

PERINATAL DEPRESSION

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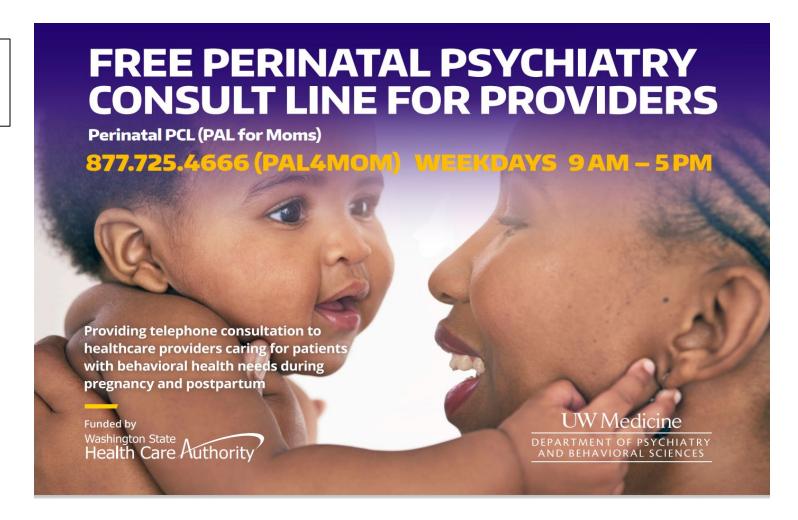






SPEAKER DISCLOSURES

Medical Director Perinatal PCL





PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

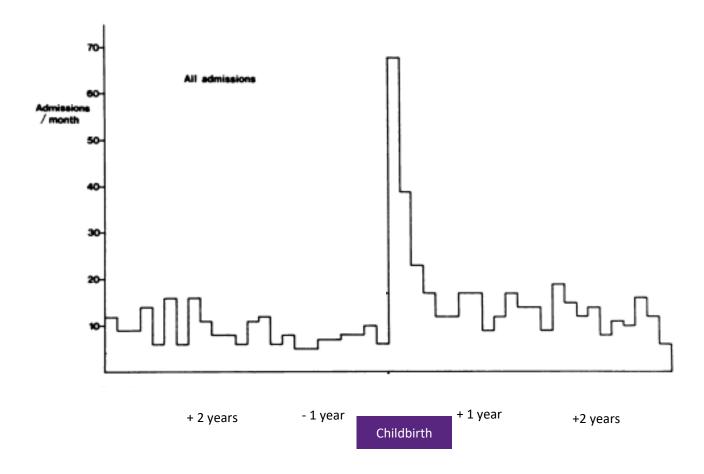
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OBJECTIVES

- 1. Describe screening, assessment, diagnosis, and differential diagnosis of depression during the perinatal period
- 2. Compare the risks of untreated depression with the risks of psychotropic medication during pregnancy and lactation
- 3. Discuss non-medication treatments for perinatal depression





Temporal Relation Between Psychiatric Hospitalization and Childbirth

Kendell, 1987; Connor et al, 2019



CASE

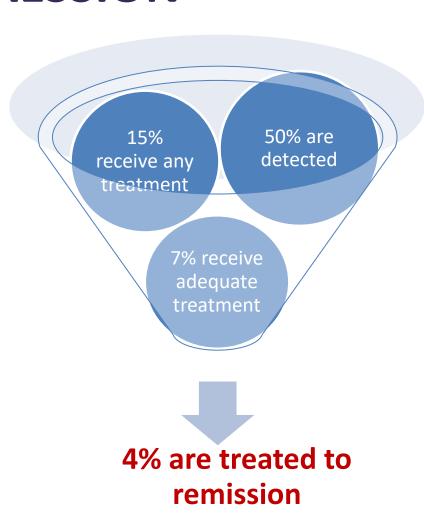
Jasmine is at 16 weeks in her first pregnancy. She tells you that she has been feeling "down" and anxious for the past 2 months. She is having trouble sleeping and her appetite is poor. She is struggling to feel bonded to this pregnancy and she has withdrawn from her friends. She is having trouble dragging herself out of bed in the morning to go to work.



