Perinatal Bipolar Disorder:

Screening, Management, and Prevention During Pregnancy & Postpartum

REBECCA LEVAL, MD, MPH

Staff Psychiatrist, Center for Women's Mental Health
Attending Psychiatrist, Acute Psychiatric Services

Massachusetts General Hospital

Disclosures

Neither Rebecca Leval nor her spouse have any financial interest/arrangements that would be considered of interest.

OBJECTIVES

- Recognize the presentation, recurrence risk, and medical implications of bipolar disorder during pregnancy and the postpartum period.
- Apply evidence-based approaches to screening, diagnostic evaluation, and pharmacologic management of perinatal bipolar disorder.
- Evaluate the reproductive safety and lactation considerations of commonly used medications for bipolar disorder, including valproic acid, second-generation antipsychotics, lithium, and lamotrigine.
- Develop prevention strategies to reduce relapse risk during pregnancy and the postpartum period through medication optimization, sleep protection, and other nonpharmacologic interventions.

Bipolar Disorder Fundamentals

Bipolar Disorder (BPAD): Presentation

[Unipolar Depression/Major Depressive Disorder]

Depressive Episode(s)

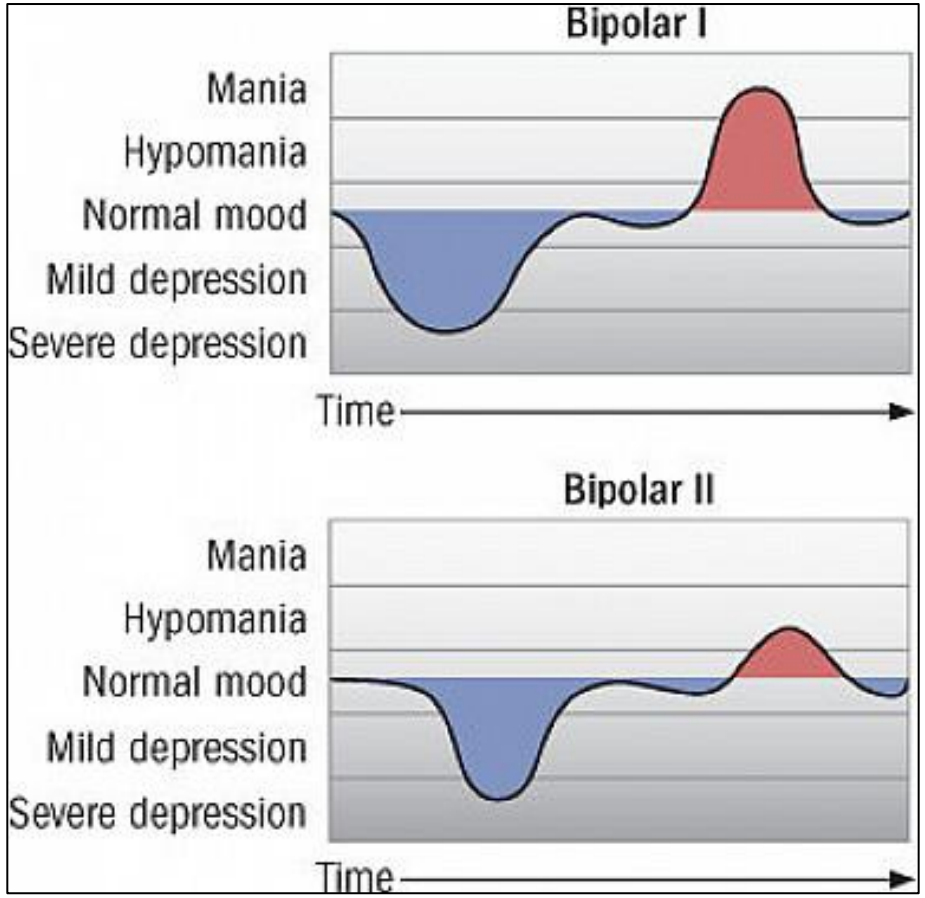
Bipolar I Disorder:

Mania (at least 1) +/- Depressive Episode(s)

Bipolar II Disorder:

*Hypo*mania + Depressive Episode(s)

DSM Specifier: With peripartum onset



Features of Mania/Hypomania

"Abnormal/persistently elevated, expansive, or irritable mood & abnormally and persistently increased activity or energy…" (DSM-5)

Mania: 1 week + of symptoms

- If symptoms warrant hospitalization → mania
- If psychotic symptoms present → mania

Hypomania: 4 days + of symptoms

> "The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization…" (DSM-5)

3+ Symptoms:
(4+ if mood is irritable)

Precipitants of Mania/Decompensation Triggers

56% of patients cannot identify any external trigger
(Smedler et al, 2020)

- Childbirth
- Sleep Deprivation/Circadian Rhythm Disruption
- Antidepressant Use
- Substance Use
- Stressful Life Events
- Seasonal Changes (spring/summer)
- Hormonal Changes
- Medication Nonadherence
- Others: Energy drinks, OTC supplements, viral infections, steroids, etc.

Bipolar Depression

One study found that in individuals with BPAD, 79% of completed suicides occurred during a major depressive episode.
(Isometsa et al., 1994)

BPADI:

- Depressive episodes occur three times more frequently than manic symptoms (Yatham et al., 2023)

BPADII:

- Greater chronicity of illness
- Spend more time in the depressive phase, higher frequency of episodes
  - 40% more time in depressive states than BPADI (Mantere et al., 2008)

Screening

Importance of Perinatal BPAD Screening

1) Pregnancy is a Period of High Vulnerability to BPAD Illness Recurrence:

- Overall risk of recurrence of illness within pregnancy: 71%
  - Depressive/mixed – 74%
  - Timing of episodes: → T1: 47%, T2: 31.9%, T3: 18.8%

- Discontinuation of Mood Stabilizers:
  - Recurrence risk twofold greater
  - Median time to first recurrence was fourfold shorter
    - 9 weeks after discontinuation
    - 40 weeks+ with continued treatment
  - Proportion of weeks ill was 5x greater

(Viguera et al., 2007)

Importance of Perinatal BPAD Screening

1) Pregnancy is a Period of High Vulnerability to Illness Recurrence

- Labor & delivery is one of the most potent precipitants of mania/hypomania
- Postpartum is the highest lifetime risk of psychiatric hospitalizations

2) Elevated Risk of Psychosis (= delusions, hallucinations, disorganized thoughts/behaviors)

- BPAD is the strongest predictor of postpartum psychosis

100-fold increased risk compared to general population

- Women with BPAD have an increased risk of psychosis: 7%-17%

3) Elevated risk of Depression

- Perinatal mood/anxiety disorders have risen from 18.4 to 40.4 per 1,000 deliveries in the US (2015)
- 50% of "postpartum" depressive episodes begin prior to delivery

(ACOG 2023)

(DSM5)

