



Peripartum Psychiatry

Supporting Family Mental Health During a
Critical Time of Development



NC MATTERS

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Peripartum Psychiatry

All the Usual Things of Psychiatry Only Now You
have the Complexity of the Peripartum Period



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Introductions



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Program Coordinator, Attachment Network of North Carolina

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Disclosures

PI of independent investigator research study of brexanolone and postpartum psychosis funded by Sage Therapeutics

Spouse has stock with Abbvie Labs as part of his retirement portfolio

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Objectives

- Participants will be able to formulate the “risk”/”risk” analysis discussion with patients about any medications their patients may take during pregnancy and with lactation.
- Participants will be able to increase knowledge of what is known (and not known) of some newer and older medications in pregnancy (e.g., LAI, Lithium).
- Participants will increase knowledge base about the use of brexanolone and supplements (e.g., probiotics).

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EH is a 38-year-old who is 2-months postpartum with her first baby. At her well child visit, she complains of pain and latch issues in breastfeeding, and is also found to have an Edinburgh score of 18. The pediatrician referred the patient to a lactation consultant, encouraged sleep hygiene/self-care strategies, and encouraged EH to follow up with her existing therapist. In addition, her Ob/Gyn started her on an SSRI antidepressant.

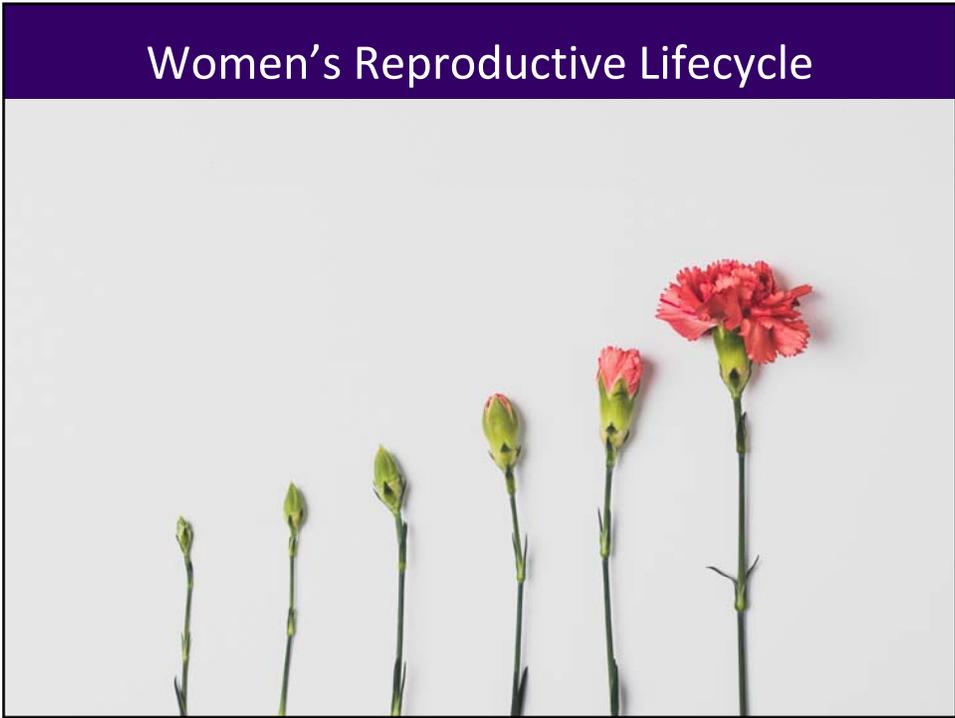
At 6-months postpartum, EH tells the pediatrician that she was discharged from OB care and now sees her PCP. She does not feel that her PCP is effective in addressing her postpartum mood symptoms. She says she is having upsetting images of a scissors in her son’s head. EH is reluctant to say she now feels more irritable, “out of control,” and “explosive;” and as this has worsened she has started increasing her alcohol intake to get to sleep.

Her additional concerns include: financial strain, marriage strain, strain with her mother who has bipolar disorder, hair loss, and low sex drive. She has tried to reconnect with her therapist, but has not been successful in getting an appointment. EH is motivated to build a care team, but does not know where to go for support.

