Screening & Treating Maternal Mental Health Conditions: Understanding & Utilizing the 2023 Clinical Practice Guidelines from ACOG

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Dr. Hoffman Disclosures

Dr. Hoffman:

- SAGE/Biogen: disease state speaker on Postpartum Depression
- Balchem: speaker on prenatal choline supplementation

LEARNING OBJECTIVES

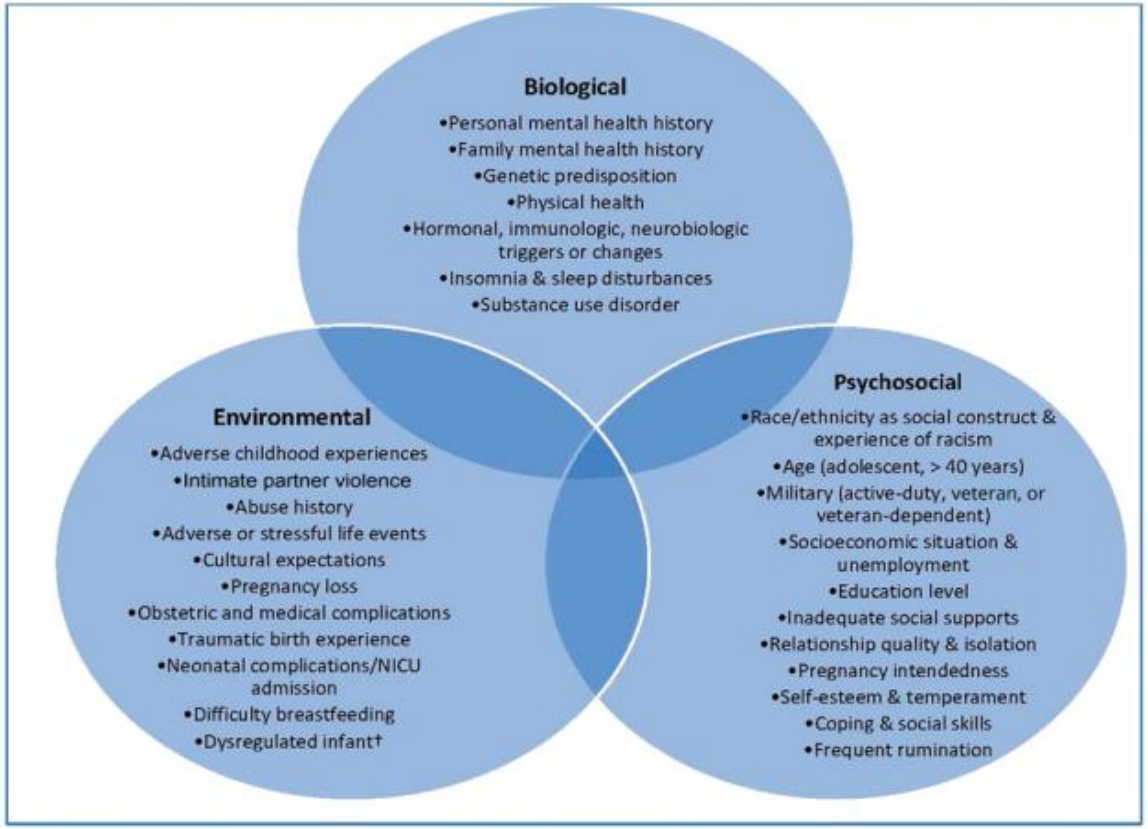
After this presentation, you should be able to:

- Provide examples of validated screening tools for perinatal mental health conditions and how to respond to the score(s).
- Understand when & which psychopharmacologic interventions to recommend for perinatal mental health disorders.
- Explain evidence-based screening, diagnostic & preliminary treatment approaches for acute postpartum psychosis and perinatal suicidality.

Background, Screening & Assessment

Perinatal mental health conditions are one of the most common complications of pregnancy & postpartum

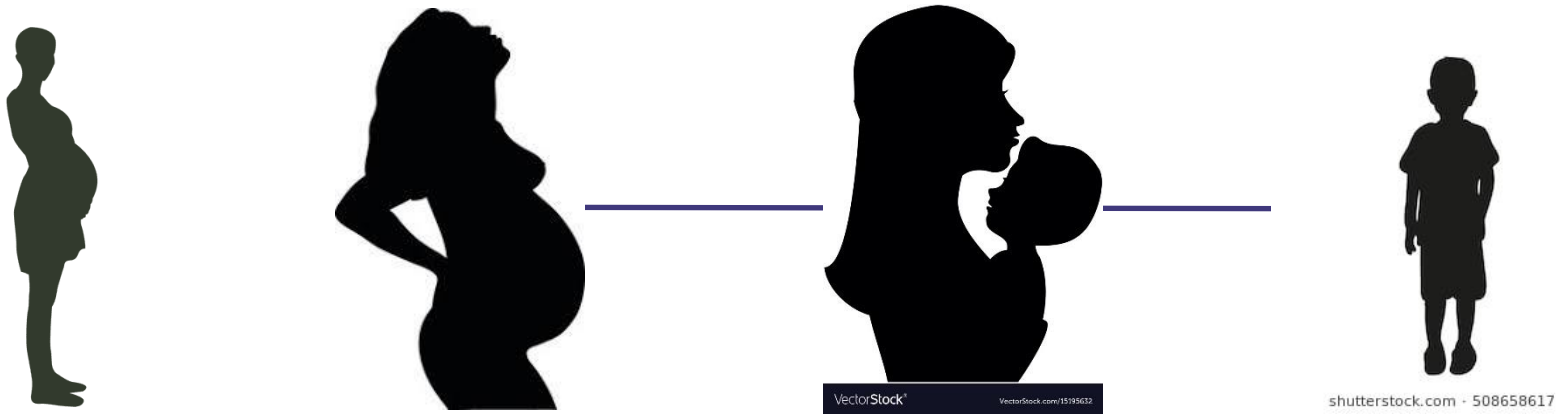
Numerous Risk Factors



Prenatal Mental Health Affects Mom, Child and Family

Preterm delivery
Low birth weight
NICU admissions

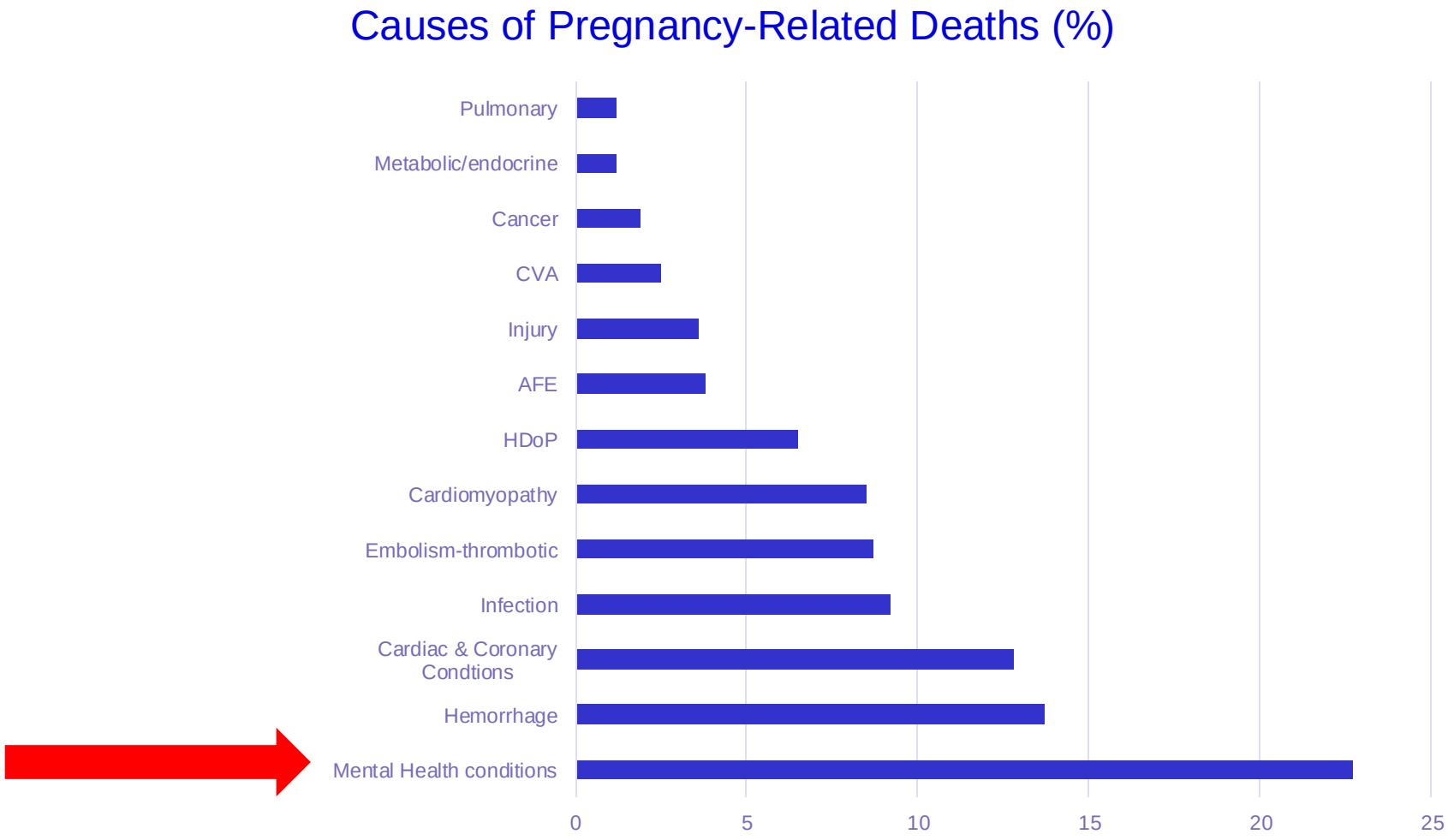
Cognitive delays
Motor & Growth issues
Behavioral problems
Mental health disorders



Less engagement in medical care
Smoking & substance use

Lactation challenges
Bonding issues
Adverse partner relationships

Mental Health Conditions are the Leading Cause of Pregnancy Related Deaths (22.7%)



Pregnancy-Related Deaths: Data from Maternal Mortality Review Committees in 36 US States, 2017–2019

MMRIA MATERNAL MORTALITY REVIEW INFORMATION APP

Susanna Trost, MPH; Jennifer Beauregard, MPH, PhD; Gyan Chandra, MS, MBA; Fanny Njie, MPH; Jasmine Berry, MPH; Alyssa Harvey, BS; David A. Goodman, MS, PhD

Key Findings

- Pregnancy-related deaths occurred during pregnancy, delivery, and up to a year postpartum.
- The leading cause of pregnancy-related death varied by race and ethnicity.
- Over 80% of pregnancy-related deaths were determined to be preventable.

Maternal Mortality Review Committees (MMRCs) are multidisciplinary committees that convene at the state or local level to comprehensively review deaths during or within a year of pregnancy (pregnancy-associated deaths). MMRCs have access to clinical and nonclinical information (e.g., vital records, medical records, social service records) to more fully understand the circumstances surrounding each death, determine whether the death was pregnancy-related, and develop recommendations for action to prevent similar deaths in the future.

Data on 1,018 pregnancy-related deaths among residents of 36 states from 2017–2019 were shared with CDC through the Maternal Mortality Review Information Application (MMRIA).