Importance of Perinatal BPAD Screening

4) Elevated Risk of Suicide/Homicide

- ~15%-20% of people with BPAD die by suicide (Nierenberg et al., 2023)
- PPP: ~4% infanticide rate, ~1%-5% suicide rate (Alford et al., 2025)

5) Elevated Risk of Maternal Impulsivity Leading to Reckless and Harmful Behaviors

- Substance use, poor adherence with prenatal care, poor nutrition, promiscuity, reckless spending, self-harm behaviors, violence/aggression

Importance of Perinatal BPAD Screening

6) Risk of Mood Switching When Starting Antidepressants (SSRIs, SNRIs, TCAs)

- Risk of switching into hypomania/mania/mixed episode if not adequately mood stabilized (Cordeiro et al., 2023)
- Antidepressant monotherapy in BPAD patients: 2.8-fold increased hazard risk of mania in first three months of treatment (Viktorin et al., 2014)

7) Permits Earlier Treatment Initiation

- More favorable prognosis – mean delayed onset of treatment by ~ 9 years after initial MDE (Nierenberg et al., 2023)
- Association between increasing number of acute BPAD episodes and further treatment resistance (da Costa et al., 2016)

Importance of Perinatal BPAD Screening

8) Untreated Illness Poses Medical Risk:

- Intrauterine growth restrictions
- Low birth weight
- Microcephaly
- Preeclampsia
- Preterm delivery
- C-section delivery
- Neonatal hypoglycemia
- Adverse neurodevelopmental outcomes

Boden et al., 2012
Galbally et al., 2010
Jablensky et al., 2005
Nierenberg et al., 2023

Screening for BPAD

22.6% of women with positive perinatal depressive screen will have BPAD when further evaluated.

ACOG: Universal screening for depression and anxiety at initial prenatal visit, later in pregnancy (T3), and postpartum visits

Ideally screen all patients in some capacity before prescribing antidepressants.

Additionally, consider BPAD screening in patients with:

1) High scores on depression screening tools (EPDS, PHQ-9)
2) History of treatment resistance, polypharmacy

Screening for BPAD

Consider Bipolar Screening in patients with:

3) First-onset psychiatric episode
   - The age of onset of BPAD occurs within prime reproductive years (17-42 years old) (Bolton et al., 2021)

4) Family history of BPAD, psychotic disorders
   - Heritability 60%-85% (BPADI> BPADII) (McIntyre et al., 2020)
   - 1st degree relative: 5-10% lifetime risk (compared to ~1% in general population) (DSM-5)

5) Patients on mood stabilizers/antipsychotics

Bipolar Screening

- Screeners:
  - Mood Disorder Questionnaire (MDQ)
    - Self administered
  - Composite International Diagnostic Interview Bipolar Stem (CIDI)
    - Clinician administered

Screening should focus on identifying a *discrete lifetime episode* of co-occurring symptoms consistent with mania or hypomania, rather than individual symptoms, which commonly occur in isolation or in other conditions without meeting diagnostic criteria.

- Speak with collateral sources: family, other treaters
- D/D: Substance-Induced Mood Episode, Borderline Personality Disorder

Management

Medical Evaluation: Rule Out Organic Etiologies

First Episode Acute Mania Potential Workup

**** Rule out organic etiologies ****

- Exams:
  - Physical exam
  - Neurological exam
  - Mental status exam
- Neurological symptoms:
  - Head imaging
  - CSF analysis
    - Anti-NMDA receptor antibodies
  - Serum ammonia

- Laboratory Work-Up:
  - CBC/CMP
  - Utox
  - Thyroid Panel
  - Calcium
  - Vitamin B12
  - Thiamine/Folate level
  - Inflammatory markers
  - [HIV, RPR]

Acute Depression Potential Work Up

**** Rule out organic etiologies ****

- CBC/iron studies
- TSH
- Vitamin D
- Vitamin B12/Folate
- [Urine toxicology]

Fundamentals of Psychiatric Medication Management in Pregnancy

Risk – Risk Decision

Both the illness and the treatments have potential risks.

No decision is risk-free.

Individualized decision.

Consider the severity of the underlying illness.

The greater the severity of illness, often the easier the decision.

Omission Bias:

Tendency to judge harm/risks of an action taken as worse than equal/greater harm from inaction.

PSYCHOTROPICS

The lack of an FDA-approved psychotropic for use in pregnancy does not constitute a contraindication.

All medications diffuse readily across the placenta.

No psychiatric medications have been FDA-approved for use within pregnancy.

Only FDA-approved medication for *postpartum* mental illness:

zuranolone (Zurzuvae): approved for postpartum depression

Brexanolone, the 60-hour IV infusion was commercially withdrawn Dec 2024

Goals of Treatment

More than 50% of patients with BPAD are not adherent to treatment.
(Nierenberg et al., 2023)

While balancing maternal wellness, to the greatest extent possible…

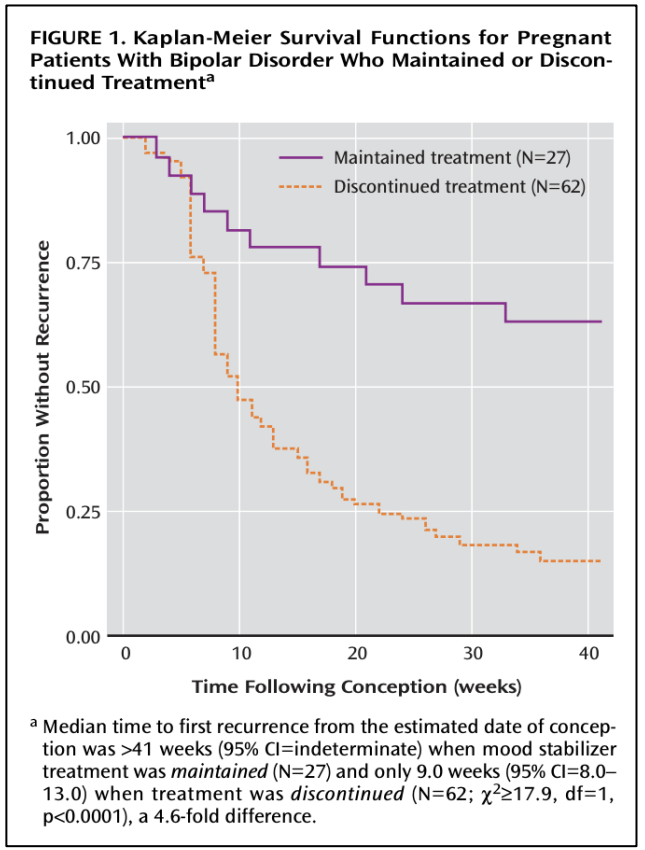
- Use the fewest medications
- Optimize non-pharmacological treatments
- Use the lowest *effective* dose
- Avoid known teratogens (ex. valproic acid, topiramate)
- Avoid starting/stopping medications
- Older agents preferred to newer agents
- Previously trialed agents preferred to untried agents
- Try not to reinvent the wheel
- Work to gain patient buy-in

Risks of Abrupt Cessation of Medications

- Reemergence of underlying symptomatology:
  - With medication discontinuation: 85.5%
  - With medication continuation: 37%
  - Fourfold shorter median time to recurrence (47% in T1)
  - Five times greater proportion of weeks ill during pregnancy

(Viguera et al., 2007)

- Stress/anxiety
- Withdrawal symptoms



(Image: Viguera et al 2007)

General Rule: Unless a patient has not taken the medication for 7 days+ continue at current dose. If more than 7 days, likely need to resume medication at starting dose & retitrate.