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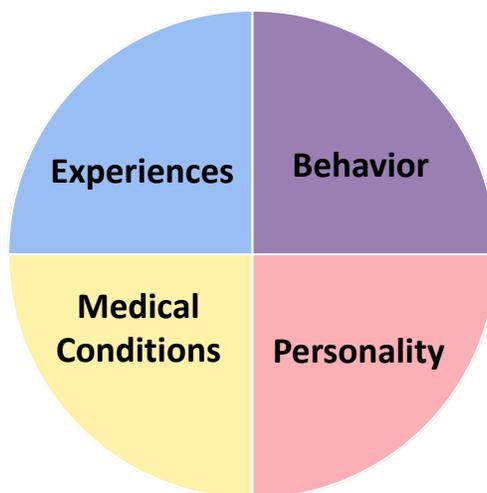


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Four Aspects of Mental Wellness

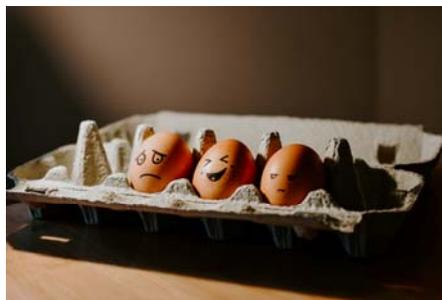


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“Normal” Psychological Changes in Peripartum

- First Trimester: Mild anxiety (ambivalence, worry), changes in energy, appetite, libido
- Third Trimester: increased anxiety about labor and delivery, impending role change
- Pregnancy and Postpartum:
 - Mild forgetfulness, confusion, distractibility
 - Worry: health of baby, responsibilities, finances etc.
 - Heightened awareness of prior relationships, losses, esp. family of origin



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Hormonal Changes in Peripartum

Internal environment	External environment
<ul style="list-style-type: none">• <u>Hormonal fluctuations</u><ul style="list-style-type: none">• Estrogen + Progesterone - rise dramatically in 3rd trimester, fall even more dramatically at parturition• Oxytocin – rises during labor - role in attachment, lactation• Hyperactive HPA Axis with high plasma cortisol• <u>Brain Circuitry Changes</u><ul style="list-style-type: none">• Increased neuronal activity - increased vigilance and protectivity• More sensitive reward and motivation circuitry - increased sensitivity to infant cues	<ul style="list-style-type: none">• Body• Mind• Relationships• Work• Sleep

Relative hormone concentration

Weeks of pregnancy

Postpartum

Estrogens

Progesterone

Human chorionic gonadotropin

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The Perinatal Depression “Treatment Cascade”

50-70% of cases go undetected

85% of cases go without treatment

91-93% of cases are not adequately treated

95-97% of cases are without remission of symptoms

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Perinatal/Postpartum Anxiety is the most common PMAD and often goes undiagnosed.

Symptoms to look for include:

- Excessive worrying
- Racing thoughts
- Feelings of dread
- Feeling overwhelmed
- Obsessive thoughts
- Rapid heartbeat

Symptoms that often are mistaken as *normal* during pregnancy and postpartum:

- Difficulty concentrating
- Trouble sleeping
- Changes in eating/sleeping patterns
- Sense of memory loss
- Nausea, dizziness, hot flashes
- Irritability
- Persistent fatigue

1 Misri, S., Abizadeh, J., Sanders, S., & Swift, E. 2015

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Intrusive Thoughts

What would happen if I left the baby in the bathtub and walked away?

I keep imagining dropping the baby while I walk down the stairs

I keep imaging myself on a respiratory

I keep imagining scissors sticking out of my son's head

How do you feel when patients share this with you?

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**(Some of the)
Spectrum of
Disorders in
the
Peripartum
Period**

- Depression
- Anxiety
- Panic Disorder
- Obsessive Compulsive Disorder
- Post Traumatic Stress Disorder
- Bipolar Disorder or Primary Psychotic Disorder
- Postpartum Psychosis

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Consequences of Not Treating During Pregnancy

Pregnancy is not protective!

Increased impulsivity, substance abuse, poor nutrition and self-care	Increased risk for preeclampsia, pre-term births, low birth weight, IUGR	Congenital defects/malformations; toxic stress of the newborn
Disability depression or anxiety	Suicidality, self-injury	Psychotic symptoms, poor judgment, delusional beliefs
	Infanticide	

