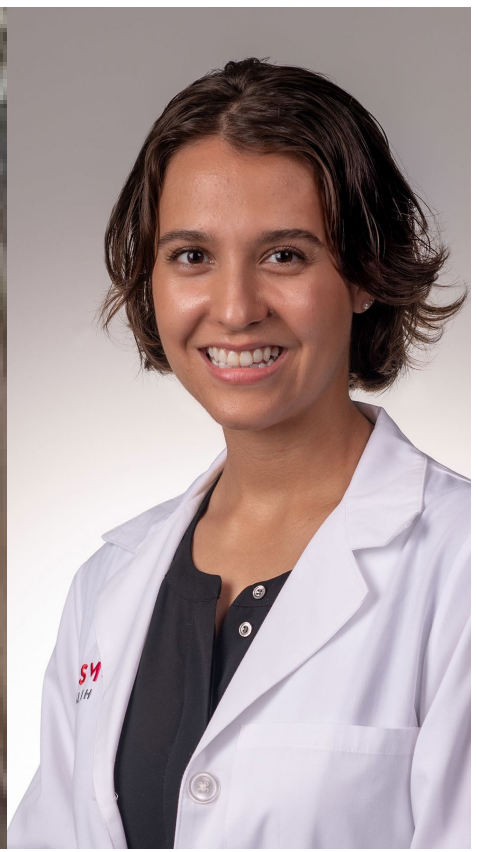
Identification and Treatment of Perinatal Depression and Anxiety Disorders

Neha Hudepohl MD
Stephanie Berg MD
Kelly Helms LISW-CP
Jessica Obeysekare MD

April 5, 2024



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- Clin Assoc Prof of Psychiatry, USC SOM Greenville

Goals

- Identify perinatal depressive disorders and their treatments – Stephanie Berg MD
- Identify new treatments with neuroactive steroids for postpartum depression – Neha Hudepohl MD
- Identify perinatal obsessive-compulsive disorder and its treatment - Neha Hudepohl MD
- Identify therapeutic interventions for management of intrusive thoughts in perinatal anxiety – Kelly Helms LISW-CP
- Identify screening for perinatal mood and anxiety disorders – Stephanie Berg MD and Neha Hudepohl MD on behalf of Jess Obeysekare MD

Identification and Treatment of Perinatal Depression

Stephanie Berg MD
Prisma Health Midlands Behavioral Day Treatment
Prisma Health Perinatal Mood Disorders Clinic

Disclaimer

- I have no financial relationships to disclose
- Discussion of medications is off label as no medications are FDA approved in pregnancy

Objectives

- Introduction
- Depression in pregnancy
- Baby blues
- Postpartum depression
- Postpartum psychosis

Case example

- Ms. M has a long history of depression and anxiety, requiring 2 previous inpatient psychiatric hospitalizations. She was admitted to PHP at 22 weeks pregnant as her gynecologist had discontinued Prozac with pregnancy. She had panic attacks, difficulty sleeping, suicidal thoughts, worries about her ability to parent, and struggling with nausea such that she had difficulty eating.

Depression in Pregnancy

- 13-21% of women during pregnancy
- Up to 30% in low-income populations

Diagnosis of Perinatal Depression

- 2 weeks or more of:
  - Depressed mood
  - Loss of interest or pleasure in usual activities
  - Insomnia or hypersomnia
  - Significant increase/decrease in appetite or weight gain/loss
  - Psychomotor agitation or retardation
  - Fatigue or loss of energy
  - Feelings of worthlessness or excessive/inappropriate guilt
  - Poor concentration or indecisiveness
  - Suicidal ideation
- With peripartum onset specifier
  - Onset of symptoms within 4 weeks of delivery
  - DSM V specifies that symptoms can start in pregnancy

American Psychiatric Association
Diagnostic and Statistical Manual of Mental Disorders (5th edition)

Depression in Pregnancy Risk Factors

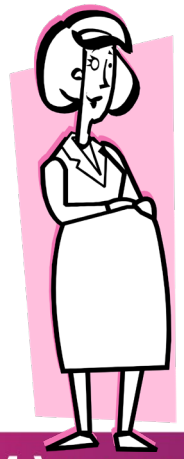
- Previous episode of depression
- Family history of depression
- Poor social support
- Ambivalence about pregnancy
- Young age - adolescents
- Not working

Onset of Perinatal Depression	
Before pregnancy	27%
During pregnancy	33%
Postpartum	40%

Fall et al 2013, Wisner et al 2013

What happens to the untreated?

- High relapse risk
  - Relapse rate of 26% with continuing antidepressants
  - Relapse rate 68% with discontinuing antidepressants



Cohen et al. 2006

Depression in Pregnancy

- Risks of untreated depression
  - Preeclampsia
  - Placenta abnormalities
  - Low birth weight
  - Preterm labor
  - Fetal distress

Depression in Pregnancy

- Risks of untreated depression
  - Poor follow up with OB appointments
  - Poorer nutrition, less likely to take folate
  - More likely to smoke, use alcohol, or other substances
  - Greater likelihood to develop postpartum depression
  - Marital difficulties
  - Parenting difficulties
  - Decreased breastfeeding
  - Suicide

Treatment in Pregnancy

An individual decision that is made on a case by case basis

Balancing

Exposure to maternal illness

Exposure to medication
***Dose**
***Number of agents**

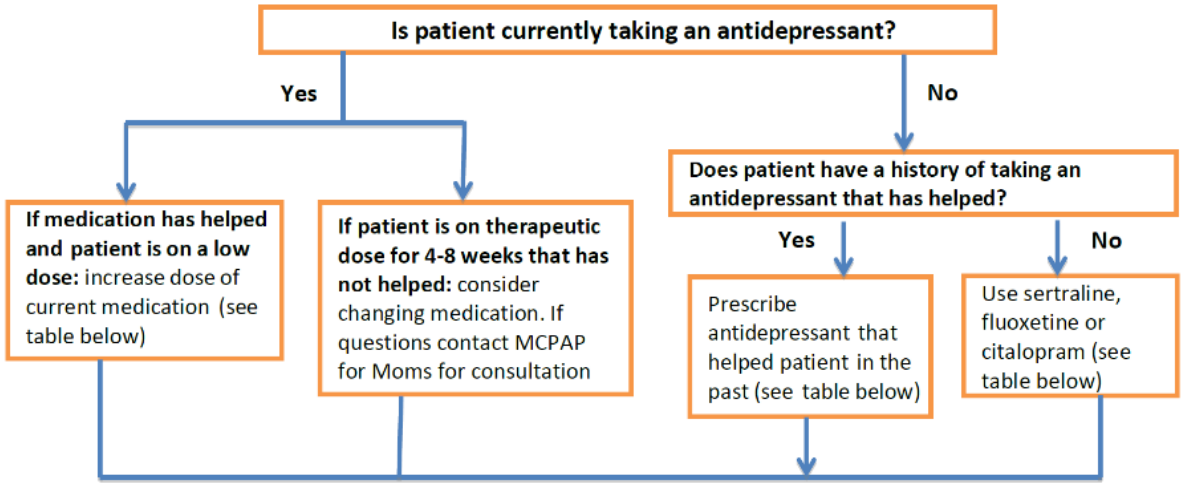
Best treatment for perinatal depression

THE ONE THAT WORKS

Massachusetts Child Psychiatry Access Project
MCPAP For Moms

Antidepressant Treatment Algorithm

(use in conjunction with **Depression Screening Algorithm for Obstetric Providers**)



To minimize side effects, half the recommended dose is used initially for 2 days, then increase in small increments as tolerated.

First line treatment (SSRIs)			
***sertraline (Zoloft) 50-200 mg** *Increase in 50 mg increments*	**fluoxetine (Prozac) 20-60 mg** *Increase in 10 mg increments*	**citalopram (Celexa) 20-40 mg** *Increase in 10 mg increments*	**escitalopram (Lexapro) 10-20mg** *Increase in 10 mg increments*
Second line treatment			
SSRIs	**SNRIs**	**Other**	**If a first or second line medicine is currently helping, continue it**
*paroxetine (Paxil) 20-60mg *Increase in 10 mg increments*	venlafaxine (Effexor) 75-300mg *Increase in 75 mg increments*	bupropion (Wellbutrin) 300-450mg *Increase in 75 mg increments*	**Strongly consider using first or second line medicine that has worked in past**
*fluvoxamine (Luvox) 50-200mg *Increase in 50 mg increments*	duloxetine (Cymbalta) 30-60mg *Increase in 20 mg increments*	mirtazapine (Remeron) 15-45mg *Increase in 15 mg increments*	
*Considered a safer alternative in lactation as it has the lowest degree of translactal passage and fewest reported adverse effects compared to other antidepressants. **In general, if an antidepressant has helped it is best to continue it during lactation.**			

Reevaluate depression treatment in 2-4 weeks via EPDS & clinical assessment

Slide courtesy of Dr. AJones

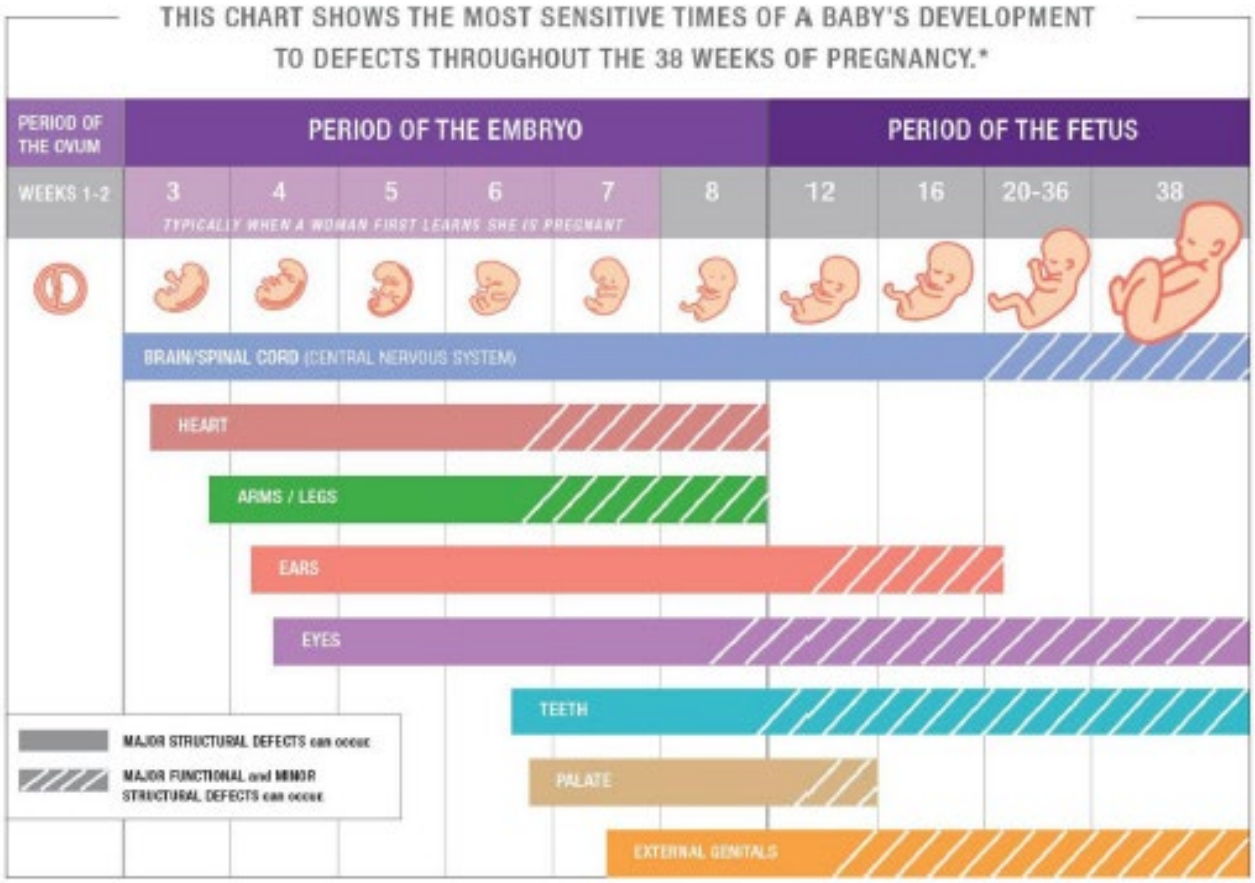
PRISMA HEALTH

What should we be concerned about?

- Teratogenicity
  - Miscarriage
- Preterm Delivery
- Lower gestational weight
- Neonatal adaptation
- Long term behavioral abnormalities

Medication Background

- Women usually find out when already 5-7 weeks gestation
- Therefore, may want to keep same medication if it's working



*Adapted from Moore 1993, and the National Organization of Fetal Alcohol Syndrome (NOFAS) 2009.

Treatment in Pregnancy

- SSRI/SNRI risks
  - Miscarriage - disproven 2013
  - Malformations - disproven 2013 and 2014
  - Earlier delivery?
  - Persistent Pulmonary Hypertension of the Newborn
  - Neonatal Adaptation Syndrome
  - autism (1.1 -> 1.7%?)