PERINATAL DEPRESSION

Depression during pregnancy and the 12 months afterwards

Prevalence 10-20%

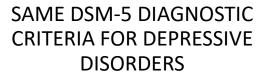


Mental health and substance use combined are the leading cause of maternal mortality (suicide, overdose: CDC, September 2022)



HOW IS PERINATAL DEPRESSION DIFFERENT FROM DEPRESSION AT OTHER TIMES?







SIMILAR TREATMENTS

- Stigma, guilt, fears of CPS involvement
- DSM-5 peripartum onset specifier
 - Pregnancy or in 4 weeks after pregnancy
- Bipolar disorder (1 in 5)
- Risk-risk discussion re medications
- Brexanolone and zuranolone indicated for postpartum depression
- Psychotherapy adapted for perinatal period



RISK FACTORS

- History of depression, bipolar disorder, anxiety disorders
- Family history of depression or perinatal mental health disorders
- Discontinuation of antidepressant medications (60-70% relapse rate)
- Antenatal depression -> 4x risk for postpartum depression
- Unplanned/unwanted pregnancy
- Difficult/traumatic birth, medical problems in infant
- Intimate partner violence
- Adolescent
- Financial problems
- Poor sleep



HEALTH INEQUITIES

- Perinatal individuals who are Black, Indigenous and People of Color (BIPOC) are less likely to be screened and treated for mental health and substance use disorders
- Non-Latina Black birthing parents have higher rates of depressive symptoms during pregnancy
- Black birthing parents are less likely to initiate perinatal depression treatment (counseling or medications), to receive follow up treatment, and to refill antidepressant prescriptions
 - Declercq E et al. Birth 2022; Edge D. Gen Hospital Psychiatry 2010



ACOG GUIDELINES FOR SCREENING

- Screening for depression and anxiety at:
 - Initial prenatal visit
 - Later in pregnancy
 - At postpartum visits
- Anyone answering a self-harm or suicidal ideation question affirmatively should receive immediate risk assessment
- Screening for bipolar disorder before starting medication for depression or anxiety
 - ACOG Clinical Practice Guideline No. 4, Obstet Gynecol June 2023



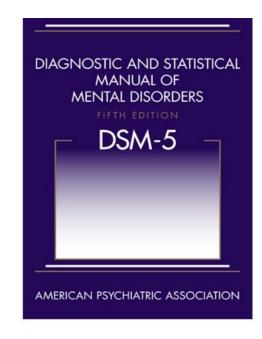
SCREENING: PHQ-9

0-4 = no depression 5-9 = mild

10-14 = moderate

≥ 15 = severe

 Feeling Trouble sleepin Feeling Poor ap Feeling 	terest or pleasure in doing things down, depressed or hopeless falling asleep, staying asleep, or g too much tired or having little energy petite or overeating	0 0	1 1 1	2	3
 Feeling Trouble sleepin Feeling Poor ap Feeling 	down, depressed or hopeless falling asleep, staying asleep, or g too much tired or having little energy	0			3
 Trouble sleepin Feeling Poor ag Feeling 	falling asleep, staying asleep, or g too much tired or having little energy		1		
5. Poor ap 5. Feeling	tired or having little energy	0		2	3
5. Poor ap 6. Feeling			1	2	3
		0	1	2	3
ranare	bad about yourself - or that you're a or have let yourself or your family down	0	1	2	3
reading	concentrating on things, such as the newspaper or watching television	0	1	2	3
3. Moving people being s	or speaking so slowly that other could have noticed. Or, the opposite - o fidgety or restless that you have oving around a lot more than usual	0	1	2	3
	ts that you would be better off dead urting yourself in some way	0	1	2	3
	Column	Totals		+ +	·
	Add Totals To	gether			





SCREENING: EPDS



0-3 points per question. Add all points (total score 0-30)

Items 1, 2, and 4 are reverse-scored

Conventions for determining severity:

