Fight for the Family's Future:

Establishing Psychiatric Leadership in PPD Detection and Treatment

MasterClass

Supported by an educational grant from Supernus Pharmaceuticals and Biogen.

Faculty

Craig Chepke, MD, DFAPA

Adjunct Associate Professor of Psychiatry, Atrium Health

Medical Director, Excel Psychiatric Associates

Chief Medical Officer, Psych Congress

Melanie Barrett, MD, DFAPA

Board of Directors, The International Society of Reproductive Psychiatry (ISRP)

Outpatient Psychiatry at Life Stance Health; Edmond, Oklahoma

International Society of Reproductive Psychiatry

Faculty Disclosures

- **Craig Chepke, MD, DFAPA:** Advisory Board—AbbVie, Acadia, Alkermes, Axsome, Biogen, Bristol Myers Squibb, Compass Pathways, Corium, Eli Lilly, Idorsia, Intra-Cellular, Jazz, Johnson & Johnson, Lundbeck, Moderna, Neurocrine, Otsuka, Sage, Sumitomo, Takeda, Teva; Consultant—AbbVie, Acadia, Alkermes, Axsome, Biogen, BoehringerIngelheim, Bristol Myers Squibb, Cingulate, Corium, Eli Lilly, Intra-Cellular, Jazz, Johnson & Johnson, Lundbeck, MedinCell, Moderna, Neurocrine, Otsuka, Sage, Sumitomo, Supernus, Teva; Research Grant/Support—Acadia, Axsome, Harmony, Neurocrine, Teva; Speaker's Bureau—AbbVie, Acadia, Alkermes, Axsome, Bristol Myers Squibb, Corium, IntraCellular, Jazz, Johnson & Johnson, Lundbeck, Luye, Merck, Neurocrine, Otsuka, Sumitomo, Takeda, Teva
- **Melanie Barrett, MD, DFAPA**: no relevant disclosures

Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration).
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Learning Objectives

- Describe the burdens and risks associated with PPD and the role of mental health clinicians in relation to other healthcare providers across the continuum of care for affected patients and families
- Assess PPD in accordance with current diagnostic criteria and guidelines, including recommended screening tools, triage and care escalation procedures, and differentiation from PPP and BD
- Evaluate novel and investigational pharmacotherapies for PPD as well as patient-centered strategies for overcoming challenges during its treatment to ensure optimal outcomes

PPD = postpartum depression, PPP = postpartum psychosis, BD = bipolar disorder

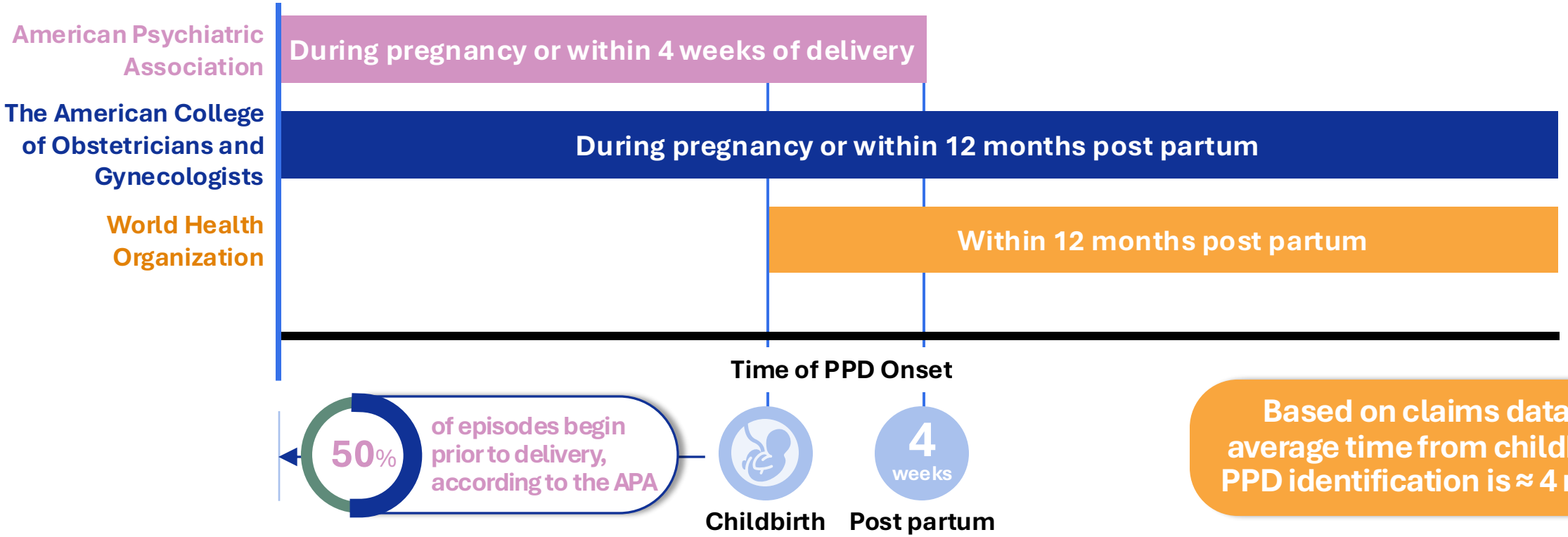
Understanding PPD

Postpartum Depression is Bluer than Just 'Baby Blues'

BABY BLUES	POSTPARTUM DEPRESSION
Onset: 2–3 days postpartum	Lasts > 2 weeks; may begin during pregnancy to up to 12 mo. postpartum
Resolves ≤ 2 weeks	Depressed mood, anhedonia
Tearful, irritable, overwhelmed	Guilt, poor bonding, sleep/appetite changes
No major impairment	Functional impairment, possible suicidal ideation

Stewart DE, Vigod SN. *Annu Rev Med*. 2019;70:183-196.

The Definition of PPD Varies Across Organizations



Based on claims data, the average time from childbirth to PPD identification is ≈ 4 months

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed; 2013. ACOG Committee Opinion No. 757. *Obstet Gynecol*. 2018;132(5):e208-e212. World Health Organization. International Classification of Diseases 11th Revision. Feb 2022.

PPD is One of the Most Common Medical Complications Associated with Childbirth

Up to 20%
of women globally experience PPD

Yet, about half (~50%)
do not receive treatment and remain undiagnosed

Who is at risk for PPD?

- Prior depression or anxiety
- History of bipolar disorder
- Limited social support, partner conflict
- Lower socioeconomic status
- Pregnancy and/or birth complications (e.g., preterm birth, NICU)

~20%
of postpartum deaths are due to suicide

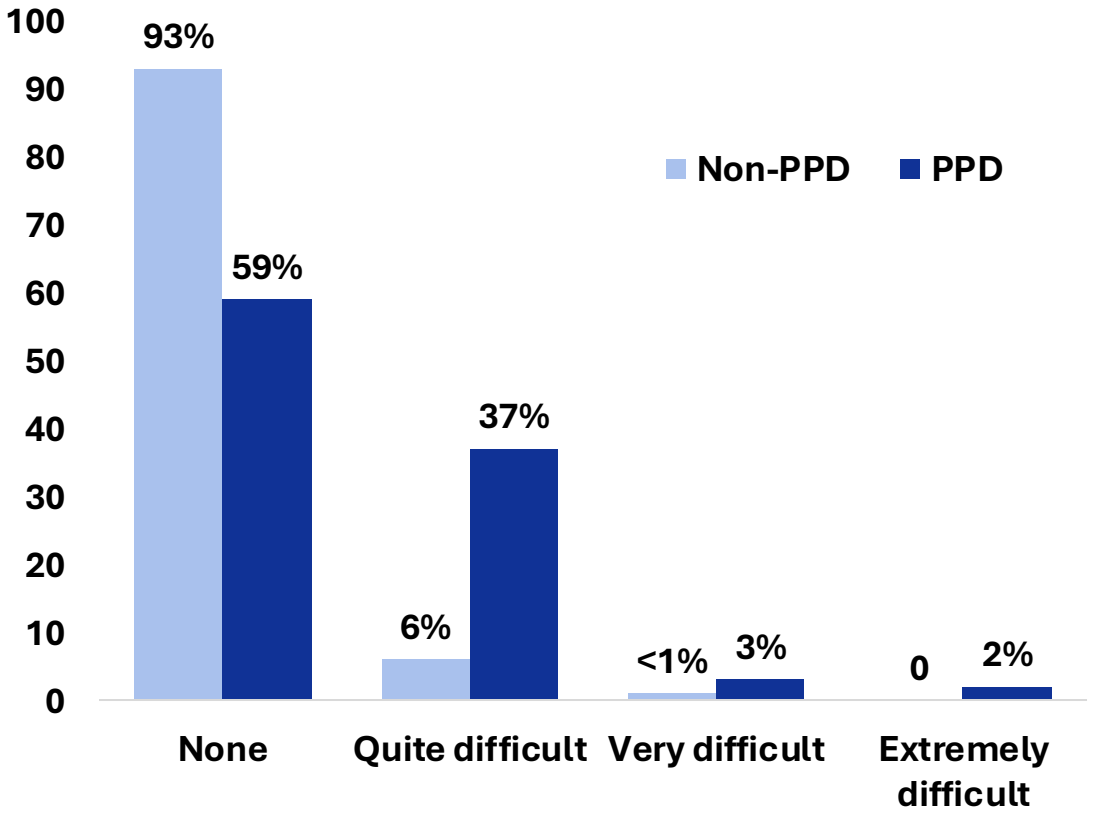
Mental health conditions are **the leading preventable cause of maternal death** in the U.S

