# How can I safely prescribe psychotropics to pregnant patients?

## An evidence-based approach to considering medications in the treatment of psychiatric disorders in pregnancy/lactation

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# Disclosures

No relevant financial relationship with a commercial interest to disclose.

# Do you treat patients with psychiatric diagnosis who can become pregnant ?

# Do you feel prepared to care for perinatal individuals on psychiatric medications ?

1. Always
2. Often
3. Sometimes
4. Rarely

# General Consideration

- 50% of all pregnancies in general population are unplanned
- 65% of all pregnancies in patients with psychiatric vulnerability are unplanned
- 83% of mothers breastfeed, 60% until 6 months and 30% until 12 months
- 10.3% women in reproductive age on antidepressants
- 6.8% use anti-depressants in first trimester
- 6-15% of pregnant patient with psychiatric d/o are prescribed antipsychotic

Ref: Finer et al 2014, Dawson et al 2016, Pratt et al 2017, Ko JY et 2012, Edinoff et al 2022, Hanley 2014, Schonewille et al., 2022.

# Common reasons for unease with perinatal prescribing

- Concern around potential effects on baby
- Concerns related to pregnancy outcomes and delivery
- Concerns related to breastfeeding
- Concerns related to long term neurodevelopmental outcomes
- Lack of training related to prescribing psychotropic medications during perinatal period

# Current limitations

- Lack of randomized clinical trials
- Limited information on medication efficacy, alternative treatments, or dosage alterations given pharmacokinetic changes in pregnancy
- Treatment decisions based only on observational studies
- Previous studies compared outcomes of depressed women on antidepressants with healthy women, with incomplete adjustment for confounding factors

# Considering the literature

*Certain studies may be more likely to misrepresent risk:*

- **Self-report**: Early databases relied on self-report registries, which introduced reporting bias and other inaccuracies, without input from clinicians on diagnosis and dosing.
- **Polypharmacy**: Early studies were less rigorous in controlling for polypharmacy and co-morbid medical conditions.

*Advances in literature over the past 30 years*

- Electronic medical records have increased the power of retrospective studies
- More recent studies control for confounding factors and account for risks associated with underlying mental illness

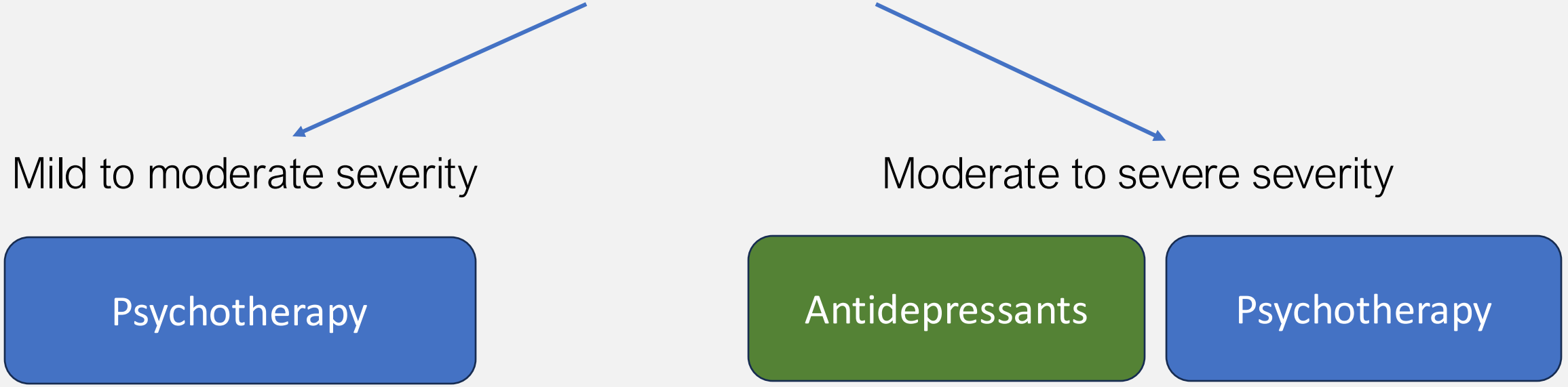
*Continued challenges*

- Though increasing, continue to have relatively fewer studies on long term outcomes for various perinatal medication exposures
- Rare Randomized controlled prospective studies

# Prescribing in the perinatal period

- Encourage patient to have psychiatric care during and after pregnancy.
- All medication changes should be done before pregnancy if possible.
- Ideally patient should be psychiatrically stable before attempting pregnancy.