Congenital Malformations:

- Meta-Analysis 2013
  - No increased risk of congenital malformations
  - Statistically significant risk of CV but not clinically significant
- Population Based Study 2014
  - No increased risk of CV malformations
- Concern about paroxetine – category D

- SNRI (2015 Meta-analysis)
  - Venlafaxine
    - 5 Studies
      - 3 cohort prospective studies found no significant association
      - 1 case control hypospadias
      - 1 case control anencephaly, ASD, COA, cleft palate, gastroschisis
      - NEW STUDY AUGUST 2020
  - Duloxetine
    - 4 studies
      - 3 no CM (case reports)
      - 1 clubfoot, kidney agenesis, hydronephrosis (1.8%) was within baseline of general population (prospective)

Congenital Malformations:

Small absolute risk

Data mixed for certain medications, particularly paroxetine

Recent Data Reassuring

Ross, JAMA Psychiatry 2013, Chun Fai Chen 2005

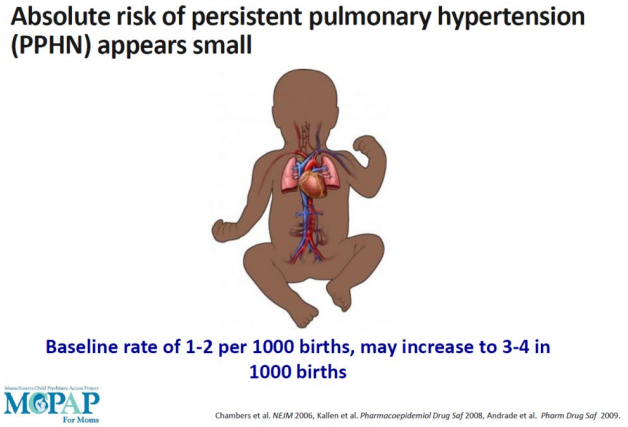
Paroxetine

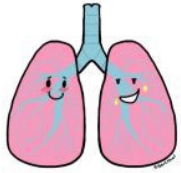
- Has FDA warning against using in first trimester due to increased risk of cardiac defects
- Paroxetine with increased risk of malformations when dose > 25mg daily
- 2008 study did not show paroxetine causes heart defects
- Ban 2014
  - Paroxetine with slight risk of heart anomalies aOR 1.78

Berard 2007, Einarson 2008, Ban 2014

SSRIs and Persistent Pulmonary Hypertension of the Newborn

- 1 % risk in babies born to mothers taking SRIs after 20 weeks gestation
- Risk increases from 2/1000 to 4/1000
- Most recent studies have not shown an association





Chambers 2006 NEJM
Wichman 2009 Mayo Clinic Proceedings
Andrade 2009 Pharmacoepi Drug Safety

Neonatal Adaptation Syndrome

- Present in up to 30% of babies born to mothers taking antidepressants late in pregnancy
- Peak
  - 3 days for term
  - 5 days for premies
- Monitor for 48 hours after delivery
- Self limiting

Moses-Kolko EL et al, 2005 JAMA
Levinson-Castiel R, 2006 Arch Pediatr Adolesc Med

Neonatal Adaptation Syndrome

- Tremors
- Increased muscle tone
- Feeding difficulties
- Irritability
- Respiratory problems
- Increased reflexes
- Increased crying
- Sleep changes
- Seizures

Moses-Kolko EL et al (2005) JAMA 293: 2372-2382

SSRI Long Term Effects

- Children's IQ, language, development, temperament assessed and compared
  - Ages 15 -71 months
- No differences between groups
  - IQ negatively associated with duration of depression
  - Language negative associated with # MDD episodes after delivery

Nulman et al (2002) AJP 159: 1889-1895.

SSRI Long Term Effects

- Looked at children 3 years - 7years
  - Depressed women taking Effexor
  - Depressed women taking SSRIs
  - Depressed women not taking antidepressants
  - Nondepressed women
- Depression children with lower IQs
  - Higher rates of acting out

Nulman et al (2013) AJP 169: 1165-1174.

Risk of Autism with SSRIs

HUFFPOST

HEALTHY LIVING

Major Study Links Autism To Antidepressant Use During Pregnancy

But this study doesn't necessarily mean you should quit your meds.

Dec 15, 2015

SCIENTIFIC AMERICAN™ SUBSCRIBE

REUTERS

HEALTH

Antidepressants in Pregnancy Tied to Autism

The new findings do not prove SSRIs cause autism, but they raise more questions about taking such medications late in pregnancy

December 14, 2015

The Washington Post

To Your Health

Maternal exposure to anti-depressant SSRIs linked to autism in children

A 140

By Ariana Eunjung Cha December 17, 2015

Follow @arianaeunjung

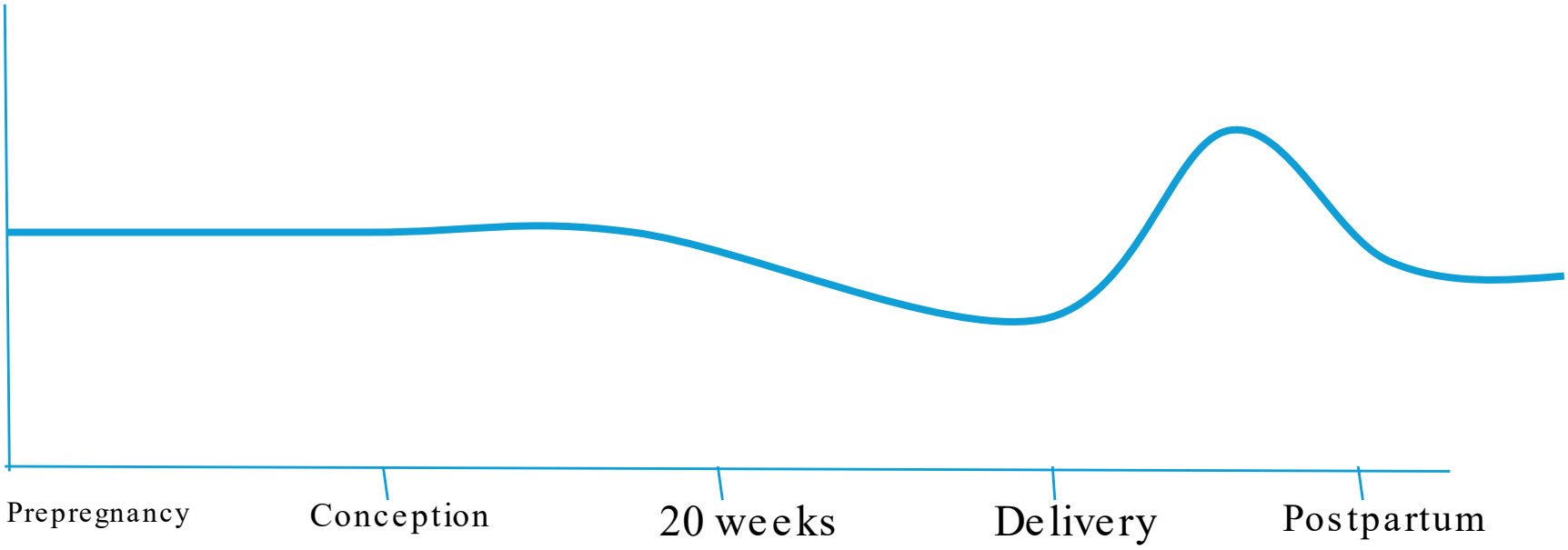
PRISMA HEALTH

August 2016
Systematic Review and Meta-Analysis
5 Case Control, 3 Cohort

The present systematic review and meta-analysis of case-control and cohort studies indicated a higher risk of ASD in the SSRI-exposed group compared to the SSRI-unexposed group. However, when compared to the other AD exposure or to no SSRI exposure in the population of mothers with the past and/or present history of psychiatric disorders, the increased ASD risk in the SSRI-exposed group was no longer significant.

Slide courtesy of Dr. A Jones

SSRI Blood Levels and Pregnancy



Adapted from Sit et al 2008


K. Haring

Postpartum Psychiatric Disorders

Disorder	Incidence	Time Course	Clinical Features
Postpartum Blues	70 – 80 %	Within first week →14 days	• Tearfulness • Anxiety • Insomnia • Mood Instability
Postpartum Depression	10 %	Within first month (technically)	• Depression • Guilt • Anxiety • Fear of harm to baby • Obsessions
Postpartum Psychosis	0.1 – 0.2 %	Within first month	• Disorientation • Confusion • Delusions • Hallucinations • Rapid Mood Cycling

Postpartum Blues Case

- Three days after she brought her baby home from the hospital after an uneventful pregnancy and delivery, Ms. S started worrying that she wouldn't be the best mom she could be and found herself become emotional while watching television. She was able to sleep when her baby slept and was eating normally. This resolved by the time her baby was two weeks old.

Postpartum Blues

- A.K.A. Baby Blues
- Common
  - 70 – 80% of women

Postpartum Blues

- Symptoms
  - Mood swings
    - Euphoria and dysphoria
    - 10 % meet criteria for hypomania
  - Irritability
  - Tearfulness (50 - 80%)
    - Not necessarily due to sadness
  - Confusion (64%)
  - Feeling tired
  - Sensitivity
  - Not depression or apathy

Postpartum Blues

- Treatment
  - Reassurance
  - Support
  - Education
  - Monitoring
- 1 out of 5 women will progress to Postpartum Depr

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Postpartum Depression

- Ms. Twas admitted to PHP 4 weeks after her 2nd son was born. She had a previous episode of depression after her older son was born 16 months ago. She has panic attacks, decreased interests, decreased appetite, teariness, hyperventilating, guilt about not wanting to spend time with her children, and thoughts to run away to escape.

Postpartum Depression

- Later onset than Postpartum Blues
  - Technically by 4 weeks
    - but most likely by 6 months
- Symptoms
  - Depression, crying
  - Inability to sleep when the baby sleeps
  - Intrusive thoughts
    - Thoughts of hurting the baby
    - Thoughts of hurting self
  - Suicidal thoughts
  - Loss of appetite
  - Lack of interest in the baby
  - Anxiety and panic attacks

Postpartum Depression Risk Factors

- Family history
- Psychosocial Factors
  - Social/partner support
- Related to hormonal related depressions
  - PMS
  - Seasonal
  - Perimenopausal
- Multiples
- Difficulty with breastfeeding
  - Watch with weaning
- Irritable babies (not just colicky)
- Younger age
- Ambivalence toward pregnancy
- Preeclampsia
- Domestic violence

Postpartum Depression Risk Factors

- Risk is not reduced with subsequent children
  - maybe increased
- Risk of recurrence:
  - 1 episode – 50%
  - 2 episodes – 75 – 80%

Postpartum Depression

- Consequences
  - Inconsistent use of birth control
  - Parenting difficulties
  - Family and marriage difficulties
  - Developmental, behavioral, and emotional problems in children
  - Personal suffering
  - Suicide

Postpartum Depression

- Consequences
  - Places child at risk down the road
    - Lower self-esteem
    - More acting out
    - Nursing infants gain less weight
    - Duration of mother's episode correlated with degree of impairment in child

Medications in Breastfeeding

- Most medications excreted into breast milk
- Drug levels in breast milk are less than what crosses the placenta
- Low levels in breastmilk of
  - Paroxetine (Paxil)
  - Sertraline (Zoloft)

Are they taking a medication for Depression or Anxiety?

Yes

- ❑ Is it working?
  - ❑ Remission or Response
- ❑ Are they breastfeeding?
  - ❑ Data for lactation
- ❑ Are there concerning/ potentially concerning side effects?

No

- ❑ Ensure accurate diagnosis
- ❑ What has worked before?
- ❑ Is medication indicated for the disorder?
- ❑ Examine for potential interactions, contraindications, or side effects.
- ❑ Are they breastfeeding?
  - ❑ Data for lactation

Nonpharmacological (therapy, caffeine use, sleep)

Risk Assessment

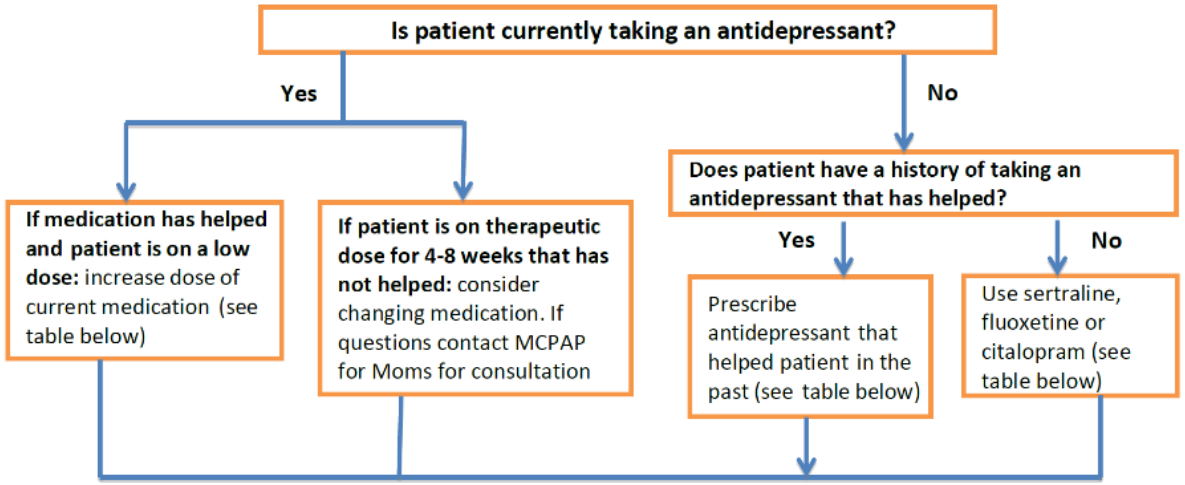
Level of Care

Slide courtesy of Dr. A Jones

Massachusetts Child Psychiatry Access Project
MCPAP For Moms

Antidepressant Treatment Algorithm

(use in conjunction with **Depression Screening Algorithm for Obstetric Providers**)



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Reevaluate depression treatment in 2-4 weeks via EPDS & clinical assessment

Slide courtesy of Dr. AJones

PRISMA HEALTH

Medications in Breastfeeding

- RID

  When assessing the compatibility of a drug with breastfeeding, the relative infant dose (RID) provides an estimate of a baby's exposure to that drug from breast milk. If the RID is less than 10%, the medication is generally considered safe for breastfeeding.[3] Calculations are based on the mother's weight-adjusted dose, using an infant's average daily milk intake of 150 mL/kg/day.[1] Keep in mind that differences exist among patients, so monitor the breastfed infant for any clinically significant changes (see table below).[1]

  - InfantRisk.com
  - LactMed
    - https://www.ncbi.nlm.nih.gov/books/NBK501922/
- Advise mother to monitor for oversedation, especially with cosleeping

Balancing

Exposure to maternal illness

Exposure to medication
***Dose**
***Number of agents**

Postpartum Depression – Treatment

- Check thyroid function
- Increase support
- Psychotherapy
  - Interpersonal Psychotherapy
- Phototherapy
- ECT

Postpartum Depression in Fathers

- More common than you would think
  - 10.4 % overall from 1st trimester to 1 year after delivery
  - 25.6% at 3-6 months
- Biggest correlation is with depression in the partner
  - But also associated with marriage problems

Postpartum Psychiatric Disorders

Disorder	Incidence	Time Course	Clinical Features
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Postpartum Psychosis

- Ms. S was hospitalized 3 weeks after her baby was born. She thought that her neighbors were poisoning her water and planning to steal her 2 older children from their school. She heard the neighbors talking through the walls of her house. She felt that there was no choice but to kill herself and her children and made plans to drive them into a tree.