0-6 = none or minimal depression

7 - 13 = mild depression

14 - 19 = moderate depression

20 - 30 = severe depression



DIFFERENTIAL DIAGNOSIS

A positive screen warrants further assessment

- Depressive disorders e.g., major depression, persistent depressive disorder
- Situational factors/adjustment disorder/postpartum or baby blues
- Other psychiatric disorders
 - Bipolar disorder, psychotic depression, PTSD, personality disorder, anxiety disorder
- Medical conditions, substance use/withdrawal, medications



FOLLOWING UP ON A POSITIVE SCREEN



- Follow up on any report of suicidal thoughts
 - Columbia Suicide Severity Rating Scale, ASQ
- Reassurance
- Education
- Referrals
- Treatment
- Follow up on referrals 11-37%
 - Increase with education, engaging social supports, facilitated referrals



COLUMBIA SUICIDE SEVERITY RATING SCALE (C-SSRS)

- 6 INTERVIEW questions as a broadbased screener.
- Ask 1st two questions and if "no" answers just go to final question
- Any positive answer said to recommend a mental health referral
- ...more urgent help with "high risk" response

Always ask questions 1 and 2.	Past	Month	
1) Have you wished you were dead or wished you could go to sleep and not wake up?			
2) Have you actually had any thoughts about killing yourself?			
If YES to 2, ask questions 3, 4, 5 and 6. If NO to 2, skip to question 6.			
3) Have you been thinking about how you might do this?			
4) Have you had these thoughts and had some intention of acting on them?		High Risk	
5) Have you started to work out or worked out the details of how to kill yourself? Did you intend to carry out this plan?		High Risk	
Always Ask Question 6	Life- time	Past 3 Months	
6) Have you done anything, started to do anything, or prepared to do anything to end your life? Examples: Took pills, tried to shoot yourself, cut yourself, tried to hang yourself, or collected pills, obtained a gun, gave away valuables, wrote a will or suicide note, took out pills but didn't swallow any, held a gun but changed your mind or it was grabbed from your hand, went to the roof but didn't jump, etc. If yes, was this within the past 3 months?		High Risk	



If YES to 2 or 3, seek behavioral healthcare for further evaluation.

If the answer to 4, 5 or 6 is YES, get immediate help: Call or text 988, call 911 or go to the emergency room.

STAY WITH THEM until they can be evaluated.



Protocol

ASQ

- "Yes" to any = recommend therapy referrals
- "Yes" to item 5 = need to assess for safety now
- The ASQ is free, available from NIMH
- Other language translations available
- https://www.nimh.nih.gov/research /research-conducted-at-nimh/asqtoolkit-materials



In the past few weeks, have you wished you were dead?	O Yes	ONo
In the past few weeks, have you felt that you or your family would be better off if you were dead?	O Yes	O No
In the past week, have you been having thoughts about killing yourself?	O Yes	O No
Have you ever tried to kill yourself?	○ Yes	O No
If yes, how?		
When?		
the patient answers Yes to any of the above, ask the following ac		O No
the patient answers Yes to any of the above, ask the following ac	cuity question: ••• Yes	O No
the patient answers Yes to any of the above, ask the following ac Are you having thoughts of killing yourself right now? If yes, please describe:	cuity question: ••• Yes	O No
the patient answers Yes to any of the above, ask the following ac Are you having thoughts of killing yourself right now? If yes, please describe:	Cuity question: O Yes ary to ask question #5).	O No
the patient answers Yes to any of the above, ask the following ac Are you having thoughts of killing yourself right now? If yes, please describe: Next steps: If patient answers "No" to all questions 1 through 4, screening is complete (not necess	Cuity question: O Yes ary to ask question #5).	ONG
the patient answers Yes to any of the above, ask the following act Are you having thoughts of killing yourself right now? If yes, please describe: Next steps: If patient answers "No" to all questions 1 through 4, screening is complete (not necess No intervention is necessary (*Note: Clinical judgment can always override a negative scr If patient answers "Yes" to any of questions 1 through 4, or refuses to answer, they a	ary to ask question #5). re considered a	O No

sQ Suicide Risk Screening Toolkit NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH) 🥢 NIH) 7/1/2021