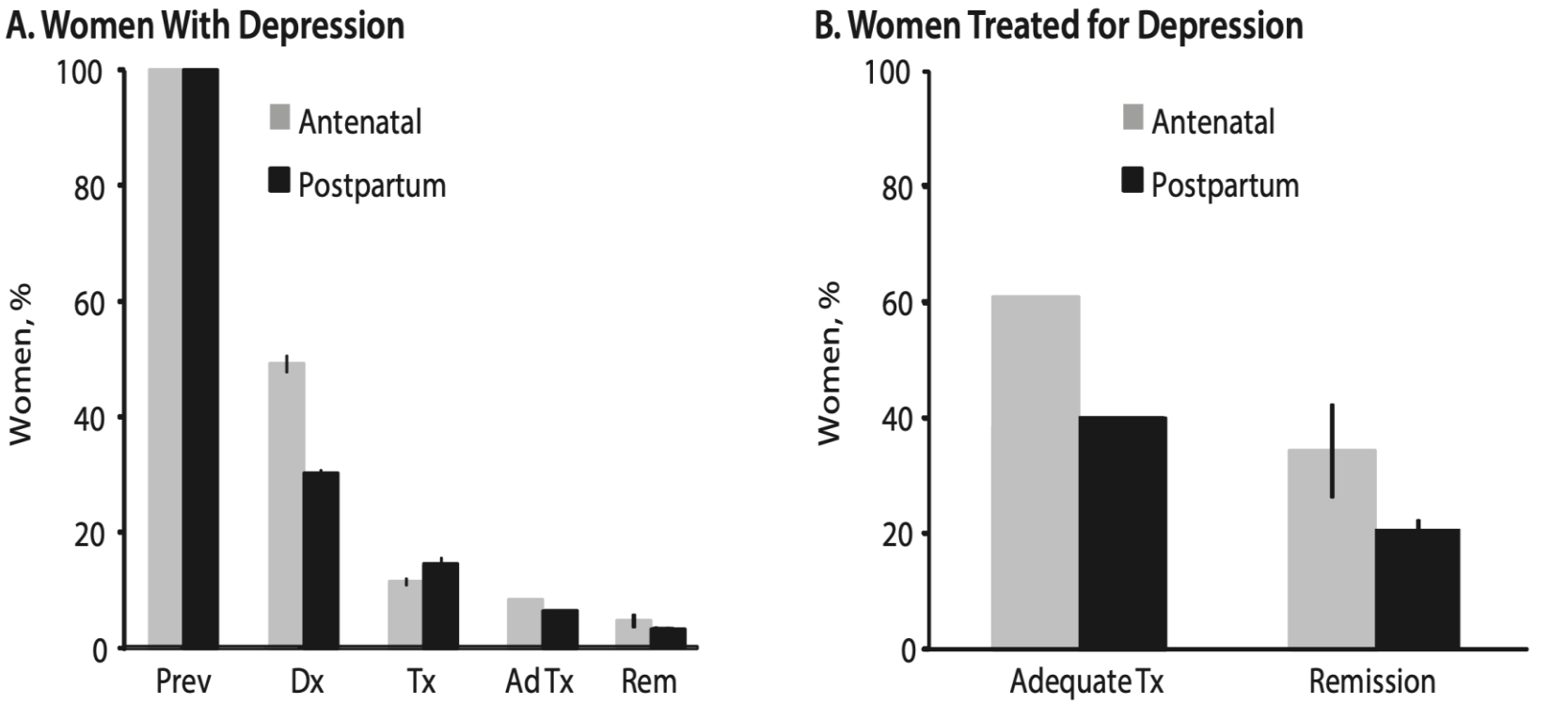
Table 1. Characteristics of pregnancy-related deaths, data from Maternal Mortality Review Committees in 36 US States, 2017–2019 (N=1,018)*

	N	%
Race and ethnicity		
Hispanic	144	14.4
non-Hispanic American Indian or Alaska Native	9	0.9
non-Hispanic Asian	34	3.4
non-Hispanic Black	315	31.4
non-Hispanic Native Hawaiian and Other Pacific Islander	6	0.6
non-Hispanic White	467	46.6
non-Hispanic other/multiple races	27	2.7
Age at death (years)		
15–19	29	2.9
20–24	155	15.3
25–29	227	22.4
30–34	297	29.3
35–39	225	22.2
40–44	70	6.9
≥45	10	1.0
Education		
12th grade or less; no diploma	135	13.7
High school graduate or GED completed	396	40.1
Some college credit, but no degree	192	19.4
Associate or bachelor's degree	218	22.1
Advanced degree	47	4.8

*Race or ethnicity was missing for 16 (1.6%) pregnancy-related deaths; age was missing for 5 (0.5%) pregnancy-related deaths; education was missing for 30 (2.9%) pregnancy-related deaths.

National Center for Chronic Disease Prevention and Health Promotion
Division of Reproductive Health

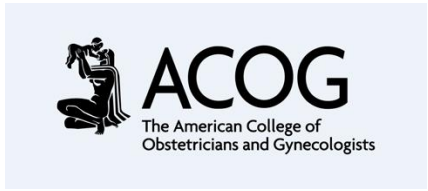
Perinatal Mental Health Conditions are Under-detected and Under-treated



Abbreviations: Ad Tx = adequate trial of treatment, Dx = diagnosis, Prev = prevalence, Rem = remission, Tx = treatment

Cox, E. Q., et al. (2016). "The Perinatal Depression Treatment Cascade: Baby Steps Toward Improving Outcomes." J Clin Psychiatry 77(9): 1189-1200., Byatt et al. (2015). Ob Gyn

Professional Societies and Policy Makers Recognize This as a Significant Public Health Issue



ACOG Guidelines & Recommendations
Available on ACOG website and 'Green Journal' (Obstetrics & Gynecology)

ACOG
The American College of Obstetricians and Gynecologists

CLINICAL PRACTICE GUIDELINE

NUMBER 4
JUNE 2023
REPLACES COMMITTEE OPINION 757, NOVEMBER 2018

Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum

Committee on Clinical Practice Guidelines—Obstetrics. This Clinical Practice Guideline was developed by the ACOG Committee on Clinical Practice Guidelines–Obstetrics in collaboration with Tiffany A. Moore Simas, MD, MPH, MEd; M. Camille Hoffman, MD, MSc; Emily S. Miller, MD, MPH; and Torri Metz, MD, MS; with consultation from Nancy Byatt, DO, MS, MBA; and Kay Roussos-Ross, MD.

The Society for Maternal-Fetal Medicine endorses this document.

The Committee on Women's Mental Health of the American Psychiatric Association reviewed and provided feedback on this document.

PURPOSE: To review evidence on the current understanding of mental health conditions in pregnancy and postpartum, with a focus on mood and anxiety disorders, and to outline guidelines for screening and diagnosis that are consistent with best available scientific evidence. The conditions or symptoms reviewed include depression, anxiety and anxiety-related disorders, bipolar disorder, suicidality, and postpartum psychosis. For information on psychopharmacologic treatment and management, refer to American College of Obstetricians and Gynecologists (ACOG) Clinical Practice Guideline Number 5, "Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum" (1).

TARGET POPULATION: Pregnant or postpartum individuals with mental health conditions. Onset of these conditions may have predated the perinatal period or may have occurred for the first time in pregnancy or the first year postpartum or may have been exacerbated in that time.

METHODS: This guideline was developed using an a priori protocol in conjunction with a writing team consisting of one specialist in obstetrics and gynecology and one maternal–fetal medicine subspecialist appointed by the ACOG Committee on Clinical Practice Guidelines–Obstetrics and two external subject matter experts. ACOG medical librarians completed a comprehensive literature search for primary literature within Cochrane Library, Cochrane Collaboration Registry of Controlled Trials, EMBASE, PubMed, and MEDLINE. Studies that moved forward to the full-text screening stage were assessed by two authors from the writing team based on standardized inclusion and exclusion criteria. Included studies underwent quality assessment, and a modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) evidence-to-decision framework was applied to interpret and translate the evidence into recommendation statements.

RECOMMENDATIONS: This Clinical Practice Guideline includes recommendations on the screening and diagnosis of perinatal mental health conditions including depression, anxiety, bipolar disorder, acute postpartum psychosis, and the symptom of suicidality. Recommendations are classified by strength and evidence quality. Ungraded Good Practice Points are included to provide guidance when a formal recommendation could not be made because of inadequate or nonexistent evidence.

ACOG
The American College of Obstetricians and Gynecologists

CLINICAL PRACTICE GUIDELINE

NUMBER 5
JUNE 2023
REPLACES PRACTICE BULLETIN NUMBER 92, APRIL 2008

Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum

Committee on Clinical Practice Guidelines—Obstetrics. This Clinical Practice Guideline was developed by the ACOG Committee on Clinical Practice Guidelines–Obstetrics in collaboration with Emily S. Miller, MD, MPH; Torri Metz, MD, MS; Tiffany A. Moore Simas, MD, MPH, MEd; and M. Camille Hoffman, MD, MSc; with consultation from Nancy Byatt, DO, MS, MBA; and Kay Roussos-Ross, MD.

The Society for Maternal-Fetal Medicine endorses this document.

The Committee on Women's Mental Health of the American Psychiatric Association reviewed and provided feedback on this document.

PURPOSE: To assess the evidence regarding safety and efficacy of psychiatric medications to treat mental health conditions during pregnancy and lactation. The conditions reviewed include depression, anxiety and anxiety-related disorders, bipolar disorder, and acute psychosis. For information on screening and diagnosis, refer to American College of Obstetricians and Gynecologists (ACOG) Clinical Practice Guideline Number 4, "Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum" (1).

TARGET POPULATION: Pregnant or postpartum individuals with mental health conditions with onset that may have predated the perinatal period or may have occurred for the first time in pregnancy or the first year postpartum or may have been exacerbated in that time.

METHODS: This guideline was developed using an a priori protocol in conjunction with a writing team consisting of one specialist in obstetrics and gynecology and one maternal–fetal medicine subspecialist appointed by the ACOG Committee on Clinical Practice Guidelines–Obstetrics and two external subject matter experts. ACOG medical librarians completed a comprehensive literature search for primary literature within Cochrane Library, Cochrane Collaboration Registry of Controlled Trials, EMBASE, PubMed, and MEDLINE. Studies that moved forward to the full-text screening stage were assessed by two authors from the writing team based on standardized inclusion and exclusion criteria. Included studies underwent quality assessment, and a modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) evidence-to-decision framework was applied to interpret and translate the evidence into recommendation statements.

RECOMMENDATIONS: This Clinical Practice Guideline includes recommendations on treatment and management of perinatal mental health conditions including depression, anxiety, bipolar disorders, and acute postpartum psychosis, with a focus on psychopharmacotherapy. Recommendations are classified by strength and evidence quality. Ungraded

ACOG recommends that everyone receiving well-woman, prepregnancy, prenatal, and postpartum care be **screened for depression and anxiety using standardized validated instruments**.

ACOG recommends that **screening for perinatal depression and anxiety occur at the initial prenatal visit, later in pregnancy, and at postpartum visits.**

ACOG recommends that mental health screening be implemented with **systems in place to ensure timely access** to assessment and diagnosis, effective treatment, and appropriate monitoring and follow-up based on severity.

ACOG recommends **screening for bipolar disorder before initiating pharmacotherapy** for anxiety or depression, if not previously done.

