



Management of Mood Disorders in Perinatal Patients

Review and discuss the evaluation and treatment of MDD and Bipolar Disorder among pregnant and postpartum patients.

Disclosures

- 1 Receive funding from NIH for the HBCD study that is not relevant to today's topic.
- 2 All thoughts are my own and do not necessarily reflect those of my employer or NIH.
- 3 This a broad overview of a complex topic and there will be two, maybe three tangents.



Women's Mental Health Program



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Psychiatrist



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Psychiatrist



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Psychiatrist

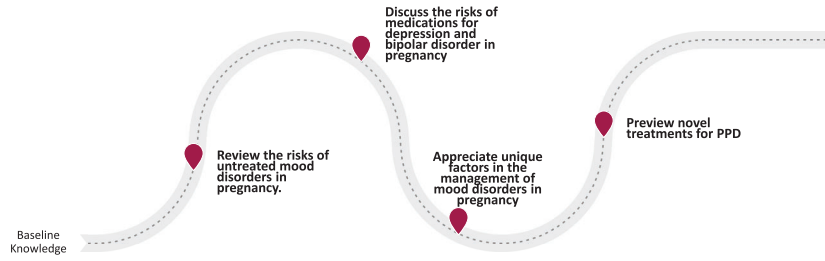


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Agenda



Overview of Mood Disorders



Postpartum Depression

NOT a specified DSM diagnosis
Symptoms consistent with MDD episode
During end of pregnancy or within 4 weeks postpartum



Bipolar I Disorder

Involves episodes of mania and depression



Bipolar Spectrum

Cyclothymia
Bipolar II Disorder

Mood disorders during pregnancy can significantly impact both the mother and child if left untreated.



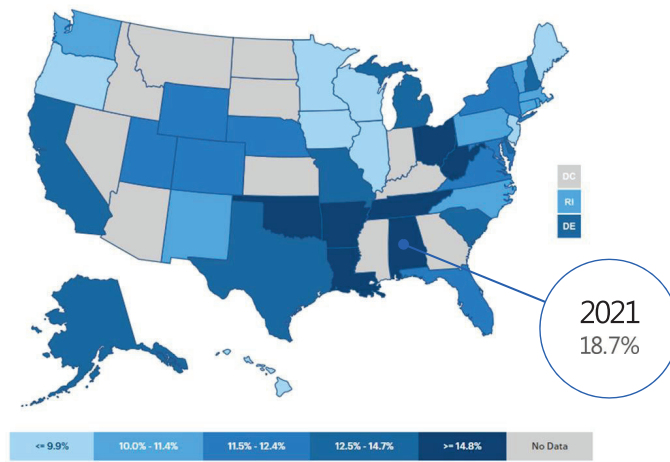
Baby Blues



Meet criteria for Postpartum Depression



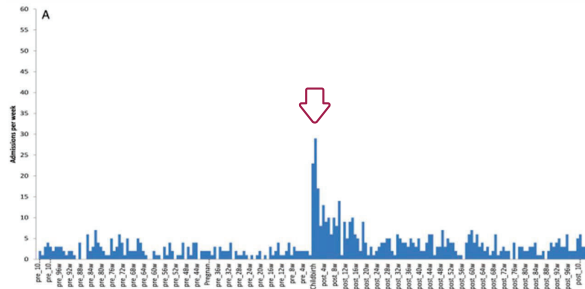
Bipolar Disorder during Pregnancy



Psychiatric Admissions

Data evaluating 4 years pre and post childbirth. Danish cohort.

