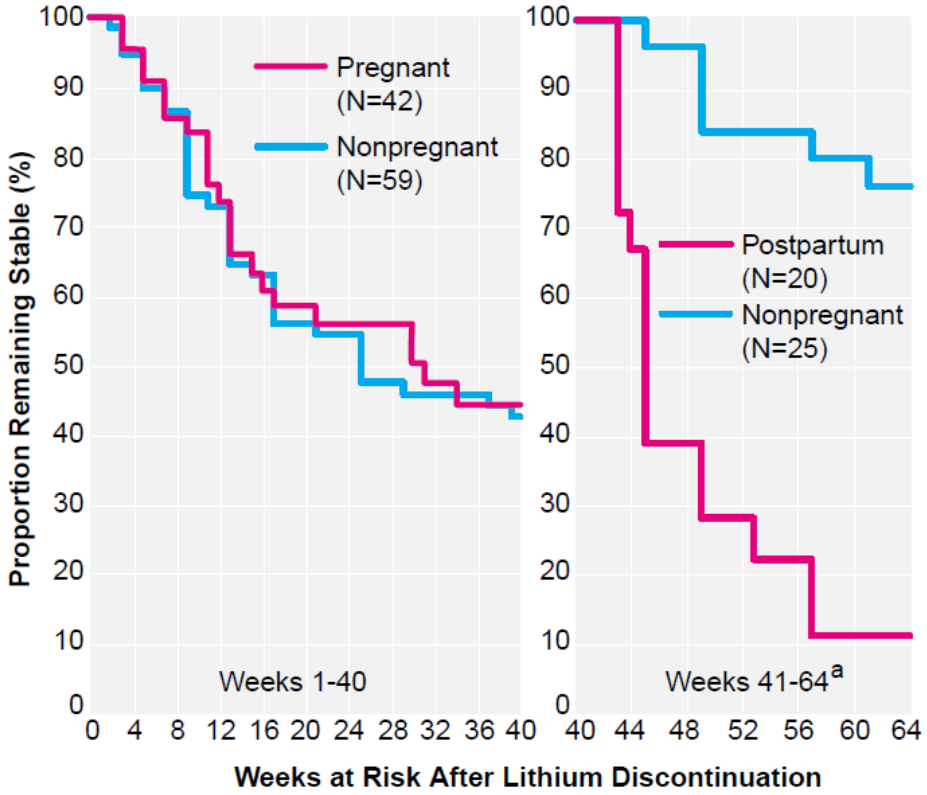
- Match the state! The choice of medication is driven by clinical presentation and state of disorder.
- Do not prescribe valproic acid and carbamazepine in women of childbearing age as known teratogens.
- Neither gabapentin nor topiramate are FDA approved for BD, hence their use not justified for this indication.
- Be mindful of potential interactions between psychiatric medications and contraceptives.
- We have the most data on medications we have been prescribing the longest.
- Dose adequately! Keep in mind pharmacokentic changes of pregnancy.

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Lithium and BD

- Lithium remains the mainstay treatment of bipolar disorder in the peripartum period.
- For patients with a known history of bipolar disorder who discontinued psychotropic medications during pregnancy, initiating prophylactic treatment immediately after delivery is advised.
- Adequate sleep protection in the postpartum period is a key non-pharmacologic strategy for reducing the risk of psychiatric decompensation in bipolar disorder.

FIGURE 1. Kaplan-Meier Survival Analysis of Bipolar Disorder Recurrence Risk After Lithium Discontinuation During Pregnancy and Postpartum and During Equivalent Time Periods in Nonpregnant Women



[a] Subjects in this second analysis were those who had remained stable over the first 40 weeks after discontinuing lithium.

Viguera et al, 2007

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Postpartum Psychosis – Medical Emergency!

- Women with BD have the highest risk for PPP:
  - Baseline rate 1-2/1000
  - Bipolar women significantly higher risk (up to 20%)
  - 72-88% women with PPP have history of BD
- Typically presents fulminantly within days to weeks after giving birth.
- Symptoms include not only psychosis, but also confusion and dysphoric mania.
- Symptoms often wax and wane, that complicates or delay diagnosis.
- Psychiatric hospitalization is required to protect both mother and baby

Friedman et al., 2019.

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Postpartum Psychosis

- Bergink et al., 2016: The authors reviewed the epidemiologic and genetic research and physiological postpartum triggers (endocrine, immunological, circadian) of psychosis.
- After an incipient episode, 20%- 50% of women have isolated postpartum psychosis.
- The remaining women have episodes outside the perinatal period, usually within the bipolar spectrum.
- The mechanism of onset is related to physiological changes after birth (e.g., hormonal, immunological, circadian), which precipitate disease in genetically vulnerable women.

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Postpartum Psychosis

- Distinguish from pre-existing stable psychotic disorder
- Patient needs immediate psychiatric evaluation and cannot be alone with the infant (usually needs psych ER)
- If in doubt, call **Project TEACH**
- Medical workup: look for other causes of delirium, intoxication, immune dysfunction
  - CBC, LFTs, TFTs, BMP, B12, Folate, Utox
  - Consider imaging if focal findings

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Postpartum Psychosis - Treatment

- The largest study (N=64) provided evidence that lithium is highly efficacious for both acute and maintenance treatment.
- Another report (N=34) described successful ECT treatment.
- Inpatient care is usually required to ensure safety, complete the diagnostic evaluation, and initiate treatment.
- The relapse risk after a subsequent pregnancy for women with isolated postpartum psychoses is 31% (95%,CI=22–42).
- Strategies for prevention of postpartum psychosis include lithium prophylaxis immediately postpartum and proactive safety monitoring.