Validated screening instruments exist for perinatal mental health conditions (all self-administered except CIDI)

EPDS
Depression & Anxiety

Depression
PHQ9 (≥10, #9)) or EPDS (≥10, #10)

The Patient Health Questionnaire (PHQ-9)

Patient Name _____ Date of Visit _____

Over the past 2 weeks, how often have you been bothered by any of the following problems?	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 asleep, 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're 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
Column Totals		_____ +	_____ +	_____
Add Totals Together				_____

Edinburgh Postnatal Depression Scale[1] (EPDS)

Name: _____ Address: _____

Your Date of Birth: _____ _____

Baby's Date of Birth: _____ Phone: _____

As you are pregnant or have recently had a baby, we would like to know how you are feeling. Please check the answer that comes closest to how you have felt **IN THE PAST 7 DAYS**, not just how you feel today.

Here is an example, already completed.

I have felt happy:
- ☐ Yes, all the time
- ☒ Yes, most of the time — This would mean: "I have felt happy most of the time" during the past week.
- ☐ No, not very often — Please complete the other questions in the same way.
- ☐ No, not at all

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

Anxiety
GAD7 (≥5) or EPDS subscale #3-5 (≥6)

Generalized Anxiety Disorder 7-item (GAD-7) scale

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all sure	Several days	Over half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it's hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3
Add the score for each column	+	+	+	
Total Score *(add your column scores)* =				

If you checked off any problems, how difficult have these made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all _____
Somewhat difficult _____
Very difficult _____
Extremely difficult _____

Source: Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder. *Arch Intern Med.* 2006;166:1092-1097.

Bipolar Disorder
MDQ or CIDI

THE MOOD DISORDER QUESTIONNAIRE

Instructions: Please answer each question to the best of your ability.

	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 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 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?	○	○

Table 3. Composite International Diagnostic Interview (CIDI) Bipolar Screen*

Screen for bipolar disorder[†]
1. Some people have periods lasting several days or longer when they feel much more excited and full of energy than usual. Their minds go too fast. They talk a lot. They are very restless or unable to sit still and they sometimes do things that are unusual for them, such as driving too fast or spending too much money. Have you ever had a period liked this lasting several days or longer?
2. Have you ever had a period lasting several days or longer when most of the time you were so irritable or grouchy that you started arguments, shouted at people, or hit people?

If YES to questions 1 and/or 2

Continue screen for bipolar disorder[†]
3. People who have episodes like this often have changes in their thinking and behavior at the same time, like being more talkative, needing very little sleep, being very restless, going on buying sprees, and behaving in ways they would normally think are inappropriate. Did you ever have any of these changes during your episodes of being (excited and full of energy/very irritable or grouchy)?

If YES to question 3

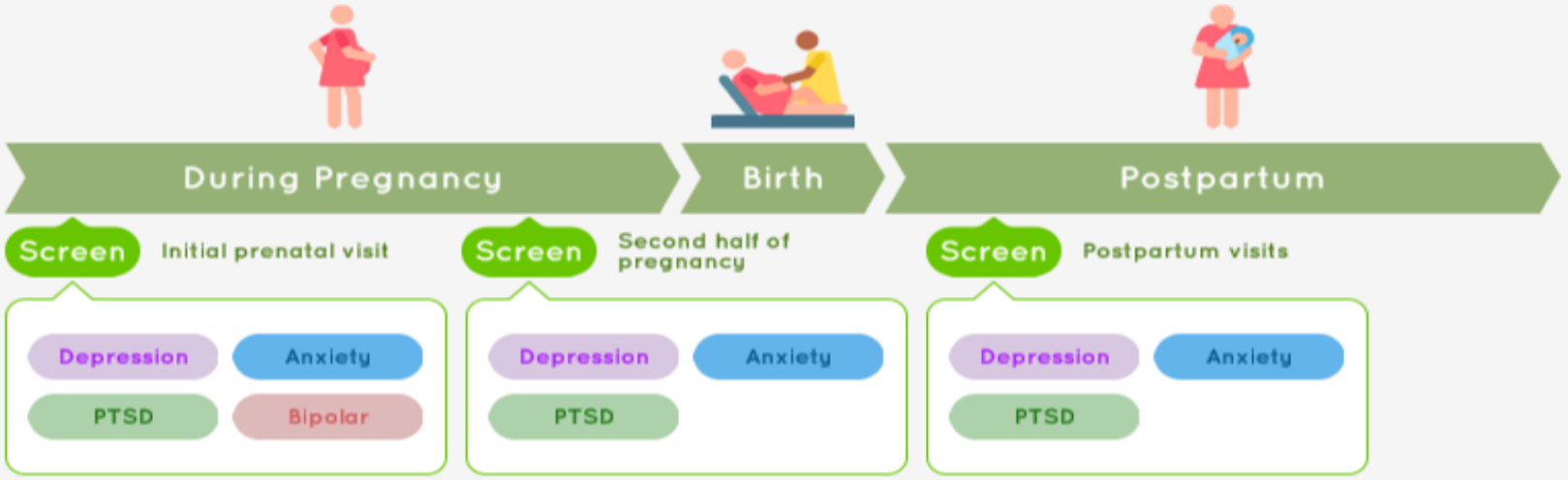
The screen suggests the patient may have bipolar disorder
If currently symptomatic or anticipating prescribing for other perinatal mood or anxiety disorder, consider consultation with mental health professional, including those available through Perinatal Psychiatry Access Programs across the country.

*In this algorithm, the provider speaks the *italicized text*.

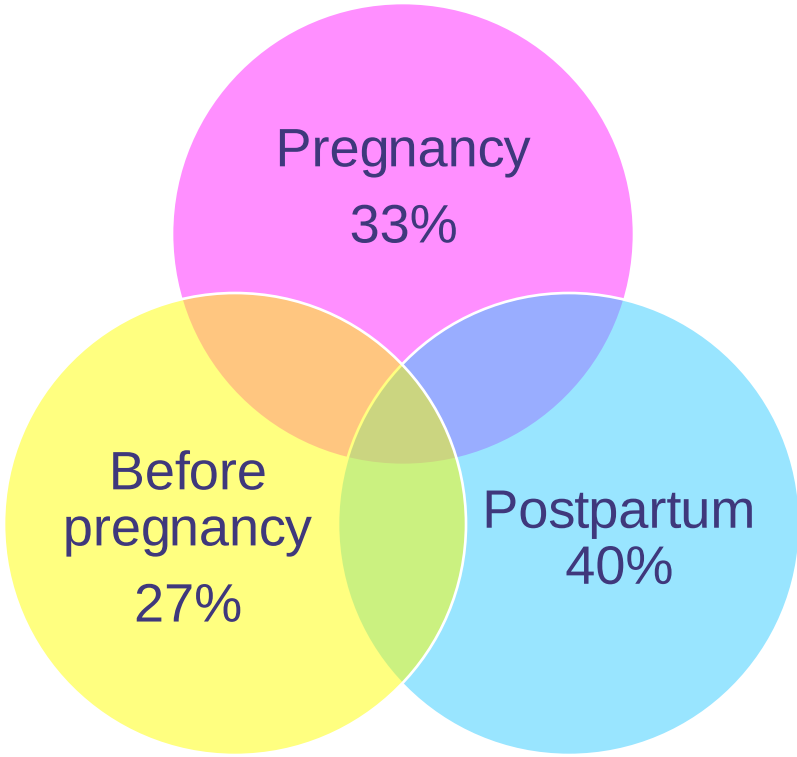
†Taken from the Composite International Diagnostic Interview-Based Bipolar Disorder Screening Scale (Kessler, Akiskal, Angst et al., 2006).

Modified from Massachusetts Child Psychiatry Access Project. MCPAP for Moms toolkit. MCPAP; 2014. Accessed February 7, 2023. https://www.mcpapformoms.org/Docs/Adult%20Toolkit.pdf

When to Screen

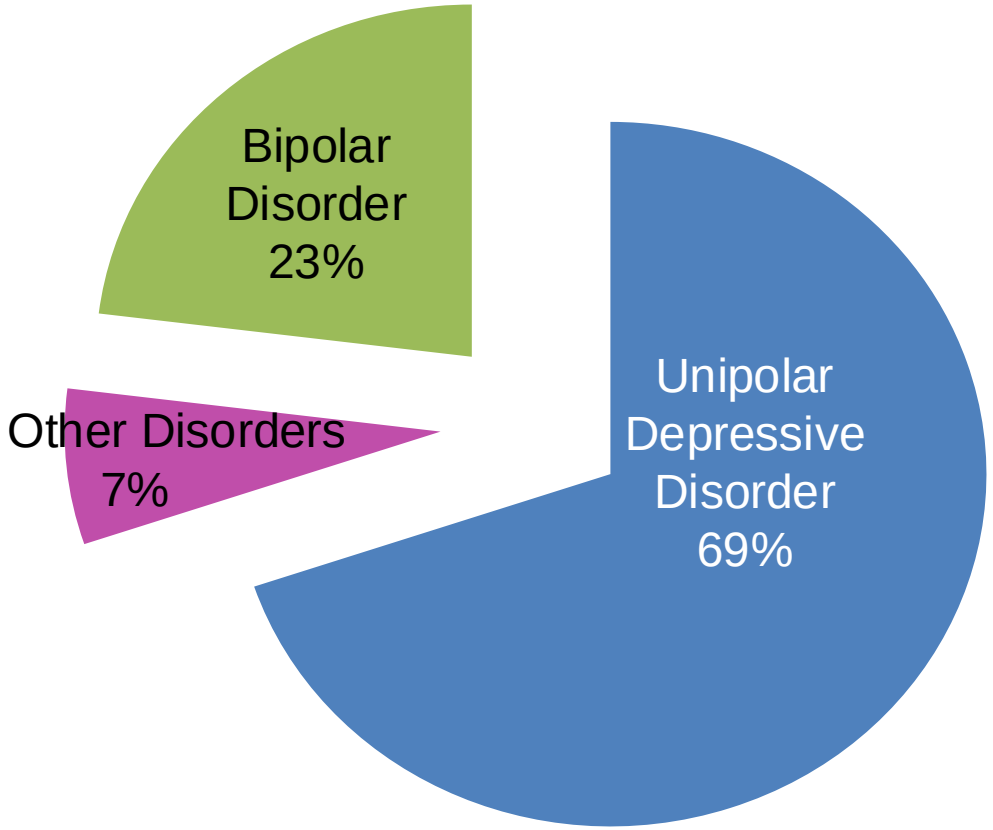


Given these recommendations and the prevalence of mental health conditions in the perinatal period, Lifeline for Moms recommend screening for depression, bipolar disorder, anxiety, and PTSD at these time points.