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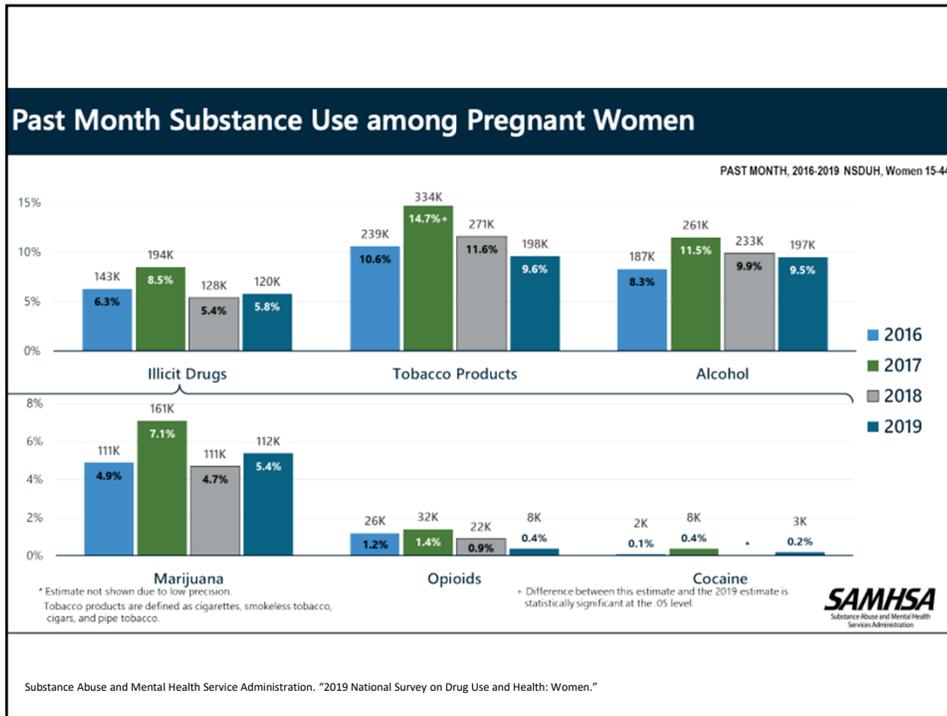
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Consequences of Not Treating Postpartum

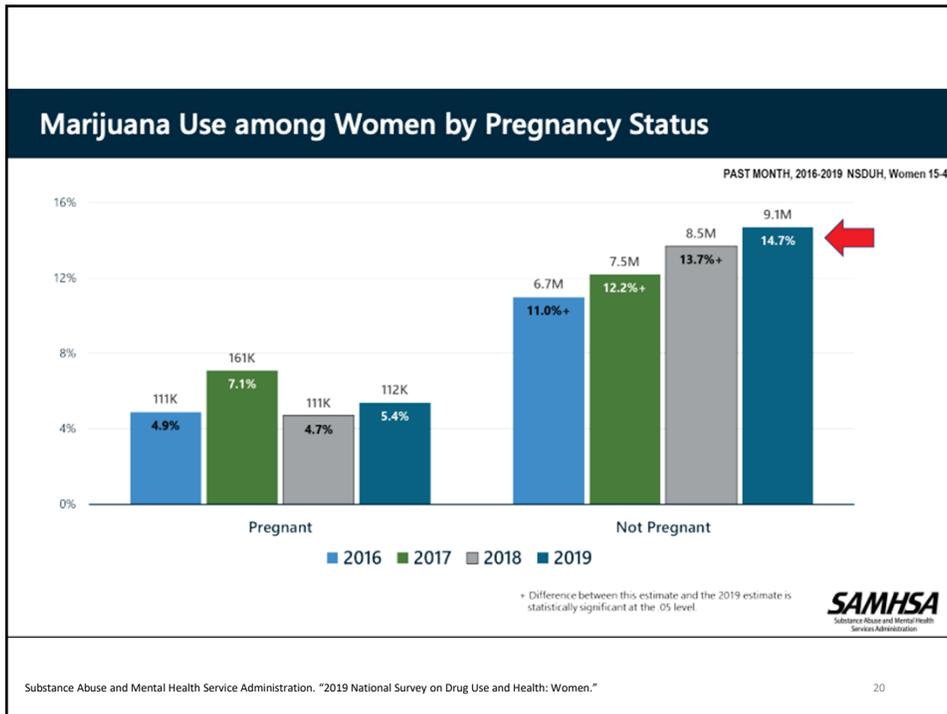
Toxic stress of the newborn	Lactation failure	Insecure attachment
Poor bonding	Lower cognitive scores in the child	Affect dysregulation in the child
Increase rates later in life of suicidality	Higher rates of ADHD and conduct disorder in the child	Impacts on Family Dynamics, higher rates of divorce and other discord

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PMADs and Families

- Partners are affected by postpartum depression by supporting and coping with their partner's symptoms:
 - **Confusion**
 - **Anger**
 - **Fear**
 - **Feeling overwhelmed**
- May also experience depression:
 - **1 in 10 fathers experience depression in the first year**