Martin, et al. (2016) BMJ Open



Risk Factors

Biological Factors

Genetics, hormones, brain chemistry

Psychological Factors

Stress, trauma, anxiety, low self-esteem

Social Factors

Lack of social support, difficult relationships, poverty

Previous Mood Disorders

History of depression or other mood disorders

Major Life Changes

Pregnancy, childbirth, parenting stresses

- Preterm Labor
- Increased Substance Use/Poor Nutrition/High Risk Behaviors
- Maternal Death
- Poor Prenatal Care
- Small for Gestational Age
- Poor Maternal-Infant Bonding
- Cognitive Development/Milestones
- Miscarriage/IUFD



Risks of Untreated Psychiatric Conditions

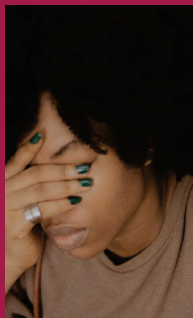
Tangent #1

Messages around pregnancy and postpartum.



Case #1

Depression during Pregnancy



Ms. A is a 34 y/o woman at 26 weeks gestation presenting with worsening depressive symptoms for the past 4 weeks.



She was taking paroxetine prior to pregnancy, but stopped once she had a positive UPT. She did well until one month ago.



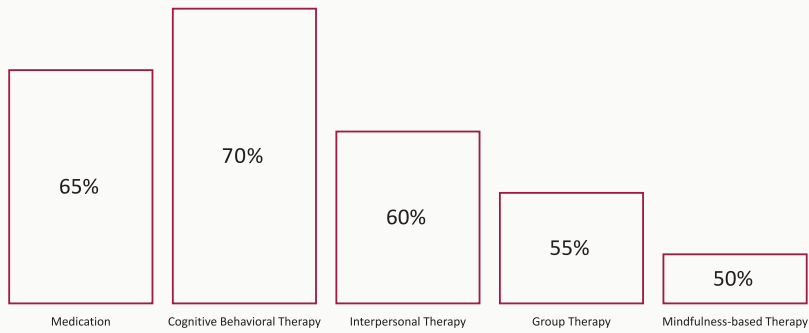
She has good social support and had similar symptoms with her previous pregnancy 3 years ago.



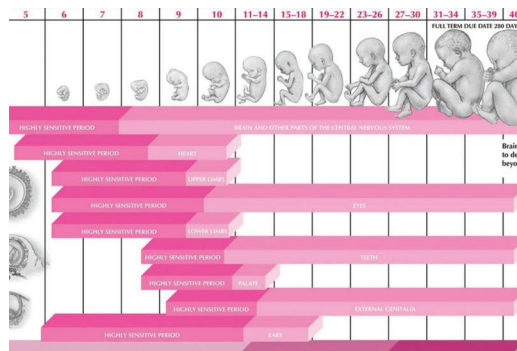
Reports poor sleep, depressed mood, feelings of guilty, low appetite, and anhedonia.

Treatment Options

Percent effectiveness over 12 weeks



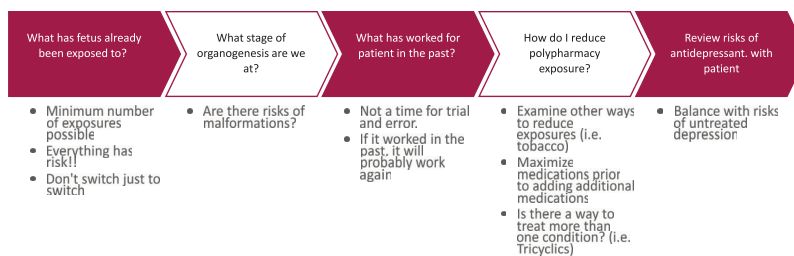
Stages of Organogenesis



Risk of Exposure?

- Most organ develop occurs during first trimester
- Importance of managing risk prior to pregnancy

What Antidepressant Do You Recommend?



Risks of Antidepressants in Pregnancy



Increased risk of low birth weight and preterm delivery
Antidepressants like SSRIs and SNRIs may increase the risk of low birth weight, preterm delivery and admission to a neonatal intensive care unit.



Risk of newborn complications
Antidepressant use in late pregnancy can cause short-term withdrawal symptoms like irritability, increased muscle tone, tremors and breathing issues in newborns.



Risk of persistent pulmonary hypertension
Some studies show an association between late pregnancy exposure to SSRIs and a small increased risk of persistent pulmonary hypertension in newborns.