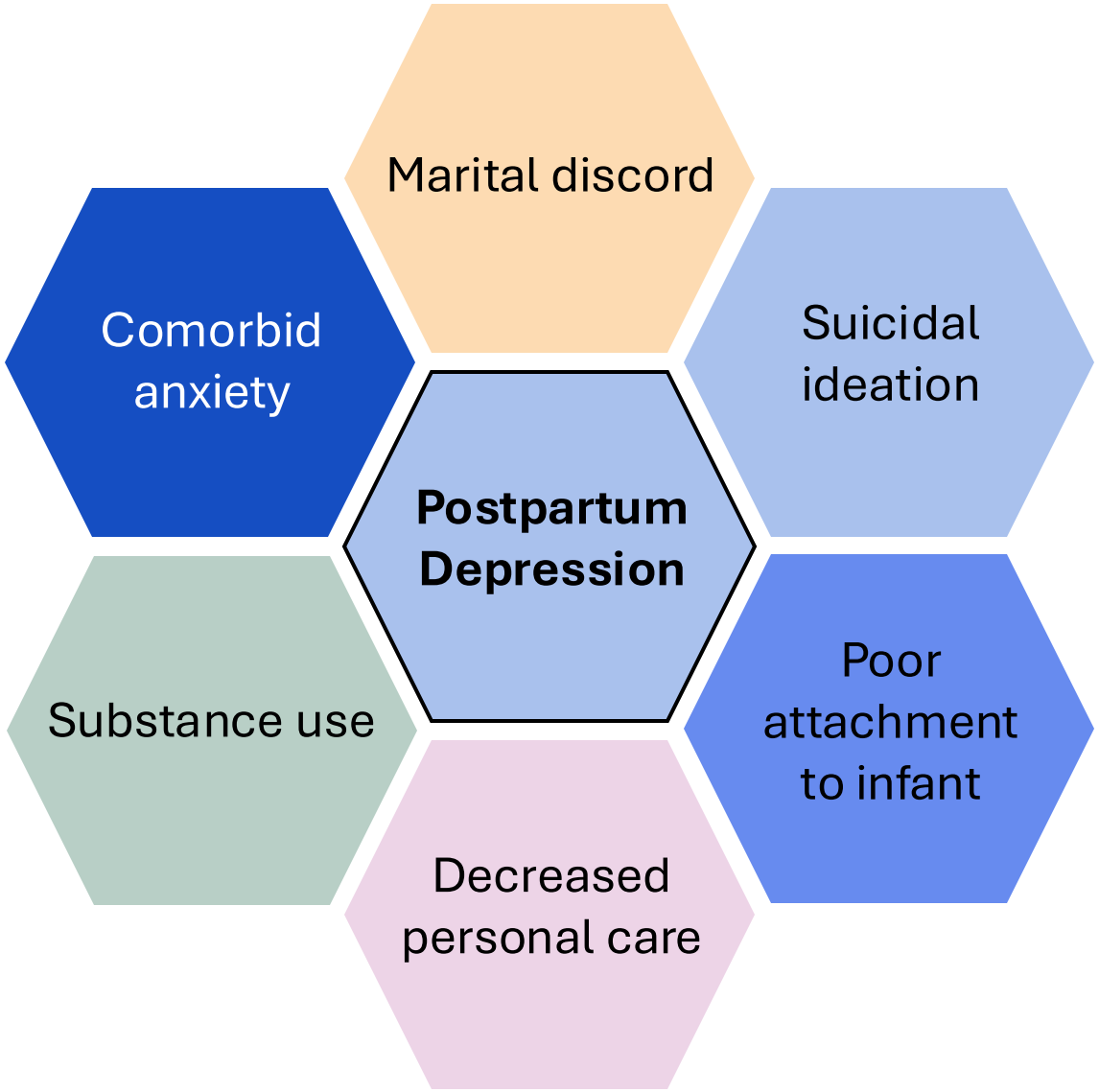
Peak suicide risk occurs around **9-12 months postpartum**

Khamidullina Z, et al. J Clin Med. 2025;14(7):2418.

Maternal Complications of PPD

Mothers with PPD report significantly higher levels of functional impairment

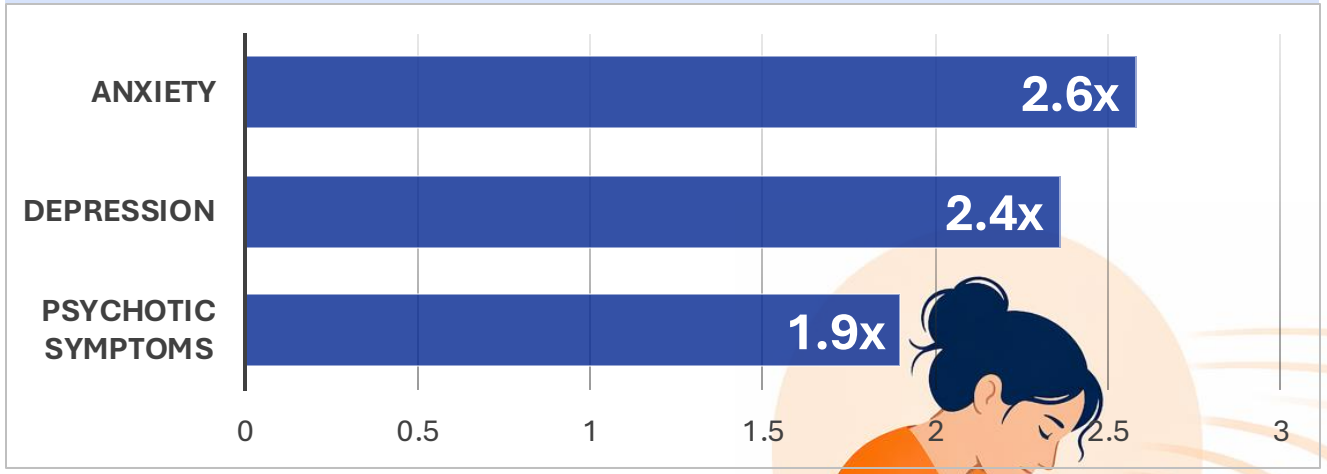


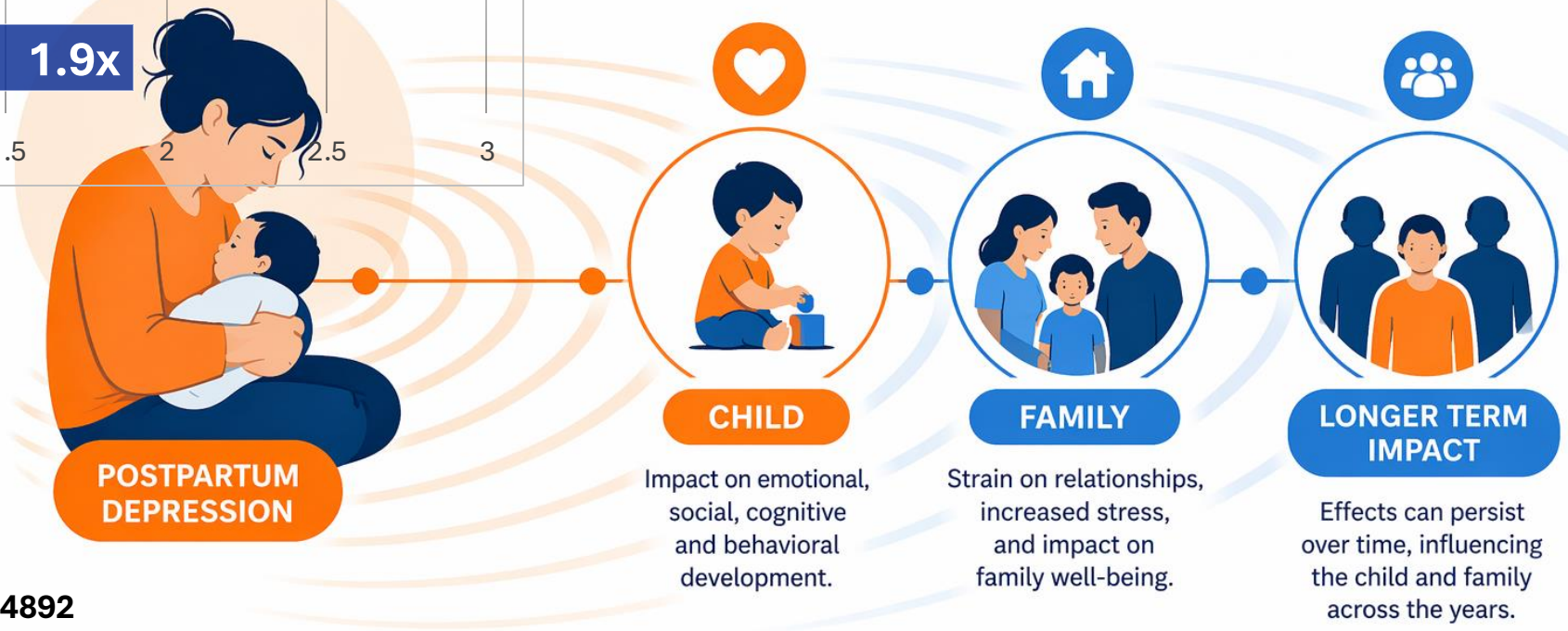


Keven MC, et al. *BMC Pregnancy Childbirth*. 2026;26(1):152.

The Ripple Effect of PPD: Offspring, Family, and Beyond

Maternal depression is associated with ~2-fold increased risk of psychiatric symptoms in their offspring





Feibel A, et al.. *JAMA Netw Open*. 2026;9(4):e264892

Identifying PPD Is A Shared Responsibility

Screening should occur across all points of care

OB/GYN

- Screen during pregnancy and postpartum
- Identify early symptoms and risk factors

PEDIATRICS

- Screen at well-child visits
- Monitor maternal functioning and well-being

WE ALL PLAY A CRITICAL ROLE

PRIMARY CARE

- Recognize ongoing or late-onset symptoms
- Reassess beyond the postpartum period

PSYCHIATRY

- **Diagnose and treat**
- **Coordinate care and support recovery**

Sit DK, Wisner KL. *Clin Obstet Gynecol*. 2009;52(3):456-468; American College of Obstetricians and Gynecologists (ACOG). *Obstet Gynecol*. 2018;131(5):e140-e150

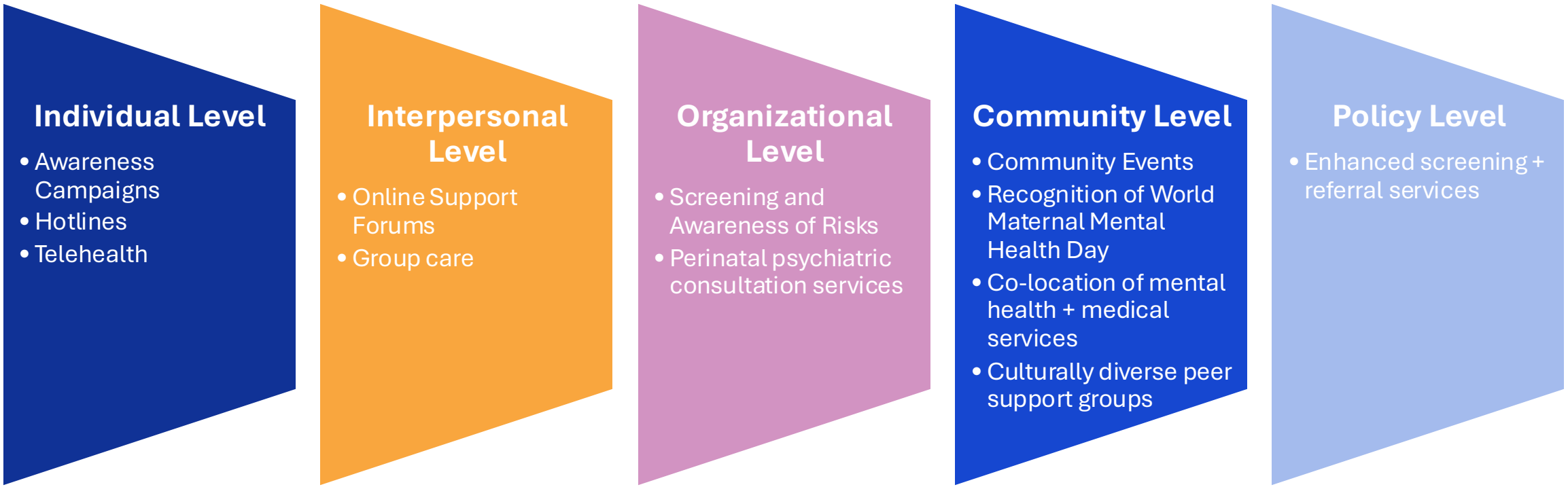
Key Learning Points

- PPD is a common, serious, and often underdiagnosed condition with symptoms that can begin during pregnancy or up to 12 months postpartum
- PPD carries substantial maternal and societal burden, including functional impairment, increased risk of suicide, and significant downstream effects on infant development and family well-being
- Early identification requires coordinated, cross-disciplinary screening and care throughout the perinatal period

Detection and Assessment of PPD

Seeking Help for Postpartum Depression

Barriers + Facilitators for Seeking Care



Place JMS, et al. *Front Glob Womens Health*. 2024 May 24;5:1335437.