# Treatment of perinatal mood and anxiety disorders



# C

- When choosing a medication to prescribe during pregnancy, frequently the best option is a medication that was helpful for the individual in the past, due to known efficacy and tolerability for that patient.

- When possible, monotherapy in adequate dose is preferred to polypharmacy.

- The goal of treatment is full symptom remission, and medications should be adjusted to the lowest efficacious and fully therapeutic dose.

# Risk Stratification

- Diagnosis
- History of recurrence
- Severity of illness
- Availability of resources
- Age
- Psychosocial factors

# Risk of Relapse of MDD

- Cohen et al., 2006. A prospective naturalistic investigation using longitudinal psychiatric assessments on a monthly basis across pregnancy.

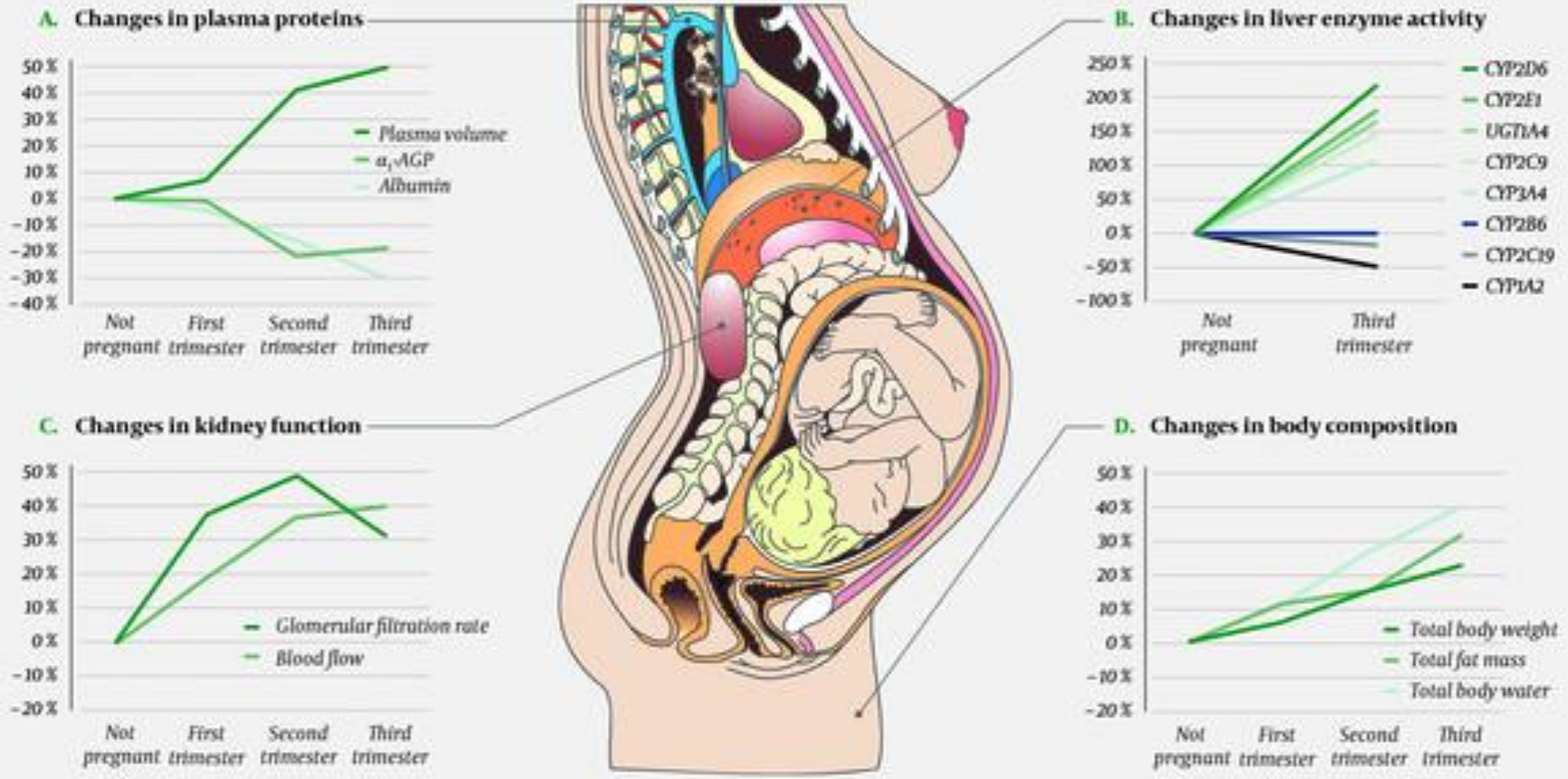
- Among the 201 women in the sample, 86 (43%) experienced a relapse of major depression during pregnancy.
- Among the 82 women who maintained their medication throughout their pregnancy, 21 (26%) relapsed compared with 44 (68%) of the 65 women who discontinued medication.
- Women who discontinued medication relapsed significantly more frequently over the course of their pregnancy compared with women who maintained their medication (hazard ratio, 5.0; 95% confidence interval, 2.8-9.1; P<.001).