OTHER SUICIDE RISK ASSESSMENT RESOURCES

- Patient Safety Screener (PSS)
- 3-item screening questionnaire + secondary screener + suicide care management plans + videos
- https://sprc.org/micro-learning/the-patient-safety-screener-a-brief-tool-to-detect-suiciderisk/
- Stanley-Brown Safety Planning document
- https://suicidesafetyplan.com/forms/
- Lethal means counseling
- Zero Suicide: https://zerosuicide.edc.org/
- Suicide prevention resources | Washington State Health Care Authority



MDQ (MOOD DISORDERS QUESTIONNAIRE)

- Brief (<5 mins)
- Self-report
- Sensitivity 73%, specificity 90% in psychiatric patients

Positive screen:

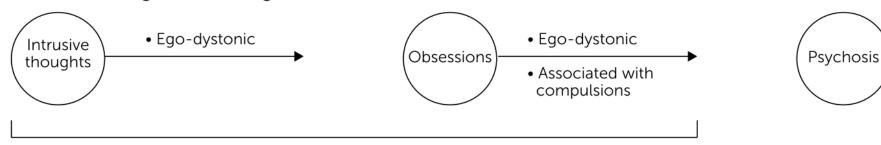
- YES to 7/13 symptoms
- YES to question 2
- Moderate/serious problem on question 3

1. Has there ever been a period of time when you were not your usual self and	YES	NO
you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?		
you were so irritable that you shouted at people or started fights or arguments?		
you felt much more self-confident than usual?		
you got much less sleep than usual and found that you didn't really miss it?		
you were more talkative or spoke much faster than usual?		
thoughts raced through your head or you couldn't slow your mind down?		
you were so easily distracted by things around you that you had trouble concentrating or staying on track?		
you had more energy than usual?		
you were much more active or did many more things than usual?		
you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?		
you were much more interested in sex than usual?		
you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?		
spending money got you or your family in trouble?		
2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time?		
B. How much of a problem did any of these cause you - like being unable to work; having family, money or legal troubles; getting into arguments or fights? No problems Minor problem Moderate problem Serious problem		



THOUGHTS OF HARMING THE BABY

FIGURE 1. Thoughts of harming the infant



Seen in 50% of new mothers without a psychiatric diagnosis and 40% to 80% of mothers with major depressive disorder

- It's common to have thoughts of harm coming to the baby and of harming the baby, either accidentally or on purpose
- Have you had thoughts like this?

Toor et al 2024



• Ego-syntonic

Associated with labile

mood, hallucinations

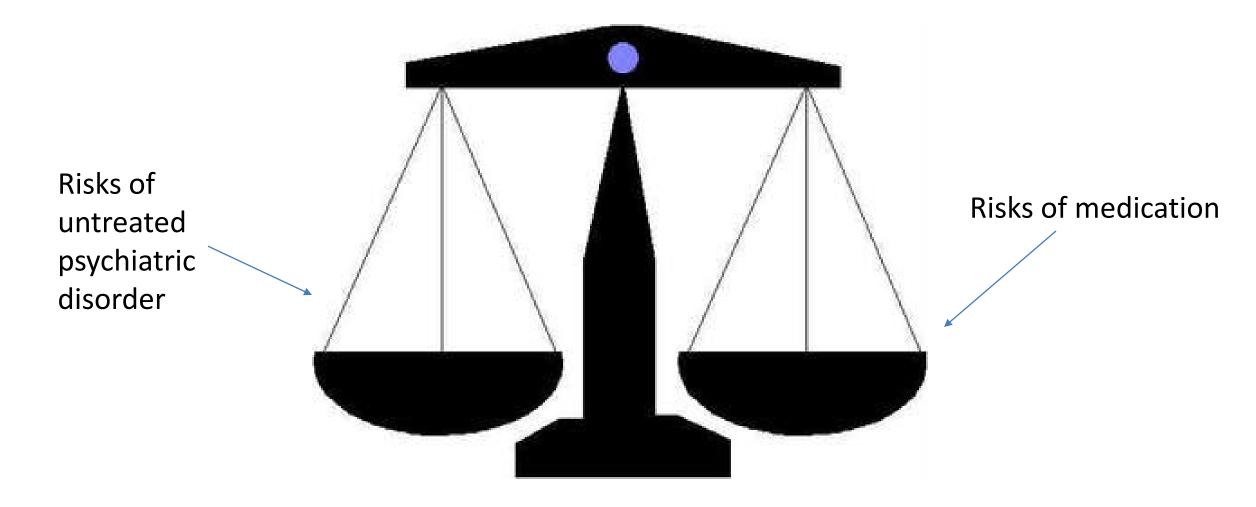
CASE (CONTINUED)

 Jasmine has a PHQ-9 score of 17 and you diagnose her with major depression. She has had some hopeless thoughts but denies thoughts of self-harm. How would you approach her treatment?