Postpartum Psychosis

- Rare
  - 1 to 3 cases per 1000 births
- Abrupt onset
  - Usually by postpartum day # 3
- Dangerous
  - 4 % risk of infanticide
  - 5 % risk of suicide
- Related to Bipolar Disorder
- HOSPITALIZE

Postpartum Psychosis

- Symptoms
  - Confusion
  - Bizarre behavior
  - Hallucinations
  - Delusions
  - Mood lability
  - Restlessness
  - Agitation

Postpartum Psychosis - Treatment

- Treatment
  - Hospitalize

TRUE PSYCHIATRIC EMERGENCY

Box 8
Treatment recommendations for acute postpartum psychosis

- Benzodiazepine (lorazepam 0.5–1.5 mg 3 times a day)
- Antipsychotic (high potency preferred, haloperidol 2–6 mg or olanzapine 10–15 mg)
- Lithium (to achieve serum level of 0.8–1.2 mmol/L)
- Tapered benzodiazepine and antipsychotic once symptom remission achieved
- Continued lithium monotherapy for 9 months (can lower to achieve serum level of 0.6–0.8 after symptom remission if severe side effects)
- For future pregnancies: prophylactic lithium monotherapy beginning during pregnancy or immediately post partum

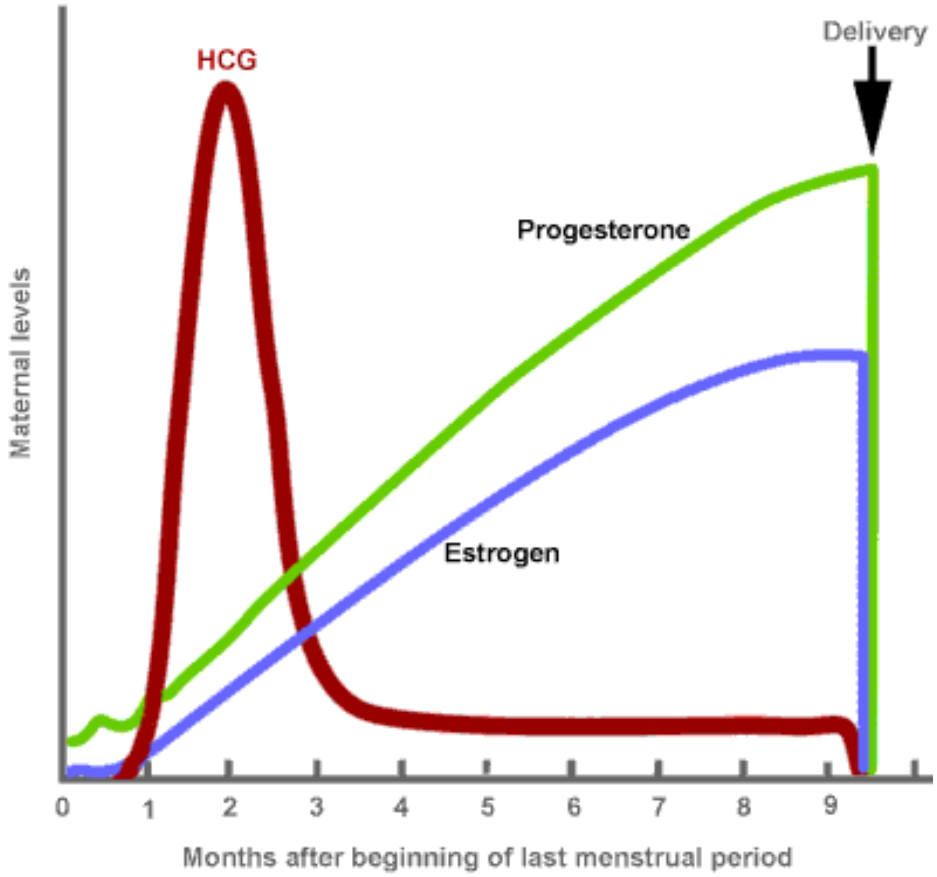
- Consider prophylactic mood stabilizer treatment starting at birth with next pregnancy
  - Women with Bipolar Disorder should probably continue treatment through pregnancy

Osborne LM (2014)
Bergink V et al (2016)

PRISMA HEALTH SM

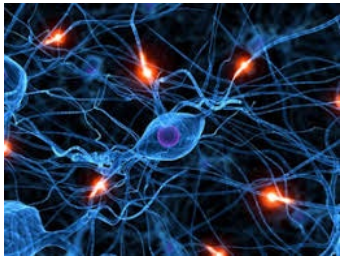
Neuroactive Steroids and PPD

Neha Hudepohl, MD


Delivery
HCG
Progesterone
Estrogen
Maternal levels
0
1
2
3
4
5
6
7
8
9
Months after beginning of last menstrual period

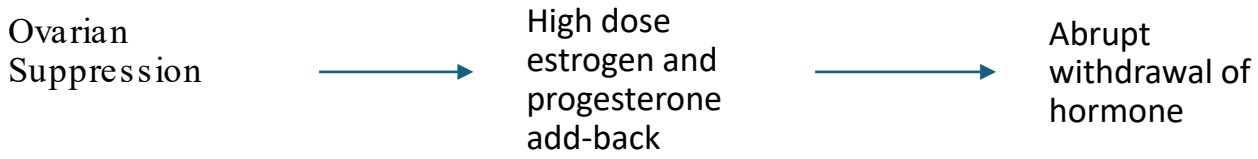
Neurobiology of Hormone-Sensitive PPD

- Impact of normally fluctuating hormone levels in perinatal period may create abnormal neural response in women who are susceptible to PPD
- Evidence of reduced connectivity between amygdala and prefrontal regions **dysregulation of the limbic system**
- Neural abnormalities are unique to the perinatal period, and are unmasked by changes in reproductive hormone concentrations



Schiller CE et al *The role of reproductive hormones in postpartum depression* CNS Spectrums 2015;20:48-59.

Impact of Hormonal Change on PPD



- In women with a history of PPD, **increased** depressive symptoms during hormone add-back and withdrawal
- In women with no history of PPD, no change in mood

Bloch M, Schmidt P, Danaceau J, et al.: Effects of gonadal steroids in women with a history of postpartum depression. Am J Psychiatry 2000, 157:924–930.

Neurosteroid Regulation of Affect

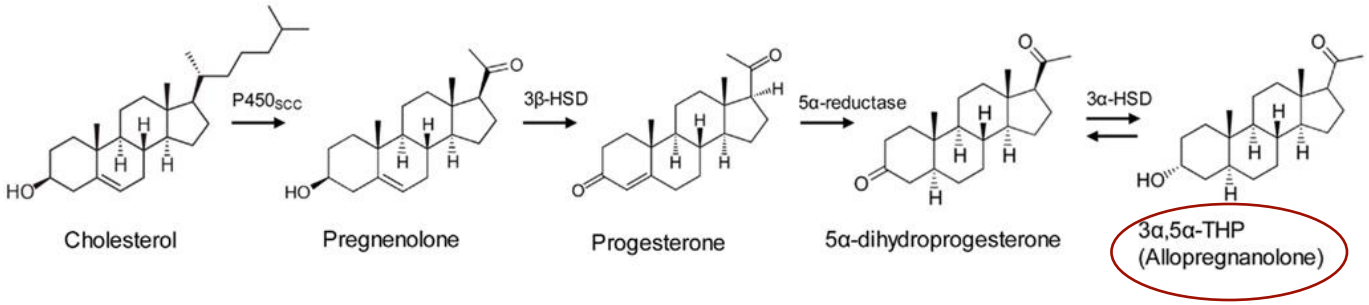
Neuroactive steroids = metabolites of steroids that are synthesized in brain/nervous system and modulate GABA and glutamate

- DHEA (dehydroepiandrosterone)
  - Abnormal secretion implicated in MDD
  - DHEA is effective antidepressant in men and women
- ALLO (allopregnanolone)
  - Positive allosteric modulator of GABAa- both synaptic and extrasynaptic receptors

Why are we talking about Allopregnanolone (ALLO)?

- Peripartum fluctuations in reproductive hormones as having a role in postpartum depression
- Treatment with antidepressants is suboptimal
- Animal models show that ALLO is a potent PAM of GABA and is implicated in lack of stress response inhibition in PPD

What is Allopregnanolone?



What is Allopregnanolone?

- Neuroactive steroid
- Positive endogenous allosteric modulator of $GABA_A$ receptor function
  - Synaptic and extra-synaptic receptor activity
  - GABA is the major inhibitory neurotransmitter
  - Activation of $GABA_A$ receptors anesthetic, sedative-hypnotic, anticonvulsant properties
- This GABA-ergic neuroactive steroid decreases the activity of the HPA system via corticotrophin-releasing hormone neurons in the paraventricular nucleus of the hypothalamus

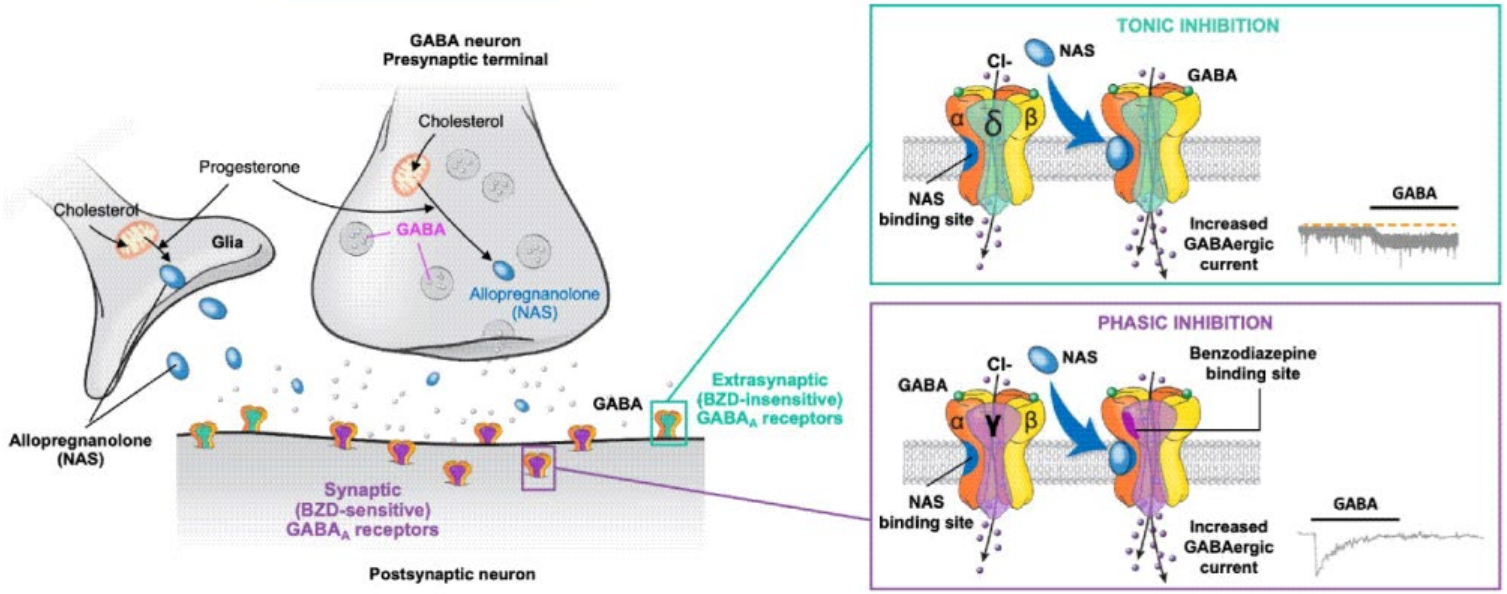
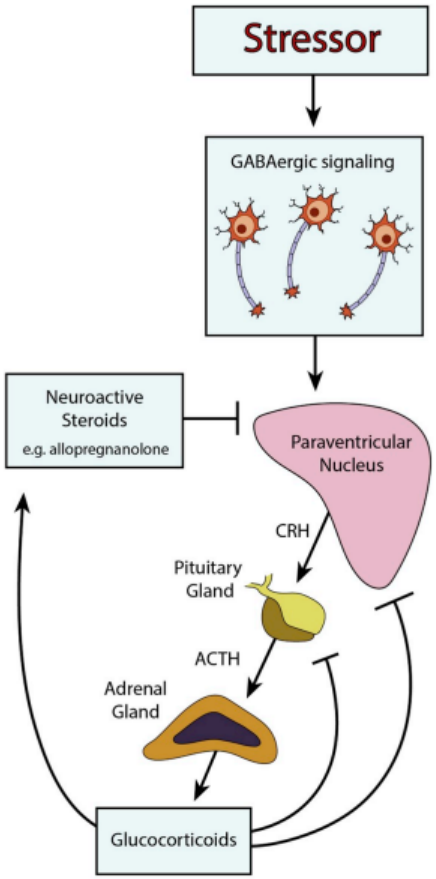


FIGURE 1 Mechanism of action of the positive allosteric modulator allopregnanolone on synaptic and extrasynaptic $GABA_A$ receptors. Allopregnanolone binds both synaptic and extrasynaptic $GABA_A$ receptors, acting as a positive allosteric modulator to increase the frequency and duration of channel opening, thus increasing hyperpolarizing GABAergic current.[46,93] BZD, benzodiazepine; GABA, γ-aminobutyric acid; $GABA_A$, γ-aminobutyric acid type A; NAS, neuroactive steroid



Adapted from: Gunn et al. Front Neurosci. 2011 Dec 5;5:131

Fig. 3. GABAergic signaling and neuroactive steroids with $GABA_AR$ positive allosteric modulator activity can act on the paraventricular nucleus of the hypothalamus to regulate the HPA axis.