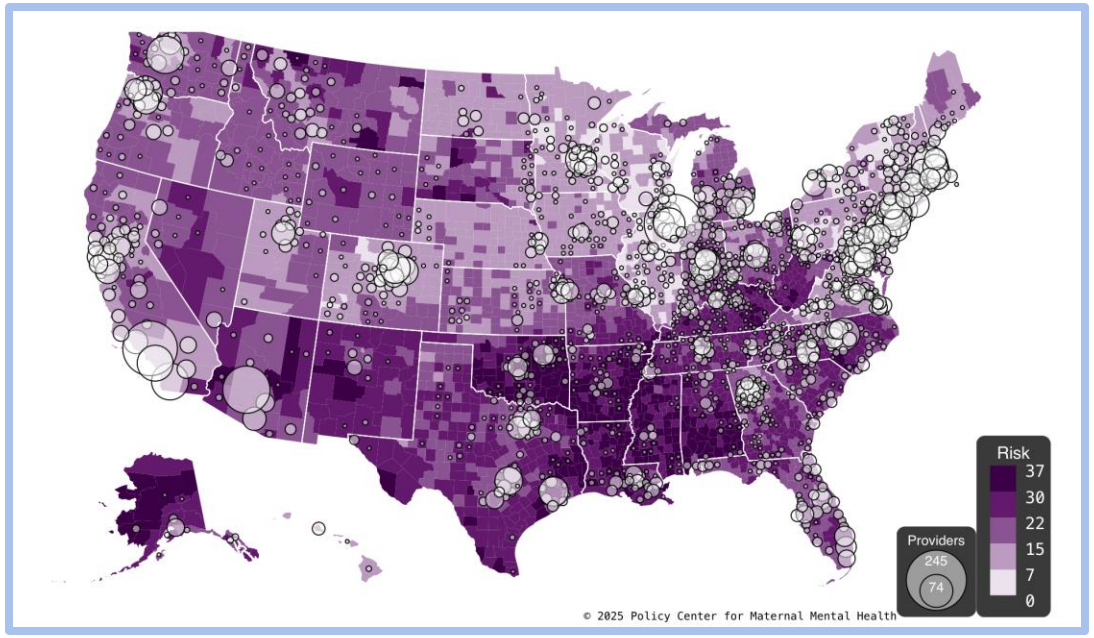
2025 U.S. Maternal Mental Health Risk and Resources by County

Policy Center For Maternal Mental Health

Counties with “severe” risk **tripled since 2023**

84%

of birthing-age women live in US maternal mental health resource shortage areas



~150 counties

are considered Maternal Mental Health “Dark Zones”

High risk + Large Resource Shortages (TX, AL, LA, OK, TN)

Policy Center for Maternal Mental Health (2025, May). 2025 U.S. Maternal Mental Health Risks and Resources by County. *https://policycentermmh.org/2025-us-maternal-mental-health-risk-and-resources/*

Diagnostic Criteria and Guidelines

DSM-5: **Major Depressive Disorder (MDD) With Peripartum Onset Specifier**

Major depressive episode that begins during pregnancy or within 4 weeks of delivery

APA's Position Statement on Screening & Treatment of Mood & Anxiety Disorders During Pregnancy and Postpartum

Assess	Educate	Screen	Educate

• All Pregnant & Postpartum Women
  • Presence of risk factors for a psychiatric disorder
	• How to recognize symptoms	• Using a validated screening tool
		• Systematic Response
			• Risks of untreated illness during pregnancy and lactation
			• Risks/benefits of treatment
			  • For mom and baby

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed., Text Revision, American Psychiatric Publishing, 2022. https://psychiatryonline.org/doi/epub/10.1176/appi.pn.2019.3b19

Edinburgh Postnatal Depression Scale (EPDS)

Validated screening tool designed to assess depressive symptoms in postpartum individuals over the previous 7 days

SCORING	
Total Score	**Indication**
0-6	None or minimal depression
7-13	Mild depression
14-19	Moderate depression
20-30	Severe depression

Any positive response to item 10 requires immediate clinical assessment for safety and suicidality ⚠

- QUESTIONS 1, 2, & 4 (without an *) are scored 0, 1, 2 or 3 with the first response bubble scored as 0 and the last response bubble scored as 3.
- QUESTIONS 3, 5, 6, 7, 8, 9, 10 (marked with an *) are reverse scored, with the first response bubble scored as a 3 and the last response bubble scored as 0

Lydsdottir LB, et al. *J Clin Psychiatry*. 2014 Apr;75(4):393-8; Cox, J.L., et al. *British Journal of Psychiatry* 150:782-786; Wisner, B. L. et al., *N Engl J Med* vol. 347, No 3, July 18, 2002, 194-199

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

***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

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

***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

***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

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

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

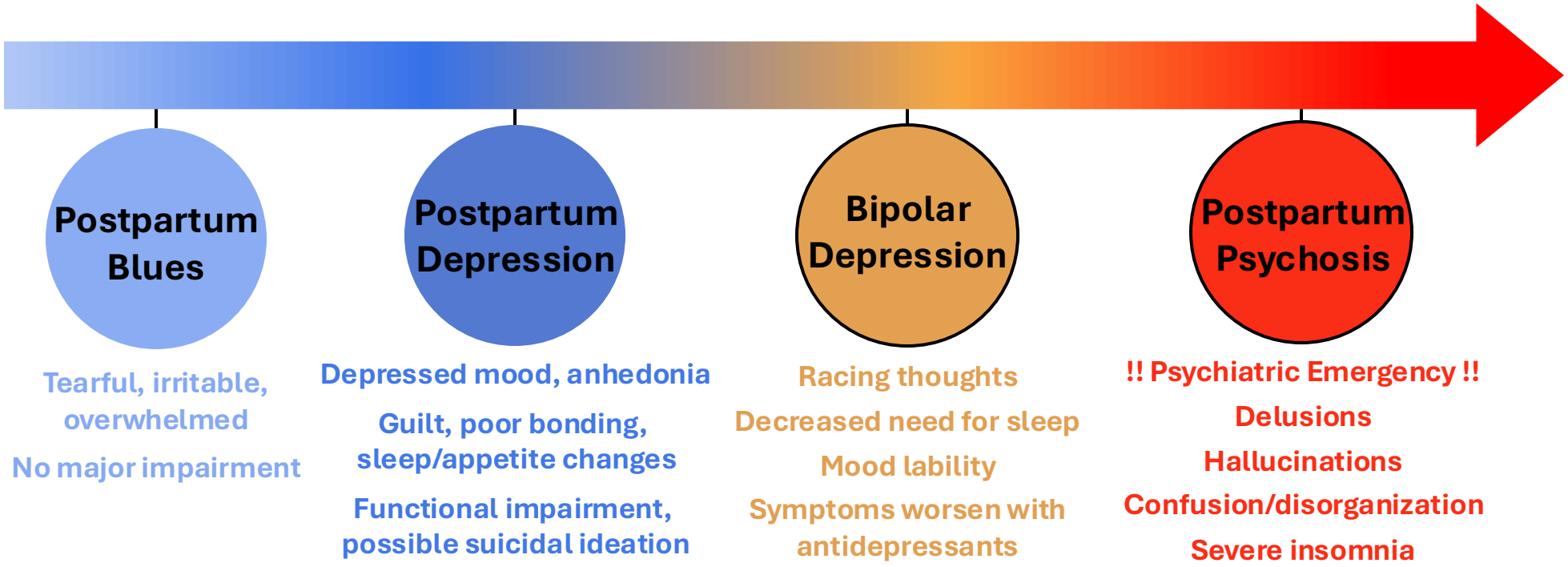
***9. I have been so unhappy that I have been crying**
- ❑ Yes, most of the time
- ❑ Yes, quite often
- ❑ Only occasionally
- ❑ No, never

***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

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

Recognizing Red Flags: When Symptoms Suggest Something More

While postpartum depression is common, certain clinical features may indicate **bipolar disorder** or **postpartum psychosis** and warrant urgent reassessment



Stewart DE, Vigod SN. *Annu Rev Med*. 2019;70:183-196; Bergink V, et al. *Biol Psychiatry*. 2026;99(9):740-747.

Screening for Bipolar Disorder

Mood Disorder Questionnaire (MDQ)

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

3. How much of a problem did any of these cause you - like being unable to work; having family, money or legal troubles; getting into arguments or fights?

☐ No problems ☐ Minor problem ☐ Moderate problem ☐ Serious problem

SCORING

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

MDQ + EPDS improved the distinction of unipolar depression from bipolar depression at the level of screening in **50%-70% of women**

MDQ = Mood Disorder Questionnaire

Clark CT, et al. Depress Anxiety. 2015 Jul;32(7):518-26; Hirschfeld RM, et al., Am J Psychiatry. 2000 Nov;157(11):1873-5.