Persistent Pulmonary Hypertension



3M+ pregnancies in US

- Medicaid patients
- "May have increased risk of PPHN" with late exposure to SSRI-antidepressants. Absolute risk is small.
- adjusted OR = 1.10 (CI 0.94-1.29)

Huybrechts, et al. (2015) JAMA

Cardiac Malformations



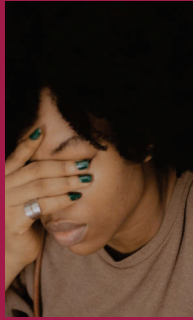
Paroxetine

- **23%** increased risk in major malformations
- **28%** increased risk of cardiac malformations
- When using case control, **2-fold** increase risk of atrial septal defects

Revard, et al. (2012) British Journal of Clinical Pharmacology

Case #1

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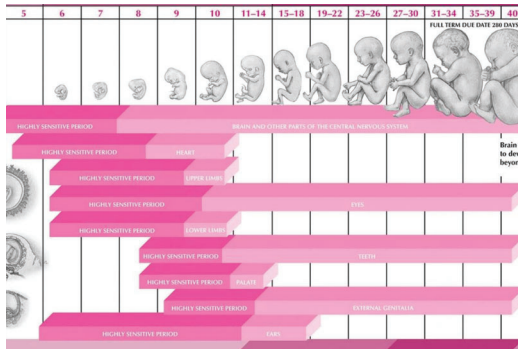


She has good social support and had similar symptoms with her previous pregnancy 3 years ago.



Reports poor sleep, depressed mood, feelings of guilty, low appetite, and anhedonia.

Stages of Organogenesis



Risk of Exposure?

- Most organ development occurs during first trimester
- Importance of managing risk prior to pregnancy

Case #2

Bipolar Disorder during Pregnancy



Ms. D is a 25 y/o woman at 8 weeks gestation who is presenting for a first appointment for bipolar disorder.



Lithium 900 mg QHS (6 years) and Aripiprazole 5 mg daily (3 years)



First manic episode was at age 19 and she has been stable for the past 2 years with last depressive episode 3 years ago.



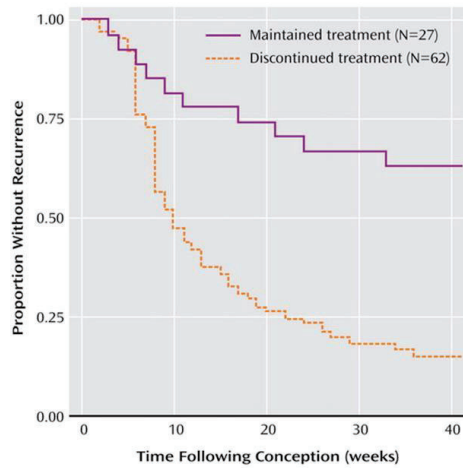
Tobacco: 1/2 ppd and Alcohol 1-2 glasses of wine per week and stopped at KOC

- Preterm Labor
- Increased Substance Use/Poor Nutrition/High Risk Behaviors
- Maternal Death
- Poor Prenatal Care
- Small for Gestational Age
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- Cognitive Development/Milestones
- Miscarriage/IUFD



Risks of Untreated Psychiatric Conditions

High Risk of Recurrence with medication discontinuation.



Vignera et al. (2007) AJP

Risks of Mood Stabilizers in Pregnancy



Neural Tube Defects and Intellectual Disability

Oxcarbamazepine and Valproic Acid contraindicated for women of reproductive age.