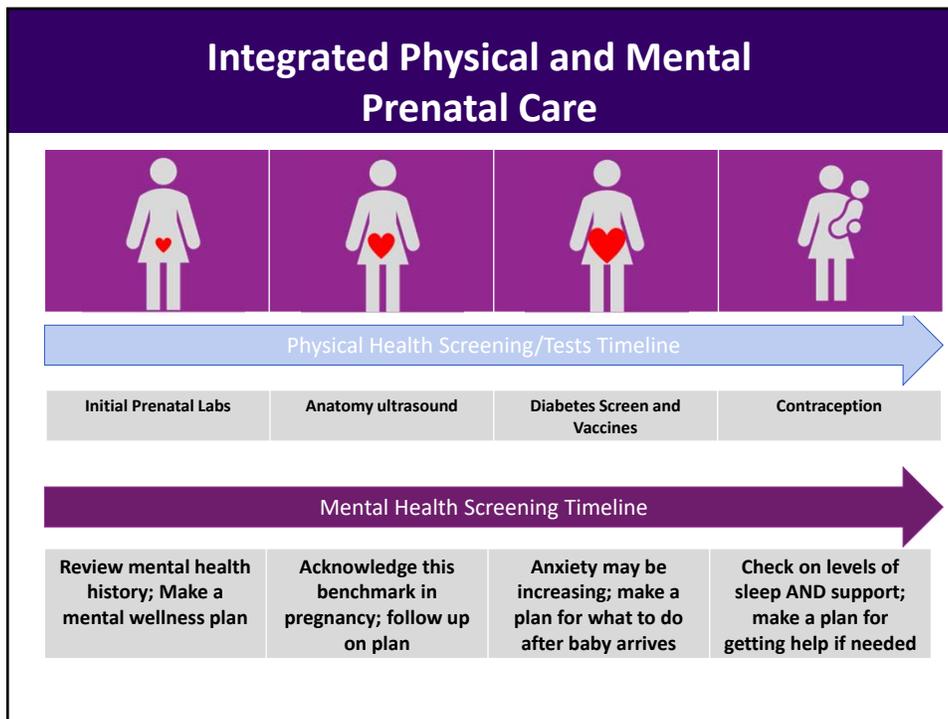
Paulson & Bazemore (2010); Kessler et al. (2003)

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What's to be done?

- Screening by providers who know how to treat or where to make appropriate referrals
- Initiate or optimize treatment for identified patients
- Treatment to remission

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Psychotropic Medications

- Goal – minimization of risk
- Risk of untreated maternal illness on the mother and the fetus vs. Risk of medications in pregnancy
- **No decision is risk-free**
- Use **lowest effective dose** but goal is symptom remission
- Remember that may need higher doses as pregnancy progresses due to increased plasma volume and rate of clearance → BUT THIS IN PART DEPENDS ON RELATED HEPATIC CYP

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Risk of Medication Exposure in Pregnancy

- All medications transmit to the placenta in varying amounts; no psychotropic is FDA approved for use in pregnancy
- Though FDA currently changing from “Categories” (i.e. C, X) to defining risks/benefits of medications
- Concerns of patients include:
 - Risk of malformations (beyond 2-4% risk in general population off medication)
 - Risk of toxicity and/or withdrawal
 - Risk of long-term developmental outcomes
- **Mothertobaby.org**



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Risk of Medication Exposure in Breastmilk

- Exposure in breastmilk less than through placenta
- If starting new medication postpartum, most antidepressants/antianxiety medications (SSRIs are first-line) are compatible with breastfeeding and felt to be safe
 - Sertraline (Zoloft) is likely negligible into milk at doses of 100 mg and less
- **LACTMED database from NIH**



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Psychopharmacology

- You may have heard that “Preferred medications during the perinatal period include sertraline and citalopram. Breastfeeding is encouraged with sertraline as preferred medication.”
- However, if woman is stable on another AD, switching is not recommended
- Could lead to relapse (don’t know if new AD will work) and exposure to more meds



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Treatment Algorithm Perinatal Depression

Pharmacologic Treatment of Perinatal Depression

Mary C. Kimmel, MD, Elizabeth Cox, MD, Crystal Schiller, MD, Edith Gettes, MD, Samantha Meltzer-Brody, MD, MPH

KEYWORDS

- Depression • Peripartum • Mental health • Medication • Treatment considerations

KEY POINTS

- Clinicians treating pregnant and postpartum women should be familiar with a range of pharmacologic treatment options, gain comfort with prescribing, and know when to consult a mental health provider.
- Treatment decisions should weigh the risks of medication exposure to fetus or infant with the risks of maternal psychiatric illness on the mother and her family.
- Clinicians should communicate to patients that perinatal depression is a treatable medical condition.