Notable exceptions: lamotrigine (5 days), stimulants (could be abruptly stopped/started)

Risks of Switching Medications

- Risk of relapse/ineffectiveness
- Risk of multiple exposures
  - Original medication, new medication, decompensated illness
- Risk of new side effects
- Risk of nonadherence
- Risks of pill quantity buildup in the home
  - Accidental or intentional use by patient
  - Accidental or intentional use by children or vulnerable adults

Risks of Decreasing Dose Preconception

- Increased drug elimination of many psychotropics in pregnancy

- If the medication dose is decreased & dose requirements increase → blood levels drop below the therapeutic threshold

❖ mother is at high risk of relapse

❖ fetus is at risk of exposure to both medication and illness

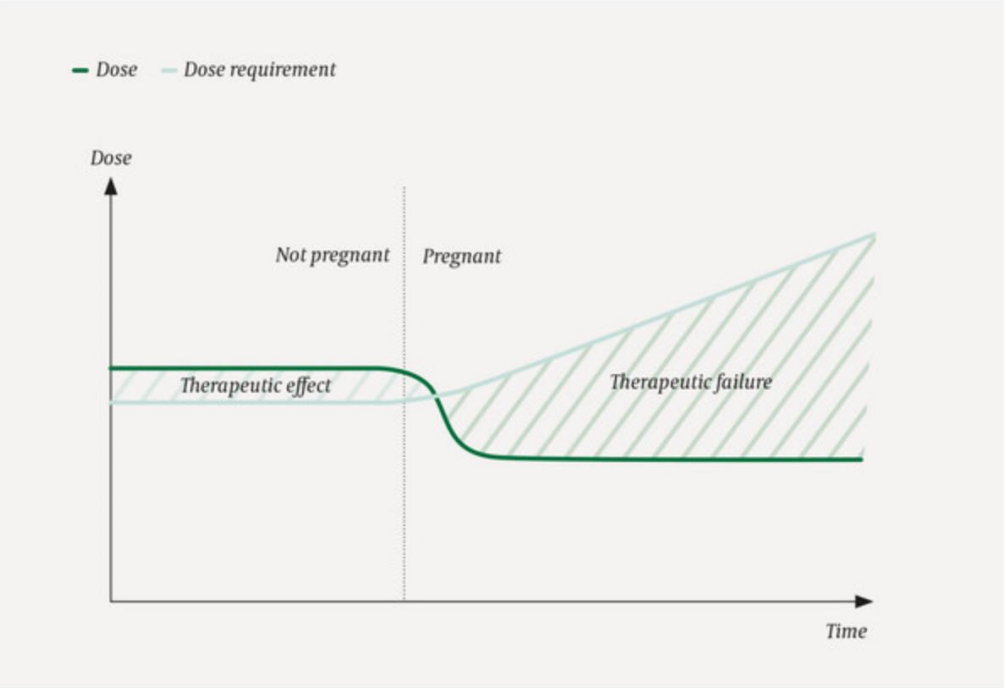


Figure 2 *Risk of therapeutic failure in pregnant women. The figure shows why pregnant women are at risk of suboptimal dosing and therapeutic failure. In this hypothetical scenario the patient takes a drug X. The dose is indicated by the green line. When the patient discovers that she is pregnant, she agrees with her doctor to reduce the dose of X, out of concern for the fetus. At the same time, the woman's dose requirement increases due to increased elimination of X. Both events (reduced dose and increased dose requirement) contribute to widening the gap between the dose she needs and the dose she receives, thus putting her at risk of therapeutic failure.*

(Westin et al., 2018)

FDA Pregnancy Risk Categories

ABOLISHED!

1975: 5 risk categories (A,B,C,D,X)

Based on data from human & animal studies.

Faced criticism for being potentially misleading.

2015: Pregnancy and Lactation Labeling Rule (PLLR)

Required removal of pregnancy labeling categories from all prescription drugs (except those approved prior to 6/30/2001).

More comprehensive narratives on potential risks/benefits to the dyad & how risks may change during the course of pregnancy.

General Principles of Medication Management in BPAD

Treatment Approaches/Options

Not an exhaustive list!

85% of patients on 2+ agents. (Fornaro et al., 2016)

Consider phase of illness:

Acute Depression

- Quetiapine
- Lamotrigine
- Olanzapine-fluoxetine
- Lurasidone +/- lithium
- Cariprazine

Acute Mania

- Lithium
- Quetiapine
- Olanzapine
- Aripiprazole
- Risperidone
- Cariprazine

Maintenance

- Lithium*
- Quetiapine*
- Lamotrigine (depression)
- Olanzapine
- Aripiprazole (mania)
- (Cariprazine)*

Severe Illness: **ECT**

* Potential use as monotherapy

(CANMAT & ISBD 2018 Guidelines for Management of Bipolar Disorder)

Reproductive Safety Profiles of Mood Stabilizers

Valproic Acid in Women of Reproductive Age

DON'T!

VALPROIC ACID RISKS

Teratogenicity

- Major congenital malformation rate ~10%

Neural tube, Craniofacial, Cardiovascular, Limb Malformations, Hypospadias

Not meaningfully reduced with high-dose Folic Acid

(Andrade et al., 2018)

Adverse Neurodevelopmental Outcomes

- Lower IQ: 8-10 pts: 2-5-fold increased risk
- ASD: 2-4-fold increased risk
- ADHD
- Language/Hearing Impairments
- Developmental Milestone Delays/Global Developmental Delays

(Honybun et al., 2024)

Gynecologic

- Increased Risk of PCOS/PMOS (OR: 6.86)

(Guo et al., 2023)

And yet… ONLY 24.5% of women on valproic acid treatment had concomitant contraceptive coverage!