Postpartum Psychosis (PPP) Is a Psychiatric Emergency

***Estimated incidence**: 1-2 cases per 1000 women*

Clinical Presentation

- Rapid onset (usually days to 2 weeks postpartum)
- Delusions or hallucinations
- Severe insomnia and agitation
- Confusion/disorganized behavior
- Depression, anxiety, and/or mania
- Paranoia or bizarre beliefs involving the infant

Risk Factors

- Bipolar disorder history
- Prior postpartum psychosis
- Family history of bipolar disorder
- Sleep deprivation
- Primiparity

Psychiatric Emergency

- Suicide risk
- Infanticide risk
- Rapid clinical deterioration
- Requires immediate psychiatric evaluation
- Hospitalization often necessary

Early recognition of PPP is critical to protect maternal and infant safety

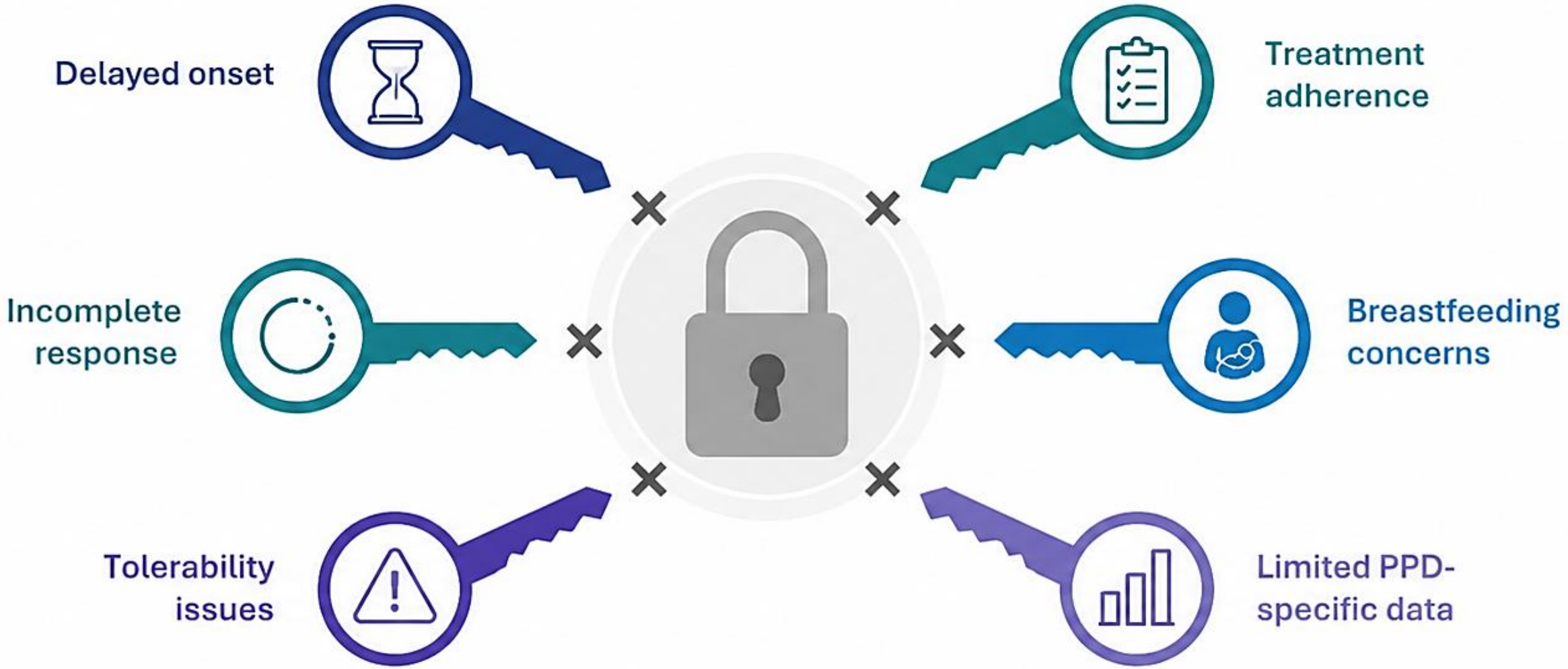
Friedman SH, et al. *Curr Psychiatry Rep*. 2023 Feb;25(2):65-72; Osborne LM. *Obstet Gynecol Clin North Am*. 2018;45(3):455-468

Key Learning Points

- Assess all pregnant and postpartum women for the presence of and risks for postpartum depression
  - *Routine screening during pregnancy and postpartum is essential for early identification of depressive and bipolar-spectrum symptoms*
- Positive screening results should prompt systematic clinical assessment, including evaluation for bipolar disorder and suicidality
  - *Screen → Diagnose*
- Postpartum psychosis is **a psychiatric emergency** requiring immediate recognition, safety assessment, and urgent psychiatric intervention

Novel and Investigational Pharmacologic Treatments for PPD

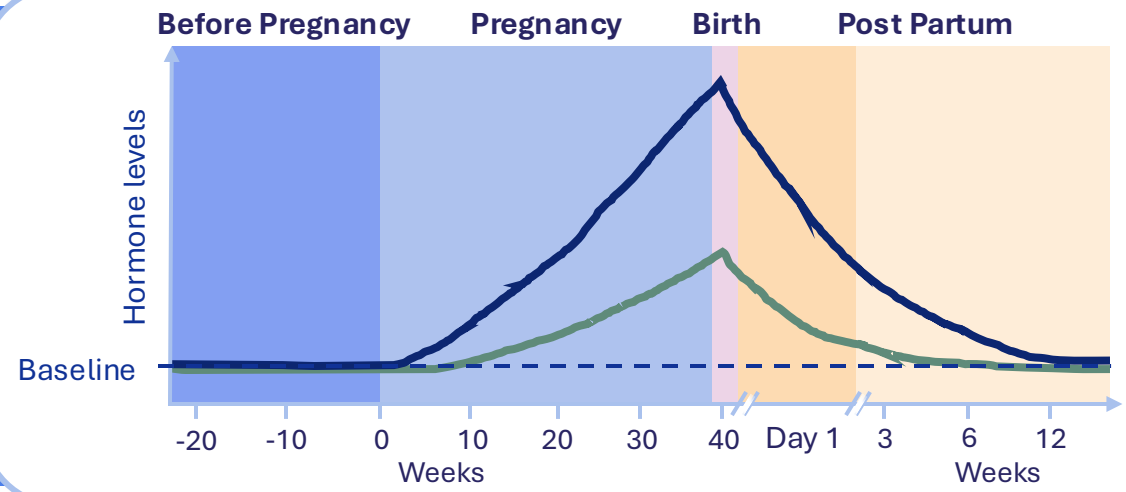
Key Unmet Needs Remain With Conventional Pharmacologic Treatments



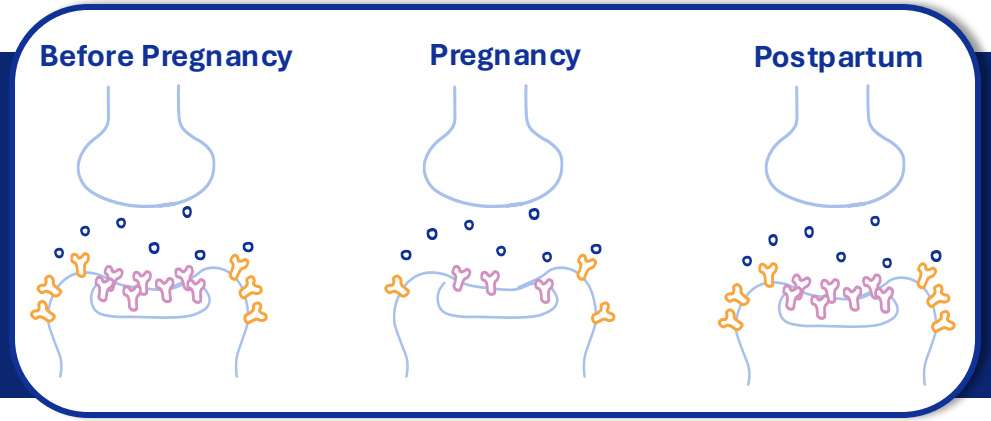
Frieder A, et al. *CNS Drugs*. 2019;33(3):265-282; Deligiannidis KM, Clayton AH. *J Clin Psychiatry*. 2023;84(Suppl 1):SG22045SU1C.

Perinatal Changes in Allopregnanolone May Disrupt GABA Signaling, and Potentially Lead to PPD

Fluctuating levels of **allopregnanolone**, a metabolite of progesterone, during the perinatal period...

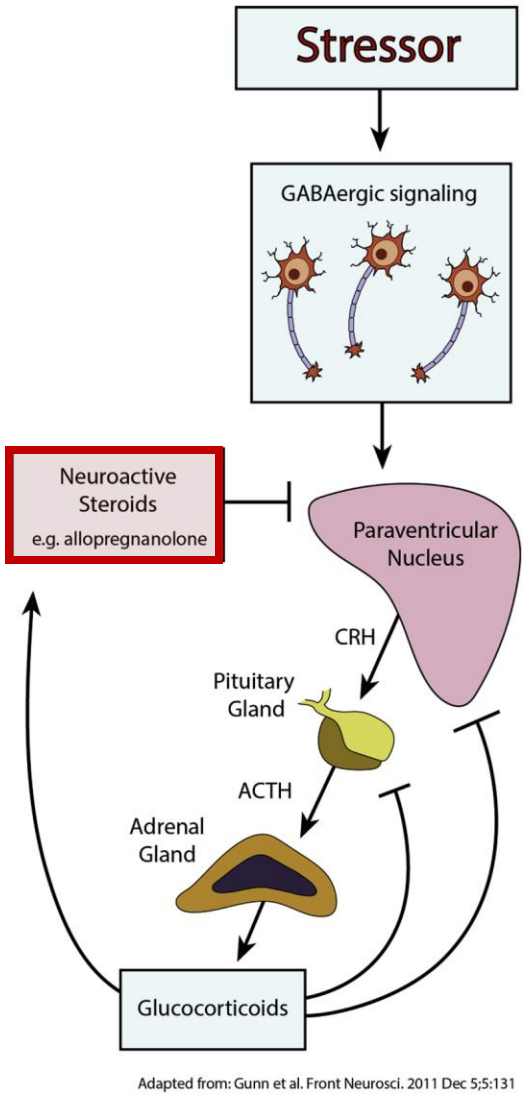


...may alter $GABA_AR$ expression and GABAergic signaling, **resulting in reduced inhibitory signaling, which may contribute to depression**



GABA = gamma-aminobutyric acid; $GABA_AR$ = GABA type A receptor.
Figure adapted from Meltzer-Brody S, Kanes SJ. Neurobiol Stress. 2020;12:100212.

Neuroactive Steroids Play An Active Role In Stress Circuitry



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

DURING PREGNANCY

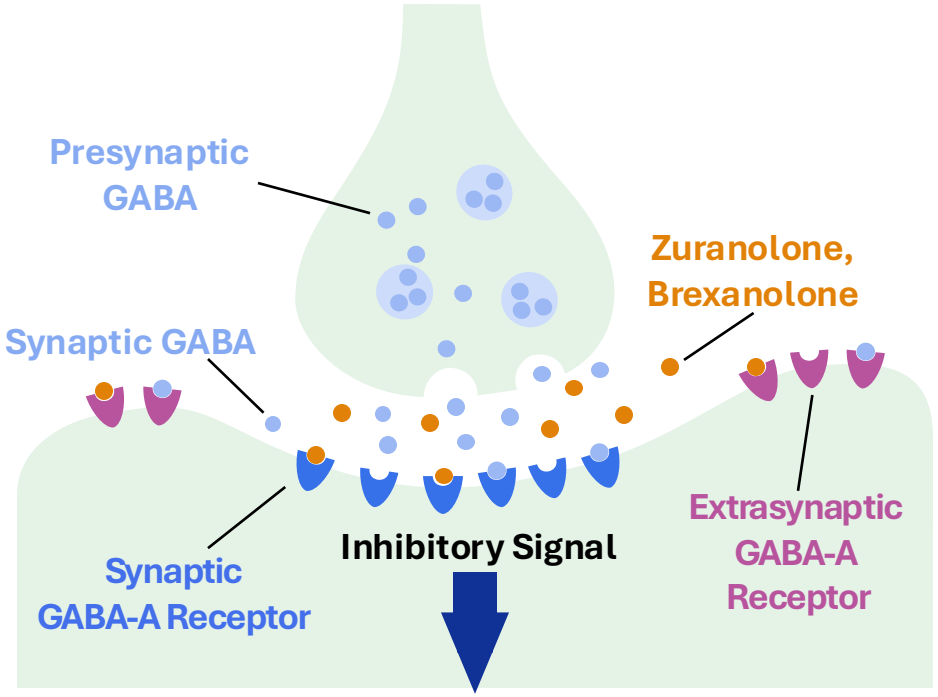
- High neuroactive steroid levels
- Enhanced GABAergic signaling
- Increased inhibitory tone on stress circuitry
- Stable HPA regulation

AFTER DELIVERY

- Sharp decline in neuroactive steroid levels
- Disrupted GABAergic signaling
- Reduced inhibitory tone on stress circuitry
- Dysregulated HPA activity
- **Increased vulnerability to mood symptoms, including PPD**

Deligiannidis KM, Clayton AH. *J Clin Psychiatry*. 2023;84(Suppl 1):SG22045SU1C.