BACKGROUND AND PREVALENCE

Perinatal depression, defined as depressive symptoms occurring either during pregnancy (antenatal depression [AND]) or postpartum (postpartum depression [PPD])^{1,2} is exceedingly common and has serious implications when not adequately identified and treated. It has been estimated that between 14% and 23% of women experience AND,³ and up to 22% of women develop PPD within the first 12 months after delivery.⁴ Yet, it has also been estimated that only 20% to 50% of women with AND or PPD are identified in clinical settings, and an even smaller number (14%–16%) receive any treatment for their symptoms.⁵

CONSEQUENCES OF PERINATAL DEPRESSION

Untreated AND has been associated with increased risks for preeclampsia and preterm birth, as well as the development of numerous chronic health complications in

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SSRIs

Generic Names	Trade Name	Dosage Range	Unique Considerations
Sertraline	Zoloft	50-200 mg, increase by 25 mg or 50 mg for very anxious patients 12.5 mg	Due to half-life, small, even negligible amounts transmitted into breast milk
Fluoxetine	Prozac	20-80 mg, increase by 10 mg or 20 mg	Longer half-life → withdrawal less likely if doses are missed, but also longer to get out of the system if there are adverse effects, likely greater amount in breast milk, thought to be more activating
Citalopram	Celexa	20-40 mg, increase by 10 mg or 20 mg	FDA Drug Safety Communication that > 40 mg could result in life-threatening heart arrhythmia.
Escitalopram	Lexapro	10-20 mg, increase by 5 mg or 10 mg	
Paroxetine	Paxil	10-60 mg, increase by 10 mg or 20 mg, CR in 12.5 mg doses	Older data demonstrated potential for a 1.5 to 2.0 fold increase risk in cardiovascular malformations, leading to a 2005 warning. Recent data show no consistent information to support teratogenic risks
Fluvoxamine	Luvox	25-150 mg, increase by 25 mg	More often used for treatment of obsessive compulsive disorder

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SNRIs

Generic	Trade	Dosage	Unique Considerations/Indications
Venlafaxine	Effexor, Effexor XR	37.5-375mg, increase by 37.5mg	Older and most data available
Duloxetine	Cymbalta	20-120mg, increase by 20mg-30mg	

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Other Antidepressants

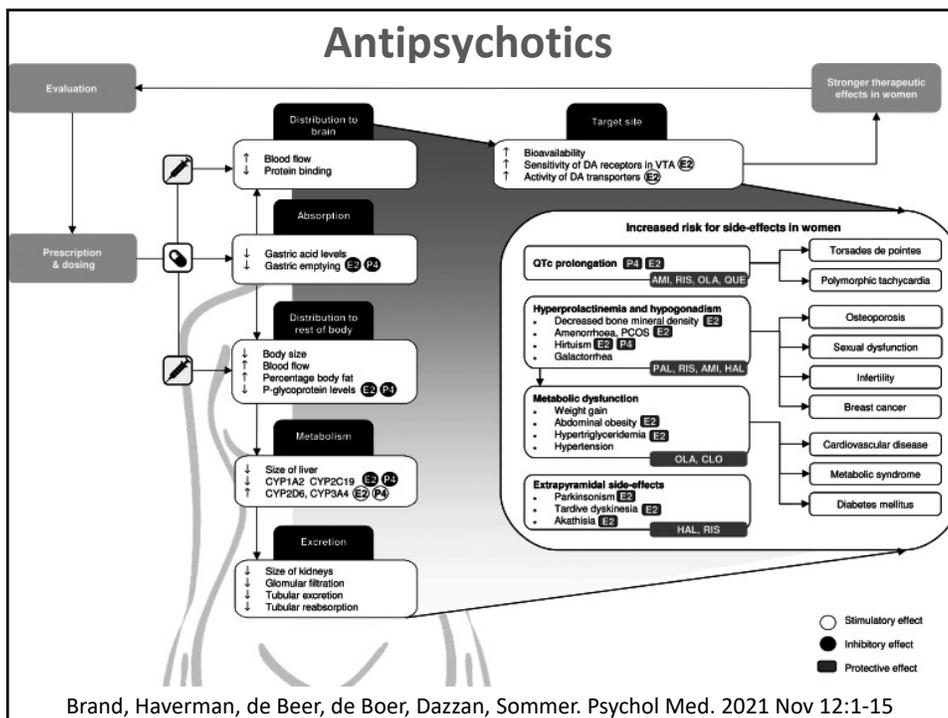
Generic	Trade	Dosage	Unique Considerations/Indications
Bupropion	Wellbutrin SR, Wellbutrin XL, Zyban, Aplenzin, Forfivo XL	150-450 mg, increase by 150 mg, SR BID dosing	Not to exceed 450 mg due to increased risk of seizure. Helpful in smoking cessation and even evidence for lowering prematurity risk for smokers. May help ADHD and other addictive disorders, such as overeating.
Mirtazapine	Remeron	15-45 mg, increase by 7.5 mg, 15 mg	Antiemetic effects in addition to antidepressant and anxiolytic effects, and helps with sleep and decreased appetite
Trazodone	Oleptro, Desyrel, Serzone	50-400 mg, ½ tablet (25 mg)-100 mg for sleep	Sleep aid at lower dosages, higher dosages more antidepressant affects. No differences in the rate of major malformations