(Smolinski et al., 2024)

Antipsychotics

Not considered to be major teratogens.
(Huybrechts et al., 2023)

General Associated Risks:

- Preterm birth (Quinne et al., 2026)
- Large for gestational age (Joseph-Delaffon et al., 2024)
- Gestational diabetes (Zhang et al., 2026)
  - Early GTT, weight monitoring
  - Olanzapine > quetiapine > risperidone
- Poor neonatal adaptation (Viguera et al., 2023)

MGH National Pregnancy Registry for Atypical Antipsychotics:
https://womensmentalhealth.org/research/pregnancyregistry/atypicalantipsychotic/

Antipsychotics

- Best characterized 2nd generation antipsychotics:
  - ❖ Quetiapine
    - Lowest demonstrated transfer and the least inter-individual variability
    - Metabolic effects/gestational diabetes
  - ❖ Olanzapine
    - Highest placental passage
    - Potential association with risks of oral clefts (2.1; 95% CI, 1.1-4.3) – hypothesis-generating safety signal (Huybrechts et al., 2022)
    - Metabolic effects/gestational diabetes
  - ❖ Aripiprazole
    - May lower prolactin (consider impact on breastfeeding)
  - ❖ Risperidone
    - Highest risk for prolactin elevation (consider impact on fertility)
    - Potential signal for cardiac malformations, not confirmed in subsequent larger international study

(Huybrechts et al., 2022)

- Increased clearance in pregnancy – consider dose increases in later pregnancy

Lithium: Cardiac Risks

Ebstein's Anomaly:
Apical displacement of the septal & posterior tricuspid valve leaflets into the right ventricle.

	Exposed vs. Unexposed
Right Ventricular Outflow Tract Obstructions:	0.6% vs. 0.18%
Any Cardiac Malformation:	2.41-3% vs. 0.8-1.15%

(Patorno et al., 2017)
(Roddy Mitchell et al., 2026)

Risk appears to be dose dependent:

Above 900 mg/day the risk is more significant.

601-900 mg/day RR 1.60 (95% CI 0.67-3.80) & > 900 mg/day RR: 3.22 (95% CI 1.47-7.02)
(Patorno et al., 2017)

FDA Recommendation: consider fetal echo between 16-20 weeks gestation with T1 lithium exposure.

Lithium in Pregnancy: Associated Risks

Pregnancy/Delivery Complications: **Exposed vs. Nonexposed**

Preterm delivery: **8.7% vs. 3%** (Hastie et al., 2021)

Data mixed. Meta analysis showing no associated risk. (Fornaro et al., 2020)

Large for gestational age: **9-14% vs. 3-6%** (Hastie et al., 2021) (Roddy Mitchell et al., 2026)

Floppy Baby Syndrome: respiratory distress, cyanosis, hypotonia, lethargy

Neonatal readmission within 28 days: **27.5% vs. 14.3%** (Fornaro et al., 2020)

Lithium in Pregnancy: Associated Risks

- Neurodevelopmental Outcomes:
  - Small study showing no differences in brain structure between lithium-exposed and non-exposed children age 8-14 years old (Poels et al. 2023)
  - Small study showing no difference in lithium exposure and neuropsychological functioning (including IQ) in children 6-14 years old

(Poels et al., 2022)

Lithium Level Fluctuations in Pregnancy

- Therapeutic range, generally **0.6-0.8** mEq/L for long-term maintenance and prevention of renal insufficiency

- Serum concentrations decline in pregnancy – jeopardizing therapeutic effect

  Nadir: ~17 weeks (Wesseloo et al., 2017)

- Serum concentrations then steadily rise until delivery – risking lithium toxicity

Checking Lithium Levels in Pregnancy

- No universally accepted approach to checking lithium levels
  - More conservative approach: close monitoring (every 3-4 weeks) until 34 weeks, weekly until delivery, twice weekly for first two weeks postpartum

    (Wesseloo et al., 2017)
  - Less conservative approaches: monthly; by trimester; symptomatically

- Check lithium level if:
  - Mood symptoms develop
  - Signs of preterm delivery, preeclampsia
  - Illnesses changing hydration status (ex. hyperemesis)
  - Renal dysfunction
  - Concern for lithium toxicity (tremor, weakness, ataxia, vision changes, slurred speech, tinnitus)

Lithium Dosing

- Recent data suggests that lithium dose does not need to be lowered/discontinued predelivery (in contrast to earlier FDA label recommendation and ACOG consideration)
  - Discontinuing poses high risk of maternal relapse
  - Neonatal complications did not appear to be related to lithium levels at delivery
  - Dose reduction/discontinuation does not improve neonatal outcomes

(U.S. Department of Veterans Affairs & U.S. Department of Defense, 2023)
(Molenaar et al., 2024)

Lamotrigine

Less effective in prevention of BPAD mania.

- NAEED Pregnancy Registry observed associated risk of oral clefts – not observed in other large international registries or meta-analyses (US Food & Drug Administration [FDA], 2025)
- Significant increases in lamotrigine elimination clearance during pregnancy
  - Clearance can increase by 76% in T1 and up to 230% in T3, but substantial interindividual variability (Harden et al., 2009)
  - Changes in dose increase ranged from 100-600 mg during pregnancy (Pennell et al., 2026)
  - Levels increase significantly postpartum due to shifts in metabolism resulting from sharp and quick decline in estrogen
- Value of levels
  - (Unlike when used as an antiepileptic): Only to rule out lamotrigine toxicity or to establish an individual therapeutic blood level

Relationship of Lamotrigine & Estrogen

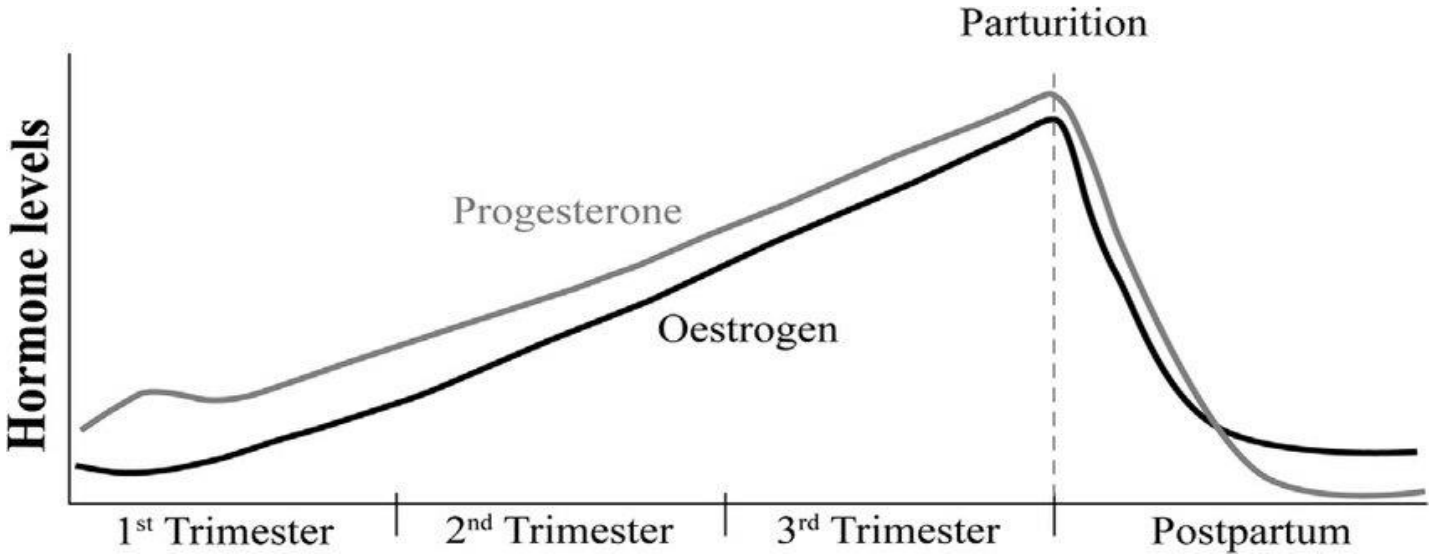


Image Source: Researchgate

- Estrogen significantly increases clearance of lamotrigine
  ~ Can decrease lamotrigine plasma concentrations by ~50%

- Combined oral contraceptives (cocps) can decrease lamotrigine concentrations; lamotrigine does not reduce the effectiveness of cocps

FDA Drug Label (2025)

Breastfeeding

Monitor infants for changes in behavior, feeding, sleep with any medication change.
Consider consultation with pediatrician, NICU team.