Bergink et al. 2016

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Antipsychotics in Pregnancy

- Antipsychotic use during pregnancy has increased significantly, driven by expanding indications, rapid onset of effect, and lower acute toxicity compared to alternative agents.
- Available data do not suggest significant risks of congenital malformations with AP use in pregnancy, with several large epidemiological studies reporting malformation rates comparable to unexposed comparison groups.
- Large register-based studies similarly show no significant increase in neurodevelopmental disorder diagnoses in children with antenatal AP exposure, supporting a generally reassuring developmental safety profile for the class.
- Safety data for newer AP agents remain limited or entirely absent, warranting caution with their use in pregnancy.

Reviewed in Bergink et al., 2025

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First Generation Antipsychotics in Pregnancy

- **Haloperidol** is the only first-generation AP with specific BD efficacy data, carrying higher extrapyramidal symptom risk but no significant malformation signal in human studies of over 750 pregnancies.
- **Phenothiazines (chlorpromazine, prochlorperazine, levomepromazine)** have more extensive human pregnancy data given their use for hyperemesis gravidarum, though neonatal motor abnormalities and adaptation syndrome have been reported at higher doses.

- **Clozapine carries the most concerning perinatal safety signals**, including case reports of floppy infant syndrome, agranulocytosis, meconium plug, fetal drug accumulation, and a possible signal for anorectal atresia, warranting particular caution despite its necessity in treatment-refractory patients.

Reviewed in Bergink et al., 2025

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Second Generation Antipsychotics in Pregnancy

- **Women treated with antipsychotics (APs) during pregnancy should be classified as high risk**, requiring coordinated care between psychiatry and obstetrics or maternal-fetal medicine, with close attention to metabolic health and pregnancy outcomes.
- **Second-generation APs carry well-recognized risks for gestational diabetes and weight gain**; early glucose tolerance testing and dietary/lifestyle counseling are recommended, with agent selection favoring lower metabolic risk options such as aripiprazole over quetiapine or olanzapine in patients with pre-existing metabolic dysfunction.
- **Quetiapine has the lowest placental and breast milk transfer rates among APs**, making it a useful option for sleep, though it carries the highest metabolic and gestational diabetes risk; malformation data are available from over 11,000 pregnancies.
- **Risperidone** carry risks for hyperprolactinemia, which may impair fertility and conception; malformation data for risperidone are available from nearly 3,000 pregnancies without significant concern.
- **Aripiprazole** carries the lowest gestational diabetes risk among second-generation APs but may impair lactation variably due to its partial dopamine agonist mechanism, and can be either activating or sedating depending on the individual.
- **Ziprasidone and lurasidone have more limited but generally non-alarming data**; ziprasidone carries a theoretical cardiac conduction risk relevant to women with additional cardiac risk factors, while lurasidone may be acceptable when other agents have failed.

Reviewed in Bergink et al., 2025

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Relative Infant Dose of Most commonly Used Antipsychotics and Mood Stabilizers

Medication	RID %
Haldol	0.12%-12%
Clozapine	1.33%-1.4%
Olanzapine	0.28%-2.24%
Quetiapine	0.02% - 0.1%
Risperidone	2.8%- 9.1%
Aripiprazole	0.7%-6.44%
Ziprasidone	0.07%-1.2%
Lurasidone	0.44%
Lithium	0.87%- 7.29%
Lamotrigine	6.62%- 18.27%

- RID = A valuable tool and practical guide to indicate the extent of drug exposure to the infant while breastfeeding.
- The RID calculates the weight adjusted dose in the infant relative to the weight adjusted dose in the mother.
- RID level <2% = minimal exposure
- RID level 2-5% = small exposure
- RID level <10% = likely safe for the infant
- RID level >25% =potentially unsafe levels

Based on Hale's medications and mothers' milk, 2025-2026

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Perinatal Relapse Prevention Plan

1. A collaborative perinatal relapse prevention plan should be developed with the patient, family, and obstetric team, documented in writing and made available to the patient and medical record with appropriate consent.
2. A individualized risk-benefit assessment should guide medication decisions during pregnancy, with strong consideration for continuing prophylactic treatment throughout the perinatal period to sustain maternal euthymia.
3. A postpartum medication plan targeting optimal therapeutic levels should be established prior to delivery, with lithium representing the most evidence-based agent for relapse prevention, particularly for patients who were medication-free during pregnancy.
4. Preferred mode of delivery and intrapartum pain management should be clearly outlined in advance in coordination with the obstetric team.
5. A proactive feeding plan and structured sleep strategy — including family or partner support for night feedings — should be established to protect circadian rhythm stability in the early postpartum period.
6. Early relapse warning signs should be identified and documented based on the patient's individual history, with a clear intervention plan and designated contacts for the patient and family to reach out to if symptoms emerge.

Bergink et al., 2025

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Resources

- **Project TEACH**: https://projectteachny.org/
- Mothertobaby.org (free resources including fact sheets for patients)
- Reprotox.org (subscription site)
- Lactmed: https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm
- Postpartum Support International: www.postpartum.net
- MGH Center for Women's Mental Health www.womensmentalhealth.org