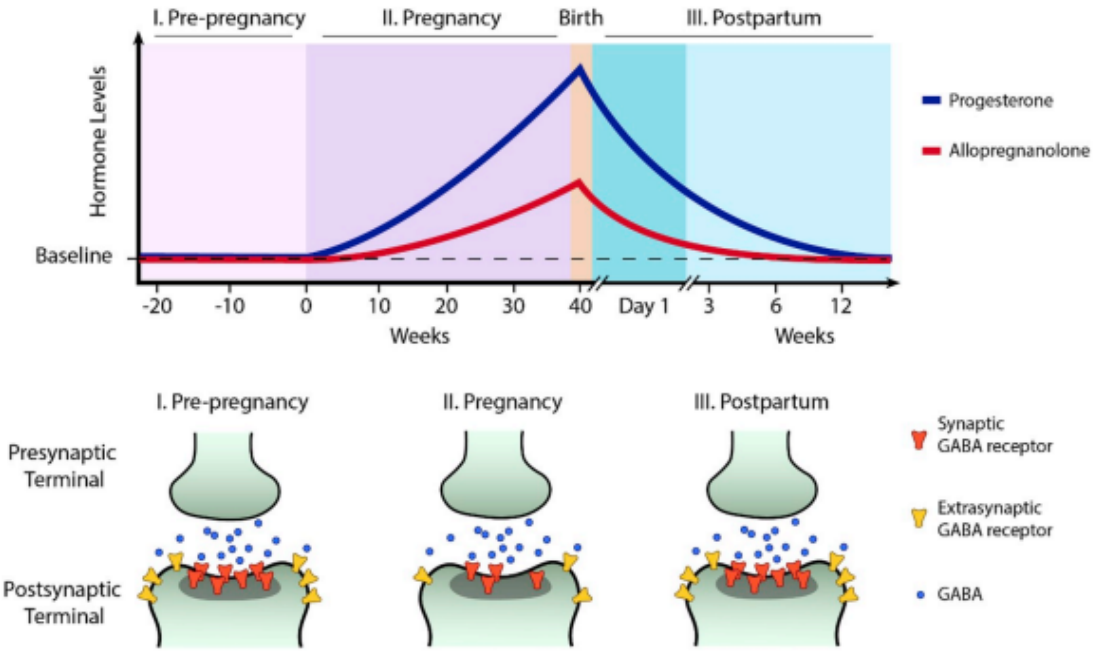
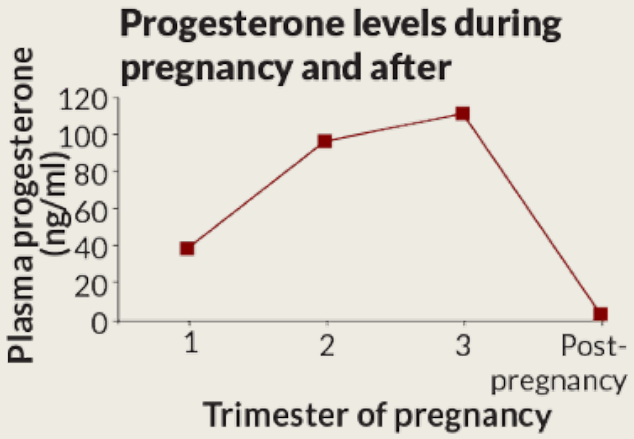


Fig. 2. GABAergic signaling in the perinatal period may be altered by fluctuations in neuroactive steroid levels and changes in the expression of $GABA_AR$ subunits. Altered expression of $GABA_AR$ subunits could alter both the number and localization of $GABA_ARs$.

- Concentrations rise in concert with progesterone throughout pregnancy, reaching highest concentrations in the third trimester
- After childbirth, concentrations drop abruptly
- $GABA_A$ receptors activity or expression is thought to be altered to prevent shifting the balance too favor in favor of inhibition
- These changes need to be quickly reversed at parturition to compensate for the rapid decline in ALLO levels
- Failure of the $GABA_A$ receptors to adapt to this drop may play a role in triggering postpartum depression in some women
- Replicated in animal studies

Allopregnanolone



*Source: K.D. Pennell, M.A. Woodlin and P.B. Pennell/*Steroids *2015*

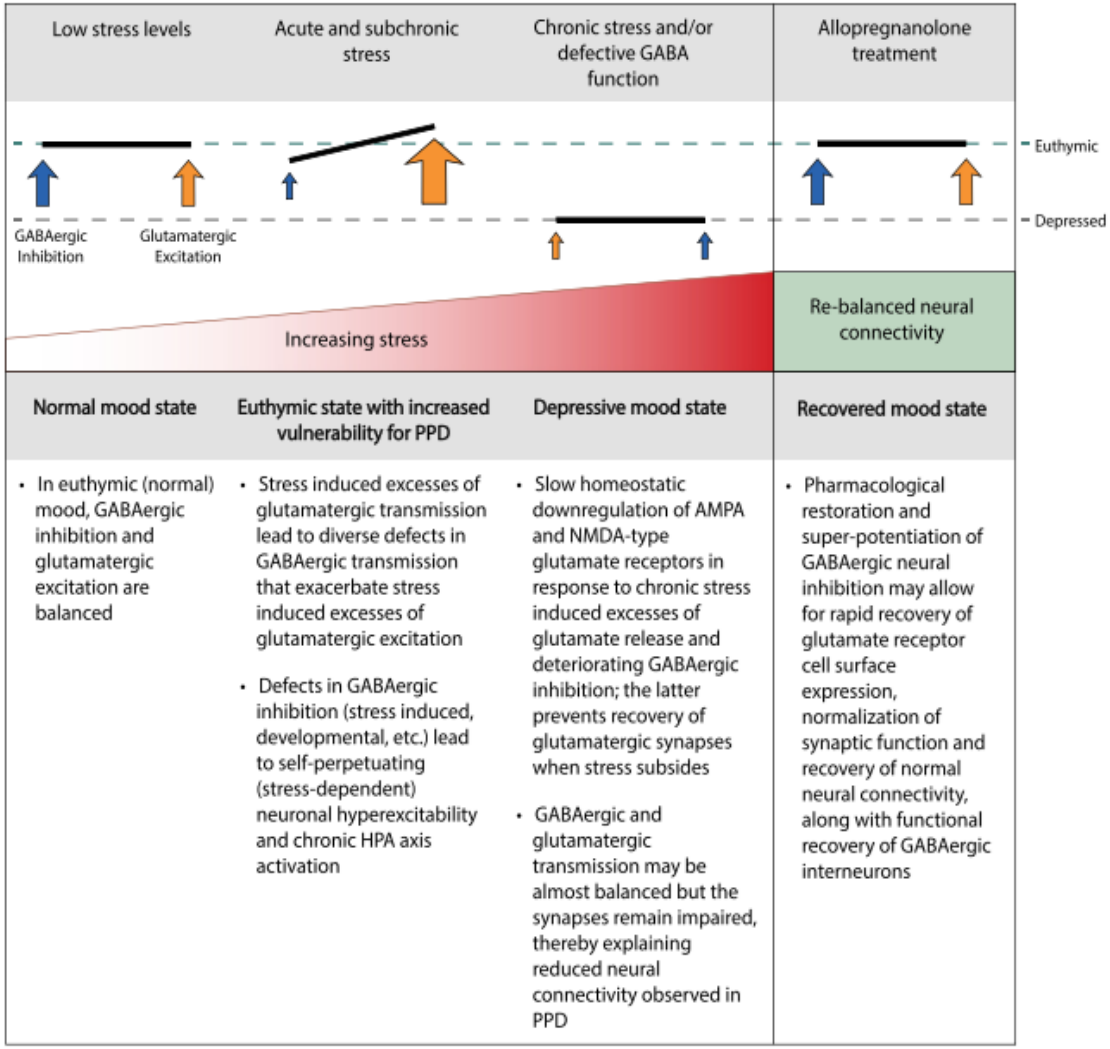
Allopregnanolone

- Preclinical studies in mice:
  - During pregnancy in mice, expression of $GABA_A$ receptor δ subunit is downregulated as ALLO concentrations increase
  - $GABA_A$ receptor δ subunit levels return to baseline as ALLO concentrations drop steeply
  - $GABA_A$ receptor δ subunit deficient mice do not adapt to the change in ALLO
    - Showed depression-like and anxiety-like behaviors
    - Normal behaviors prior to pregnancy but insensitivity to ALLO during pregnancy

Theory

Women with onset of severe depression in 3rd trimester or triggered by delivery:

- Associated with rapid fluctuations in gonadal steroids
- More likely to have a hormone-responsive form of PPD
- Sensitive to the effects of decreased ALLO and GABA function on HPA axis and other stress response systems
- Could respond to doses of neuroactive steroids such as allopregnanolone to re-equilibrate these changes



Adapted from Luscher and Mohler. F1000Res. 2019. May29:8.

Fig. 5. Acute stress can result in imbalances between GABAergic and glutamatergic signaling, and further adaptation to chronic stress may result in a new balance of GABAergic and glutamatergic signaling at lower levels, contributing to depression. Restoring GABAergic signaling through brexanolone injection offers the potential to restore the original balance and level of signaling. Abbreviations: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA), N-methyl-D-aspartate (NMDA).

Brexanolone (Zulresso)

- Indicated for moderate-severe PPD up to 6 months PP
- Requires inpatient admission for 60-hour infusion
- High associated cost
- Accessibility due to requirement of inpatient stay

- High efficacy
- Difficult to obtain depending on institution

Brexanolone: Phase 3

- 2 multicentre, double blind, randomized, placebo-controlled phase 3 trials
- Ambulatory female participants age 18-45
- Discontinued lactation or agreed to cease until 4 days after end of infusion
- MDD with onset in third trimester or up to 4 weeks postpartum
- 6 months or less PP at screening
- HAM-D score
  - >/= 26 for first study
  - 20-25 for second study
- Stable dose of AD medication for 14 days prior to screening

Brexanolone: Phase 3

Study 1

BRX90 = brexanolone injection 90µg/kg/h

BRX60 = brexanolone injection 60µg/kg/h

Placebo

Study 2

BRX90 = brexanolone injection 90µg/kg/h

Placebo

Brexanolone Phase 3

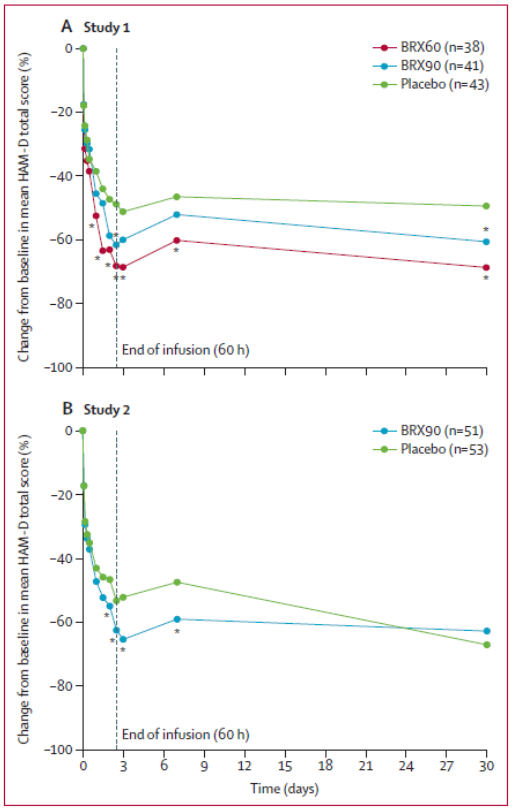


Figure 2: **Percentage change from baseline in mean HAM-D total score in study 1 (A) and 2 (B)**
p values were calculated by two-sided *t* test. BRX60=brexanolone injection 60 µg/kg per h. BRX90=brexanolone injection 90 µg/kg per h. *p<0·05 *vs* placebo.

Brexanolone Phase 3

	Study 1			Study 2	
	Placebo (n=43)	BRX60 (n=38)	BRX90 (n=41)	Placebo (n=53)	BRX90 (n=51)
Overall					
Any adverse event	22 (51%)	19 (50%)	22 (54%)	24 (45%)	25 (49%)
Severe adverse event	0	1 (3%)	0	1 (2%)	2 (4%)
Serious adverse event	0	1 (3%)	0	0	1 (2%)
Adverse event leading to discontinuation of study treatment	1 (2%)	1 (3%)	0	0	2 (4%)
Deaths	0	0	0	0	0
Adverse events in three or more patients					
Headache	7 (16%)	7 (18%)	6 (15%)	6 (11%)	9 (18%)
Dizziness	1 (2%)	6 (16%)	6 (15%)	4 (8%)	5 (10%)
Somnolence	3 (7%)	7 (18%)	2 (5%)	2 (4%)	4 (8%)
Infusion site pain	1 (2%)	1 (3%)	4 (10%)	2 (4%)	5 (10%)
Nausea	3 (7%)	1 (3%)	0	2 (4%)	5 (10%)
Dry mouth	0	4 (11%)	0	1 (2%)	2 (4%)
Fatigue	0	1 (3%)	1 (2%)	2 (4%)	3 (6%)

Data are n (%). Treatment-emergent adverse events were defined as an adverse event with onset after the start of study drug, or any worsening of a pre-existing medical condition or adverse event with onset after the start of study drug. Treatment-emergent adverse events were coded according to the Medical Dictionary for Regulatory Activities version 19.1 or later. BRX60=brexanolone injection 60 μg/kg per h. BRX90=brexanolone injection 90 μg/kg per h.

Table 3: **Treatment-emergent adverse events**

FDA NEWS RELEASE

FDA approves first treatment for post-partum depression

SAGE THERAPEUTICS

Zulresso (brexanolone) injection for IV use

- Received approval 3/19/2019
- First drug approved for treatment of postpartum depression
- Priority review
- Breakthrough therapy designation

Zuranolone

- Positive allosteric modulator of synaptic and extrasynaptic GABAa receptor
- Neuroactive steroid
- Oral, once daily x 14 day

- Phase 3 studies completed at both 30mg daily and 50mg daily for PPD

Zuranolone Phase 3

- Double=blind, randomized, placebo-controlled, parallel-group study
- Age 18–45-year-old women
- Less than or equal to 12 months PP
- Major depressive episode with onset in third trimester or up to 4 weeks postpartum
- 6 months or less PP at screening
- HAM-D score
  - >/= 26 for first study
- Stable dose of AD medication for 30 days or more prior to first study treatment dose
- All patients ceased lactation or did not provide breastmilk through 7 days post the last dose
- Exclusion:
  - History of bipolar disorder
  - Psychotic disorders
  - Attempted suicide
  - Risk of suicide in current episode of PPD

Zuranolone: Phase 3
Self administration of 50mg/day or placebo once daily in the evening with fat-containing food for 14 days

Primary Outcome Measure:

Change from baseline in HAM-D total score at day 15

Secondary analyses:

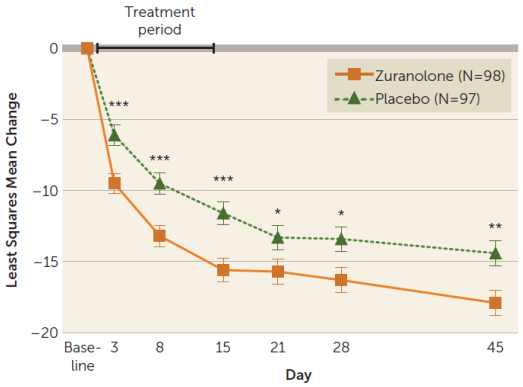
Changes in HAM-D from baseline at days 3, 28, 45

Change from baseline in CGI severity score at day 15

HAM-D response (reduction >50%) and remission (total score <8) on days 15, 45

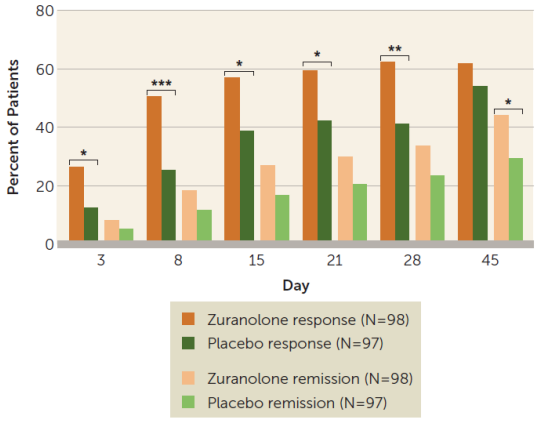
Zuranolone
2023

FIGURE 2. Change from baseline in HAM-D score in a placebo-controlled trial of zuranolone 50 mg/day for postpartum depression (full analysis set)[a]



[a] The primary endpoint was change from baseline in score on the 17-item Hamilton Depression Rating Scale (HAM-D) at day 15, and the key secondary endpoints included change from baseline in HAM-D score at days 3, 28, and 45. Multiplicity was accounted for when analyzing primary and key secondary endpoints. All other secondary endpoints were not adjusted for multiplicity and are to be interpreted with nominal p values. Error bars indicate standard error. *p<0.05. **p<0.01. ***p<0.001.