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Mood Stabilizers

Generic	Trade	Dosage	Unique Considerations/Indications
Lamotrigine	Lamictal	>50mg, start at 25mg daily and increase by 25mg every 2 weeks (decrease risk of Stevens-Johnson syndrome)	Augmentation in TRD, OCD, possible OCD, mood dysregulation, aggression in BPD (often comorbid with MDD)
Atypical antipsychotics (aripiprazole, quetiapine, olanzapine...)	Abilify, Seroquel, Zyprexa...		Inc. likelihood of remission when used for augmentation; when controlling for other factors exposure does not associate with increased risk OB complications except GDM
Lithium 		Increase by 150mg or 300mg, therapeutic blood level 0.4-0.8 (depression) and 0.8-1.2 (mood stabilization)	Monotherapy and, augmentation MDD< also bipolar disorder and PPP

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Antipsychotics

Table 1. Summary of drug-specific pharmacokinetic properties, side-effects and overdosing risks in women

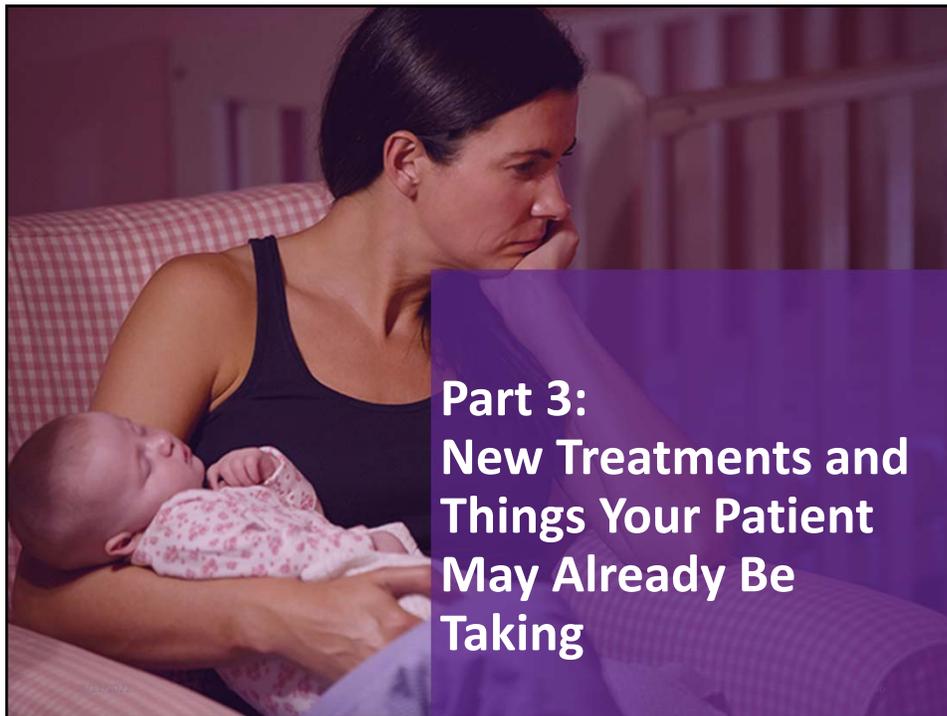
	Pharmacokinetics			Risk for side-effects					
	Metabolism ¹	CYP-activity in females as compared to males ^{2,3,4,5,6}	P-gp binding ^{7,8,9}	QTc prolongation	Prolactin elevation	EPS and akathisia ¹⁰	Metabolic dysfunction		Risk of overmedicating women as compared to men
						Weight gain ¹¹	Lipid/glucose abnormalities ¹²		
Amisulpride	>90% renal excretion		+/+++	+++ ¹⁰	+++ ^{10,12}	+ ¹⁰	+	++ ¹²	++
Aripiprazole	CYP2D6, CYP3A4	(+), (+ +)	++	- ¹⁰	- ^{10,12}	-/+ ¹⁰	+ ¹⁰	- ¹²	+
Chlorpromazine	CYP1A2 ² , CYP2D6	(- -), (+)	+	++ ^{11v}	+ ^{10v}	++ ^{10v}	+++ ¹⁰	+++ ^{12v}	++
Clozapine	CYP1A2², CYP2C19³, CYP3A4	(- -), (-), (+ +)	+	++ ^{11v}	- ^{10,12}	- ¹⁰	+++ ¹⁰	+++ ¹³	+++
Flupentixol	CYP2D6²	(+)	?	+ ^{11v}	- ¹⁰	+++ ¹⁰	+++ ¹⁰	?	+
Haloperidol	CYP2D6², CYP3A4	(+), (+ +)	+	+ ^{10v}	+++ ^{10,12}	+++ ¹⁰	+ ¹⁰	- ¹³	+
Lurasidone	CYP3A4	(+ +)	?	- ¹⁰	+/+ ^{10,12}	+++ ¹⁰	+ ¹⁰	- ¹³	+/-
Olanzapine	CYP1A2²	(- -)	+/+++	+++ ¹⁰	+ ^{10,12}	- ¹⁰	+++ ¹⁰	+++ ¹³	+++
Paliperidone	CYP3A4, UGT1A1, 50% renal excretion	(+ +), (+)	+/+++	+ ¹⁰	+++ ^{10,12}	+ ¹⁰	+ ¹⁰	+++ ¹³	++
Quetiapine	CYP3A4, CYP2D6²	(+ +), (+)	-/+	+++ ¹⁰	- ^{10,12}	- ¹⁰	+++ ¹⁰	+++ ¹³	-
Risperidone	CYP2D6², CYP3A4	(+), (+ +)	+++*	+++ ¹⁰	+++ ^{10,12}	+++ ¹⁰	+++ ¹⁰	+ ¹³	++
Sulpiride	Renal excretion only		+/+++	++	+++ ^{12v}	+++ ^{10v}	+++ ¹⁰	?	++
Zucloperithol	CYP2D6	(+)	?	?	?	+++ ¹⁰	+ ¹⁰	?	+