- Severe depression
- Generally, medication and therapy



RISK-RISK ASSESSMENT



Alternative treatments



RISKS OF PERINATAL DEPRESSION

- Distress, functional impairment, hospitalization, suicide
- Poor prenatal and self-care, higher rates of perinatal substance use
- Antenatal depression is major risk factor for postpartum depression
- Impaired bonding
- In child, higher rates of failure to thrive, developmental delay, hospitalization and mortality in first year of life
- Higher rates of internalizing and externalizing disorders
- Increased depression risk through adolescence
 - Jacques et al., 2019; Field et al., 2014



SSRIS IN PREGNANCY

- Citalopram (Celexa), escitalopram (Lexapro), fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft)
- No consistent evidence for increase in malformations
 - ?paroxetine
- Limited information available for fluvoxamine
- Persistent pulmonary hypertension of the newborn (PPHN)
- Neonatal adaptation syndrome
- Sertraline preferred



PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN (PPHN)

- Meta-analysis, 11 studies, 156,978 exposed women
- 1.8/1000 baseline risk
- 2.9/1000 with SSRI exposure
- NNH = 1000

•	Lowest	risk with	sertra	line

_	Masarwa	et al.	2018
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SSRI	Placental Passage	P Score
Sertraline	30%	0.83
Escitalopram	50%	0.69
Paroxetine	-	0.49
Citalopram	70%	0.21
Fluoxetine	65%	0.16



NEONATAL ADAPTATION SYNDROME

- 30% of SSRI-exposed babies
- High-pitched cry, sleep disturbance, tremor, hypertonicity/myoclonus, tachypnea, gastrointestinal symptoms, seizures
- Peaks within 2 days after birth, resolves in about 4 days
- Worse with SSRI + benzodiazepine
- Reducing dose in 3rd trimester does not prevent NAS
- May be related to prematurity, hypoglycemia
 - Moses-Kolko 2005; Warburton 2010



ANTIDEPRESSANTS AND LACTATION

- Relative infant doses generally 10% of maternal dose or lower
 - Lowest for:
 - bupropion, mirtazapine, duloxetine, fluvoxamine, paroxetine, sertraline

• Safety index (adverse events/exposures) lowest (most favorable) for sertraline, paroxetine

Berle and Spigset 2011



SSRIS AND CHILD OUTCOMES

- Physical outcomes (5 studies asthma, cancer, BMI, epilepsy): conflicting associations for BMI.
- Neurodevelopmental outcomes (18 studies cognition, behavior, IQ, motor development, speech, language, and scholastic outcomes): no consistent associations
- Psychiatric outcomes (11 studies: ASD, ADHD, affective disorders): associations with affective disorder
 - Rommel et al., 2018



ALTERNATIVE/NON-MEDICATION TREATMENTS

- Psychotherapy
- Sleep
 - 4-5 hours uninterrupted sleep at night postpartum
- Bright light therapy
 - 10,000 lux, morning, 30 min
- Exercise
- Yoga
- Omega-3-fatty acids





EVIDENCE-BASED PSYCHOTHERAPIES

- Cognitive-behavioral therapy (CBT)
 - Emotional distress and maladaptive behaviors are caused/exacerbated by dysfunctional patterns of thought
 - Effective for perinatal depression and in prevention of postpartum depression
 - Sockol LE. J Affect Dis 2015.
- Interpersonal therapy (IPT)
 - Emphasizes role of interpersonal relationships in psychological distress
 - Areas of focus: role transition, role dispute, grief
 - Effective for treatment and prevention of perinatal depression
 - Sockol LE. J Affect Dis 2018.