Brexanolone/Zuranolone May Treat PPD by Modulation of Synaptic and Extrasynaptic GABA-A Receptors



Synaptic GABA-A Receptors

- Mediate **phasic inhibition** (rapid, transient)
- Primary target of benzodiazepines

Extrasynaptic GABA-A receptors

- Mediate **tonic inhibition** (sustained, baseline)
- **Highly sensitive to neuroactive steroids**

Zuranolone & Brexanolone

- Act on **both** synaptic and extrasynaptic GABA-A receptors as ***positive allosteric modulators***
- Enhance tonic inhibitory signaling, and may be able to reset the excitatory/inhibitory balance of neural networks

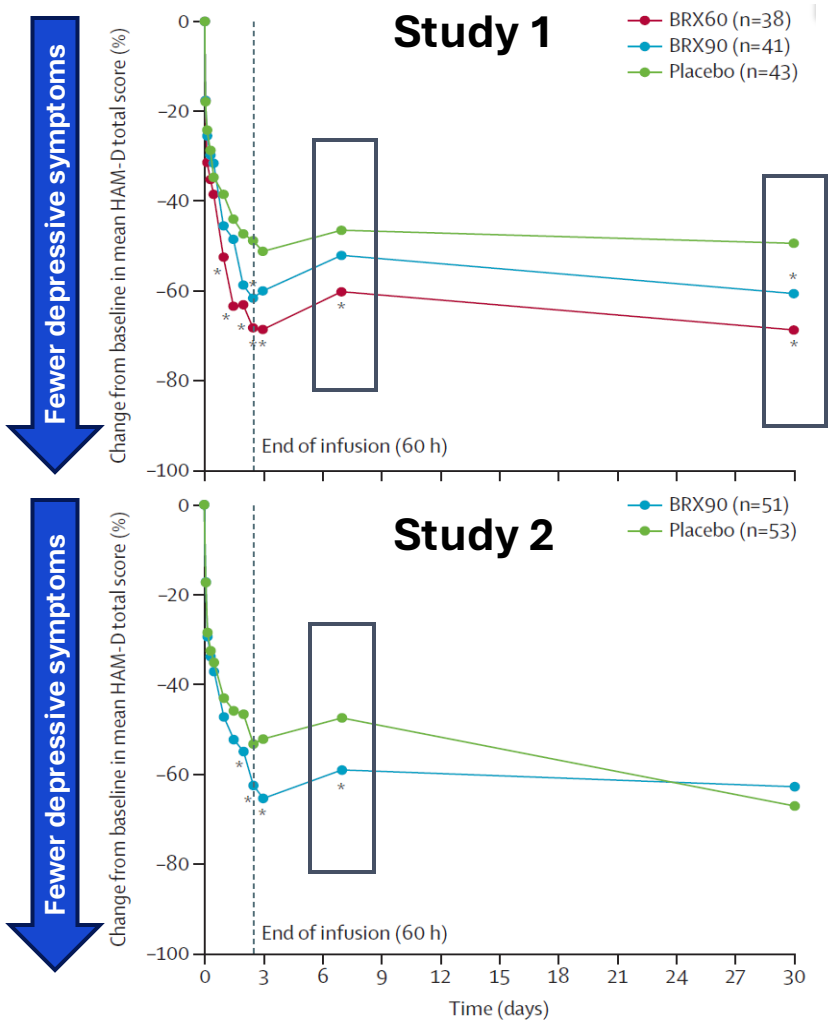
Benzodiazepines in MDD

- Act primarily at **synaptic GABA-A receptors;** require endogenous GABA for effect
- **Do not** significantly modulate extrasynaptic inhibition
- No demonstrated antidepressant efficacy in RCTs for MDD

MDD = major depressive disorder; RCT = randomized controlled trial.

Farrant M, Nusser Z. *Nat Rev Neurosci*. 2005;6(3):215-229; Althaus AL, et al. Neuropharmacology. 2020;181:108333; Morrison KE, et al. Drugs Today (Barc). 2019;55(9):537-544.

Single 60-Hour IV Infusion Brexanolone Persistently Reduced Depressive Symptoms



First medication FDA-approved specifically for PPD

Requires clinical monitoring

Black box warning for the potential for excessive sedation and sudden loss of consciousness

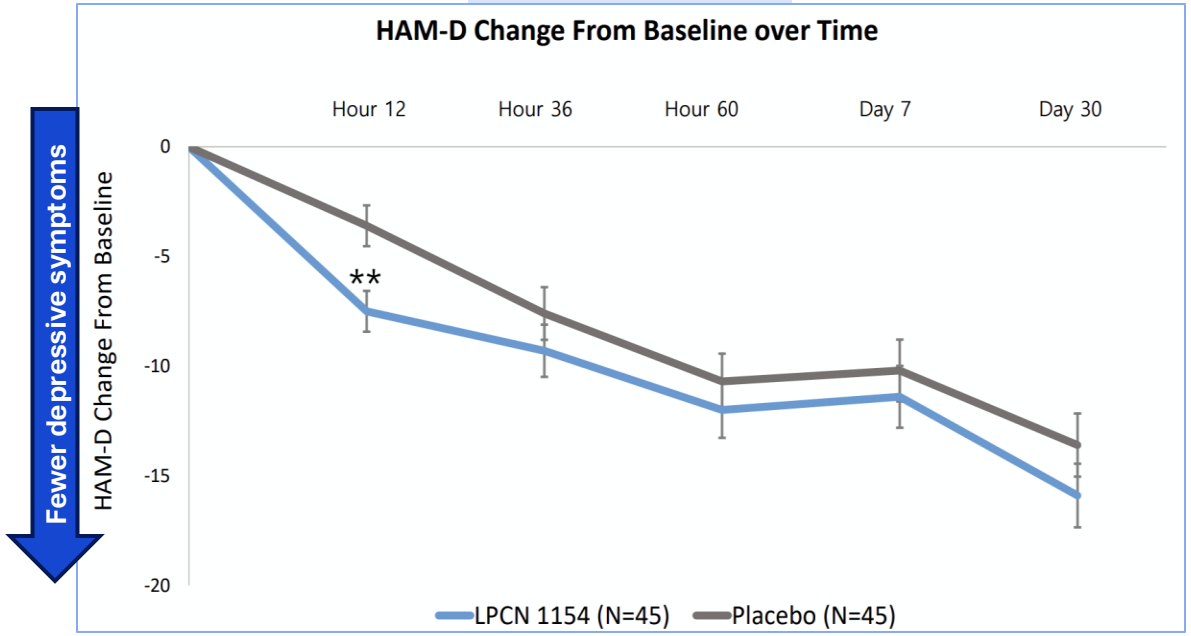
The relative infant dose (RID) is low: **1% to 2%** of the maternal weight-adjusted dosage

	Study 1			Study 2	
AE in ≥3 patients	**Placebo N=43**	**BRX 60mg N=38**	**BRX 90mg N=41**	**Placebo N=53**	**BRX 90mg N=51**
Headache	16%	18%	15%	11%	18%
Dizziness	2%	16%	15%	8%	10%
Somnolence	7%	18%	5%	4%	8%
Infusion site pain	2%	3%	10%	4%	10%
Nausea	7%	3%	0	4%	10%
Dry mouth	0	11%	0	2%	4%
Fatigue	0	3%	2%	4%	6%

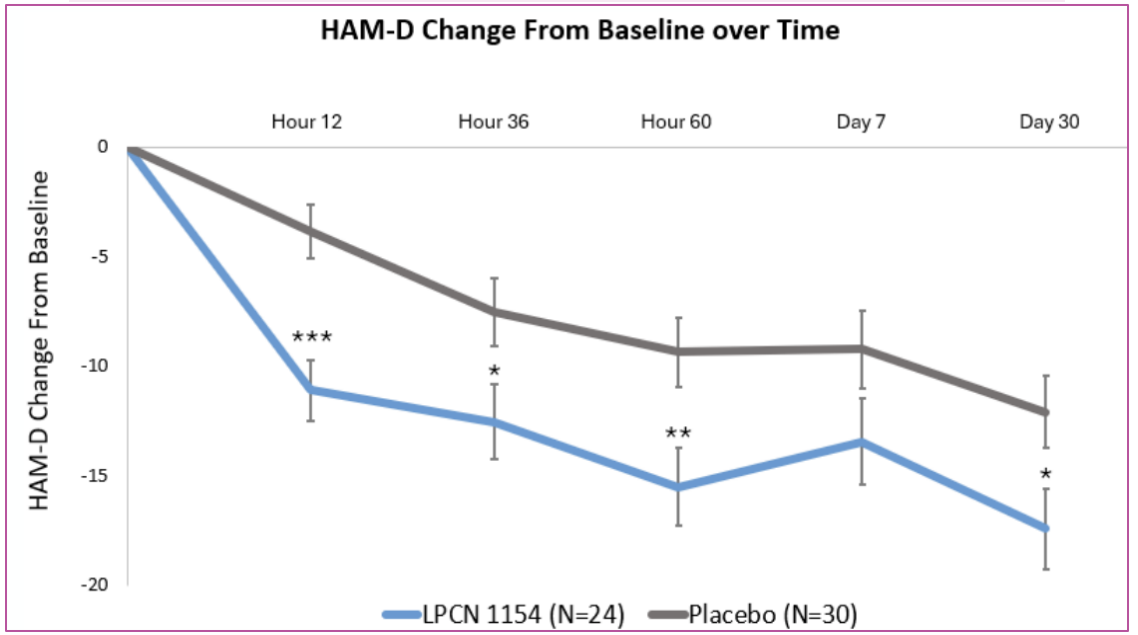
Meltzer-Brody S, et al. *Lancet*. 2018;392(10152):1058-1070.

