

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.

UAMS Women's Mental Health Program



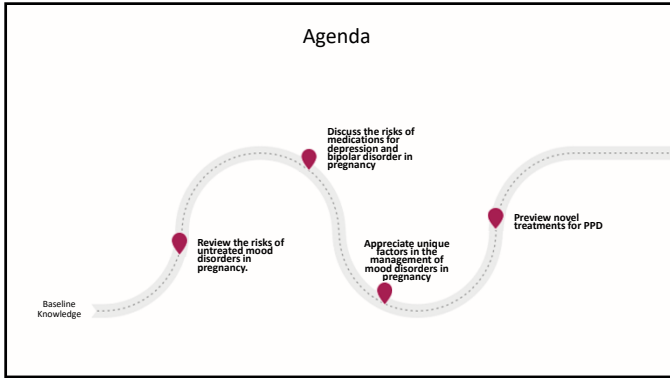
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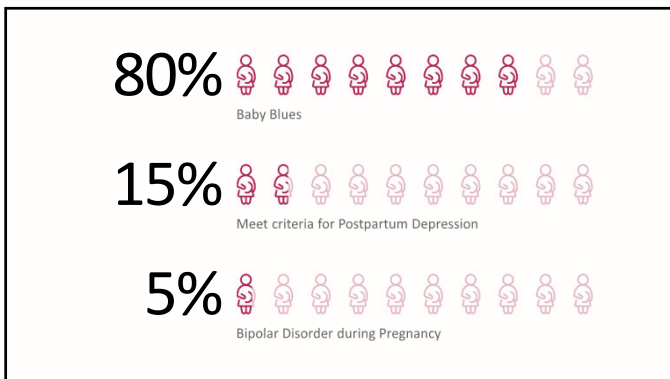
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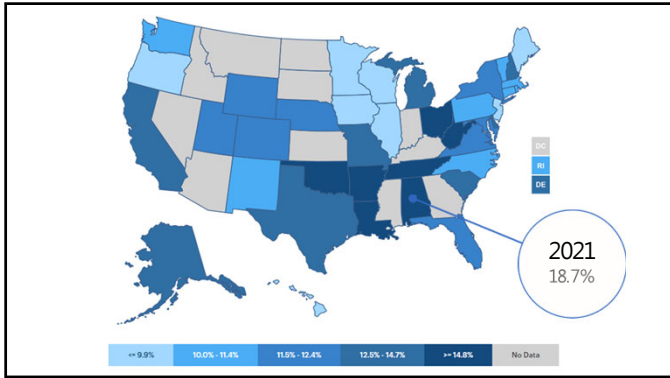


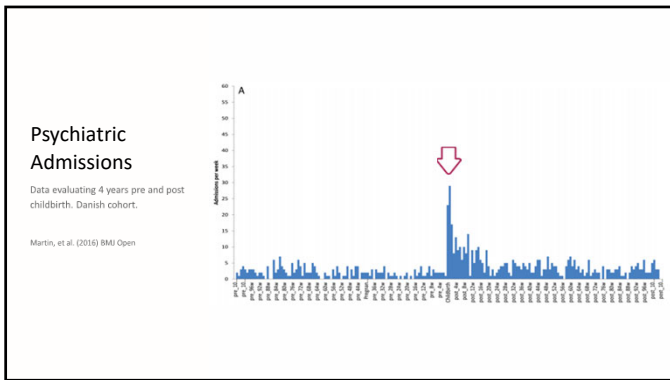
Overview of Mood Disorders

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











- 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.