# Risk of relapse of bipolar disorder

- Viguera et al., 2011: Among women with bipolar disorder who were clinically treated, 23% had illness episodes during pregnancy and 52% during the postpartum period.

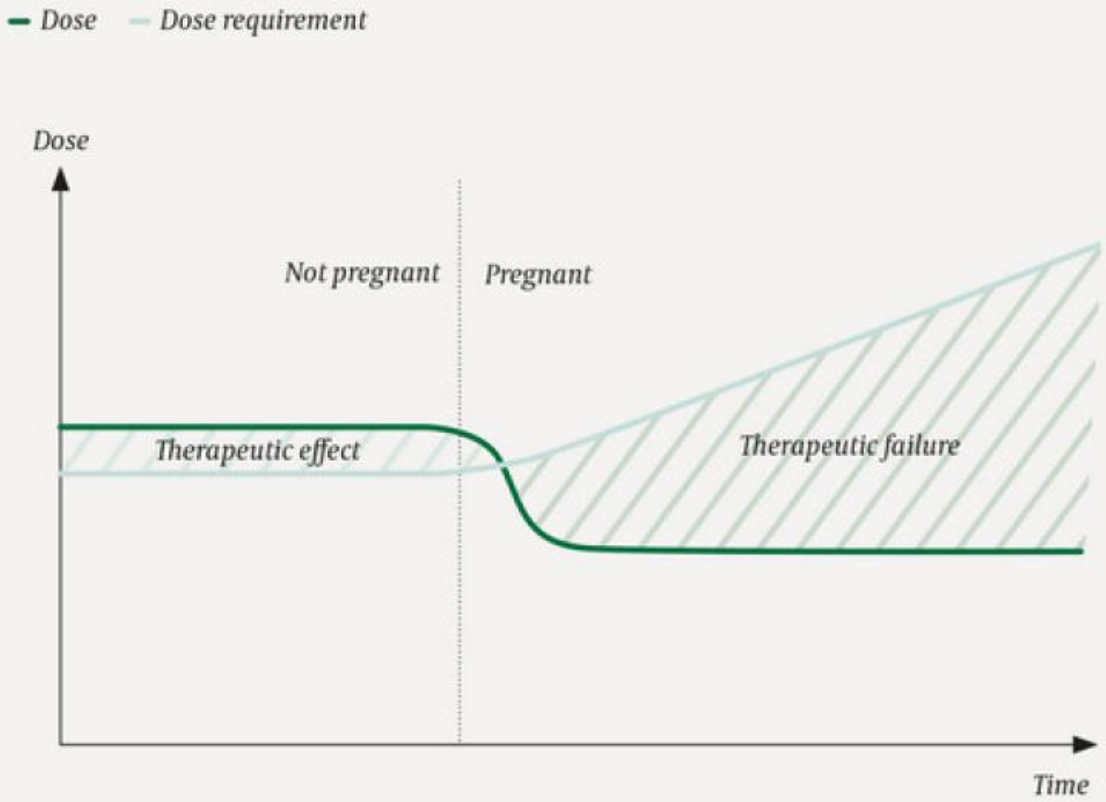
- Perry et al., 2022: 128 women with DSM-5 BD were followed from week 12 of pregnancy (baseline) to 12-weeks postpartum.
  - Perinatal recurrence of illness was common - 57% (BD-I) and 62% (BD-II) experienced a mood episode during pregnancy.
  - Women with BD-I were more likely to experience mania/psychosis during pregnancy than women with BD-II (13.5% vs. 0%).
  - Women with BD-I were more likely to experience mania/psychosis within 6 weeks postpartum (23%) compared to women with BD-II (4%).
  - In women with BD-I, mania/psychosis during pregnancy was associated with a sevenfold increased risk of postpartum mania/psychosis (RR 7.0, $p<0.001$).