Wisner et al. *JAMA Psychiatry* 2013

Bipolar Disorder Needs to be Considered with a Positive Depression Screen Especially Prior to Initiating Pharmacotherapy

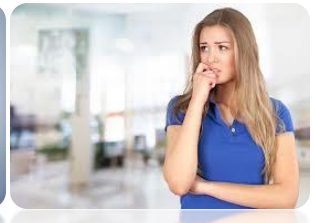


Wisner et al. JAMA Psychiatry 2013

Prescribing unopposed antidepressant can precipitate mania and increase risk of other negative outcomes

Consider the Differential Diagnosis


Depression


Anxiety


OCD


PTSD


Bipolar Disorder


Psychosis

Assess for Co-morbidities and Medical Causes

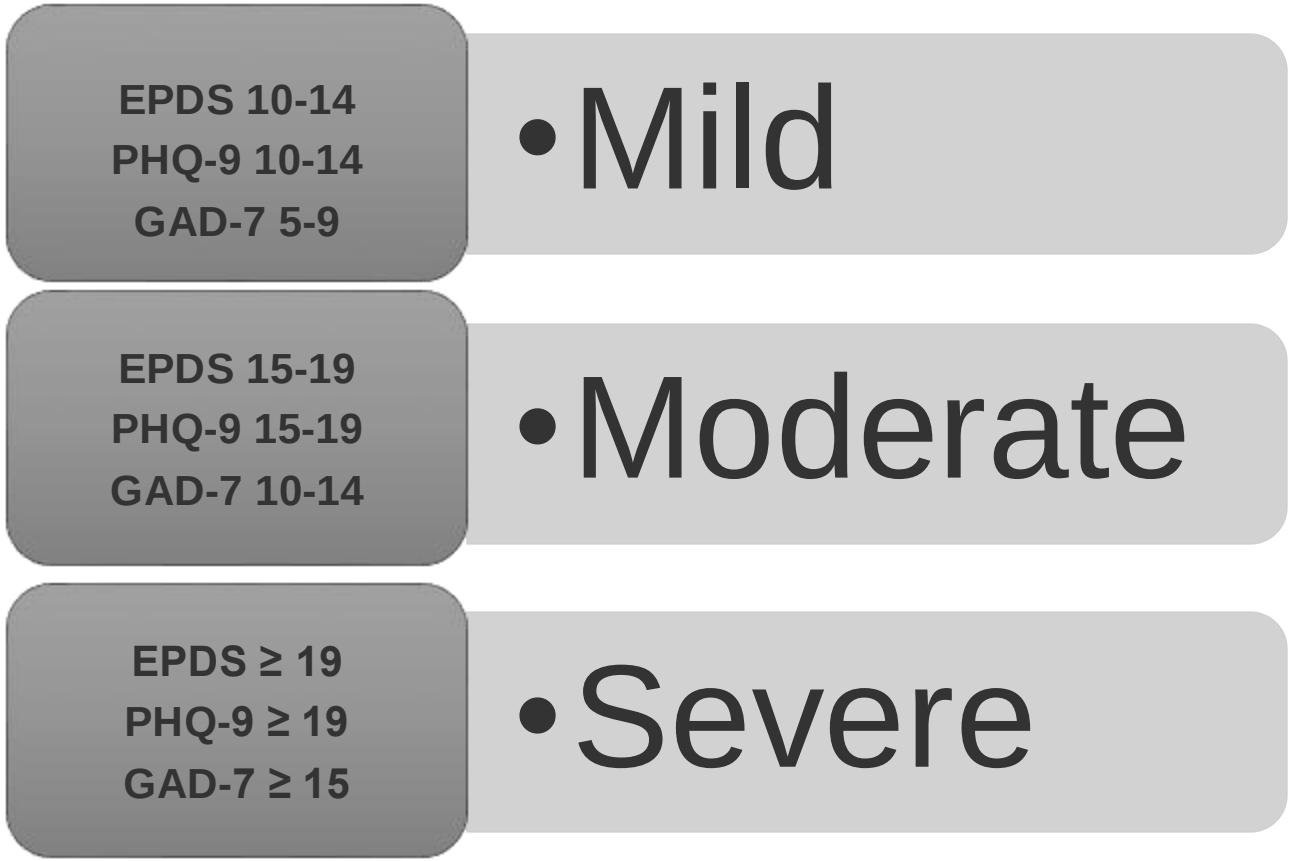
Medical causes (thyroid function, anemia

Check TSH, CBC, B12, Vitamin D, and folate

Medications

Substance use disorder (e.g. EtOH, opioids)

Score on Screeners Correlates with Illness Severity, However Further Assessment is Needed



Symptom severity directs treatment intensity

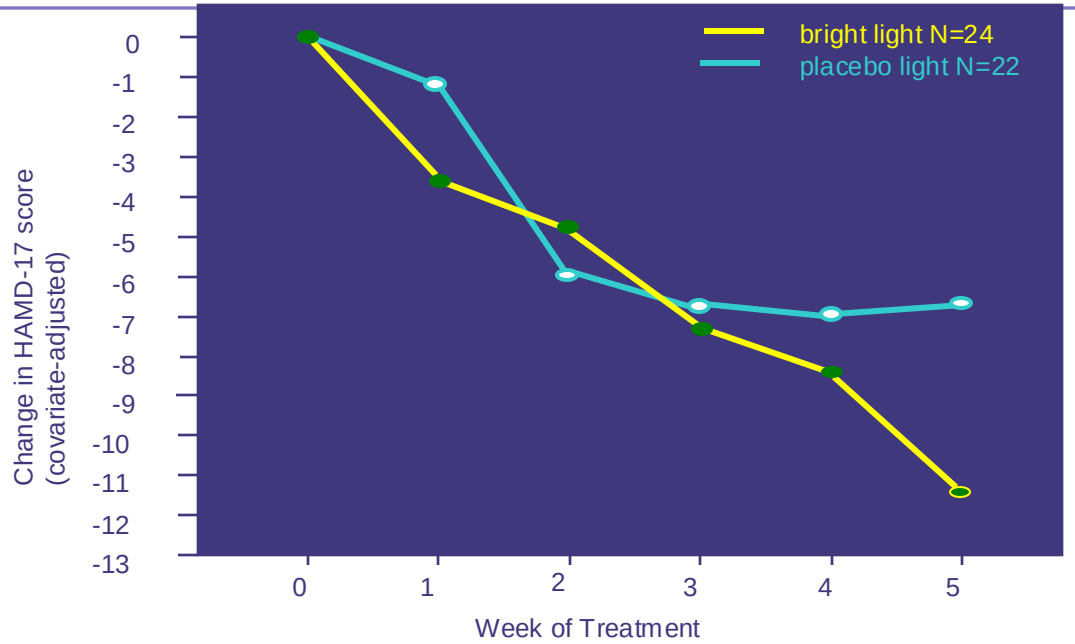
Treatment

Non-pharmacologic treatment of depression and anxiety

- Psychotherapy! CBT and IPT have strongest evidence base (moderate symptoms)

Bright AM Light Therapy in Pregnancy

www.cet.org



Wirz-Justice et al: A randomized, double-blind, placebo-controlled study of light therapy for antepartum depression. J Clin Psychiatry 2011;72(7):986-993

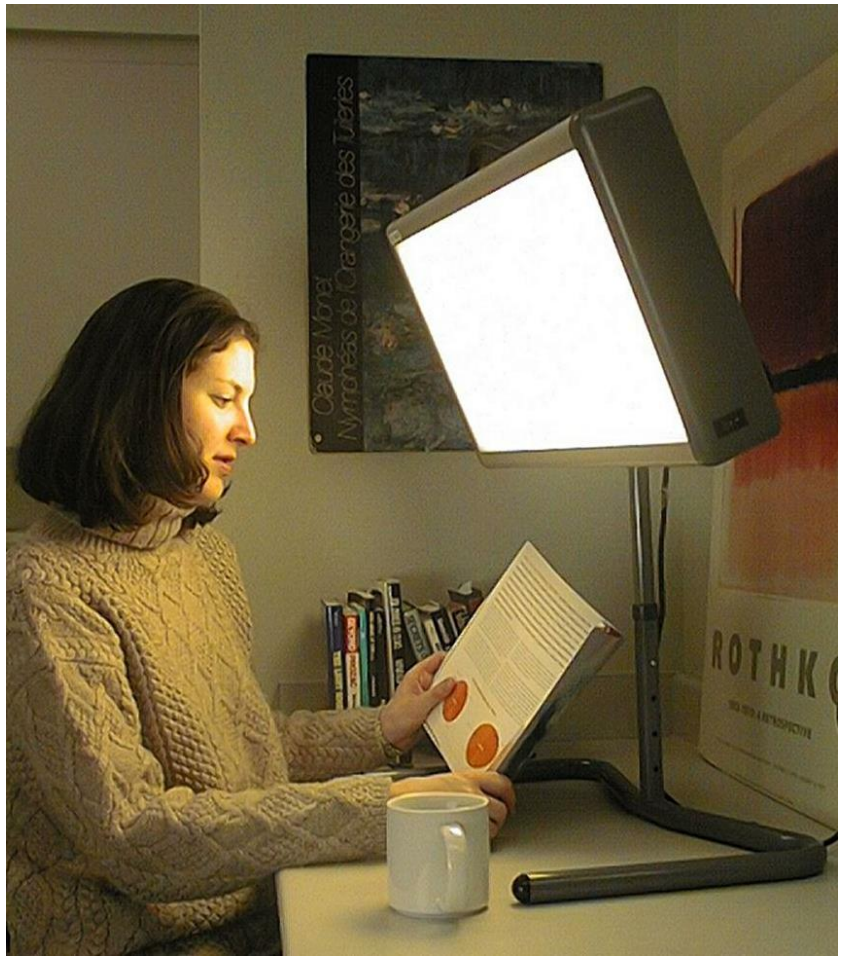
* p<.05

	Response			Remission		
	bright	placebo		bright	placebo	
HAMD 17*	13/24 (54.2%)	5/22 (22.7%)	0.029	11/24 (45.8%)	4/22 (18.2%)	0.045
SIGHADS 29*	12/24 (50.0%)	4/22 (18.2%)	0.024	5/24 (20.8%)	2/22 (9.1%)	0.245

*Bolded values depict the response and remission rates for randomized women; N=24 bright white and N=22 dim red LT

Bright Morning Light Therapy

- Bright Morning Light Therapy, 10,000 lux commercial UV blocked box; pregnancy-- *Epperson et al. J Clin Psych 65:421-425, 2004; Oren DA et al.* Am J Psych *159:666-669, 2002.*
- Data support efficacy in non-seasonal depression
- Non-pharmacologic augmentation strategy
- Lam, *JAMA Psychiatry.* 2016;73(1):56-63.

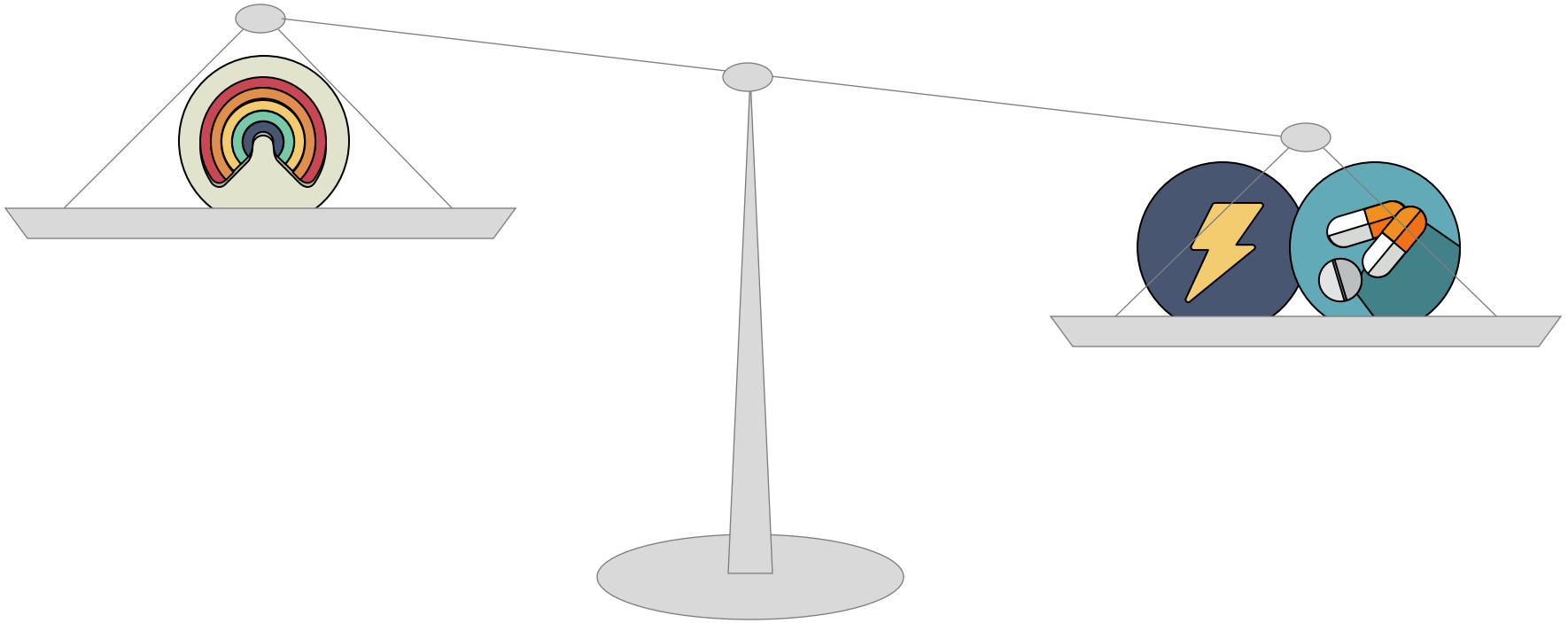


ACOG recommends that obstetricians* be prepared to **counsel patients** on the benefits and risks of psychopharmacotherapy for perinatal mental health conditions