ANOTHER CASE...

 Maria and her partner are planning pregnancy. Maria has a history of recurrent episodes of depression and 2 psychiatric hospitalizations following suicide attempts. She has tried several antidepressants, including sertraline, fluoxetine, citalopram, and bupropion, without success. For the past year, she has had a stable mood without depression on duloxetine 60 mg daily. She wants to know whether she can take this medicine during pregnancy.

- 50% of pregnancies are unplanned
- Risk-risk discussion for anyone of childbearing potential



DULOXETINE (SNRI)

- Limited information
- No overall increase in malformations
- Possible small increase in heart defects (RR=1.3)
- Increased risk of postpartum hemorrhage (RR=1.5)
- ? Gestational hypertension
- Neonatal adaptation syndrome (like SSRIs)
- Low transmission in breast milk; considered compatible with breast/chest feeding
 - Lassen, 2016; Huybrechts et al., 2020





BUPROPION

Less studied than SSRIs

No increased rate of malformations (?LVOT)

Possible elevated risk of attention deficit disorder in child

Can exacerbate anxiety disorders

2 case reports of neonatal seizures during lactation

Avoid in people with bulimia, seizure disorders



OTHER ANTIDEPRESSANTS

- Venlafaxine (Effexor; SNRI)
 - No increase in malformations
 - PPHN, NAS as with SSRIs
 - Increased rate of gestational hypertension
 - RID 3-12%; rare reports of adverse effects in infants
- Mirtazapine (Remeron)
 - No increase in malformations
 - Neonatal adaptation syndrome
 - RID<2%; limited data but no adverse effects reported in infants
- Vortioxetine (Trintellix), vilazodone (Viibryd)
 - Very limited data



ECT AND TMS

Electroconvulsive therapy (ECT)

- Rapid, effective, for severe depression/suicide risk
- APA, ACOG, systematic reviews suggest ECT relatively safe during pregnancy, including first trimester
- Reported adverse events include fetal arrhythmia, premature birth, miscarriage, uterine contractions,
 vaginal bleeding, placental abruption
 - Coshal 2019

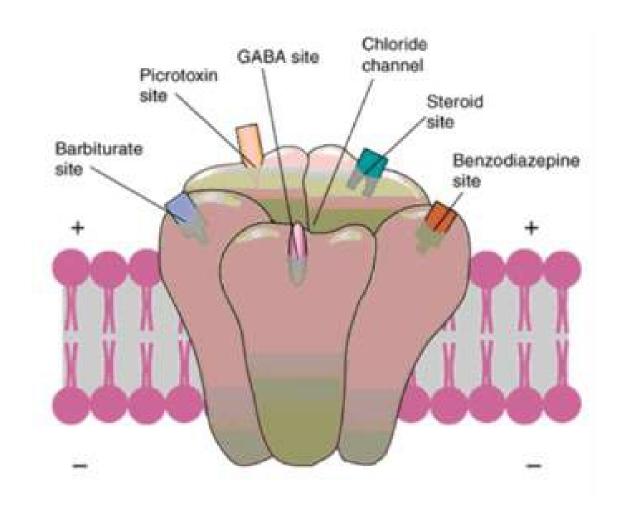
Transcranial Magnetic Stimulation (TMS)

- RCT; 22 women with MDD in 2nd/3rd trimester (11 TMS, 11 sham), 20 sessions, stimulation of right dorsolateral PFC
- Response in 81.8% vs. 45.4%; remission 27.3% vs. 18.3%
- Preterm birth (35-36 wks) in 3 women receiving active TMS
 - Kim 2019