FIGURE 3. HAM-D response and remission (full analysis set) in a trial of zuranolone 50 mg/day for postpartum depression[a]



[a] Response was defined as a reduction ≥50% from baseline in score on the 17-item Hamilton Depression Rating Scale (HAM-D), and remission was defined as a HAM-D score ≤7. Secondary endpoints were not adjusted for multiplicity and are to be interpreted with nominal p values. *p<0.05. **p<0.01. ***p<0.001.

FDA NEWS RELEASE

FDA Approves First Oral Treatment for Postpartum Depression

For Immediate Release: August 04, 2023

Who is Zurzuvae good for?

- Primary diagnosis of PPD
  - Onset of symptoms in pregnancy or early in the PP period
  - Hormonally sensitive depression
- Not indicated for bipolar depression, postpartum anxiety, OCD, or postpartum psychosis

PRISMA HEALTH SM

Perinatal OCD

Neha Hudepohl, MD

Clinical Associate Professor, University of South Carolina School of Medicine Greenville

Clinical Associate Professor, Clemson University School of Health Research

April 5. 2024

Perinatal OCD

- Estimates at prevalence vary widely by study
  - 0.3-29% in pregnant women
  - 1.7-9% in postpartum women
- High prevalence of O-C symptoms in PP women in general, non-clinical samples have seen rates as high as 80%
- Retrospective studies indicate that many women with a diagnosis of OCD trace onset of symptoms to pregnancy or childbirth (18-40%)
- 60-80% comorbidity with MDD

- Can affect care of the infant and mother-infant bonding

Obsessive-Compulsive Disorder

- Underappreciated
- 11% prevalence 2 weeks postpartum
  - peak onset 2 weeks
- 18%-40 % of women with OCD have perinatal onset
- OCD worsens in pregnancy and the postpartum

- 60-80% comorbidity with MDD

Brandes 2004, Miller 2013

Perinatal OCD

- Intrusive anxious thoughts
  - Contamination
  - Harm coming to infant (accidental or intentional)
  - Urges for symmetry
- Ritualistic compulsions
  - Compulsive cleaning
  - Excessive checking on child to ensure well-being
  - Avoidance of child/obsessional cues
  - Mental rituals, neutralizing

- Preserved reality testing
- Patients do not act on aggressive thoughts

Sit D et al (2006) *Journal of Women's Health* 15(4):352-368.

Harming Infant Thoughts

- PP Depression associated with:
  - Repeated, intrusive thoughts of harming infant (usually mild, ego-dystonic)
    - 1999 study: 41% of mothers with PPD endorsed
  - Overwhelmed fear of being alone with infant (25% of depressed mothers)
  - Feel unable to care for infant (11% of depressed mothers)

Donahue Jennings K "Thoughts of harming infants in depressed and nondepressed mothers." (1999) *Journal of Affective Disorders* 54:21-28.

Intrusive Thoughts

- 100% of all new parents have intrusive thoughts of accidental harm
- 49.5 % have intrusive thoughts of intentional harm
  - 86.7 % physical
  - emotional (screaming)

Obsessive-Compulsive Disorder

Intrusive thoughts, images, impulses

- contamination fears
- stabbing baby
- throwing the baby
- sexually abusing baby
- drowning the baby accidentally
- SIDS
- dropping the baby
- baby choking
- poor parenting

Intrusive Thoughts

- May be seen with depression
- E**go-dystonic** thoughts
- Often violent thoughts of harm to child

- Compulsions
  - Checking
  - Cleaning

Risk of harm to baby

OCD/anxiety	Postpartum Psychosis
• Good insight • Thoughts are intrusive and scary • No psychotic symptoms • Thoughts cause anxiety	• Poor insight • Psychotic symptoms • Delusional beliefs or distorted reality present
Low risk	High risk

Massachusetts Child Psychiatry Access Project
MCPAP For Moms

Intrusive Thoughts

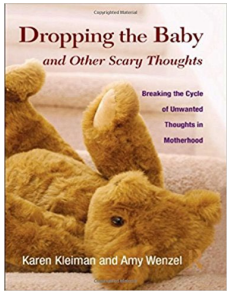


Table 1 Thoughts of intrusive harm to the child: distinguishing between obsessions and delusions

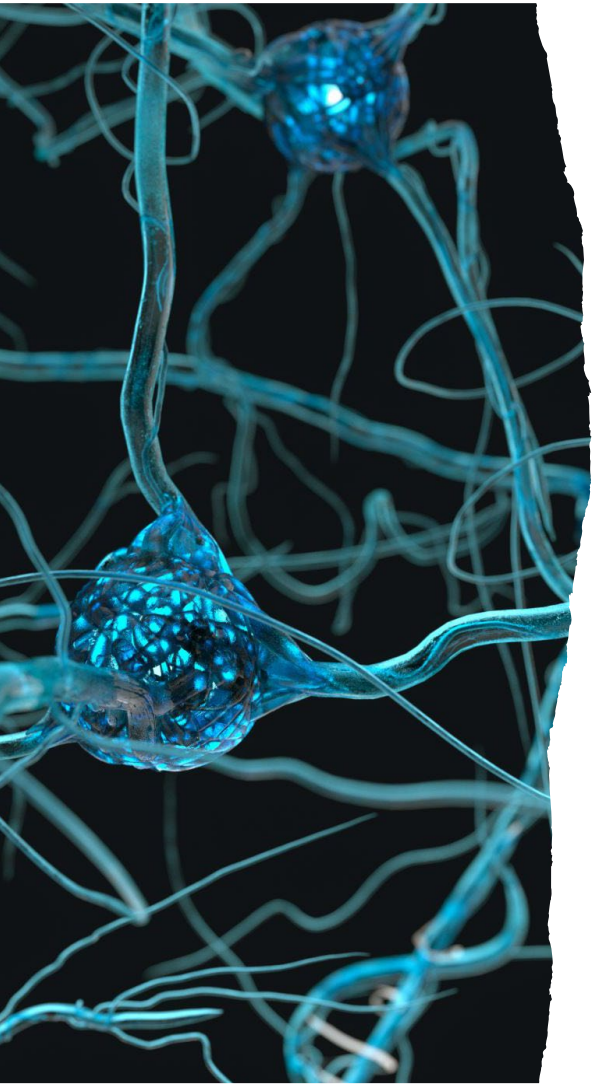
Obsessions	Delusions
Intrusive thoughts are unwanted and extremely distressing (ego-dystonic)	Intrusive thoughts may be unbidden but do not cause significant distress (ego-syntonic)
Can be sexual, religious, or violent	Can also be sexual, religious, or violent; content often bizarre or unusual
Patient has no desire to act on thoughts	Patient may want to or feel compelled to act on thoughts
Patient may engage in avoidance or in checking/reassuring compulsions to ease distress	No compulsions
Preserved insight	Poor insight, distortion of reality
Example: Mother has intrusive thoughts about throwing baby out the window. She locks all windows, closes blinds, repeatedly checks locks, and refuses to go to the side of the room where windows are.	Example: Mother believes child has sinned and that God has commanded mother to drop child out the window to punish this sin.

Screening Question

"It's not uncommon for new mothers to experience intrusive, unwanted thoughts that they might harm their baby. Have any such thoughts occurred to you?"

Pregnancy Risks of Untreated Anxiety

- Studies have shown preterm birth associated with anxiety
- Shortened gestational age
  - Anxiety in 3rd trimester
  - Severe anxiety in all 3 trimesters
- Lower birth weight + shorter length
  - Trait anxiety at 2nd and 3rd trimester
  - Severe anxiety for at least 2 trimesters



Risks of Perinatal OCD

- Gestational hypertension
- Preeclampsia
- Poor fetal growth
- Preterm birth
- Elevated inflammatory markers in neonate

Risks of Perinatal OCD

- Poorer quality of life
- Greater distress
- Lower maternal responsiveness

Untreated Anxiety in Post-Partum

- Bonding
- Maternal – Infant Relationship
- Insomnia
- Relationship with partner
- Self Esteem
- Guilt

Etiology

GENETIC FACTORS

IMMUNE DYSFUNCTION

HORMONES

SLEEP DEPRIVATION

Perinatal Treatment of OCD

- Reassurance
- Cognitive behavioral therapy
- Family education
- SSRIs
  - Require higher doses

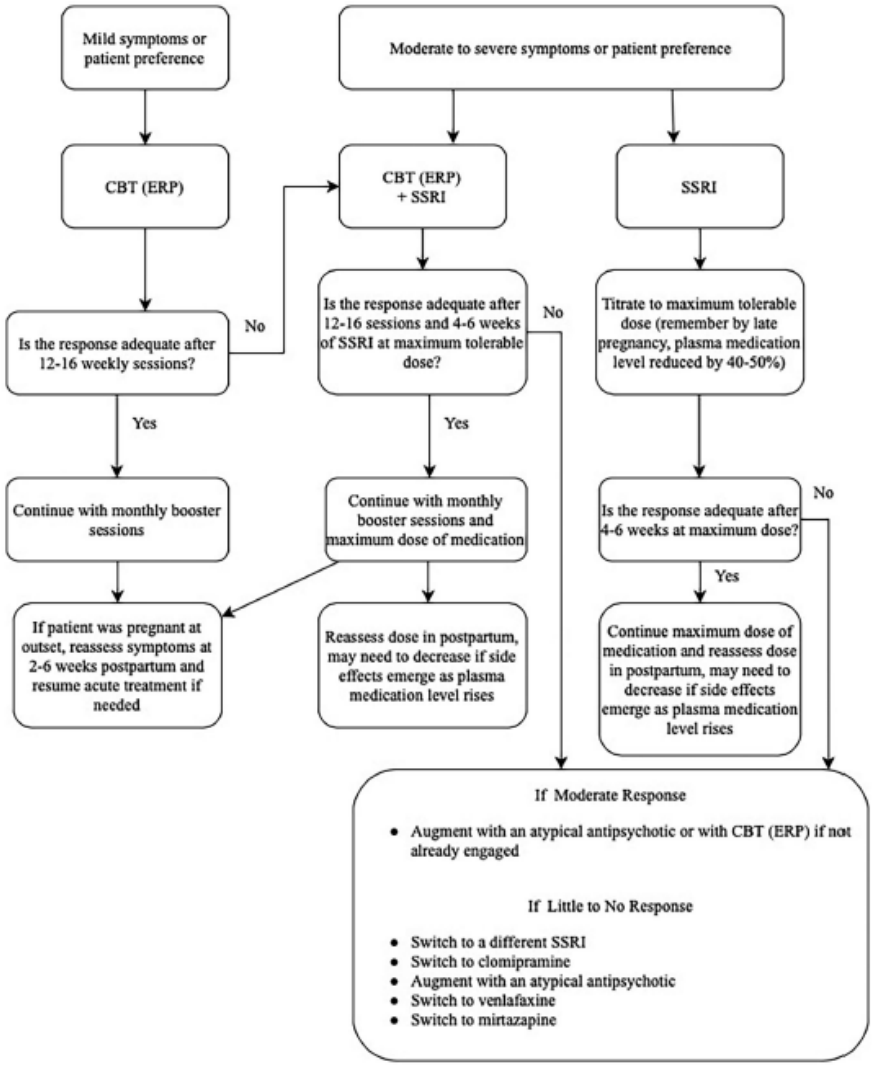


Fig. 1 Treatment algorithm for perinatal OCD. From Hutner et al. eds., *The APA Textbook of Women's Reproductive Mental Health (Washington, DC: APA Publishing, 2021)*

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•Kelly et al. Neonatal Benzodiazepines Exposure During Breastfeeding. Journal of Pediatrics, 2002

•Ross et al. Selected Pregnancy and Delivery Outcomes After Exposure to Antidepressant Medication. JAMA Psychiatry, 2013

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Therapeutic Interventions for Intrusive Thoughts in Perinatal Anxiety

Kelly Helms LISW-CP

Disclaimer

- I have no financial relationships to disclose

Screening

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Disclosure

No financial interest in or affiliation with any commercial supporter to disclose.

Learning Objectives

- At the conclusion of this activity, participants will be able to:
  - Describe the evidence base for screening for PMADs
  - Describe the barriers to implementation of universal screening for perinatal depression

What does screening add?

- Women may not realize they are depressed
  - 78 women who were diagnosed with PPD for a research study were interviewed after the diagnosis
    - 97% reported feeling "worse than usual"
    - 32% believed they had depression
      - Other explanations: tiredness, problems with partner/baby/kiddos

Whitton, A., Warner, R., & Appleby, L. (1996). The pathway to care in post-natal depression: women's attitudes to post-natal depression and its treatment. *The British journal of general practice : the journal of the Royal College of General Practitioners*, *46*(408), 427–428.

What does screening add?

- Women may not disclose sx of depression
  - Of those 78 women:
    - 12% disclosed to a healthcare provider
    - 81% did not want medications
      - 51% thought sx would improve without tx
      - 19% were afraid of addiction

Whitton, A., Warner, R., & Appleby, L. (1996). The pathway to care in post-natal depression: women's attitudes to post-natal depression and its treatment. *The British journal of general practice : the journal of the Royal College of General Practitioners*, *46*(408), 427–428.