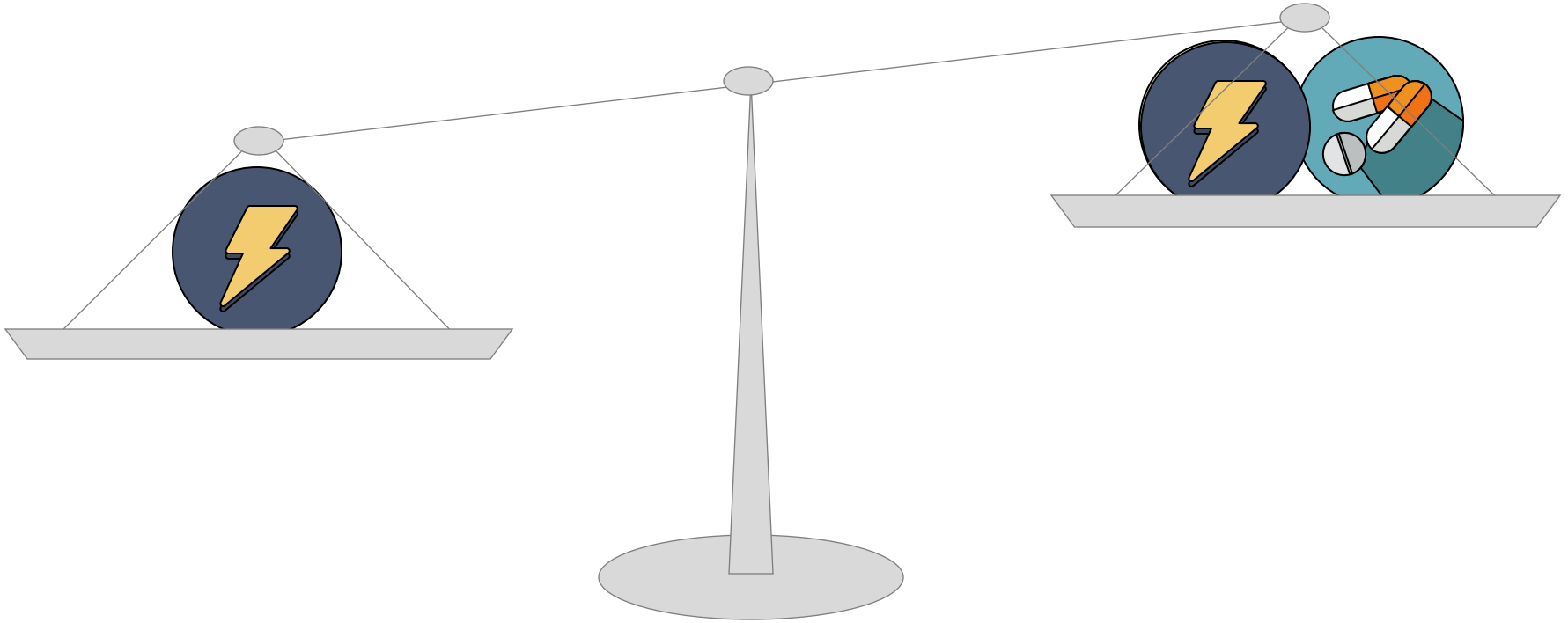
…and **initiate psychopharmacotherapy** for perinatal depression or anxiety disorders.

*and other obstetric care clinicians

COUNSELING FRAMEWORK



COUNSELING FRAMEWORK



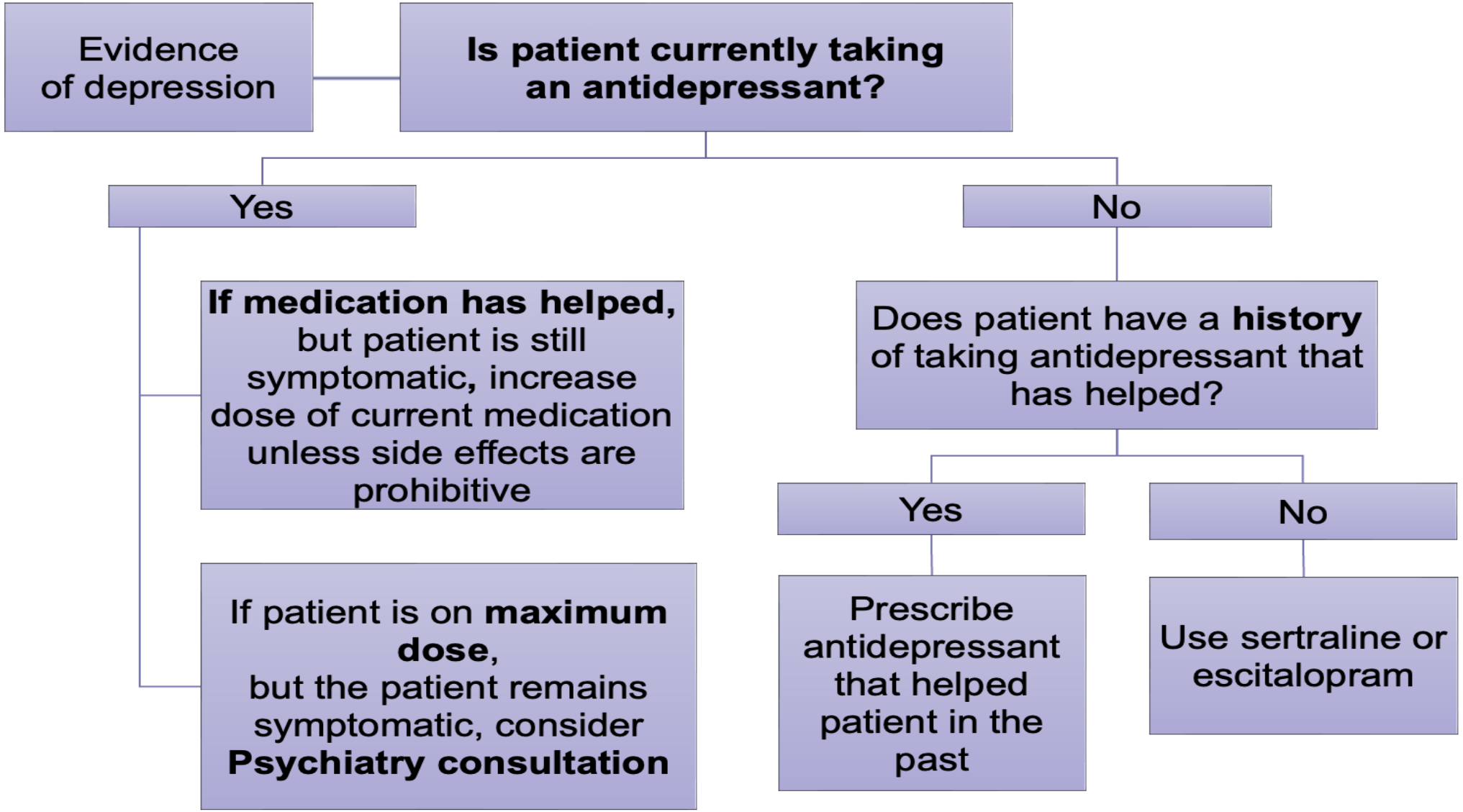
GENERAL APPROACH TO RISK COUNSELING

Untreated depression or anxiety represents an exposure

Risks of under-treatment or no treatment for depression during pregnancy include…	**Risks of antidepressant use during pregnancy include…***
Limited engagement in medical care and self-care	PPHN
Substance use	Transient neonatal adaptation syndrome
Preterm birth	Preeclampsia (SNRIs)
Low birth weight	Spontaneous abortion (SNRIs)
Preeclampsia	
Postpartum depression	
Impaired infant attachment (which carries long-term developmental effects)	
Disrupted relationship with partner	
Suicide†	

ACOG recommends that **SSRIs be used as first-line pharmacotherapy** for perinatal depression and/or anxiety. SNRIs are reasonable alternatives.

Pharmacotherapy should be **individualized** based on prior response to therapy (if applicable). If there is no pharmacotherapy history, **sertraline** or **escitalopram** are reasonable first-line medications.


Evidence of depression
Is patient currently taking an antidepressant?
Yes
No
If medication has helped, but patient is still symptomatic, increase dose of current medication unless side effects are prohibitive
If patient is on maximum dose, but the patient remains symptomatic, consider Psychiatry consultation
Does patient have a history of taking antidepressant that has helped?
Yes
No
Prescribe antidepressant that helped patient in the past
Use sertraline or escitalopram

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** **Strongly consider using first or second line medicine that has worked in past**
*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*	
*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

If no/minimal clinical improvements after 4-8 weeks

1. If patient has no or minimal side effects, increase dose
2. If patient has side effects, switch to a different med

If you have any questions or need consultation, contact MCPAP for Moms at 855-Mom-MCPAP (855-666-6272)

If clinical improvement and no/minimal side effects

Reevaluate every month and at postpartum visit. Refer back to patient's provider and/or clinical support staff for psychiatric care once OB care is complete. Contact MCPAP for Moms if it is difficult to coordinate ongoing psychiatric care. Continue to engage woman in psychotherapy, support groups and other non-medication treatments.

Educate Patient: Within first few doses, if she has marked increase in anxiety, becomes agitated, or feels energized, stop the medication and contact obstetric clinician.

*Common side effects of SSRI include: nausea, dry mouth, insomnia, diarrhea, headache, dizziness, agitation, sexual problems, and drowsiness

ACOG recommends that a validated screening tool be used to monitor for response to treatment.

If clinically indicated, the pharmacotherapy dosage should be up-titrated, with the goal of remission of depressive and anxiety symptoms.

ACOG **recommends against withholding or discontinuing medications** for mental health conditions due to pregnancy or lactation status alone.

ACOG recommends **consideration of zuranolone (brexanolone) administration** in the postpartum period for moderate-to-severe perinatal depression with onset in the third trimester or within 4 weeks postpartum.