# Key physiological changes during pregnancy




*Westin et al., 2018.*

# Risk of therapeutic failure in women







Westin AA, Reimers A, Spigset O. Tidsskr Nor Laegeforen. 2018;138(17):10.

# Prescribing in the perinatal period

- There are important physiologic changes to be aware of during pregnancy, and the dose of psychotropic medication may need to be increased due to increase in plasma volume and faster drug clearance rate.

- When possible, therapeutic monitoring of serum levels may guide dosing.

- The involvement and collaboration of psychiatry, obstetrics, and pediatrics is important to provide optimal care for these patients.

# Breastfeeding and psychotropic medications

- All psychotropic medications readily pass into breast milk.
- The amount of medication secreted into breast milk is significantly lower in most circumstances than the amount of medication that passed through the placenta during pregnancy.
- If an infant was exposed in utero to a psychiatric medication, it does not make sense to switch to another medication for breastfeeding, unless:
  - The mother's psychiatric illness has relapsed and the current medication regimen is not working
  - The mother is on a medication that has a risk of severe side effects with continued exposure to the infant (clozapine)
  - The infant appears to be having side effects or medical complications related to the medication exposure during breastfeeding.



Payne, 2019.

# Relative Infant Dose (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.
- ACOG recommends that RID<10% acceptable for lactation
- Practice of pumping and dumping is not advised
- Can consider timing short half life medications after breastfeeding
- Sleep deprivation increases risk of relapse for mother
- Collaborate with pediatrician

Ref:Burkey et al 2013

# How to stay up to date on literature

Project TEACH: https://projectteachny.org/

Mother to Baby: https://mothertobaby.org/

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

MGH: https://womensmentalhealth.org/

Reprotox: https://www.reprotox.org/

ROSE: https://www.womenandinfants.org/rose-program-postpartum-depression

LACTMED: https://www.ncbi.nlm.nih.gov/books/NBK501922/

# FDA Guidelines: 2014 Pregnancy and Lactation Labeling Rule (PLLR)

- We do not use the FDA Lettering system anymore!

| Pregnancy Category | Description |
|---|---|
| A | Appropriate human studies - no risk |
| B | Insufficient human studies, but animal research suggests safety<br>**or**: Animal studies show issues but human studies show safety |
| C | Insufficient human studies, but animal studies show problems<br>**or**: No animal studies, and insufficient human studies |
| D | Human studies, with/without animal research show fetal risks, but the drug is important to some women to treat their conditions |
| X | Fetal risks are evident; there are no situations where the risk/benefit justifies use |

- PLLR system
  - Pregnancy: risk summary, clinical considerations, available data
  - Lactation: risk summary, clinical considerations, available data
  - Female and Male Reproductive potential: impact on pregnancy testing, contraception, and infertility

# There is no decision without a risk

Risk of untreated PMADs

vs.