An Oral Formulation of Brexanolone Did Not Meet its Primary Endpoint in a Study of PPD

Total Sample



PPD with History of Psychiatric Conditions



TEAEs in ≥ 2 participants in LPCN 1154 arm

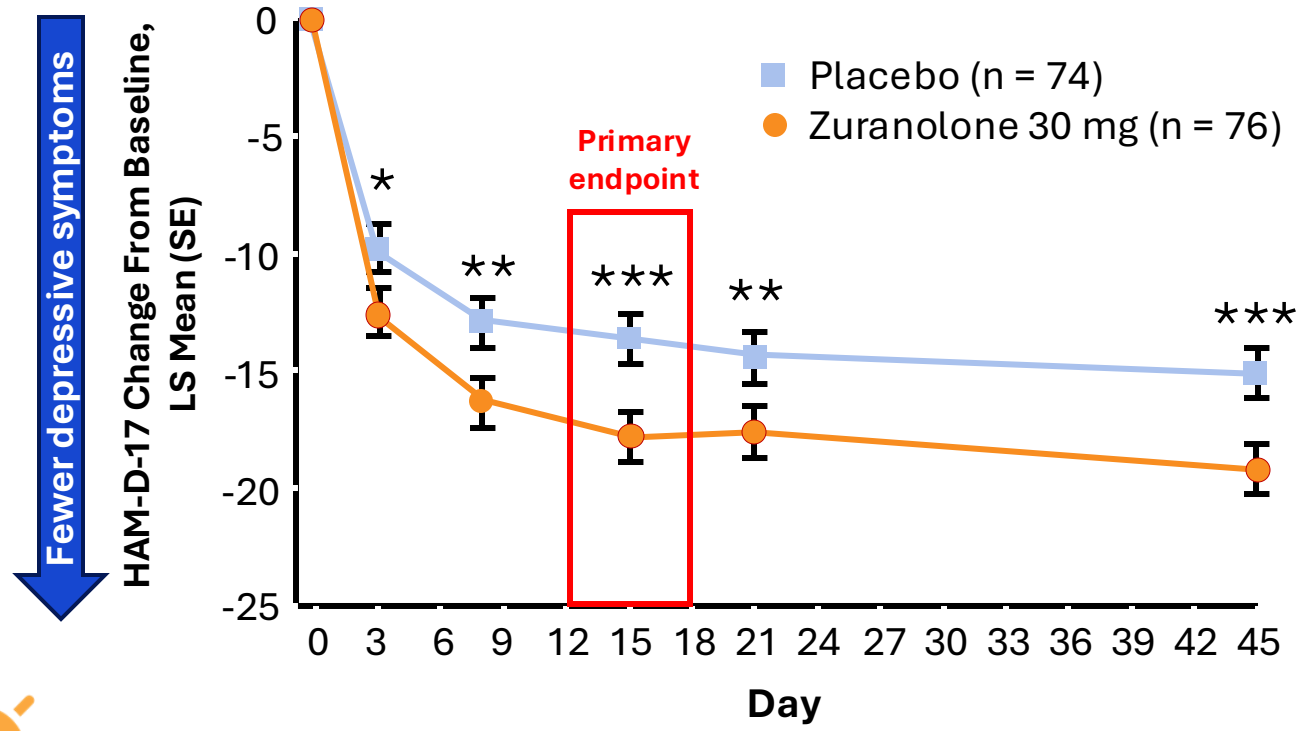
	LPCN 1154 (N=45)	Placebo (N=45)
Headache	4.4%	6.7%
Dizziness	4.4%	0
Somnolence	4.4%	0
Nausea	4.4%	0

Despite not meeting the primary endpoint, **further studies of oral brexanolone are being pursued**

*p<0,.05, **p<0.01, ***p<0.001

TEAE=Treatment-emergent adverse event. Lipocine. LPCN 1154 (Brlizio™): Oral brexanolone for postpartum depression (PPD). May 2025/2026. Accessed May 8, 2026; Lipocine Inc. Lipocine reports topline safety and efficacy results for LPCN 1154 in patients with postpartum depression [press release]. April 2, 2026. Accessed May 14, 2026

Pivotal Phase 3 Study of Zuranolone 30 mg in Postpartum Women With PPD



TEAEs ≥ 5%	Zuranolone 30mg N=78	Placebo N=73
Somnolence	15%	11%
Headache	9%	12%
Dizziness	8%	6%
URTI	8%	1%
Diarrhea	6%	3%
Sedation	5%	0
Nausea	4%	8%
Vomiting	1%	6%
Abnormal dreams	0	6%
Hyperhidrosis	0	6%

Recommended dosage is **50 mg orally once daily in the evening for 14 days**

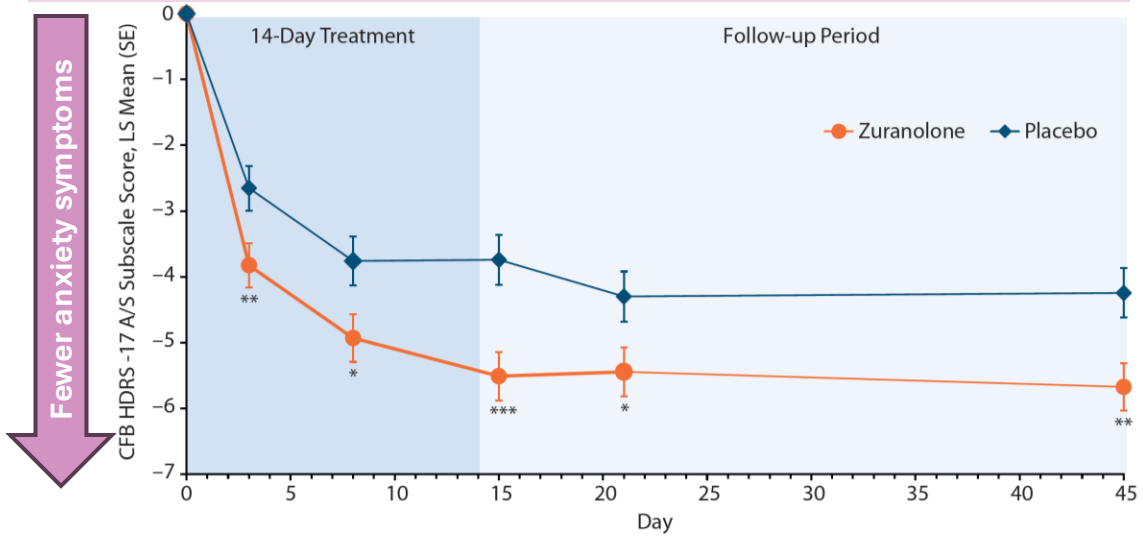
Primarily metabolized by **CYP3A4**

Discontinuations due to AEs: Zuranolone: 1, Placebo: 0

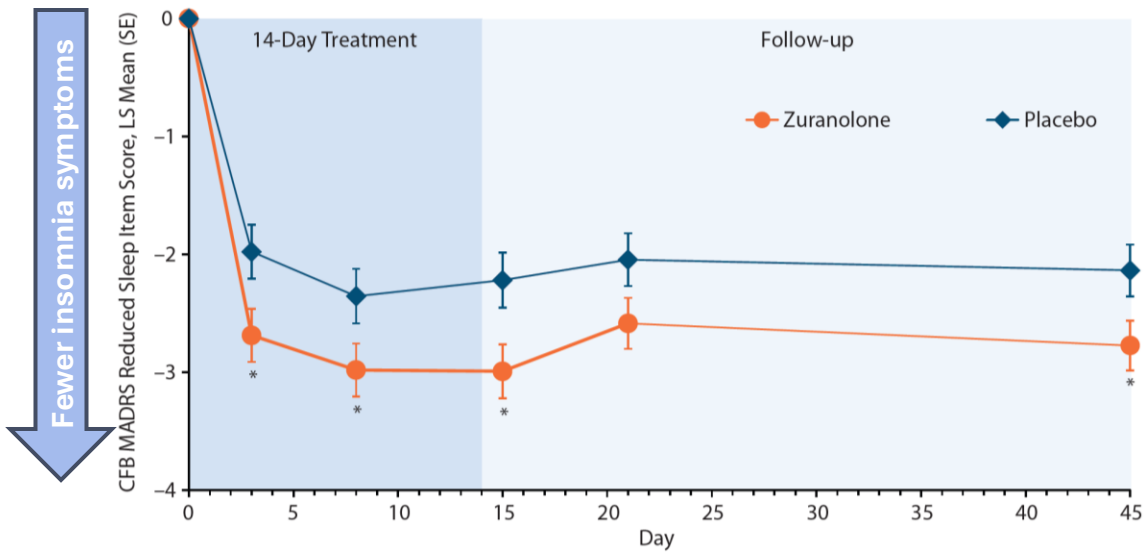
***P = .03, **P = .01, ***P = .003.**
URTI = upper respiratory tract infection.
Deligiannidis KM, et al. *JAMA Psychiatry*. 2021;78(9):951-959.

Treatment with Zuranolone Showed Signals of Improving Anxiety, Insomnia, and Perceived Functioning