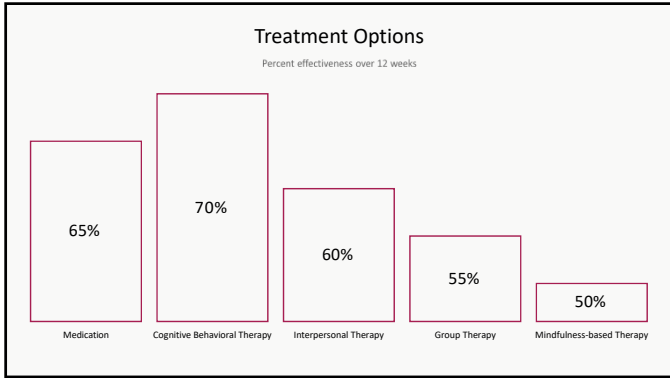


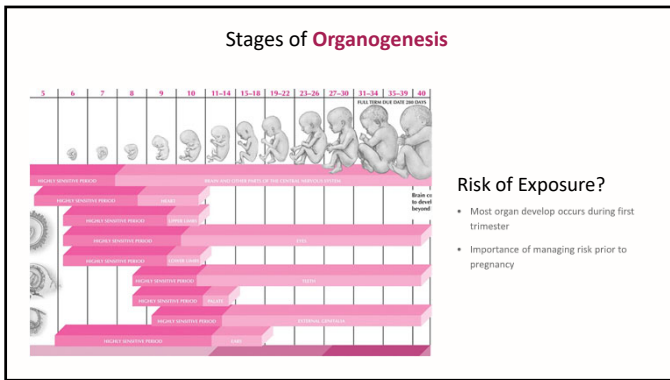
Case #1

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.





What Antidepressant Do You Recommend?

What has fetus already been exposed to?

- Minimum number of exposures possible
- Everything has risk!
- Don't switch just to switch

What stage of organogenesis are we at?

- Are there risks of malformations?

What has worked for patient in the past?

- Not a time for trial and error.
- If it worked in the past, it will probably work again

How do I reduce polypharmacy exposure?

- Examine other ways to reduce exposures (i.e. tobacco)
- Maximize medications prior to adding additional medications
- Is there a way to treat more than one condition? (i.e. Tricyclics)

Review risks of antidepressant with patient.

- Balance with risks of untreated depression

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)

Hodges et al. (2022) JAMA

Cardiac Malformations



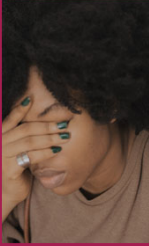
Paroxetine

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

Rezek et al. (2012) British Journal of Clinical Pharmacology

Case #1

Depression during Pregnancy



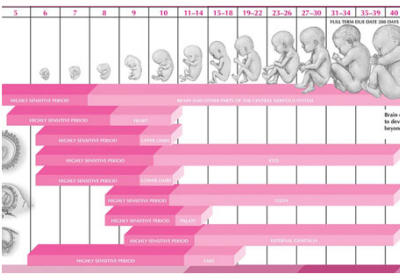
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Stages of Organogenesis




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.

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

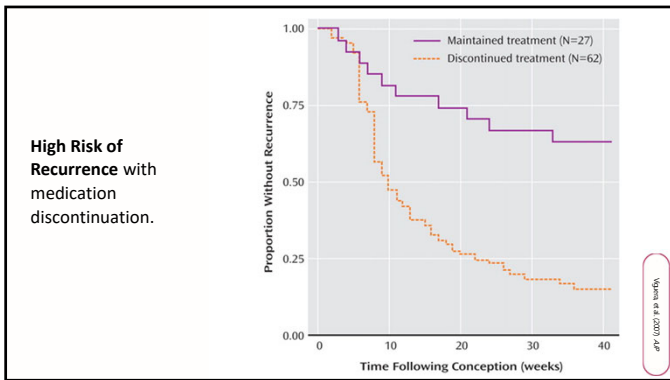
Lithium 900 mg QHS (6 years) and Aripiprazole 5 mg daily (3 years)

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
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Risks of Untreated Psychiatric Conditions




Risks of Mood Stabilizers in Pregnancy




Neural Tube Defects and Intellectual Disability
Oxcarbazepine and Valproic Acid contraindicated for women of reproductive age.