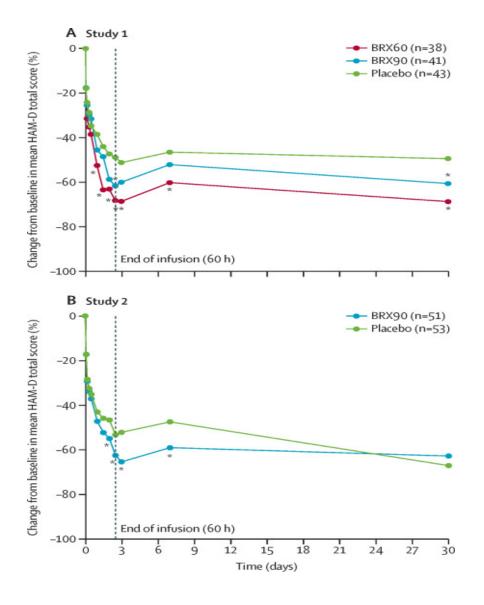
BREXANOLONE

- FDA indication for PPD in March 2019
- Novel mechanism of action
- Formulation of allopregnanolone
- What is allopregnanolone?
 - Metabolite of progesterone
 - Positive allosteric modulator of GABA-A receptors
 - Antidepressant, anxiolytic, anticonvulsant effects
 - Levels increase in pregnancy, decrease postpartum
 - Lower levels during pregnancy associated with PPD





BREXANOLONE



- Brexanolone Phase 3 trials (60-hour infusion)
- Much improved or very much improved:
- Study 1
 - 82% vs. 84% vs. 56% at 60 hours (NNT = 4)
- Study 2
 - 80% vs. 56% at 60 hours (NNT = 4)
 - Difference from placebo at 7 but not 30 days
- Side effects: headache, dizziness, sedation, loss of consciousness
- FDA warning; REMS
 - Meltzer-Brody et al., 2018



ZURANOLONE (ZURZUVAE)

- FDA approved 8/4/23
- Oral synthetic form of allopregnanolone
- Half-life 16-23 hours
- Severe MDD beginning in third trimester or first 4 weeks postpartum
- 50 mg x 14 days, in the evening with fatty meal
- Significant separation from placebo starting at day 3, effects sustained at 45 days
- Side effects: somnolence, dizziness, diarrhea
- No loss of consciousness
- No data re safety during lactation, may cause fetal harm
 - Deligiannidis et al., JAMA Psychiatry 2021 and Am J Psychiatry, July 2023



ZURANOLONE (ZURZUVAE)

- Needs to be taken with food -- 400 to 1000 calories, 25-50% from fat
- Box warning: patients should not drive for 12 hours after taking the medication
- Standard antidepressant warning about suicide risk in patients under 24, did not see particular concerns in clinical trials
- Somnolence is #1 side effect (36%) -- reduce dose to 40 mg/day.
- As with any sedating medication, there should be another adult present in the home to respond to the baby as needed and the parent should not co-sleep/bed-share
- Can be taken with another antidepressant
- Dispensed through national specialty pharmacies: contact company at www.sagerx.com



TAKE HOME POINTS

- Untreated depression is associated with risks for the birthing parent and baby
- The PHQ-9 and EPDS are similarly effective as screening tools
- Evaluate for bipolar disorder, thoughts of suicide/self-harm, substance use
- Consider non-medication treatments
- For moderate to severe depression, medications are usually indicated as well
- Prescribing medication requires a risk-risk discussion



RESOURCES

For clinicians:

Reprotox: www.reprotox.org

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

Infant Risk Center https://www.infantrisk.com

Natural Medicines: https://naturalmedicines.therapeuticresearch.com/

MGH: www.womensmentalhealth.org

UW Perinatal PCL (1-877-PAL4MOM/1-877-725-4666)

Perinatal Mental Health Care Guide https://www.mcmh.uw.edu/care-guide

Perinatal Mental Health ECHO (MAP ECHO): https://perc.psychiatry.uw.edu/map-echo-perinatal-psychiatry-case-conference-series/

Swedish Day Treatment Program for Postpartum Depression: 1-206-320-7288

For patients and families:

Perinatal Support Washington: http://perinatalsupport.org/

MothertoBaby fact sheets https://mothertobaby.org/fact-sheets-parent/

NIMH Perinatal Depression brochure: https://www.nimh.nih.gov/health/publications/perinatal-depression

National Maternal Mental Health Hotline

- 1-833-852-6262 (1-833-TLC-MAMA)
- 24/7 support, English and Spanish (interpreters for other languages available)
- https://mchb.hrsa.gov/national-maternal-mental-health-hotline/faq



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QUESTIONS

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