Zuranolone for the Treatment of Postpartum Depression

Kristina M. Deligiannidis, M.D., Samantha Meltzer-Brody, M.D., M.P.H., Bassem Maximos, M.D., E. Quinn Peeper, M.D., Marlene Freeman, M.D., Robert Lasser, M.D., M.B.A., Amy Bullock, Ph.D., Mona Kotecha, M.D., Sigui Li, M.S., Fiona Forrestal, M.Sc., Nilanjana Rana, M.B.B.S., Manny Garcia, M.D., Bridgette Leclair, Pharm.D., James Doherty, Ph.D.

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]

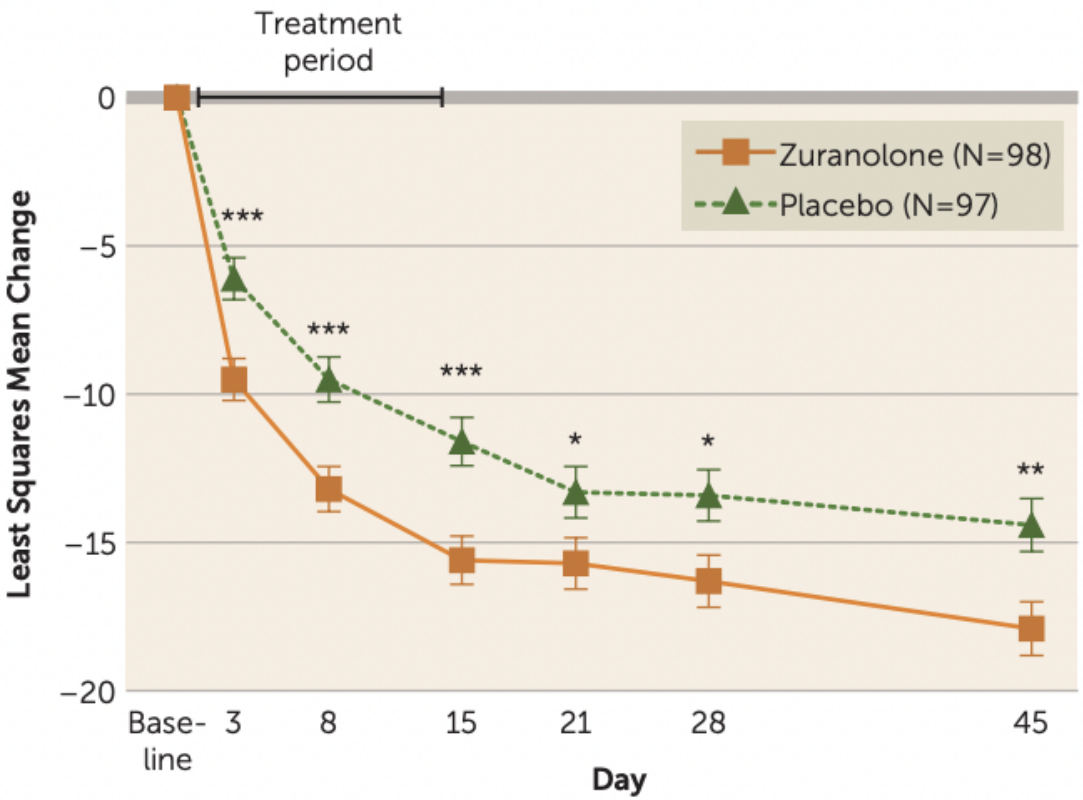
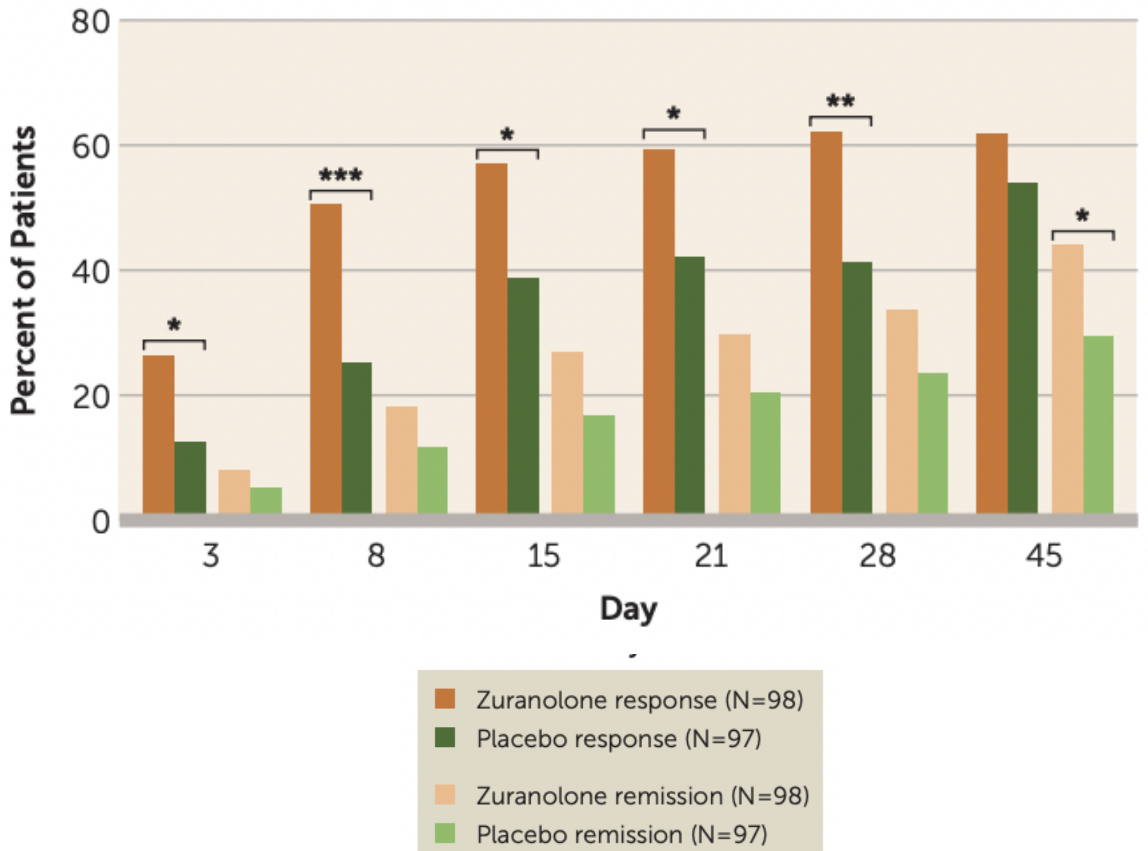


FIGURE 3. HAM-D response and remission (full analysis set) in a trial of zuranolone 50 mg/day for postpartum depression[a]



Zuranolone for the Treatment of Postpartum Depression

Practice Advisory | **August 2023**

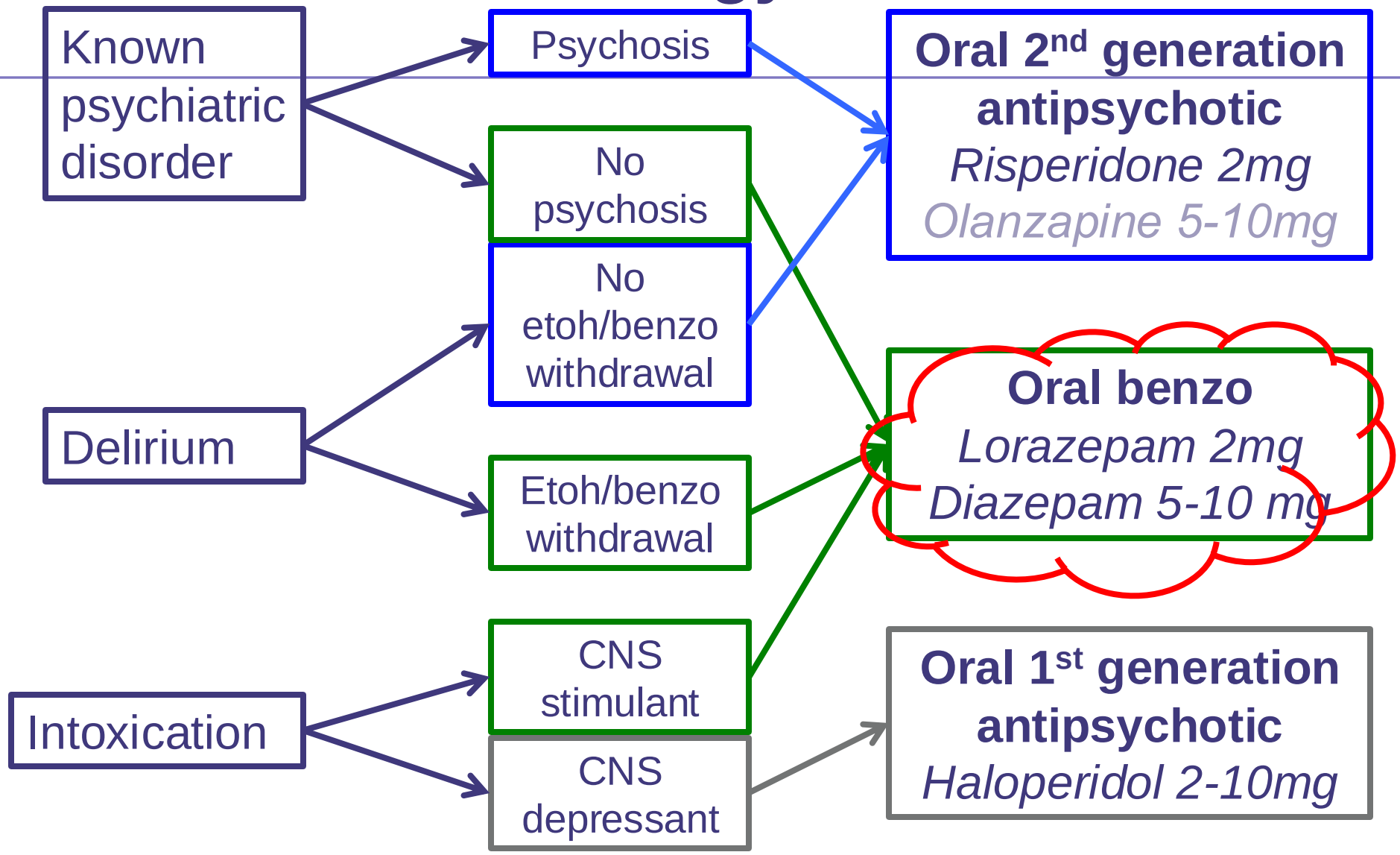
- Zuranolone (Zurzuvae)
- 14 day po course, qHS
- Improved remission at day(s):
  - 15 (31.4% vs 23.4%)
  - 45 (42% vs 30%)

Considerations for zuranolone therapy:

- The daily recommended dose of zuranolone is generally 50 mg. It is taken in the evening with a fatty meal (eg, 400 to 1,000 calories, 25% to 50% fat), for 14 days. Dosage may be reduced to 40 mg if central nervous system (CNS) depressant effects occur. In the case of severe hepatic or moderate to severe renal impairment, dosing should be initiated at 30 mg. Dose adjustments will also be needed if patients are taking medications that are strong CYP3A4 inhibitors and concomitant use with CYP3A4 inducers should be avoided.*
- If an evening dose is missed, take the next dose at the regular time the following evening; do not take extra doses on the same day. Complete 14 days of treatment total.
- Zuranolone can be used alone or as an adjunct to other oral antidepressant therapy like SSRIs and SNRIs.
- Patients should use effective contraception during the 14-day treatment course and for 1-week after the final dose. Zuranolone may cause fetal harm [2]. If pregnancy does occur, there is a registry.**
- Patients should be warned and given precautions about adverse reactions including:
  - Impaired ability to drive or engage in other potentially hazardous activities,
  - CNS depressant effects including somnolence and confusion, and
  - Increased suicidal thoughts and behaviors.
- Patients should not drive or engage in activities requiring complete mental alertness until at least 12 hours after each dose for the duration of the full treatment course. Patients may not be able to accurately assess their own degree of impairment during the treatment cycle.
- Other CNS depressing substances should be avoided (eg, alcohol, benzodiazepines, opioids, tricyclic antidepressants). If unable to avoid, a dose reduction may be necessary.
- The most common side effects include dizziness, fatigue, drowsiness, diarrhea, common cold-like symptoms, and urinary tract infections.
- Zuranolone passes into breast milk, although with a RID lower than that of SSRIs. There are no data on effects on a breastfed infant and limited data on milk production. The patient's clinical need for zuranolone and the developmental and health benefits of breastfeeding should be balanced through a shared decision-making process that considers continuation, pumping and discarding milk through 1-week past treatment completion, and cessation.