Drug	Relative Infant Dose (%)	Considerations
Aripiprazole	0.7 - 6.44	Concern for lactation failure/reduced milk supply. Limitations of data.
Lamotrigine	6.62 - 18.27	Some infants require monitoring of CBC (thrombocytosis), LFTs. Monitor for rash – no cases of SJS attributable to lamotrigine in infants.
Lithium	0.87 - 7.29	Infant toxicity reported: hypertonia, hypothermia, cyanosis, ECG changes, transient TSH elevations. No universal infant monitoring protocols. Limitations of data.
Olanzapine	0.28 - 2.24	Limitations of data.
Quetiapine	0.02 - 0.1	Limitations of data.
Risperidone	2.8 - 4.7	Limitations of data, may increase prolactin.

Hales Meds 2026

Breastfeeding Considerations in BPAD

- Potential adverse impacts on maternal mood/anxiety
  - Leading to impaired maternal functioning
  - Disruptions in bonding/attachment
  - Reduced sensitivity/responsiveness to infant cues
- Potential adverse impacts on sleep
  - Leading to mood decompensation/precipitating mood episode
- Limited lactation safety data on individual medications
- Absence of lactation safety data on polypharmacy

POSTPARTUM PSYCHOSIS

Postpartum Psychosis

- Not the presentation of any and all psychosis – distinct syndrome
- Rare: 1-2 per 1,000 women (0.1-0.2%)
- Typically, with sudden onset, occurring within the first two weeks postpartum
  - 50% within 1-3 days after delivery (Jones et al., 2001)
  - Earlier in women with Bipolar Disorder
- May represent index episode of Bipolar Disorder or may be circumscribed psychotic episode (40%+ of patients) (Gilden et al., 2020)

By comparison:

Early pregnancy loss:	1 in 10
Birth defects:	1 in 33
Preeclampsia:	1 in 25
Preterm delivery:	1 in 10

Postpartum Psychosis: *Presentation*

Waxing and Waning/Marked Fluctuation:

Delirium-like:

- Confusion
- Disorientation
- Changes in consciousness
- Catatonia

Mania:

- Abnormal mood (mania, depression, mixed, irritability)
- Insomnia/decreased need for sleep
- Thought & behavioral disorganization
- Delusional thinking
  - Persecutory delusions (75.2%)
  - Ideas of reference (55.8%)
  - Hyperreligiousity/religious delusional content
- Hallucinations
  - Visual hallucinations (52.3%)
    - Outside of the postpartum period, VH occur in about 2-3% of BPAD patients (Baethge et al., 2005)

CLASSIC PRODROME:

- Insomnia, restlessness, exhaustion, or decreased need for sleep.
- Sadness, irritability, rapid mood changes.

Preceding the emergence of delusions & hallucinations.

(Sharma et al., 2003)

(Cohen et al., 2025)

Postpartum Psychosis: *Management*

Acute Treatment: INPATIENT PSYCHIATRIC HOSPITALIZATION

- Lithium, antipsychotics, ECT
- As needed medications for anxiety, insomnia, agitation

Duration of Maintenance Medication Management:

❖ Suspicion for BPAD: will require lifelong maintenance treatment

❖ Circumscribed Episode:

- Ideally continue treatment 9-12 months postpartum with close follow up with taper.
- Prophylaxis in future pregnancies
  - Do not assume that subsequent episodes will follow the same course

POSTPARTUM PSYCHOSIS IS A HIGHLY TREATABLE ILLNESS
~99% Remission Rate & ~80% Sustained Remission Rate At 9 Months PP

(Bergink et al., 2015)

Prevention

Medication Management

- Ensure medication coverage against manic and depressive episodes
  - Adequate dosing to confer protection
    - Ex: Quetiapine → bipolar mania recommended dose: 400-800 mg/day
      → acute bipolar depression recommended dose: 300 mg/day
- Consider making PRNs available should mood destabilization occur unexpectedly
  - Consider sedating PRNs for dual purpose of sleep protection & mood protection
- Ideally, a patient would be on a stable medication regimen for 6 months prior to trying to conceive

SLEEP PROTECTION

Protecting Sleep

- Do Everything possible to PROTECT SLEEP!

- Closely monitor:
  - Within T3
  - Within L&D/Postpartum hospitalization
  - With any travel
  - With breastfeeding/postpartum

Sleep Disruptions in Pregnancy

- High progesterone during pregnancy causes daytime sleepiness and fatigue

- 80% of pregnant women experience insomnia, worse in the 3rd trimester
  - Obstructive Sleep Apnea: 10-25% of pregnancies
  - Restless Leg Syndrome: 27-30% of pregnancies

- Sleep disruptions may also occur during pregnancy due to:

  Nausea/vomiting, frequent urination, physical discomfort, fetal movements, leg cramps, heartburn, snoring, irregular uterine contractions, shortness of breath, anxiety

Gordon et al., 2021
Hashmi et al., 2016

Non-Pharmacological Interventions

- Provide tips on maintaining good sleep hygiene
- Counsel on increasing daytime activity *(as medically appropriate)*
- Prevent heartburn *(small, frequent meals, avoid eating 3 hours before bed, sleep on side, keep head elevated)*
- Consider using pregnancy pillows
- Progressive muscle relaxation
- Cognitive Behavioral Therapy for Insomnia (CBT-I)
- Night nurses/doulas

L & D Considerations for Sleep Protection

Potential considerations within the hospital setting: *(if available and medically appropriate)*

- Bundling interventions to minimize interruptions, if safe to do so
- Posting signage on the door to limit unnecessary disruptions
- Limiting visitors
- Early epidural
- Wireless monitoring, if available
- Keeping the baby in the newborn nursery, if available
- Consider placement of the patient in a room away from high-traffic, noisy areas on the unit, if available
- Providing eye masks and/or ear plugs
- Medication management for sleep, anxiety
  - Might consider: Hydroxyzine, lorazepam, olanzapine, quetiapine
  - Further optimizing pain control