Cardiac Malformations

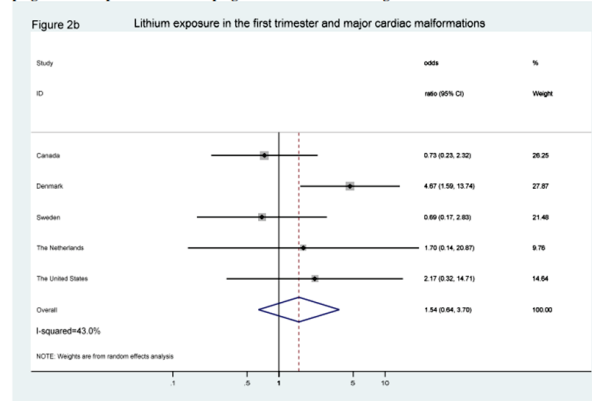


Gestational Diabetes
Atypical Antipsychotics



Dose Adjustments

Figure 2b. Pooled adjusted odds ratio of major cardiac malformations in lithium first trimester exposure pregnancies compared to reference pregnancies with maternal diagnosis of mood disorder



Adjusted for maternal age at delivery, primiparity, treatment with other psychotropic medications during pregnancy and calendar year of birth.

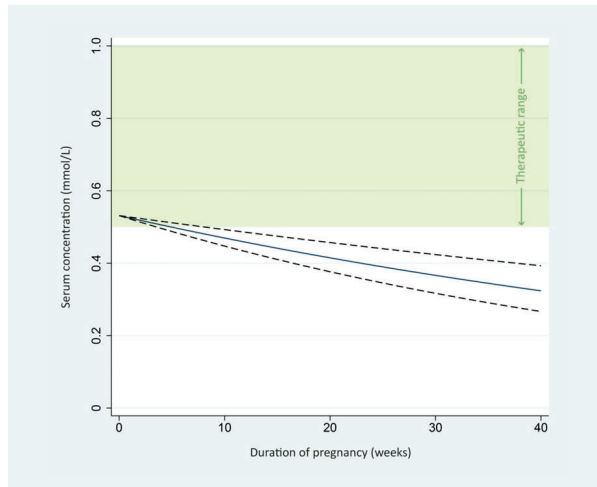
Lithium

Volume Adjustments

Recommend monthly lithium levels until month 9 and then weekly levels until delivery.

Monitor closely postpartum.

Lamotrigine shows similar decrease due to liver metabolism.



Lithium and Breastfeeding



Risks versus Benefits

- Experts do not agree.
- Individual decision based on benefits of breastmilk.
- Baby needs blood monitoring similar to adult.
- Baby lithium level is 25-50% of mother's level.

Bipolar Disorder during Pregnancy



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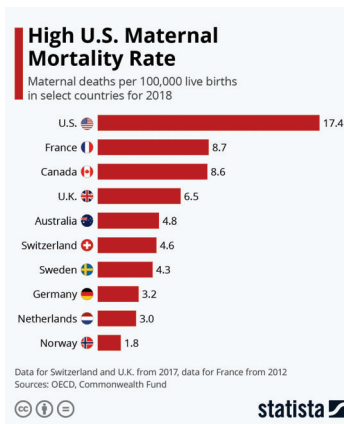
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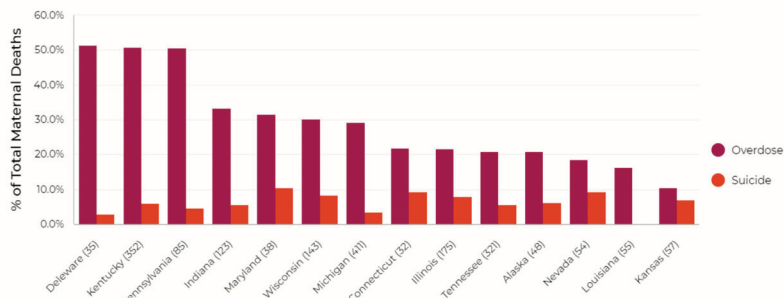
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Tangent #2