Psychiatric Emergencies

Medications for Agitation Depend on Etiology



Wilson 2012 (22451918)

Postpartum Psychosis

- 1-2/1000 women (0.1-0.2%)
- **>70% bipolar disorder**
- Of those who have a subsequent pregnancy, up to 90% at risk for another episode
- >50% will have another psychotic episode in their lifetime
- Onset usually < 1 month PP
  - PP day 3-7, peaks at 2 weeks PP
- Mood symptoms, psychotic symptoms & disorientation
- R/o medical causes of delirium
- Psychiatric emergency & most severe perinatal psychiatric d/o
- 5% suicide risk and 4% infanticide risk

afshakhan92ppd.yolasite.com

Because bipolar disorder is associated with an increased risk of psychosis, suicide, and infanticide or homicide, consider consulting a mental health professional, including those available through Perinatal Psychiatry Access Programs for assessment, management, and treatment guidance.

ACOG recommends clinicians provide immediate medical attention for postpartum psychosis

Treatment of Psychosis and Mania in the Postpartum Period

Veerle Bergink, M.D., Ph.D., Karin M. Burgerhout, M.D., Kathelijne M. Koorengevel, M.D., Ph.D., Astrid M. Kamperman, M.Sc., Ph.D., Witte J. Hoogendijk, M.D., Ph.D., Mijke P. Lambregtse-van den Berg, M.D., Ph.D., Steven A. Kushner, M.D., Ph.D.

- Nonpharmacological treatment:
  - all women received interventions to optimize mother-baby interaction (feedback from nursing, video-interaction guidance, baby massage).

- Pharmacologic INPATIENT treatment algorithm (the Netherlands):
  1. **Lorazepam** at bedtime for **3 days**
  2. Antipsychotic medication added on **day 4**
     - **Haloperidol** 2-6mg/day.
     - Atypical antipsychotic otherwise (or if previously treated with this)
  3. After 2 weeks, lithium recommended if no significant clinical response (target lithium plasma level of 0.8-1.2mmol/L)
  4. After 12 weeks on above if no response, ECT with all medications tapered to zero before ECT.
  5. Once symptoms remitted, lorazepam tapered out of regimen and other medications continued **until at least 9 months PP**
     - If antipsychotic + lithium, antipsychotic also tapered.

AJP February 2015, Luykx AJP 2019

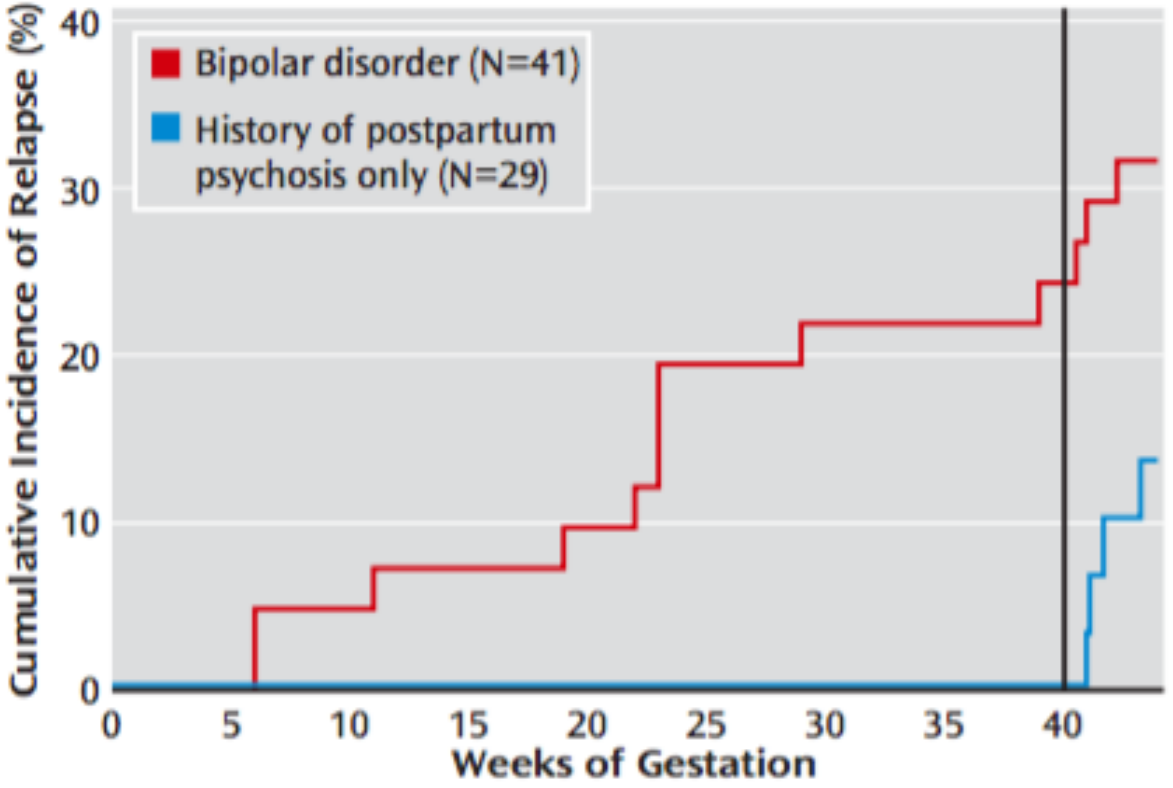
Postpartum Psychosis- Treatment

- Requires immediate hospitalization
  - Medications can include:
    - Antipsychotics
      - Immediate with haloperidol, olanzapine IM
      - Treatment with atypical anti-psychotics vs typical antipsychotics
    - Mood stabilizers
      - Lithium
    - Benzodiazepines
      - For immediate treatment consider lorazepam
  - Additional options for treatment
    - ECT
  - Until you are able to have the patient on a psychiatric floor, patient should have a sitter at all times

Rai 2015 (26330638)

Bipolar d/o in pregnancy & PPP

FIGURE 2. Cumulative Incidence of Relapse During Pregnancy and the Postpartum Period in Women With Bipolar Disorder or a History of Postpartum Psychosis Only



Most common medications:

Lamotrigine (200mg +/- qD)
Lithium (dose based on blood levels)

Other combos of atypical antipsychotics and SRIs/SNRI

Bergink V et al. Prevention of Postpartum Psychosis and Mania in Women at High Risk. AJP 2012

Postpartum OCD

- Postpartum OCD is thought to occur in approximately 1-5% of all postpartum mothers.
- Pregnant and postpartum women are more likely to experience OCD compared to the general population.
- Risk factors include:
  - a personal history of anxiety disorders and/or OCD
  - personal history of depression
- The onset of symptoms may occur rapidly, within a week of delivery.

Postpartum OCD- Treatment

- Psychotherapy
  - Exposure therapy (CBT)
- Medication
  - SSRI is considered first-line
    - Important to remember, many times treatment of anxiety/OCD will require higher dosing

Postpartum OCD

Examples of obsessions include:

- Intrusive thoughts of stabbing, throwing, or suffocating the newborn
- Disturbing images of sexually abusing the newborn
- Fear of causing harm to the newborn via exposure to germs
- Fear of newborn dying suddenly

Examples of compulsions include:

- Avoiding areas with sharp objects such as knives or scissors
- Avoiding changing diapers or bathing the newborn
- Avoiding normal activities, leaving home, letting others touch baby
- Repeatedly checking on newborn to make sure he/she is alive

Intrusive Thoughts:

Thoughts of Harming the Baby are Not Always a Psychiatric Emergency

OCD/Anxiety/Depression	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

Psych medications during lactation

Clozapine (M/P 2.8)

Lithium (15%)

Aripiprazole (1-8%)

Carbamazepine (M/P 0.6)

Clonazepam (M/P 0.3)

Olanzapine (1.6%)

Risperidone (3.6%)

Quetiapine (<1%)

Haloperidol?

paroxetine

fluoxetine

sertraline

Temazepam (lowest)

Lorazepam

Alprazolam (when < 3mg qD)

Uguz 2016 (27028982); Uguz 2016 (27297617); Kronenfeld 2017 (28714610)

ACOG recommends that, when someone answers a self-harm or suicide question affirmatively, clinicians immediately assess for likelihood, acuity, and severity of risk of suicide attempt, and then arrange for risk-tailored management

Maternal Suicide

- Suicide and overdose or poisoning are the most common causes of pregnancy-associated maternal mortality as determined by maternal mortality review committees (MMRCs)

- Additionally, the Centers for Disease Control and Prevention (CDC) in collaboration with state MMRCs have determined all maternal mortality secondary to mental health conditions to be preventable

When Using Screening Instruments for Postpartum Depression….

Always remember to review the “safety questions” on EPDS, PHQ-9

- Many times patients may be too scared or feel too guilty to verbalize thoughts of self-harm, but they may be willing to indicate it on a written screen
- It is our responsibility to always review this question and address any positive responses

EPDS

*10 The thought of harming myself has occurred to me

- ☐ Yes, quite often
- ☐ Sometimes
- ☐ Hardly ever
- ☐ Never

PHQ-9

9. Thoughts that you would be better off dead, or of hurting yourself

0	1	2	3

Suicidal ideation screening

- PHQ9
  - “Nearly every day” on the ninth question correlates with future self-harm (0.3% annual incidence
- Columbia Suicide Severity Scale (short)
  - Over the past 2 weeks, have you wished you were dead or wished you could go to sleep and not wake up?
  - Over the past 2 weeks, have you thoughts of killing yourself?

Simpson 2013 (24036589)

This screener should be administered by the obstetric care clinician.

A. DETECTION (PRIMARY SCREENING)

Ask the following questions exactly as worded. If collateral information indicates ideation or attempt, document a “yes”.

1. In the past two weeks, have you felt down, depressed, or hopeless? *(Not necessary to ask if PHQ9 was already administered – score it based on PHQ9 Item 2 response. 0=No, >0=Yes)*

☐ Yes ☐ No ☐ Patient unable to complete ☐ Patient refused

2. In the past two weeks, have you had thoughts of killing yourself? *

☐ **Yes** ☐ No ☐ Patient unable to complete ☐ Patient refused

3. In your lifetime, have you ever attempted to kill yourself? *

☐ Yes ☐ No ☐ Patient unable to complete **3a. If yes, when did this happen?** ☐ Patient refused

☐ Within past 24 hours (including today) ☐ Within last month (but not today) ☐ Between 1 and 6 months ago

☐ More than 6 months ago ☐ Patient unable to complete ☐ Patient refused

B. DETECTION RESULT

“Yes” to Item 2 (ideation) OR “Within past 24 hours”, “Within last month” or “Between 1 and 6 months ago” to Item 3a = ϒ Positive screen -> Proceed to C. Stratification

C. STRATIFICATION (SECONDARY SCREENING)

Assess the following six indicators using all data available to you, including patient self-report, collateral information, medical record review, and current observations.