Δ HDRS-17 Anxiety/Somatization Subscale Score



Δ MADRS Reduced Sleep Item Score

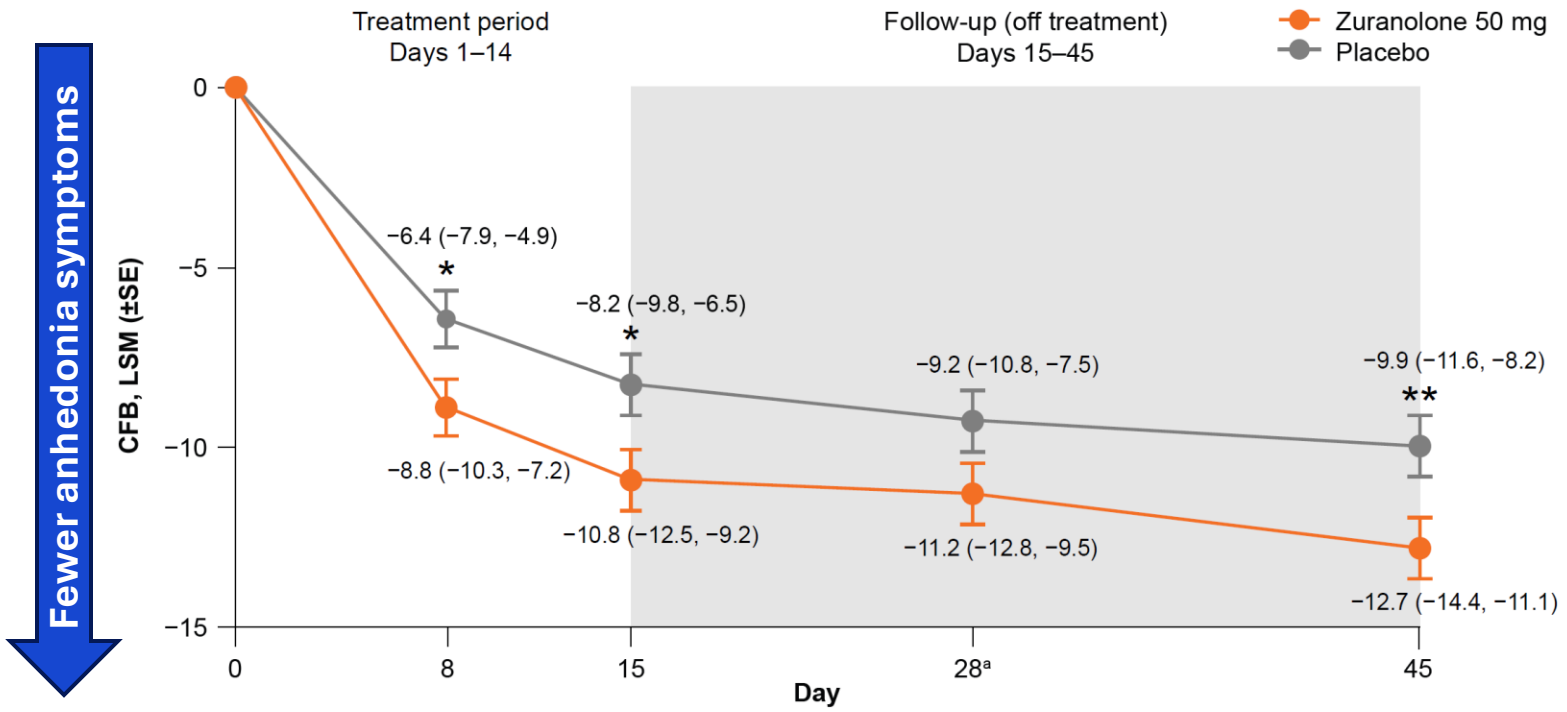


With Zuranolone treatment, patient-reported functioning and well-being (measured with the SF-36) were also improved across **social**, **mental**, and **physical** domains

***P <.05 vs placebo, **P < .01, ***P < .001.**
HDRS = Hamilton Depression Rating Scale; MADRS = Montgomery- Åsberg Depression Rating Scale; SF-36 = Short Form Health Survey.
Deligiannidis KM, et al. *J Clin Psychiatry*. 2023;84(1):22m14475.

Post-Hoc Analyses Indicate Zuranolone May Produce Rapid and Sustained Improvements in Anhedonia

Post-hoc Analysis of MADRS Anhedonia Subscale Score in Ph 3 SKYLARK Study



Post-hoc analyses of adverse event data showed **the majority of somnolence events**:

Began within 7 days of the first dose,

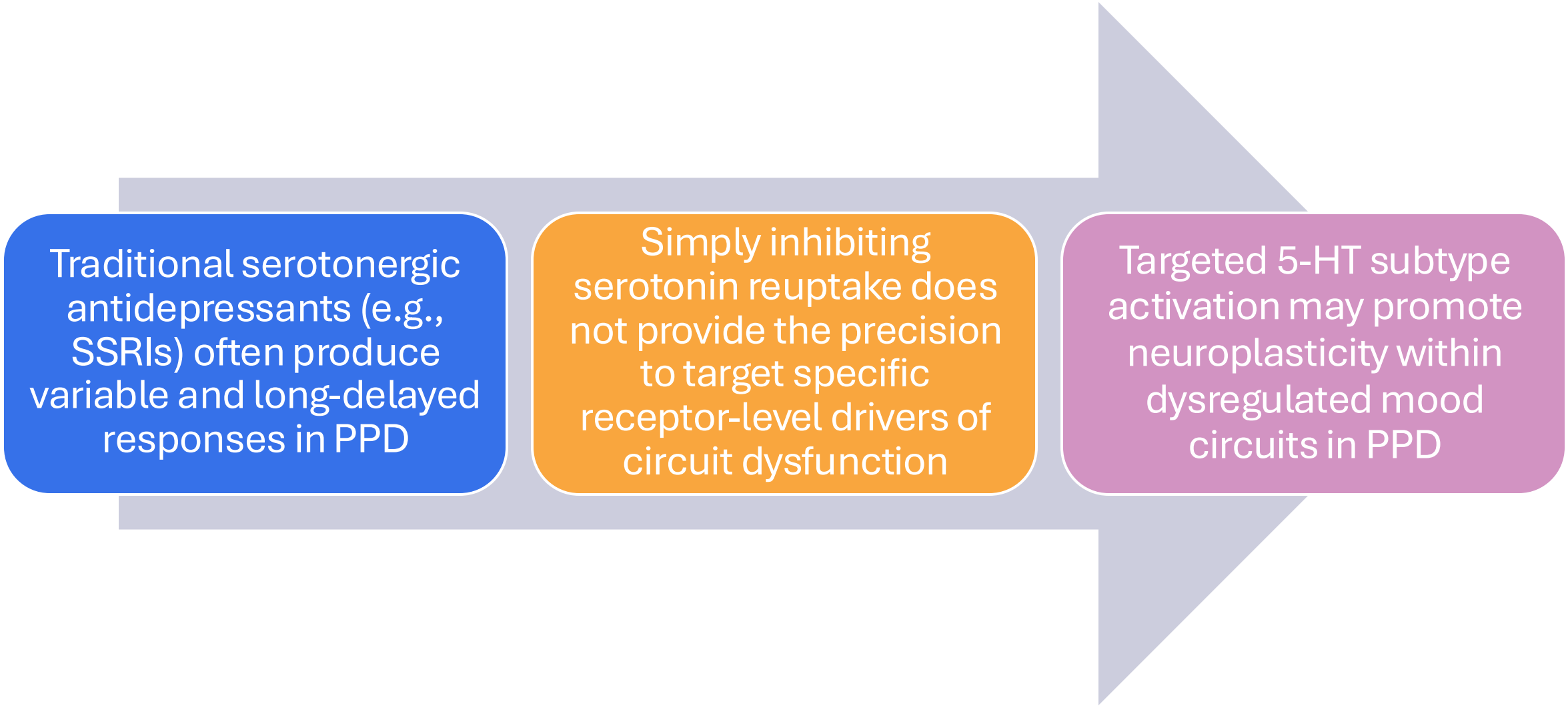
Were mild in severity, and

Resolved while **still on treatment** or **within 2 to 5 days** after the last dose

MADRS = Montgomery–Åsberg Depression Rating Scale; CFB = change from baseline; TEAE = treatment-emergent adverse event; UTI = urinary tract infection.

Chepke C, et al. Improvement in anhedonia symptoms with zuranolone in patients with postpartum depression (PPD): a post hoc analysis of the phase 3 SKYLARK study. Poster presented at: American Psychiatric Association Annual Meeting; May 17–21, 2025; Los Angeles, CA.

Revisiting Serotonin: Moving Toward More Targeted Approaches in PPD

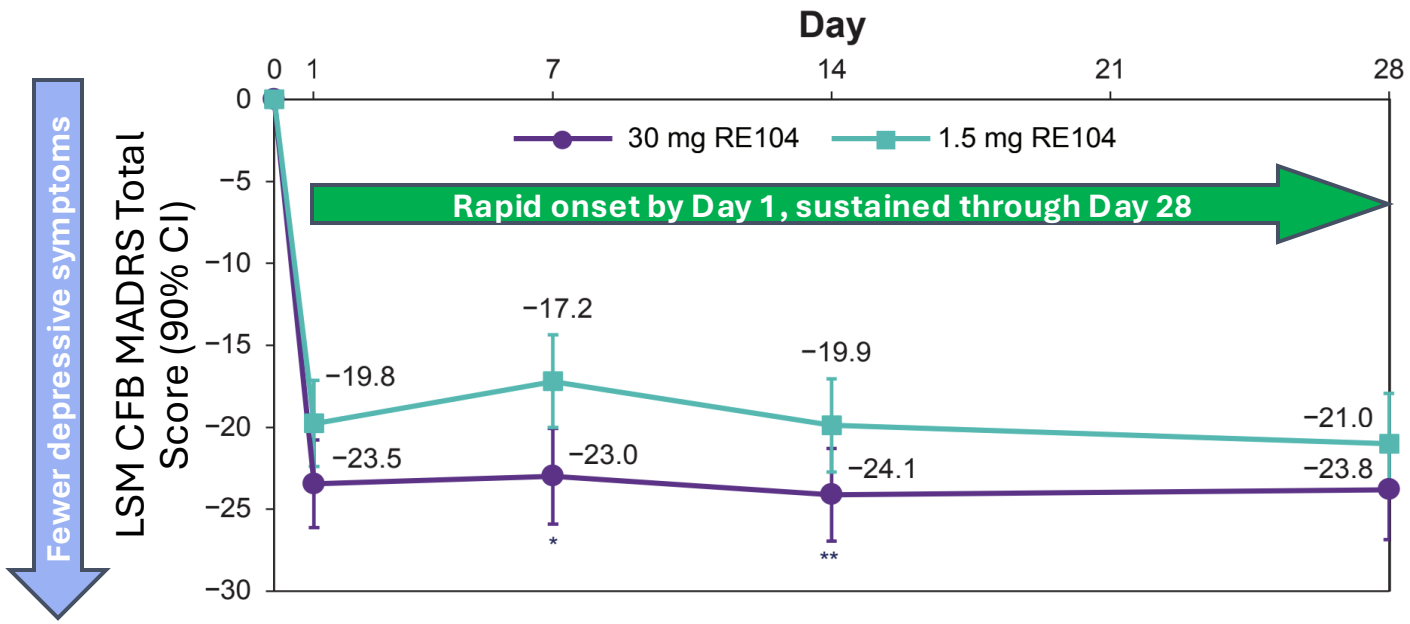


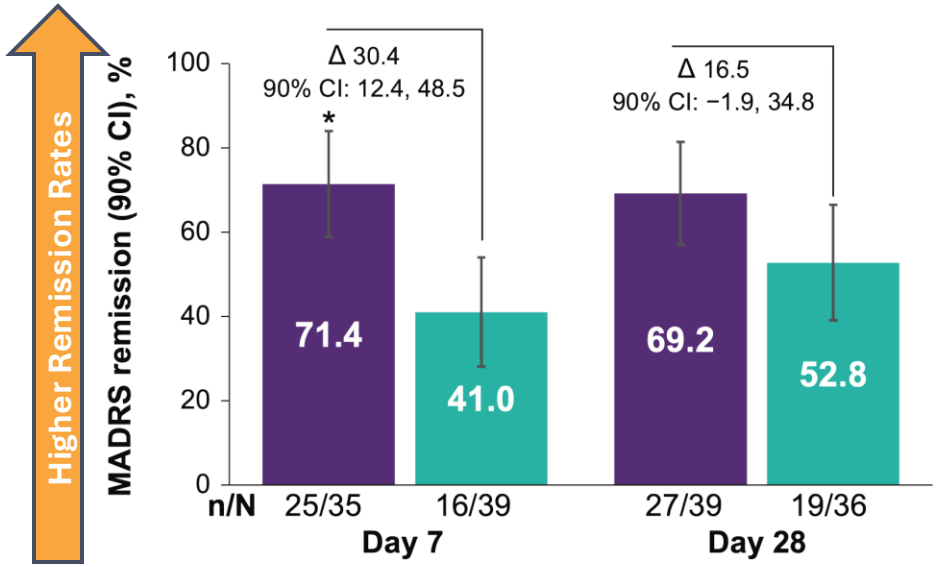
Sharma V, Sommerdyk C. Prim Care Companion CNS Disord. 2013;15(6):PCC.13r01529; Jairaj C, Rucker JJ. J Psychopharmacol. 2022;36(8):920-931.