Internal barriers to disclosing PPD

- Stigma of mental illness
- Feeling of failure as a mother
- Fearing being labeled a "bad" or "unfit" mother
- Fear of baby being removed from their custody
- Fear of psychiatric admission
- Normalization
- Too busy to seek care
- Wanting to wait it out (16% of people with depressive sx)

Sword, W., Busser, D., Ganann, R., McMillan, T., & Swinton, M. (2008). Women's care-seeking experiences after referral for postpartum depression. *Qualitative health research*, *18*(9), 1161–1173.

Outcome of screening

- 462 2-month postpartum women in Hong Kong randomized to screening with EPDS vs TAU clinical nursing assessment
  - EPDS group: 29% above cutoff
  - TAU group: 6% probable postnatal depression
- All received EPDS at 6 months:
  - 13% in intervention group had EPDS >10
  - 22% in control
- No difference between groups at 18 months

Leung SS, Leung C, Lam TH, et al. Outcome of a postnatal depression screening programme using the Edinburgh Postnatal Depression Scale: a randomized controlled trial. *J Public Health (Oxf)*. 2011;33(2):292-301.

Validated tools in pregnancy/postpartum

Table 1. Depression Screening Tools

Screening Tool	Number of Items	Time to Complete (Minutes)	Sensitivity and Specificity	Spanish Available
Edinburgh Postnatal Depression Scale	10	Less than 5	Sensitivity 59–100% Specificity 49–100%	Yes
Postpartum Depression Screening Scale	35	5–10	Sensitivity 91–94% Specificity 72–98%	Yes
Patient Health Questionnaire 9	9	Less than 5	Sensitivity 75% Specificity 90%	Yes
Beck Depression Inventory	21	5–10	Sensitivity 47.6–82% Specificity 85.9–89%	Yes
Beck Depression Inventory-II	21	5–10	Sensitivity 56–57% Specificity 97–100%	Yes
Center for Epidemiologic Studies Depression Scale	20	5–10	Sensitivity 60% Specificity 92%	Yes
Zung Self-Rating Depression Scale	20	5–10	Sensitivity 45–89% Specificity 77–88%	No

ACOG Committee Opinion Number 757: Screening for Perinatal Depression

Depression vs Pregnancy

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

Edinburgh Postnatal Depression Scale

In the past 7 days:

1. I have been able to laugh and see the funny side of things
   - ☐ As much as I always could
   - ☐ Not quite so much now
   - ☐ Definitely not so much now
   - ☐ Not at all

2. I have looked forward with enjoyment to things
   - ☐ As much as I ever did
   - ☐ Rather less than I used to
   - ☐ Definitely less than I used to
   - ☐ Hardly at all

*3. I have blamed myself unnecessarily when things went wrong
   - ☐ Yes, most of the time
   - ☐ Yes, some of the time
   - ☐ Not very often
   - ☐ No, never

4. I have been anxious or worried for no good reason
   - ☐ No, not at all
   - ☐ Hardly ever
   - ☐ Yes, sometimes
   - ☐ Yes, very often

*5 I have felt scared or panicky for no very good reason
   - ☐ Yes, quite a lot
   - ☐ Yes, sometimes
   - ☐ No, not much
   - ☐ No, not at all

*6. Things have been getting on top of me
   - ☐ Yes, most of the time I haven't been able to cope at all
   - ☐ Yes, sometimes I haven't been coping as well as usual
   - ☐ No, most of the time I have coped quite well
   - ☐ No, I have been coping as well as ever

*7 I have been so unhappy that I have had difficulty sleeping
   - ☐ Yes, most of the time
   - ☐ Yes, sometimes
   - ☐ Not very often
   - ☐ No, not at all

*8 I have felt sad or miserable
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Not very often
   - ☐ No, not at all

*9 I have been so unhappy that I have been crying
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Only occasionally
   - ☐ No, never

*10 The thought of harming myself has occurred to me
   - ☐ Yes, quite often
   - ☐ Sometimes
   - ☐ Hardly ever
   - ☐ Never

EPDS

- A2022 systematic review found that the EPDS is the most widely used tool in the community setting
  - Cut-off varied
- EPDS available in 50 languages

Bhat A, Nanda A, Murphy L, Ball AL, Fortney J, Katon J. A systematic review of screening for perinatal depression and anxiety in community-based settings. Arch Womens Ment Health. 2022 Feb;25(1):33-49.
ACOG Committee Opinion Number 757: Screening for Perinatal Depression

EPDS Cutoffs

- With a cut-off of ≥ 13, pooled sensitivity for MDD is 0.91
  - Specificity ranges from 0.84-0.99

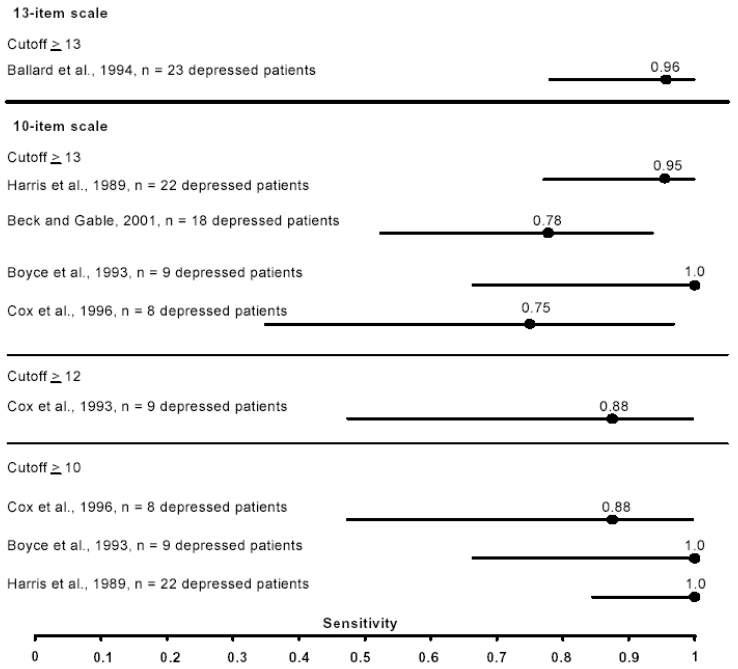


Figure 16a. Sensitivity of screening by Edinburgh Postnatal Depression Scale: postpartum period, major depression alone

Gaynes, B. N., Gavin, N., Meltzer-Brody, S., Lohr, K. N., Swinson, T., Gartlehner, G., Brody, S., & Miller, W. C. (2005). Perinatal depression: prevalence, screening accuracy, and screening outcomes. *Evidence report/technology assessment (Summary)*, (119), 1–8.

EPDS Cutoffs

Lyubenova A, Neupane D, Levis B, et al. Depression prevalence based on the Edinburgh Postnatal Depression Scale compared to Structured Clinical Interview for DSM Disorders classification: Systematic review and individual participant data meta-analysis. *Int J Methods Psychiatr Res*. 2021;30(1):e1860.

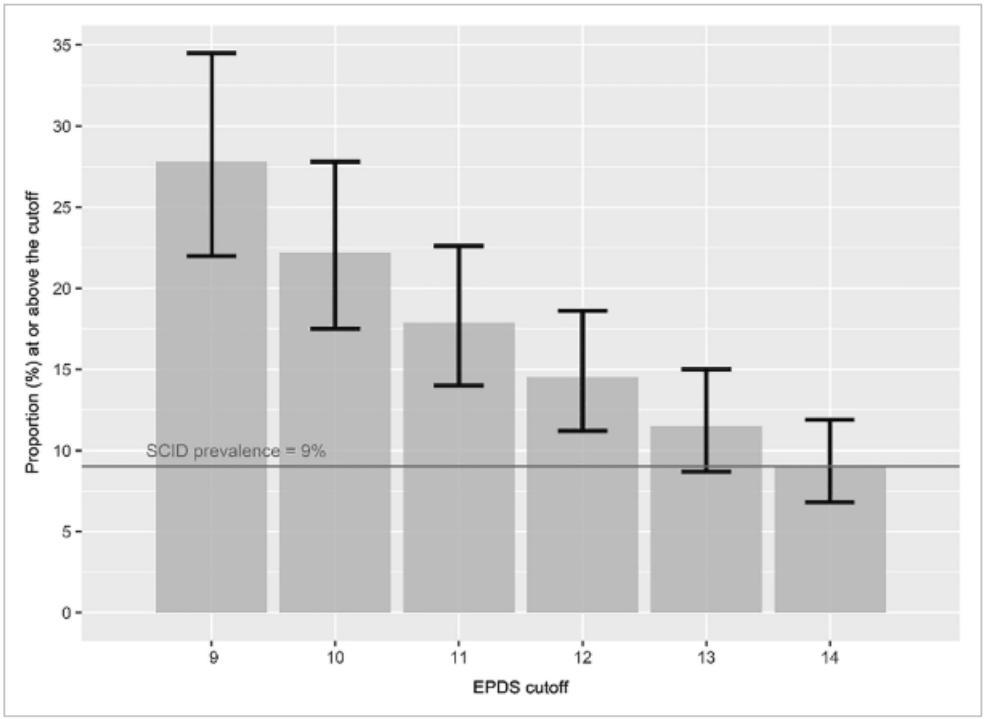
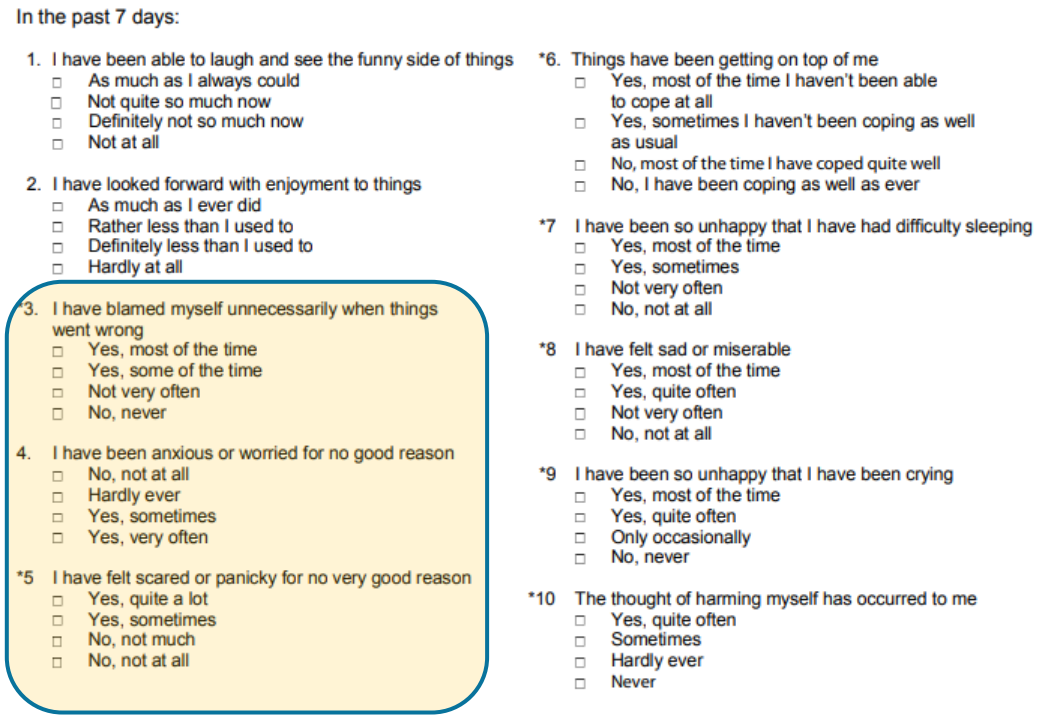


FIGURE 2 Open in figure viewer | PowerPoint

Prevalence estimates and 95% CI based on each EPDS cutoff threshold from ≥ 9 to ≥ 14. CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; SCID, Structured Clinical Interview for DSM

Anxiety subscale

- EPDS-3A
- Using a cutoff of ≥ 5 has a sensitivity of 71% and a specificity of 92% for clinical anxiety
- However, this does not capture more women than using a total EPDS cutoff of ≥ 11



In the past 7 days:

1. I have been able to laugh and see the funny side of things
   - ☐ As much as I always could
   - ☐ Not quite so much now
   - ☐ Definitely not so much now
   - ☐ Not at all

2. I have looked forward with enjoyment to things
   - ☐ As much as I ever did
   - ☐ Rather less than I used to
   - ☐ Definitely less than I used to
   - ☐ Hardly at all

*3. I have blamed myself unnecessarily when things went wrong
   - ☐ Yes, most of the time
   - ☐ Yes, some of the time
   - ☐ Not very often
   - ☐ No, never

4. I have been anxious or worried for no good reason
   - ☐ No, not at all
   - ☐ Hardly ever
   - ☐ Yes, sometimes
   - ☐ Yes, very often

*5 I have felt scared or panicky for no very good reason
   - ☐ Yes, quite a lot
   - ☐ Yes, sometimes
   - ☐ No, not much
   - ☐ No, not at all

*6. Things have been getting on top of me
   - ☐ Yes, most of the time I haven't been able to cope at all
   - ☐ Yes, sometimes I haven't been coping as well as usual
   - ☐ No, most of the time I have coped quite well
   - ☐ No, I have been coping as well as ever

*7 I have been so unhappy that I have had difficulty sleeping
   - ☐ Yes, most of the time
   - ☐ Yes, sometimes
   - ☐ Not very often
   - ☐ No, not at all

*8 I have felt sad or miserable
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Not very often
   - ☐ No, not at all

*9 I have been so unhappy that I have been crying
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Only occasionally
   - ☐ No, never

*10 The thought of harming myself has occurred to me
   - ☐ Yes, quite often
   - ☐ Sometimes
   - ☐ Hardly ever
   - ☐ Never

Smith-Nielsen J, Egmose I, Wendelboe KI, Steinmejer P, Lange T, Vaever MS. Can the Edinburgh Postnatal Depression Scale-3A be used to screen for anxiety?. *BMC Psychol*. 2021;9(1):118. Published 2021 Aug 7.

Screening for anxiety

- Screening instrument minimum criteria:
  - AUC ≥ 0.8
  - Youden's J index ≥ 0.5 (sensitivity + specificity -1)
  - NPV ≥ 0.8
  - Positive LR f ≥ 4.0 (with a positive test result, the probability the person has the disease increases 25% over pre-test probability)

Fairbrother N, Corbyn B, Thordarson DS, Ma A, Surm D. Screening for perinatal anxiety disorders: Room to grow. *J Affect Disord*. 2019;250:363-370.