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Brand, Haverman, de Beer, de Boer, Dazzan, Sommer. Psychol Med. 2021 Nov 12:1-15

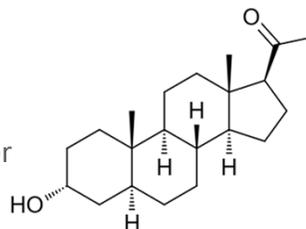
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Brexanolone (Zulresso)

- 1st drug FDA approved specifically for Postpartum Depression
 - Inpatient admission required
- Consider for...
 - Moderate to severe PPD
 - Symptom onset during the 3rd trimester or within 6 months postpartum
 - May have co-morbidities such as anxiety, OCD, PTSD
 - Symptom onset during the 3rd trimester or within 6 months postpartum

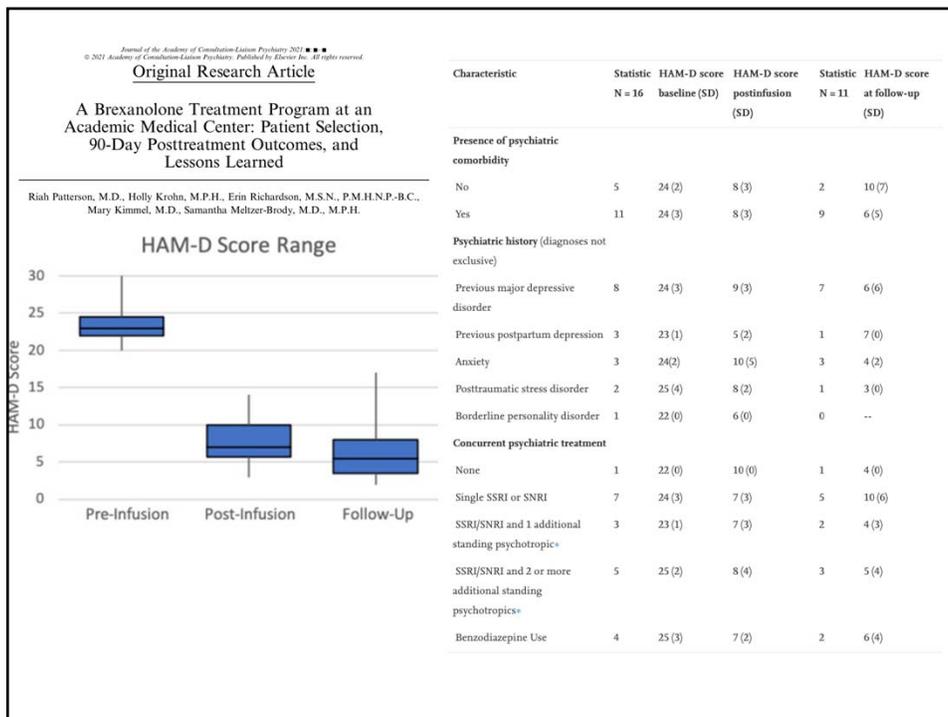


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Brexanolone (Zulresso)