Risk of prescribing medications during pregnancy

# An Approach to Medication Management

1. **Use what works!** When reasonable start with medications known to work for the patient in the past. Remember many medications are compatible with pregnancy.
2. **Less is more!** When possible, avoid polypharmacy.
3. **Treat to effect!** Use lowest medication amount needed to reach remission of symptoms, not the lowest possible dose of medication.
4. **Be mindful of pregnancy and postpartum related changes!** Due to pharmacokinetic changes seen in pregnancy, you may need to adjust the dose of medications to maintain euthymia or avoid toxicity.
5. **Most medications are compatible with breastfeeding!** Remember, exposure through breast milk is generally less as compared to transplacental passage.
6. **Discuss safe sleep practices with anyone using sedating medications**
7. **When in doubt: call Project TEACH!**

# Case Discussions

# Preconception Counselling: Case 1

A 35 y/o female with history of postpartum depression without suicide ideation with first child that responded well to Lexapro 5mg in the postpartum period. Continues to be on Lexapro 5mg 2 years after birth. Reports no other history of depressive symptoms. Is presenting for counseling around medication use in pregnancy as she is currently hoping to get pregnant.

Assessment:

- Assess for residual symptoms: currently asymptomatic
- Assess for additional supports: is married with strong social and family support. Not currently in therapy
- Assess for additional risk factors: due to job reporting plan to take around only 3 weeks of parental leave

# Case 1: Treatment recommendations

- General Risk Stratification: low
- General recommendation:
  - Complete Risk Risk Discussion
  - Can consider medication discontinuation/lowering with plan for 3-6 month stability before starting attempts to conceive. Discuss plan to restart/increase medications if evidence of symptom redevelopment
- Consider additional supports:
  - Therapy
  - Postpartum planning: Discuss concerns around childcare/provide relevant resources

# Depression in Pregnancy: Case 2

A 40 y/o female, with history of recurrent MDD disorder, history of suicidal ideation without attempt or intent, currently 10 weeks pregnant. Presenting for counseling around continued use of Zoloft

- Assess for residual symptoms: reporting some moderate symptoms of depression. Denies any current thoughts of self harm
- Assess for additional supports: reports close friends and supportive job environment
- Assess for additional risk factors: unplanned pregnancy, currently living alone. Poor family supports

Treatment recommendations

- General Risk Stratification: Moderate
- Complete risk risk discussion
  - Recommend continued medication use; in fact you will want to consider increase/augmentation as patient is currently symptomatic. Remember goal is to treat to effect!
  - Recommend additional supports: therapy, psychoeducation childbirth/parenting classes, support groups, help identify other social/community support sources etc
- If patient chooses to discontinue medication:
  - Discuss importance of close monitoring during perinatal period

# Bipolar Disorder & Pregnancy: Case 3

Case 3: A 27 year old female, with history of bipolar disorder, 2 prior hospitalizations for manic episodes, history of prior suicide attempt via cutting, presenting now with unplanned pregnancy at 16 weeks following recent manic episode; now stable on Zyprexa.

- Assess for residual symptoms: currently denying additional symptoms
- Assess for additional supports: reports close relationship with therapist
- Assess for additional risk factors: history of postpartum psychosis in grandmother, history of postpartum depression in mother

**Quick word:** Mood stabilizers such as Lithium and Depakote have higher neonatal risk profiles than antipsychotics. Recommend getting specialist support for cases with individuals on these medications

Treatment Recommendations:

- General Risk Stratification: High
- Complete risk risk discussion
  - Recommend continued medication use
  - Recommend continued therapy
  - Recommend additional supports: psychoeducation childbirth/parenting classes, support groups, help identify other social/community support sources etc
  - **Important to discuss plans around optimizing sleep in postpartum period.**
  - **Family meeting to discuss risks of the postpartum period**
  - **Inter-team disciplinary approach**
- If patient chooses to discontinue medication:
  - Discuss importance of close monitoring during perinatal period

# Thank You !