Other Considerations

- Psychotherapy
  - Individual, couples, group
- Close Psychiatric Follow Up
  - Any woman with a history of severe illness – psychosis, history of hospitalizations/suicide attempts, or high suspicion for BPAD should be followed by psychiatry beginning early in the course of pregnancy, ideally preconception
  - Women are often closely followed when working with fertility medicine & within pregnancy & may feel less supported in the highly vulnerable postpartum period
- Family Involvement
  - Consider including family in visits, bolstering social supports at home
  - Be mindful that family members are not immune to illness themselves in the postpartum (consider heritability of BPAD)

Other Considerations

- Stress Reduction
- Treating Co-Occurring Psychiatric Illness
  - Lifetime prevalence of 1 co-occurring psychiatric condition: ~65-90%; 3+ conditions: 50-60%. Most commonly anxiety disorders. (McIntyre et al., 2020) (Nierenberg et al., 2023)
- ECT Consultations
  - ECT is considered the single most effective treatment for severe or treatment-resistant BPAD
  - Response rates: 65-85% (Nierenberg et al., 2023)
- Prenatal Vitamins
  - Rate of unintended pregnancies in the U.S.: 41.6% (2019) (Resendez et al., 2023)
  - USPSTF recommends all women of reproductive age take prenatal vitamins
  - Reduce risk of neural tube and cardiac malformations

RESOURCES

Massachusetts General Hospital Center for Women's Mental Health:

- Main website: www.womensmentalhealth.org
- MGH Postpartum Psychosis Project (MGHP3): https://www.mghp3.org/ *(Free consultations to providers)*
- Virtual Rounds:

  Wednesdays 2-3 PM EST. All health care providers welcome. No cost to attend.
  Register at: https://womensmentalhealth.org/virtual-rounds-at-the-cwmh/

Postpartum Support International: https://postpartum.net/

Online Support Groups: https://postpartum.net/get-help/psi-online-support-meetings/

National Maternal Mental Health Hotline: 1-833-TLC-MAMA (text, chat, call)

https://mchb.hrsa.gov/programs-impact/national-maternal-mental-health-hotline

Thank You

Contact Information:

rleval@mgh.harvard.edu

Citations

- Accortt E, Mirocha J, Jackman S, Coussons-Read M, Dunkel Schetter C, Hobel C. Association between diagnosed perinatal mood and anxiety disorders and adverse perinatal outcomes. J Matern Fetal Neonatal Med. 2022 Dec;35(25):9066-9070. doi: 10.1080/14767058.2021.2014450. Epub 2021 Dec 8. PMID: 34879772.
- Alford, A. Y., Riggins, A. D., Chopak-Foss, J., Cowan, L. T., Nwaonumah, E. C., Oloyede, T. F., Sejoro, S. T., & Kutten, W. S. (2025). A systematic review of postpartum psychosis resulting in infanticide: missed opportunities in screening, diagnosis, and treatment. *Archives of women's mental health*, *28*(2), 297–308. https://doi.org/10.1007/s00737-024-01508-3
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). American Psychiatric Publishing.
- Andrade C. (2018). Major Congenital Malformations Associated With Exposure to Antiepileptic Drugs During Pregnancy. *The Journal of clinical psychiatry*, *79*(4), 18f12449. https://doi.org/10.4088/JCP.18f12449
- Bergink V, Burgerhout KM, Koorengevel KM, Kamperman AM, Hoogendijk WJ, Lambregtse-van den Berg MP, Kushner SA. Treatment of psychosis and mania in the postpartum period. Am J Psychiatry. 2015 Feb 1;172(2):115-23. doi: 10.1176/appi.ajp.2014.13121652. PMID: 25640930.
- Bodén, R., Lundgren, M., Brandt, L., Reutfors, J., Andersen, M., & Kieler, H. (2012). *Risks of adverse pregnancy and birth outcomes in women treated or not treated with mood stabilisers for bipolar disorder: Population based cohort study*. *BMJ, 345*, e7085. https://doi.org/10.1136/bmj.e7085
- Bolton S, Warner J, Harriss E, Geddes J, Saunders KEA. Bipolar disorder: Trimodal age-at-onset distribution. *Bipolar Disord*. 2021; 23: 341–356. https://doi.org/10.1111/bdi.13016
- Cohen, L. S., Arakelian, M., Church, T. R., Dunk, M. M., Gaw, M. L., Yoon, H. E., Kobylski, L. A., Vanderkruik, R., & Freeman, M. P. (2025). The phenomenology of postpartum psychosis: preliminary findings from the Massachusetts General Hospital Postpartum Psychosis Project. *Molecular psychiatry*, *30*(6), 2537–2544.
- da Costa SC, Passos IC, Lowri C, Soares JC, Kapczinski F. Refractory bipolar disorder and neuroprogression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2016;70:103-110. doi:10.1016/j.pnpbp.2015.09.005.
- Deligiannidis, K. M., Byatt, N., & Freeman, M. P. (2014). Pharmacotherapy for mood disorders in pregnancy: a review of pharmacokinetic changes and clinical recommendations for therapeutic drug monitoring. *Journal of clinical psychopharmacology*, *34*(2), 244–255. https://doi.org/10.1097/JCP.0000000000000087
- Elisabetta Patorno, Krista F. Huybrechts, Brian T. Bateman, Jacqueline M. Cohen, Rishi J. Desai, Helen Mogun, Lee S. Cohen, & Sonia Hernandez-Diaz. (2017). *Lithium use in pregnancy and the risk of cardiac malformations*. *New England Journal of Medicine, 376*(23), 2245–2254. https://doi.org/10.1056/NEJMoa1612222
- Fornaro, M., De Berardis, D., Koshy, A. S., Perna, G., Valchera, A., Vancampfort, D., & Stubbs, B. (2016). Prevalence and clinical features associated with bipolar disorder polypharmacy: a systematic review. *Neuropsychiatric disease and treatment*, *12*, 719–735. https://doi.org/10.2147/NDT.S100846
- Fornaro, M., Maritan, E., Ferranti, R., Zaninotto, L., Miola, A., Anastasia, A., Murru, A., Solé, E., Stubbs, B., Carvalho, A. F., Serretti, A., Vieta, E., Fusar-Poli, P., McGuire, P., Young, A. H., Dazzan, P., Vigod, S. N., Correll, C. U., & Solmi, M. (2020). *Lithium exposure during pregnancy and the postpartum period: A systematic review and meta-analysis of safety and efficacy outcomes*. *American Journal of Psychiatry, 177*(1), 76–92. https://doi.org/10.1176/appi.ajp.2019.19030228
- Galbally, M., Roberts, M., Buist, A., & Perinatal Psychotropic Review Group. (2010). *Mood stabilizers in pregnancy: A systematic review*. *Australian & New Zealand Journal of Psychiatry, 44*(11), 967–977. https://doi.org/10.3109/00048674.2010.506637
- Gilden, J., Kamperman, A. M., Munk-Olsen, T., Hoogendijk, W. J. G., Kushner, S. A., & Bergink, V. (2020). Long-Term Outcomes of Postpartum Psychosis: A Systematic Review and Meta-Analysis. *The Journal of clinical psychiatry*, *81*(2), 19r12906. https://doi.org/10.4088/JCP.19r12906
- Gordon, S. (2021, December 5). *Sleep position unlikely to affect baby's health in pregnancy, study finds*. HealthDay. Retrieved February 19, 2022, from https://consumer.healthday.com/pregnancy-information-29/pregnancy-news-543/sleep-position-unlikely-to-affect-baby-s-health-in-pregnancy-study-finds-750168.html
- Guo, J., Liu, Y., Kong, L., Sun, Y., Lu, Z., Lu, T., Qu, H., & Yue, W. (2023). Comparison of the probability of four anticonvulsant mood stabilizers to facilitate polycystic ovary syndrome in women with epilepsies or bipolar disorder-A systematic review and meta-analysis. *Frontiers in psychiatry*, *14*, 1128011. https://doi.org/10.3389/fpsyt.2023.1128011

Citations (cont.)