	Yes	No	Unable to complete
4. Did the patient screen positive on BOTH active ideation AND a past suicide a past suicide attempt	1	0	
5. Has the individual begun a suicide plan? *“Have you been thinking about how you might kill yourself?”*	1	0	
6. Has the individual recently had intent to act on his/her ideation? *Do you think you might act on your thoughts?*	1	0	
7. Has the patient ever had a psychiatric hospitalization? *Have you ever been hospitalized for a mental health or substance abuse problem?*	1	0	
8. Does the patient have a pattern of excessive substance use? *Has drinking or drug abuse ever been a problem for you?*	1	0	
9. Is the patient irritable, agitated, or aggressive? *Note: This is an observation*	1	0	
Sum score (1 for each “Yes”) **Total:**			

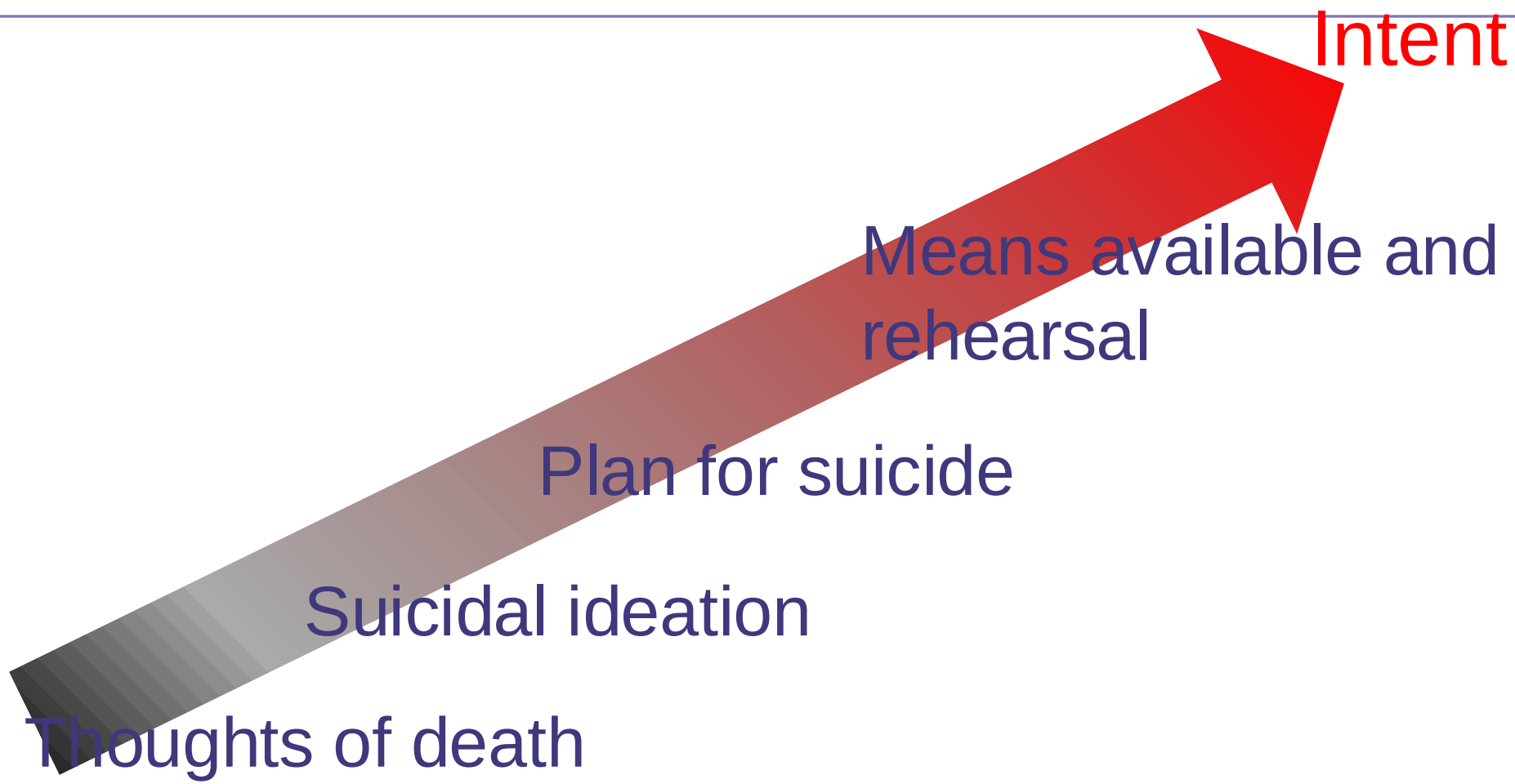
**A patient presenting with a current suicide attempt is an automatic Yes on Items 2, 3, 4, 5, and 6.*

D. STRATIFICATION RESULT

	Mild risk	Moderate risk	High risk
Score from Section C	0 – 2	3 – 4	5 – 6
Critical items		Suicide plan **or** intent (not both)	Suicide plan **and** intent
			Current attempt

Risk level based on **highest** level category endorsed **Mild** **Moderate** **High**

Inquiring about suicidal ideation



McDowell 2011 (21709131)

Evidence-based suicide risk reduction

- Treat acute symptoms
  - Intoxication, agitation, psychosis
- Complete safety planning (w/support people)
  - Triggers / Coping Skills / Contacts
- Lethal means restriction
- Provide warm hand-off to treatment
- Certain treatments based on diagnosis

Miller 2017 (28456130); Nordentoft 2017 (28760024); Woods 2002 (12072138) ; Bryan 2017 (28142085)

1. Discontinuation of antidepressants proximate to conception
2. Use of a lower dose of antidepressants during pregnancy
3. A switch to sertraline in pregnancy/PP

    **when well-controlled on something else

4. A change to a category "B" label drug
5. Discontinuation of lithium during pregnancy
6. Try supplements or alternative therapies **when well-controlled on meds prior
7. Stop breastfeeding or defer antidepressant Rx.
8. Use of non-benzo sedative-hypnotics (Ambien) instead of an occasional benzo

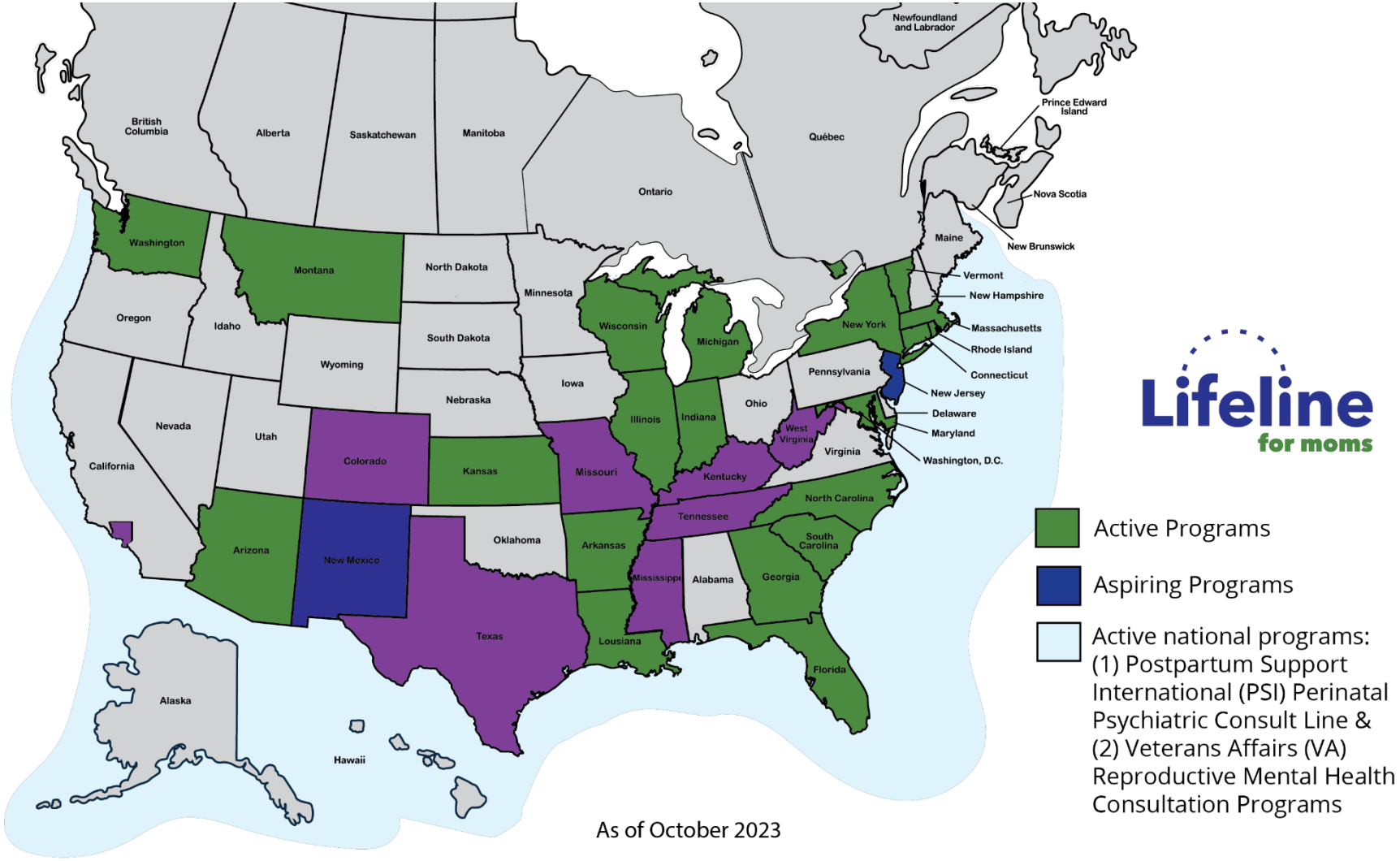
    **insomnia is common and sleep is important for mood

9. Pumping and dumping
10. Failure to bring up contraception

Conclusions

- Perinatal Mental Health is the leading cause of pregnancy-associated maternal mortality
  - Perinatal mental health conditions affect 1 in 5 pregnant and postpartum people
  - Screening is imperative in identifying those with symptoms who require further evaluation and treatment
- Obstetricians should initiate treatment and/or refer to behavioral health resources when indicated
- Screen for bipolar disorder prior to initiating antidepressant medications for depression or anxiety
- Check to see if your state has a perinatal psychiatric access program and utilize it for help in screening, evaluating, and treating mental health disorders in pregnancy and postpartum

There are now 30 state/county Perinatal Psychiatry Access Programs across the US and 2 national (PSI & VA)



RESOURCES

ACOG | Online Learning

NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

POSTPARTUM SUPPORT INTERNATIONAL
PSI

Certificate Trainings

PSI PMD 2-Day and Advanced Certificate Trainings

Trastornos del Estado de Ánimo Perinatales: Componentes de Cuidado

MMH Online Certificate Course with 2020Mom

Advanced Psychotherapy

Advanced Psychopharmacology

Psychopharmacology (2-hour) (Approved for PMH-C)

Questions?

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mental health <u>is</u> maternal health