Cardiac Malformations

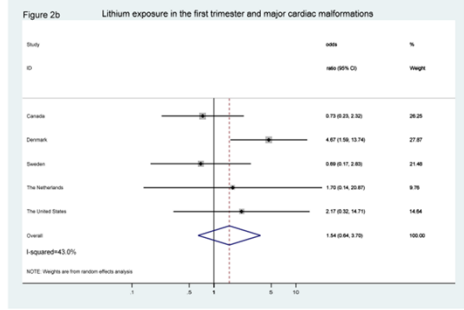


Gestational Diabetes
Atypical Antipsychotics



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.

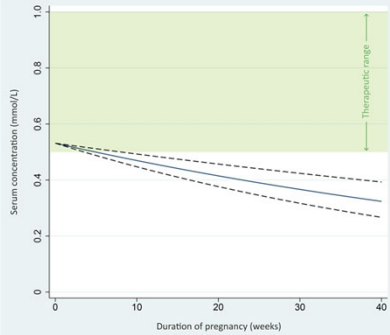
Lithium

Volume Adjustments

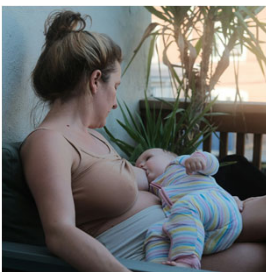
Recommend monthly lithium levels until month 9 and then weekly levels until delivery.

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.

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Tangent #2

Maternal Mortality

High U.S. Maternal Mortality Rate

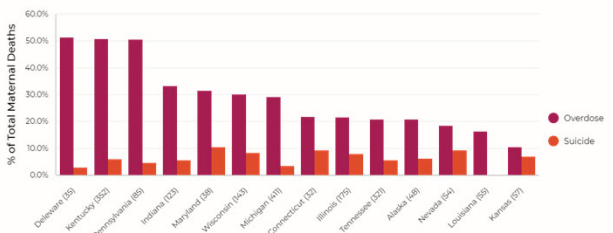
Maternal deaths per 100,000 live births in select countries for 2018

U.S.	17.4
France	8.7
Canada	8.6
U.K.	6.5
Australia	4.8
Switzerland	4.6
Sweden	4.3
Germany	3.2
Netherlands	3.0
Norway	1.8

Data for Switzerland and U.K. from 2017, data for France from 2012
Source: OECD, Commonwealth Fund

statista

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



White, et al. (2023) Archives of Women's Mental Health



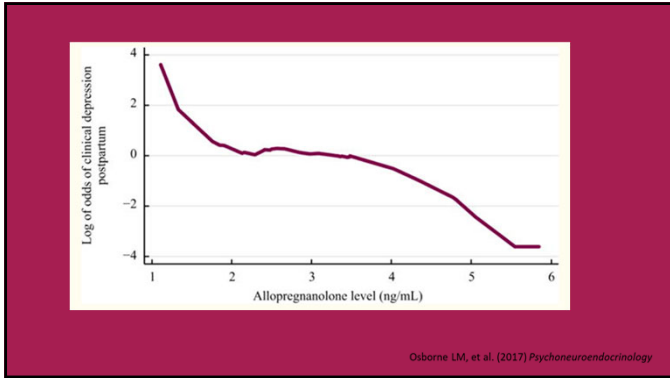
NORMAL PREGNANCY
Increased levels of Progesterone/Allopregnanolone → positive allosteric modulation of GABA receptors





**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



<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 27 Clinical sites in the US</p> 	<p>PRIMARY OUTCOME 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>

Delgannidis, K.M., Metzger-Brodsky, S., Gundak-Bruce, H., Doherty, J., Jones, J., Li, S., ... & Lauer, R. (2021). Effect of zuranolone vs placebo in postpartum depression: a randomized clinical trial. *JAMA psychiatry*, 78(6), 651-658.

Scientific Breakthrough...

FINDINGS
Individuals with postpartum depression who received zuranolone for 2 wk displayed significantly greater reductions in depressive symptoms compared with placebo at day 15

Difference in change in depressive symptoms at 15 wk, zuranolone vs placebo: -4.2 (95% CI, -6.9 to -1.5); P = .003

...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 Sokomon, *The Noontide Demon*