- Hale, T. W. (2026). *Hale's Medications & Mothers' Milk*. Springer Publishing. https://www.halesmeds.com
- Harden, C. L., Pennell, P. B., Koppel, B. S., Hovinga, C. A., Gidal, B., Meador, K. J., Hopp, J., Ting, T. Y., Hauser, W. A., Thurman, D., Kaplan, P. W., Robinson, J. N., French, J. A., Wiebe, S., Wilner, A. N., Vazquez, B., Holmes, L., Krumholz, A., Finnell, R., Shafer, P. O., … American Epilepsy Society (2009). Practice parameter update: management issues for women with epilepsy--focus on pregnancy (an evidence-based review): vitamin K, folic acid, blood levels, and breastfeeding: report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society. *Neurology*, *73*(2), 142–149. https://doi.org/10.1212/WNL.0b013e3181a6b325
- Hashmi, A. M., Bhatia, S. K., Bhatia, S. K., & Khawaja, I. S. (2016). Insomnia during pregnancy: Diagnosis and Rational Interventions. *Pakistan journal of medical sciences*, *32*(4), 1030–1037. https://doi.org/10.12669/pjms.324.10421
- Hastie, R., Tong, S., Hiscock, R., Lindquist, A., Lindström, L., Wikström, A. K., & Sundström-Poromaa, I. (2021). Maternal lithium use and the risk of adverse pregnancy and neonatal outcomes: a Swedish population-based cohort study. *BMC medicine*, *19*(1), 291. https://doi.org/10.1186/s12916-021-02170-7
- Honybun, E., Cockle, E., Malpas, C. B., O'Brien, T. J., Vajda, F. J., Perucca, P., & Rayner, G. (2024). Neurodevelopmental and Functional Outcomes Following In Utero Exposure to Antiseizure Medication: A Systematic Review. *Neurology*, *102*(8), e209175. https://doi.org/10.1212/WNL.0000000000209175
- Huybrechts KF, Straub L, Karlsson P, et al. Association of In Utero Antipsychotic Medication Exposure With Risk of Congenital Malformations in Nordic Countries and the US. *JAMA Psychiatry*. 2023;80(2):156–166. doi:10.1001/jamapsychiatry.2022.4109
- Isometsä, E. T., Henriksson, M. M., Aro, H. M., & Lönnqvist, J. K. (1994). Suicide in bipolar disorder in Finland. *The American journal of psychiatry*, *151*(7), 1020–1024. https://doi.org/10.1176/ajp.151.7.1020
- Jablensky, A. V., Morgan, V., Zubrick, S. R., Bower, C., & Yellachich, L.-A. (2005). *Pregnancy, delivery, and neonatal complications in a population cohort of women with schizophrenia and major affective disorders*. *American Journal of Psychiatry, 162*(1), 79–91. https://doi.org/10.1176/appi.ajp.162.1.79
- Jones, I., & Craddock, N. (2001). Familiarity of the puerperal trigger in bipolar disorder: Results of a family study. *American Journal of Psychiatry, 158*(6), 913–917. https://doi.org/10.1176/appi.ajp.158.6.913
- Joseph-Delaffon, K., Eletri, L., Dechartres, A., Nordeng, H. M. E., Richardson, J. L., Elefant, E., Mitanchez, D., & Marin, B. (2024). Neonatal outcomes after in utero exposure to antipsychotics: a systematic review and meta-analysis. *European journal of epidemiology*, *39*(10), 1073–1096. https://doi.org/10.1007/s10654-024-01156-y
- Mantere, O., Suominen, K., Valtonen, H.M., Arvilommi, P., Leppämäki, S., Melartin, T. and Isometsä, E. (2008), Differences in outcome of DSM-IV bipolar I and II disorders. Bipolar Disorders, 10: 413-425. https://doi.org/10.1111/j.1399-5618.2007.00502.x
- McIntyre, R. S., Berk, M., Brietzke, E., Goldstein, B. I., López-Jaramillo, C., Kessing, L. V., Malhi, G. S., Nierenberg, A. A., Rosenblat, J. D., Majeed, A., Vieta, E., Vinberg, M., Young, A. H., & Mansur, R. B. (2020). Bipolar disorders. *Lancet (London, England)*, *396*(10265), 1841–1856. https://doi.org/10.1016/S0140-6736(20)31544-0
- Molenaar NM, Poels EMP, Robakis T, Wesseloo R, Bergink V. Management of Lithium Dosing Around Delivery: An Observational Study. Focus (Am Psychiatr Publ). 2024 Jan;22(1):120-125. doi: 10.1176/appi.focus.23021031. Epub 2024 Jan 12. PMID: 38694160; PMCID: PMC11058920.
- Nierenberg AA, Agustini B, Köhler-Forsberg O, et al. Diagnosis and treatment of bipolar disorder: a review. *JAMA*. 2023;330(14):1370-1380. doi:10.1001/jama.2023.18588.
- Pennell, P. B., Li, D., Kerr, W. T., Pack, A. M., French, J., Gerard, E., Birnbaum, A. K., McFarlane, K. N., Meador, K. J., & MONEAD Study Group (2026). Antiseizure Medication Dosing Strategy During Pregnancy and Early Postpartum in Women With Epilepsy in MONEAD. *Neurology*, *106*(2), e214483. https://doi.org/10.1212/WNL.0000000000214483
- Poels, E. M. P., Kamperman, A. M., Bijma, H. H., Honig, A., van Kamp, I. L., Kushner, S. A., Hoogendijk, W. J. G., Bergink, V., & White, T. (2023). Brain development after intrauterine exposure to lithium: A magnetic resonance imaging study in school-age children. *Bipolar Disorders, 25*(3), 181–190. https://doi.org/10.1111/bdi.13297
- Poels, E. M. P., Schrijver, L., White, T. J. H., Roza, S. J., Zarchev, M. G., Bijma, H., Honig, A., van Kamp, I. L., Hoogendijk, W. J. G., Kamperman, A. M., & Bergink, V. (2022). The effect of prenatal lithium exposure on the neuropsychological development of the child. *Bipolar Disorders, 24*(3), 310–319. https://doi.org/10.1111/bdi.13133
- Quinn, D., Donnelly, M., & O'Neill, C. (2026). Antipsychotic drug use during pregnancy and neonatal outcomes: a systematic review and meta-analysis. *Archives of women's mental health*, *29*(1), 12. https://doi.org/10.1007/s00737-025-01651-5

Citations (cont.)