Screening for anxiety

Table 2
Indices of screening tool diagnostic accuracy for the full composite of the anxiety and related disorders.

Variable	Cut-off	AUC	95% CI	Sensitivity	Specificity	PPV	NPV	LR +	LR-	Correct Classification
EPDS	6	0.744	0.663–0.824	0.680	0.643	0.272	0.911	1.91	0.498	64.9%
EPDS-3A	4	0.757	0.678–0.836	0.640	0.777	0.360	0.917	2.87	0.463	75.4%
GAD-7	6	0.780	0.704–0.856	0.560	0.852	0.424	0.908	3.78	0.516	80.4%
GAD-2	2	0.752	0.675–0.829	0.560	0.815	0.373	0.904	3.03	0.540	77.1%
AD-13	11	0.863	0.811–0.914	0.694	0.847	0.466	0.935	4.54	0.360	82.2%

Note. AUC = Area under the curve; CI = Confidence intervals; PPV = Positive predictive values; NPV = Negative predictive values; LR + = Likelihood ratio of a positive test; LR - = Likelihood ratio of a negative test.

Fairbrother N, Corbyn B, Thordarson DS, Ma A, Surm D. Screening for perinatal anxiety disorders: Room to grow. *J Affect Disord*. 2019;250:363-370.

Next steps

- An elevated EPDS does not equal PPD!
- An Australian study completed a diagnostic interview on women with EPDS scores over 12
  - 16% had only MDD
  - 15% had only an anxiety disorder
  - 11% had both MDD and an anxiety disorder
  - The remainder had minor depressive sx/adjustment disorder

Rowe HJ, Fisher JR, Loh WM. The Edinburgh Postnatal Depression Scale detects but does not distinguish anxiety disorders from depression in mothers of infants. *Arch Womens Ment Health*. 2008;11(2):103-108.

Mania

- 23% of women who have an EPDS score over 10 have bipolar disorder
  - 27% of women with an EPDS score over 13 have bipolar disorder

Sharma V, Al-Farayedhi M, Doobay M, Baczynski C. Should all women with postpartum depression be screened for bipolar disorder?. *Med Hypotheses*. 2018;118:26-28.

MDQ

Instructions: Check (☑) the answer that best applies to you.
Please answer each question as best you can.

	Yes	No
1. Has there ever been a period of time when you were not your usual self and...		
...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 you didn't really miss it?	◯	◯
...you were much more talkative or spoke 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 much 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? *Please check 1 response only.*	◯	◯
3. How much of a problem did any of these cause you — like being able to work; having family, money, or legal troubles; getting into arguments or fights? *Please check 1 response only.* ◯ No problem ◯ Minor problem ◯ Moderate problem ◯ Serious problem		
4. Have any of your blood relatives (ie, children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?	◯	◯
5. Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?	◯	◯

How to Score

Further medical assessment for bipolar disorder is clearly warranted if patient:

- Answers *Yes* to 7 or more of the events in question #1

AND

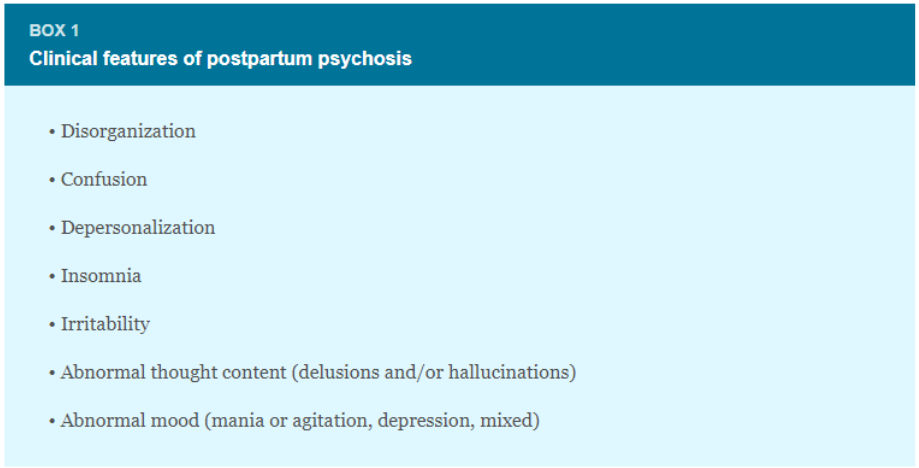
- Answers *Yes* to question #2

AND

- Answers *Moderate problem* or *Serious problem* to question #3

Postpartum Psychosis

- There is no standardized screening tool for PPP
- Onset is typically sudden and within 2 weeks postpartum



BOX 1
Clinical features of postpartum psychosis

- Disorganization
- Confusion
- Depersonalization
- Insomnia
- Irritability
- Abnormal thought content (delusions and/or hallucinations)
- Abnormal mood (mania or agitation, depression, mixed)

Osborne LM. Recognizing and Managing Postpartum Psychosis: A Clinical Guide for Obstetric Providers. *Obstet Gynecol Clin North Am*. 2018;45(3):455-468.

Postpartum Psychosis

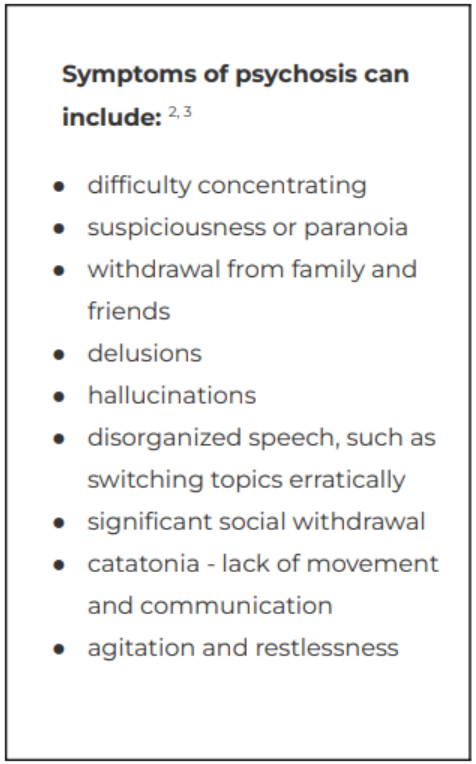
Key points

- Postpartum psychosis (PPP) is a rare psychiatric emergency that can endanger the lives of the mother and child.
- It most often arises within 10 days of childbirth and is characterized by bizarre thoughts and/or behavior, alterations of consciousness, and mood fluctuation.
- The single biggest risk factor is a personal history of bipolar disorder, and most women with PPP will go on to develop bipolar disorder.
- It carries high rates of suicide and infanticide, and suspected cases require psychiatric evaluation as soon as possible.
- Treatment requires hospitalization and aggressive pharmacologic management.

Osborne LM. Recognizing and Managing Postpartum Psychosis: A Clinical Guide for Obstetric Providers. *Obstet Gynecol Clin North Am*. 2018;45(3):455-468.

2020 Mom Psychosis Checklist

- Consensus checklist (not validated) and background 5-page info sheet



Symptoms of psychosis can include: [2,3]

- difficulty concentrating
- suspiciousness or paranoia
- withdrawal from family and friends
- delusions
- hallucinations
- disorganized speech, such as switching topics erratically
- significant social withdrawal
- catatonia - lack of movement and communication
- agitation and restlessness

OCD

- 1 in 7 women experience OCD symptoms during pregnancy or first 6 months postpartum
  - Postpartum OCD often has obsessions around harm (intentional but highly distressing or unintentional) coming to the baby
  - Checking compulsions are common

Fairbrother N, Albert A, Keeney C, Tchir D, Cameron RB. Screening for Perinatal OCD: A Comparison of the DOCS and the EPDS [published online ahead of print, 2021 Dec 30]. *Assessment*.

OCD

Table 4. EPDS and EPDS-3A ROC Analysis Data.

EPDS-Full and 3A by Assessment Point	AUC [95% CI]	J	Cutpoint	Sensitivity	Specificity	PPV	NPV	LR+
EPDS-Full								
Prenatal	0.71 [0.54, 0.88]	0.26	9.05	0.50	0.76	0.07	0.98	2.08
Early postpartum	0.79 [0.72, 0.85]	0.39	7.43	0.74	0.65	0.20	0.95	2.11
Late postpartum	0.78 [0.66, 0.90]	0.52	10.01	0.67	0.85	0.22	0.98	4.47
EPDS-3A								
Prenatal	0.73 [0.55, 0.91]	0.52	4.63	0.80	0.72	0.09	0.99	2.86
Early postpartum	0.79 [0.72, 0.86]	0.46	4.35	0.67	0.79	0.28	0.95	3.19
Late postpartum	0.80 [0.68, 0.92]	0.51	4.90	0.76	0.75	0.16	0.98	3.04

Note. EPDS = Edinburgh Postnatal Depression Scale; EPDS-3A = three-item Anxiety subscale of the EPDS; ROC = receiver operating characteristic; AUC = area under the curve; CI = confidence interval; LR+ = positive likelihood ratio; PPV = positive predictive value; NPV = negative predictive value.

Fairbrother N, Albert A, Keeney C, Tchir D, Cameron RB. Screening for Perinatal OCD: A Comparison of the DOCS and the EPDS [published online ahead of print, 2021 Dec 30]. *Assessment*.

Dimensional Obsessive-Compulsive Scale

Dimensional Obsessive-Compulsive Scale

This questionnaire asks you about 4 different types of concerns that you might or might not experience. For each type there is a description of the kinds of thoughts (sometimes called *obsessions*) and behaviors (sometimes called *rituals* or *compulsions*) that are typical of that particular concern, followed by 5 questions about your experiences with these thoughts and behaviors. Please read each description carefully and answer the questions for each category based on your experiences in the last month.

Category 1: Concerns about Germs and Contamination

Examples…

-Thoughts or feelings that you are contaminated because you came into contact with (or were nearby) a certain object or person.
-The feeling of being contaminated because you were in a certain place (such as a bathroom).
-Thoughts about germs, sickness, or the possibility of spreading contamination.
-Washing your hands, using hand sanitizer gels, showering, changing your clothes, or cleaning objects because of concerns about contamination.
-Following a certain routine (e.g., in the bathroom, getting dressed) because of contamination
-Avoiding certain people, objects, or places because of contamination.

The next questions ask about your experiences with thoughts and behaviors related to contamination over the last month. Keep in mind that your experiences might be different than the examples listed above. Please circle the number next to your answer:

1. About how much time have you spent each day thinking about contamination and engaging in washing or cleaning behaviors because of contamination?

   0 None at all
   1 Less than 1 hour each day
   2 Between 1 and 3 hours each day
   3 Between 3 and 8 hours each day
   4 8 hours or more each day

Elevated EPDS?

- Consider depression, anxiety, OCD, bipolar depression and postpartum psychosis
- Consider using the MDQ to screen for bipolar disorder
- Keep an eye out for PPP – a psychiatric emergency
- Remember that PP-OCD symptoms are common

When should I screen?

American College of Obstetrics and Gynecology

In its committee opinion 757, American College of Obstetrics and Gynecology (ACOG) recommends screening:

- At least once during the perinatal period
- At the comprehensive postpartum visit

ACOG further indicates if a patient is screened for depression and anxiety during pregnancy, additional screening should then occur during the comprehensive postpartum visit.

American Psychiatric Association

In a 2018 position statement, the American Psychiatric Association (APA) recommended a total of 6 screens throughout the perinatal period, including two screenings during pregnancy.[11]

The recommending timing of screenings conducted by obstetrician:

- At least twice during pregnancy
- At least once postpartum

They also recommend screening in the pediatric setting:

- At 1, 2, and 4 month well-child visits

Postpartum Support International

Postpartum Support International (PSI) recommends universal screening for MMH disorders during prenatal and postpartum visits with obstetricians. The recommended timing of screenings:[44]

- First prenatal visit
- At least once in second trimester
- At least once in third trimester
- Six-week postpartum obstetrical visit (or at first postpartum visit)
- Repeated screening at 6 and/or 12 months in OB and primary care settings

PSI also recommends screening in the pediatric setting at these intervals:

- At 3, 9, 12-mo pediatric well-child visits (with pediatrician)

2020 Mom: Universal Screening for Maternal Mental Health Disorders Issue Brief - https://www.issuelab.org/resources/40013/40013.pdf

Too soon?

- Screening prior to discharge?
  - In 361 women who completed a PHQ9 within 1-2 days of delivery, only 2.5% were positive

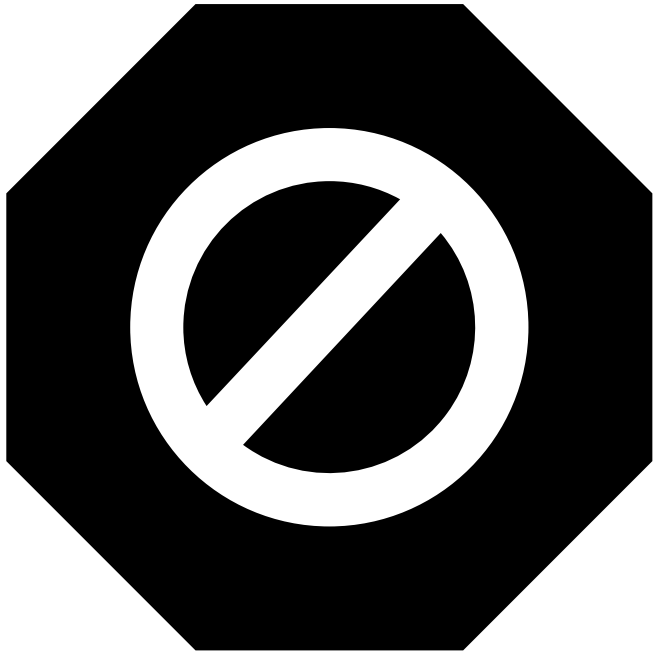
Pawar, G., Wetzker, C., & Gjerdingen, D. (2011). Prevalence of depressive symptoms in the immediate postpartum period. *Journal of the American Board of Family Medicine: JABFM*, *24*(3), 258–261

What are the expected population findings?

- Self-reported PPD rates vary by state
  - Lowest: 6.9% - Hawaii
  - Highest: 18% - Arkansas
- Average aggregate depressive sx that meet criteria for PPD: 10.1%
- Likely higher in low-income populations

Yu, M., & Sampson, M. (2016). Closing the Gap between Policy and Practice in Screening for Perinatal Depression: A Policy Analysis and Call for Action. *Social work in public health*, *31*(6), 549–556.