Maternal Mortality



Percentage of Total Maternal Death Due to Psychiatric Causes, 2013-2021



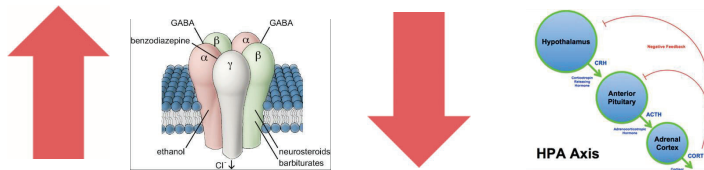


Zuranolone/Zulresso

FDA Approved for Postpartum Depression

NORMAL PREGNANCY

Increased levels of Progesterone/Allopregnanolone → positive allosteric modulation of GABA receptors

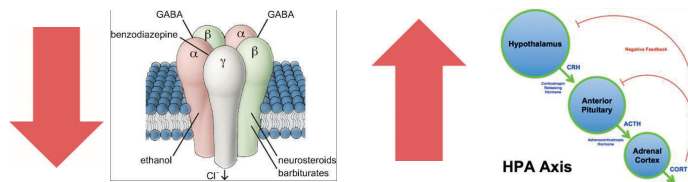


**Prevention of Pre-term Delivery?
Mood Protective**

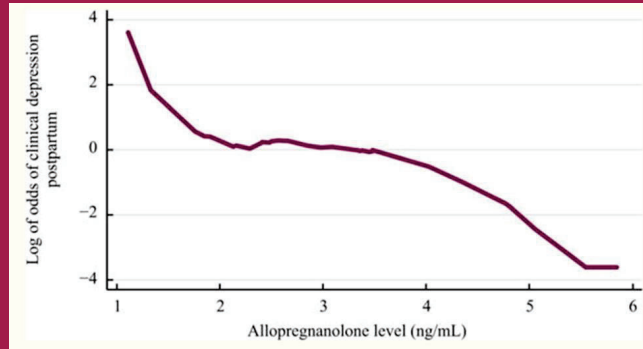
Melon LC, et al. (2018) *Psychoneuroendocrinology*
Osborne LM, et al. (2017) *Psychoneuroendocrinology*

POSTPARTUM





Drastic drop of Progesterone/Allopregnanolone → modulation of GABA receptors no longer present



Postpartum Depression

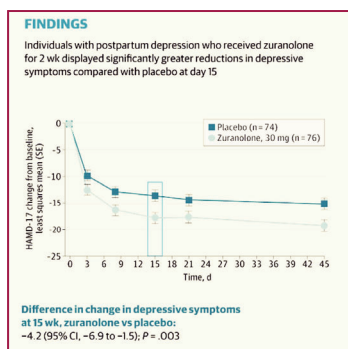


Osborne LM, et al. (2017) *Psychoneuroendocrinology*

<p>POPULATION 150 Women</p>  <p>Women ages 18-45 y with postpartum depression and Hamilton Rating Scale for Depression (HAM-D-17) score ≥ 26 Mean (SD) age, 28.3 (5.4) y</p>	<p>INTERVENTION 153 Individuals randomized</p>  <p>76 Zuranolone Oral zuranolone, 30 mg, every evening with food for 14 d</p>  <p>74 Placebo Oral placebo capsule every evening with food for 14 d</p>
<p>SETTINGS / LOCATIONS</p>  <p>27 Clinical sites in the US</p>	<p>PRIMARY OUTCOME</p> <p>Change from baseline in depressive symptoms at day 15, as measured by HAM-D-17 score (range, 0-52, with higher scores indicating more severe depression)</p>

Delgiannis, K. M., Meltzer-Brody, S., Gunduz-Bruce, H., Doherty, J., Jonas, J., Li, S., ... & Lasseur, R. (2021). Effect of zuranolone vs placebo in postpartum depression: a randomized clinical trial. *JAMA psychiatry*, 78(9), 951-959.

Scientific Breakthrough...



...but does not work for everyone.

- Most effective when depression starts in third trimester or within 4 weeks postpartum.
- Not breastfeeding or willing to "pump and dump".
- Sedation is primary risk.
- Accessibility, financial burden

“If you save the women, it has been said, they will in return save the children, and so by tracing a chain of influence one can save the country

”

Andrew Solomon, *The Noonday Demon*