A Single Subcutaneous Dose of Luvesilocin (RE104) Produced Rapid and Sustained Antidepressant Effects in PPD

Luvesilocin (RE104) is a 5-HT_{2A} partial agonist that is a prodrug of a psilocybin analog designed to produce a shorter psychedelic experience.

At the primary endpoint of Day 7,
30 mg of RE104 reduced the MADRS score
5.8 points more than the 1.5 mg comparator (P=0.0094)

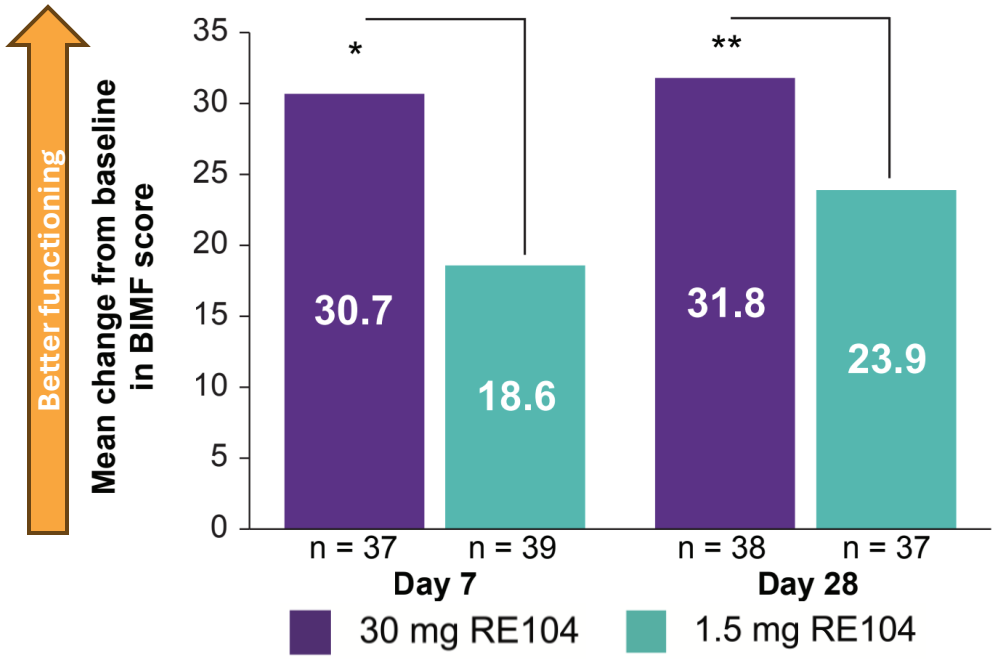




SC = subcutaneous; LSM=Least Squares Mean; CFB=Change From Baseline; MADRS remission defined as a score ≤10

Clayton AH, et al. RE104: A novel serotonergic psychedelic 4-OH-DiPT prodrug for the treatment of postpartum depression. Poster presented at: 64th Annual Meeting of the American College of Neuropsychopharmacology; January 12–15, 2026; Nassau, Bahamas

Luvesilocin (RE104) Improved Maternal Well-Being and Functioning, and was Well-Tolerated



Significantly improved **maternal functioning** at Days 7 and 28

TEAEs ≥ 10%	30mg RE104 N=41	1.5mg RE104 N=43
Nausea	44%	16%
Headache	34%	19%
Dizziness	27%	7%
Vomiting	24%	2%
Hallucinations, visual	22%	5%
Anxiety	20%	7%
Illusion	15%	5%
Tremor	12%	2%
Feeling abnormal	12%	2%
Chills	12%	0

No serious AEs or discontinuations due to TEAEs were observed in either group

All participants were discharge-ready in 4 hrs

*P < 0.01; **P < 0.05; one-sided P values. Baseline scores (SD): 30 mg RE104, 65.4 (16.0); 1.5 mg RE104, 68.6 (16.2); BIMF = Barkin Index of Maternal Functioning.

Clayton AH, et al. RE104: A novel serotonergic psychedelic 4-OH-DiPT prodrug for the treatment of postpartum depression. Poster presented at: 64th Annual Meeting of the American College of Neuropsychopharmacology; January 12–15, 2026; Nassau, Bahamas

The Future of PPD Therapeutics Looks Bright

Treatment Class/Approach	Example Agents/Modalities	Mechanism of Action	Stage of Development
Neuroactive steroids (GABA-A PAMs)	Zuranolone (post-marketing studies)	Enhances GABAergic inhibition; rapidly reduces depressive symptoms	Phase 4 (recruiting)
	LPCN 1154 (Brexanolone [oral])	Brexanolone encased in a lipid-based carrier to enhance oral absorption	Meeting with FDA to discuss design of next Phase 3 Study
Glutamatergic modulators	Ketamine (PPD-specific PK/PD studies)	NMDA receptor antagonism; rapid antidepressant effects via synaptic plasticity	Early clinical (recruiting)
Psychedelic-inspired agents	Luvesilocin (RE104): psilocybin analog	5-HT2A receptor partial agonism; alters mood, cognition, and reward processing	January 2026: Phase 2 met primary endpoint, Phase 3 to initiate in 2026
Neuromodulation	Accelerated TMS (e.g., SAINT protocol)	Modulates fronto-limbic circuits implicated in mood regulation	Early-mid clinical (recruiting)
Digital therapeutics	MamaLift Plus, chatbot-based interventions	Behavioral activation, CBT principles, and real-time support delivery	Early clinical/device trials (recruiting)

Key Learning Points

- Conventional pharmacologic treatments for PPD have notable limitations, including delayed onset, tolerability challenges, and incomplete symptom response
- PPD is associated with sharp declines in neuroactive steroid levels after delivery, contributing to disrupted GABAergic signaling and impaired stress regulation
- Novel therapies target these underlying mechanisms and can produce rapid, clinically meaningful symptom improvement

Practical Strategies to Ensure Optimal Treatment of PPD with Zuranolone and Overcome Challenges

Zuranolone Patient Selection

PPD Diagnosis, age 18+

FDA-approved as Monotherapy or Adjunctive to Traditional Oral Antidepressant

Know your patient: Severity of illness, impact on functioning, current medications and previous medication trials, support system, treatment goals

Zuranolone: Dosing Considerations

Standard Dosing

- 50mg in the evening for 14 days
  - Administer with fat-containing food (e.g., 400-1,000 calorie meal) with 25-50% fat
- 2 X 25mg capsules (quantity: 28)

Dose Adjustments

- Reduce to 30 mg if:
  - Using strong CYP3A4 inhibitors
  - Presence of severe hepatic impairment or moderate/severe renal impairment
- Consider 40 mg if:
  - CNS depressant effects/sedation

Avoid/Monitor

- Avoid CYP3A4 inducers, may decrease efficacy
- Monitor CNS depression

ZURZUVAE (zuranolone) prescribing information. April 2026. Accessed May 13, 2026.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/217369s003lbl.pdf

Zuranolone: Precautions and Warnings

Boxed Warning: Patients should NOT drive or engage in other potentially hazardous activities for at least 12 hours after administration

- Not for use in pregnancy → **Educate:** patients should use effective contraception during treatment and for one week following treatment
- Not for postpartum psychosis → **Screen, accurate diagnoses**
- **CNS Depressant Effects**: somnolence, confusion → **Caution** with sedating medicines.
  - Review medications, supplements, rule out substance use disorder
  - Consider dose reduction, discontinuation
- **Suicidal thoughts and behavior** → **Monitor** for suicidal thoughts
- Schedule IV Controlled Substance → **Rule out Active Substance Use Disorder**

ZURZUVAE (zuranolone) prescribing information. April 2026. Accessed May 13, 2026.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/217369s003lbl.pdf

Zuranolone: Breastfeeding and Prescription Info

- **<u>Breastfeeding</u>**
  - Zuranolone passes into breastmilk, low levels
  - Estimated RID of 0.984%

→ Discuss, potential risks/unknowns, benefits of breastfeeding.

- **<u>Prescription</u>**
  - Specialty pharmacy in network with patient's insurance

→ PPD Dx

Specialty pharmacy ships medication to patient's preferred address

RID = relative infant dose.

Drugs and Lactation Database (LactMed®) [Internet]. Bethesda (MD): National Institute of Child Health and Human Development; 2006–. Zuranolone. Updated November 15, 2025. Accessed May 26, 2026. Deligiannidis KM, et al. *J Clin Psychopharmacol*. 2024;44(4):337-344.

Planning for Care Continuation and Transitions

Encourage frequent follow-ups, close monitoring
Utilize telemedicine as appropriate, as needed
Involve family and other support when appropriate
Encourage therapy
Provide educational resources
Consider support groups
Know your community resources
Collaborate with OBGYN, primary care, care team

Key Learning Points

- Zuranolone is the only FDA-approved oral pharmacotherapy for adults with PPD (14-day course)
  - It can be used as monotherapy or adjunctive treatment for PPD
- Monitor for sedation, CNS depression, suicidal thoughts, and drug interactions during treatment
- Effective PPD care includes follow-up, family support, therapy, and coordinated care: plan for close/frequent follow-up of your patients with PPD

Faculty Discussion: Collaborative and Individualized Care of Patients with PPD

Setting Up Your Practice to Facilitate PPD Treatment

Consulting and Collaborating with Non-Psychiatric Clinicians in PPD

Shared Decision-Making with Patients and Care Partners in PPD

Setting Up Your Practice to Facilitate PPD Treatment

Develop	Develop a process for utilizing and evaluating screeners
Incorporate	Incorporate the option for telemedicine services
Know	Know your community resources
Develop	Develop a process for providing patient education
Implement	Implement involving family/loved ones for support as appropriate

Shared Decision-Making with Patients and Care Partners in PPD

Discussion prior to pregnancy, ideally

Discussion of risks of untreated mental illness during pregnancy and lactation and risks/benefits of treatment for mom and baby

Family/support involvement

Practical Takeaways

- **Screen early and often**: Assess for PPD throughout pregnancy and the first year postpartum using validated screening tools
- **Diagnose accurately**: Differentiate PPD from baby blues and evaluate for bipolar disorder, suicidality, and postpartum psychosis when indicated
- **Individualize treatment**: Discuss risks and benefits of available treatment options and align care with patient goals, preferences, and clinical needs
- **Collaborate across disciplines**: Partner with OB/GYN, pediatrics, primary care, and family/support systems to ensure timely identification, treatment, and follow-up