- Resendez, A. V., Copen, C. E., Zapata, L. B., D'Angelo, D. V., & Morrow, B. (2023). *Updated methodology to estimate overall and unintended pregnancy rates in the United States* (Vital and Health Statistics, Series 2, No. 201). National Center for Health Statistics. Centers for Disease Control and Prevention. https://www.cdc.gov/nchs/data/series/sr_02/sr02-201.pdf
- Roddy Mitchell, A., Lindquist, A., Hiscock, R. J., Forsythe, A., Gordon, H., Homer, C. S. E., Pritchard, N., Atkinson, J., Walker, S. P., Tong, S., & Hastie, R. (2026). Lithium Use in Pregnancy and the Risk of Spontaneous Preterm Birth: An Australian Statewide Retrospective Cohort Study. *BJOG : an international journal of obstetrics and gynaecology*, 10.1111/1471-0528.70301. Advance online publication. https://doi.org/10.1111/1471-0528.70301
- Rodrigues Cordeiro C, Côrte-Real BR, Saraiva R, Frey BN, Kapczinski F, de Azevedo Cardoso T. Triggers for acute mood episodes in bipolar disorder: a systematic review. *J Psychiatr Res*. 2023;161:237-260. doi:10.1016/j.jpsychires.2023.03.008.
- Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum: ACOG Clinical Practice Guideline No. 4: (2023). *Obstetrics & Gynecology*, *141*(6), 1232–1261. https://doi.org/10.1097/AOG.0000000000005200
- Sharma, V., & Mazmanian, D. (2003). Sleep loss and postpartum psychosis. *Bipolar Disorders, 5*(2), 98–105. https://doi.org/10.1034/j.1399-5618.2003.00015.x
- Smedler E, Sparding T, Hattab A, Sellgren CM, Landén M. Reporting trigger factors for (hypo)manic episodes in bipolar disorder: association with personality and prognosis. *Acta Psychiatr Scand*. 2020;141(6):534-540. doi:10.1111/acps.13174
- Smolinski, N. E., Sarayani, A., Thai, T. N., et al. (2024). Prenatal exposure to valproic acid across various indications for use. *JAMA Network Open, 7*(5), e2412680. https://doi.org/10.1001/jamanetworkopen.2024.12680
- U.S. Food and Drug Administration. (2025). *LAMICTAL (lamotrigine) tablets, tablets for oral suspension, and orally disintegrating tablets: Prescribing information* [Label]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/020241s068s069%2C020764s061s062%2C022251s032s033lbl.pdf
- Viktorin, A., Lichtenstein, P., Thase, M. E., Larsson, H., Lundholm, C., Magnusson, P. K., & Landén, M. (2014). The risk of switch to mania in patients with bipolar disorder during treatment with an antidepressant alone and in combination with a mood stabilizer. *The American journal of psychiatry*, *171*(10), 1067–1073.
- Viguera, A. C., McElheny, S. A., Caplin, P. S., Kobylski, L. A., Rossa, E. T., Young, A. V., Gaccione, P., Góez-Mogollón, L., Freeman, M. P., & Cohen, L. S. (2023). Risk of Poor Neonatal Adaptation Syndrome Among Infants Exposed to Second-Generation Atypical Antipsychotics Compared to Antidepressants: Results From the National Pregnancy Registry for Psychiatric Medications. *The Journal of clinical psychiatry*, *84*(1), 22m14492. https://doi.org/10.4088/JCP.22m14492
- Viguera, A. C., Whitfield, T., Baldessarini, R. J., Newport, D. J., Stowe, Z., Reminick, A., Zurick, A., & Cohen, L. S. (2007). Risk of recurrence in women with bipolar disorder during pregnancy: prospective study of mood stabilizer discontinuation. *The American journal of psychiatry*, *164*(12), 1817–1923. https://doi.org/10.1176/appi.ajp.2007.06101639
- Wesseloo, R., Wierdsma, A. I., van Kamp, I. L., Munk-Olsen, T., Hoogendijk, W. J. G., Kushner, S. A., & Bergink, V. (2017). Lithium dosing strategies during pregnancy and the postpartum period. *The British journal of psychiatry : the journal of mental science*, *211*(1), 31–36. https://doi.org/10.1192/bjp.bp.116.192799
- Westin, A. A., Brekke, M., Molden, E., Skogvoll, E., & Spigset, O. (2017). Selective serotonin reuptake inhibitors and venlafaxine in pregnancy: Changes in drug disposition. *PloS one*, *12*(7), e0181082. https://doi.org/10.1371/journal.pone.0181082
- Yatham LN, Arumugham SS, Kesavan M, et al; BEAM-BD Trial Group. Duration of adjunctive antidepressant maintenance in bipolar I depression. *N Engl J Med*. 2023;389(5):430-440. doi:10.1056/NEJMoa2300184
- Yatham, L. N., Kennedy, S. H., Parikh, S. V., Schaffer, A., Bond, D. J., Frey, B. N., Sharma, V., Goldstein, B. I., Rej, S., Beaulieu, S., Alda, M., MacQueen, G., Milev, R. V., Ravindran, A., O'Donovan, C., McIntosh, D., Lam, R. W., Vazquez, G., Kapczinski, F., … Berk, M. (2018). *Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder*. *Bipolar Disorders, 20*(2), 97–170. https://doi.org/10.1111/bdi.12609
- Zhang, H., Zhang, X., Wei, L., Chen, S., Fan, Y., & Huang, L. (2026). Antipsychotic use during pregnancy and risk of gestational diabetes: an updated meta-analysis. *Journal of affective disorders*, *395*(Pt A), 120633. https://doi.org/10.1016/j.jad.2025.120633
- Zheng, L., Tang, S., Tang, R., Xu, M., Jiang, X., & Wang, L. (2021). Dose Adjustment of Quetiapine and Aripiprazole for Pregnant Women Using Physiologically Based Pharmacokinetic Modeling and Simulation. *Clinical pharmacokinetics*, *60*(5), 623–635. https://doi.org/10.1007/s40262-020-00962-3

Citations (cont.)

Images Sources:

- https://www.foxnews.com/health/biden-oldest-president-age-80-nation-full-neurological-assessment
- https://www.health.harvard.edu/newsletter_article/Bipolar_disorder
- https://www.osmosis.org/answers/dig-fast-manic-episode-mnemonic
- https://www.researchgate.net/figure/Estrogen-and-progesterone-levels-during-pregnancy-and-after-parturition_fig4_318896767
- Westin, A. A., Reimers, A., & Spigset, O. (2018). Should pregnant women receive lower or higher medication doses. *Journal of the Norwegian Medical Association*, *138*(17). https://doi.org/10.4045/tidsskr.18.0065