Barriers to Screening



Barrier: No next step available

- USPSTF recommends screening when there are "adequate systems in place" for treatment and/or referral when patients screen positive

Siu, A. L., U. S. Preventive Services Task Force (2016) Screening for depression in adults: US preventive services task force recommendation statement. JAMA 315(4):380–387

Barrier: Patient not taking the next step

- Rates of initiation of mental health treatment among women who screen positive for PND can range from 0% to 30%
- NJ: An Act Concerning Postpartum Depression (Postpartum Depression, 2012):
  - 67% of pregnant women had received screening for antenatal depression
  - 90% of women were screened for perinatal depression at the time of hospital delivery
  - No uptrend of treatment entry was observed after passage of the legislation

Yu, M., & Sampson, M. (2016). Closing the Gap between Policy and Practice in Screening for Perinatal Depression: A Policy Analysis and Call for Action. *Social work in public health*, *31*(6), 549–556.

Barrier: "Postpartum" definition

- DSM-5: 4 weeks
- ICD-11: "about 6 weeks"
- National Institute for Health & Care Excellence (NICE): 12 months
- ACOG: 12 months

El-Den S, Pham L, Anderson I, Yang S, Moles RJ, O'Reilly CL, Boyce P, Raine KH, Raynes-Greenow C. Perinatal depression screening: a systematic review of recommendations from member countries of the Organisation for Economic Co-operation and Development (OECD). Arch Womens Ment Health. 2022 Oct;25(5):871-893.

Barrier: "Can of Worms"

- Visit time constraints
- Providers may feel "not qualified" and lack confidence in the ability to screen and treat
- A 2003 survey of 282 OBGYNs found that the probability of conducting depression screening doubled among physicians who reported adequate training as compared to physicians who did not receive adequate training to treat depression

Yu, M., & Sampson, M. (2016). Closing the Gap between Policy and Practice in Screening for Perinatal Depression: A Policy Analysis and Call for Action. *Social work in public health*, *31*(6), 549–556.

Current recommendations for screening

- **2010: The American Academy of Pediatricians (AAP)** was the first professional trade association to significantly address the need for screening among its members, publishing a clinical report.[6]
- **2015: The American College of Obstetrics and Gynecology (ACOG)** overturned its prior guideline, which noted evidence for screening was not strong enough, as screening did not in and of itself lead to treatment. The 2015 position noted patients should be screened by obstetricians at least once during the perinatal period and patients should be supported by obstetricians in obtaining treatment.[7]
- **2016: The U.S. Preventive Services Task Force (USPSTF)** followed suit, specifically including pregnant women in their recommendation that adults be screened for depression.[8]
- **2016: The Centers for Medicare and Medicaid Services (CMS)** announces state Medicaid agencies may cover screening for maternal depression as a part of a well-child visit.[9]
- **2017: The American Medical Association (AMA)** issued a public statement endorsing screening for maternal depression.[10]
- **2018: The American Psychiatric Association (APA)** issued a position on screening and treatment of depressive, anxiety, and psychotic disorders in pregnant and postpartum women.[11]

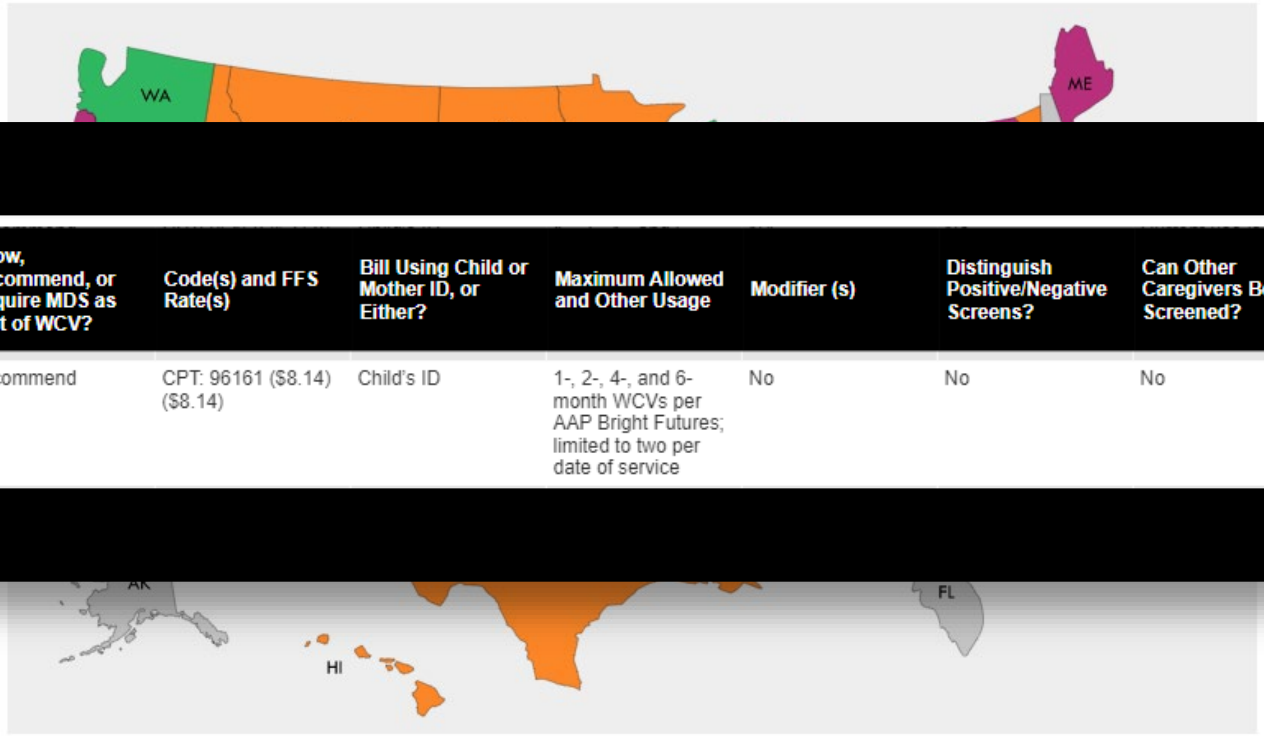
2020 Mom: Universal Screening for Maternal Mental Health Disorders Issue Brief - https://www.issuelab.org/resources/40013/40013.pdf

American Academy of Pediatrics

- 2019 Policy statement
- Routine parental screening recommended
  - Using a validated screening tool (suggested: EPDS or PHQ)
  - Should occur at well-infant visits at 1, 2, 4, and 6 months
  - +partner EPDS at 6 months

Marian F. Earls, Michael W. Yogman, Gerri Mattson, Jason Rafferty, COMMITTEE ON PSYCHOSOCIAL ASPECTS OF CHILD AND FAMILY HEALTH, Rebecca Baum, Thresia Gambon, Arthur Lavin, Lawrence Wissow; Incorporating Recognition and Management of Perinatal Depression Into Pediatric Practice. Pediatrics January 2019; 143 (1): e20183259. 10.1542/peds.2018-3259

State Medicaid Policies for Maternal Depression Screening During Well-Child Visits



State	Allow, Recommend, or Require MDS as Part of WCV?	Code(s) and FFS Rate(s)	Bill Using Child or Mother ID, or Either?	Maximum Allowed and Other Usage	Modifier (s)	Distinguish Positive/Negative Screens?	Can Other Caregivers Be Screened?	Require or Recommend Tools?
South Carolina	Recommend	CPT: 96161 ($8.14) ($8.14)	Child's ID	1-, 2-, 4-, and 6-month WCVs per AAP Bright Futures; limited to two per date of service	No	No	No	Recommend

Washington, DC recommends maternal depression screening during well-child visits and reimburses 96161 at $2.46 within the fee-for-service system.

National Academy for State Health Policy (NASHP): Maternal Depression Screening, updated 4/5/21.
https://healthychild.nashp.org/maternal-depression-screening-2/

ACOG

Recommendations and Conclusions

The American College of Obstetricians and Gynecologists (the College) makes the following recommendations and conclusions:

- The American College of Obstetricians and Gynecologists (the College) recommends that obstetrician–gynecologists and other obstetric care providers screen patients at least once during the perinatal period for depression and anxiety symptoms using a standardized, validated tool. It is recommended that all obstetrician–gynecologists and other obstetric care providers complete a full assessment of mood and emotional well-being (including screening for postpartum depression and anxiety with a validated instrument) during the comprehensive postpartum visit for each patient. If a patient is screened for depression and anxiety during pregnancy, additional screening should then occur during the comprehensive postpartum visit.
- Women with current depression or anxiety, a history of perinatal mood disorders, risk factors for perinatal mood disorders, or suicidal thoughts warrant particularly close monitoring, evaluation, and assessment.
- There is evidence that screening alone can have clinical benefits, although initiation of treatment or referral to mental health care providers offers maximum benefit. Therefore, clinical staff in obstetrics and gynecology practices should be prepared to initiate medical therapy, refer patients to appropriate behavioral health resources when indicated, or both.
- Systems should be in place to ensure follow-up for diagnosis and treatment.

ACOG Committee Opinion Number 757: Screening for Perinatal Depression. November 2018. https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2018/11/screening-for-perinatal-depression

Take Home Points

- Depression in pregnancy is common
- Untreated depression in pregnancy carries risks for both the mother and the child
  - The best treatment is the one that's effective
- Must weigh risks and benefits with the mother (and partner) on an individual basis

Take Home Points

- Postpartum blues are the norm but should resolve by 2 weeks
- Postpartum depression treatment takes into consideration breastfeeding
- Postpartum psychosis is a true psychiatric emergency
- Postpartum obsessive compulsive disorder is often overlooked and marked by intrusive thoughts
- Screening for perinatal mood and anxiety disorders are recommended but barriers still exist

Resources

MGH CENTER for Women's Mental Health
Reproductive Psychiatry Resource & Information Center

Drugs and Lactation Database (LactMed®)

Bethesda (MD): National Institute of Child Health and Human Development; 2006-.

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Infant Risk Center
AT TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

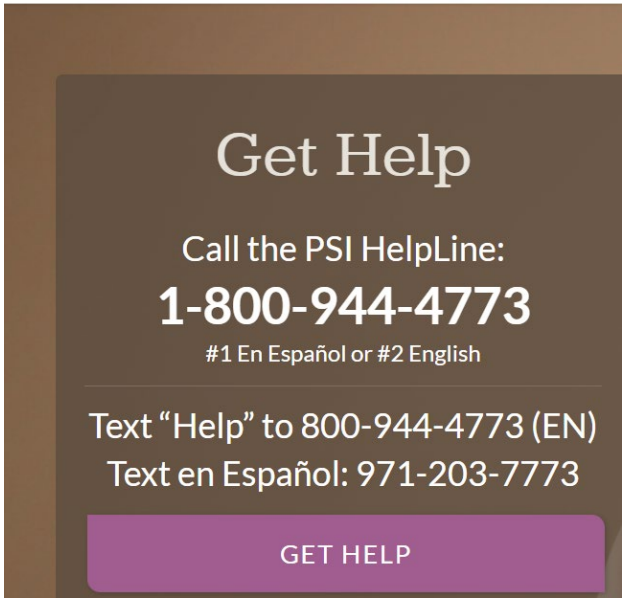
PSI POSTPARTUM SUPPORT INTERNATIONAL

MotherToBaby

Massachusetts Child Psychiatry Access Program
MCPAP For Moms

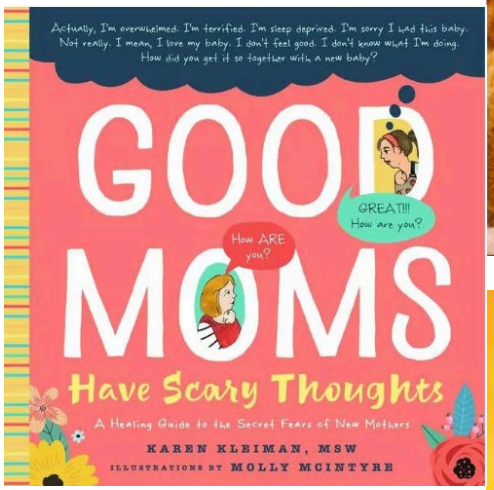
Resources

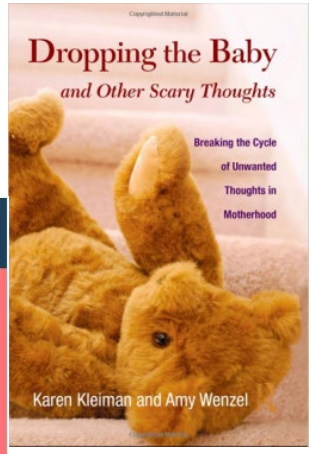
POSTPARTUM SUPPORT INTERNATIONAL

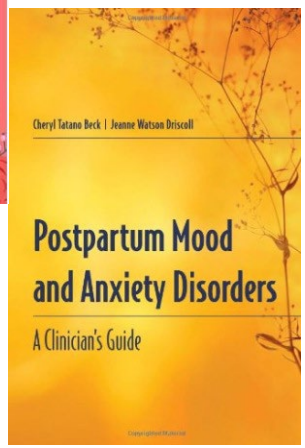


SHADES of BLUE PROJECT
MATERNAL & MENTAL HEALTH RESOURCE CENTER

POSTPARTUM SUPPORT CHARLESTON







MUGS for MOMS

TheBlueDot project

National Maternal Mental Health Hotline

1-833-TLC-MAMA (1-833-852-6262)

Published in final edited form as:
Obstet Gynecol. 2017 March ; 129(3): 422–430. doi:10.1097/AOG.0000000000001902.

Consensus Bundle on Maternal Mental Health:

Perinatal Depression and Anxiety

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Abstract

Perinatal mood and anxiety disorders are among the most common mental health conditions encountered by women of reproductive age. When left untreated, perinatal mood and anxiety disorders can have profound adverse effects on women and their children, ranging from increased risk of poor adherence to medical care, exacerbation of medical conditions, loss of interpersonal and financial resources, smoking and substance use, suicide, and infanticide. Perinatal mood and anxiety disorders are associated with increased risks of maternal and infant mortality and morbidity and are recognized as a significant patient safety issue. In 2015, the Council on Patient Safety in Women's Health Care convened an interdisciplinary workgroup to develop an evidence-based patient safety bundle to address maternal mental health. The focus of this bundle is perinatal mood and anxiety disorders. The bundle is modeled after other bundles released by the Council on

Dr. Berg References

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