- UNC Perinatal Psychiatry Program offers Zulresso (Brexanolone)
- 60-hour infusion on medical unit
- Only available through a restricted program called Zulresso REMS (Risk Evaluation and Mitigation Strategy), due to risk of excessive sedation or sudden loss of consciousness during administration
- Costly; requires insurance approval, Medicaid does cover in NC

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Brexanolone (Zulresso)

Exclusion criteria:

- Bipolar disorders, psychotic disorders, current substance abuse disorders
- Active SI with plan or intent
- Pregnant
- Renal impairment (eGFR < 15 mL/min/1.73m²)

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Zulresso (brexanolone) Treatment for Postpartum Psychosis

A research study at UNC Hospitals
Principal Investigator: Mary Kimmel, MD
For questions about the study please contact Holly Krohn at holly_krohn@med.unc.edu



What is postpartum psychosis?

Signs and symptoms of postpartum psychosis include:

- Thoughts that don't make sense
- Thoughts that others do not think make sense
- Intense thoughts or images of harm to you or your baby or family
- Extreme sense that things are hopeless
- Seeing or hearing things that aren't there

Postpartum psychosis after childbirth is a temporary but severe mood episode that can affect the way you think or feel!

- Difficulty responding to your baby
- Difficulty sleeping beyond the normal interrupted sleep of new motherhood.
- Confusion, irritability or agitation
- Extreme mood swings
- Periods of feeling excess energy good or bad
- Thoughts jumping around
- Sense of need to do things quicker or more of them

Why are you doing this study?

Postpartum psychosis is a severe illness that may require in-patient care to treat. We are hoping to learn whether Zulresso, a medication to treat postpartum depression (a related condition), can help improve symptoms of postpartum psychosis.

Who can participate in this study?

Women aged 18-45, who have delivered less than one year ago and are experiencing any symptoms listed above may be eligible.

What do I have to do if I join the study?

The study involves a screening visit, a 4-day inpatient (overnight) stay at UNC Hospitals where you will receive a 60-hour continuous infusion in your arm of the FDA approved drug Zulresso (brexanolone). After the hospital stay, there will be 6 follow-up visits at a UNC research clinic.

What is Zulresso (brexanolone)?

Zulresso (brexanolone) is an FDA-approved medication for the treatment of postpartum depression. It is given intravenously (through a small tube in your arm) over a 60-hour period while you are in the hospital.

Why should I join this study?

You can help us learn whether this medication can improve symptoms of postpartum psychosis and there is a chance it may help your symptoms. You will also be cared for by the UNC Perinatal Psychiatry team, who are experts in treating postpartum psychosis.



IRB 20-0812 IRB_subjects@unc.edu IRB Approved 12/15/2021

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Probiotics



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Research Paper
Effect of *Lactobacillus rhamnosus* HN001 in Pregnancy on Postpartum Symptoms of Depression and Anxiety: A Randomised Double-blind Placebo-controlled Trial

R.F. Slykerman^a, F. Hood^b, K. Wickens^b, J.M.D. Thompson^c, C. Barthow^d, R. Murphy^e, J. Kang^b, J. Rowden^a, P. Stone^f, J. Crane^g, T. Stanley^g, P. Abels^g, G. Purdie^h, R. Maude^h, E.A. Mitchell^{h,i,*}, the Probiotic in Pregnancy Study Group

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Probiotic
Depression
Anxiety
Randomised controlled trial
Microbiome gut brain axis

ABSTRACT

Background: Probiotics may help to prevent symptoms of anxiety and depression through several putative mechanisms.
Objective: The aim of this study was to evaluate the effect of *Lactobacillus rhamnosus* HN001 (HN001) given in pregnancy and postpartum on symptoms of maternal depression and anxiety in the postpartum period. This was a secondary outcome, the primary outcome being scores in the offspring at 12 months of age.
Design, Setting, Participants: A randomised, double-blind, placebo-controlled trial of the effect of HN001 on postnatal mood was conducted in 423 women in Auckland and Wellington, New Zealand. Women were recruited at 14–16 weeks gestation.
Intervention: Women were randomised to receive either placebo or HN001 daily from enrolment until 6 months postpartum, if breastfeeding.
Outcome Measures: Modified versions of the Edinburgh Postnatal Depression Scale and State Trait Anxiety Inventory were used to assess symptoms of depression and anxiety postpartum.
Trial Registration: Australia NZ Clinical Trials Registry: ACTRN12612000196842.
Findings: 423 women were recruited between December 2012 and November 2014. 212 women were randomised to HN001 and 211 to placebo. 380 women (89.8%) completed the questionnaire on psychological outcomes. 193 (91.0%) in the treatment group and 187 (88.6%) in the placebo group. Mothers in the probiotic treatment group reported significantly lower depression scores (HN001 mean = 7.7 (SD = 5.4), placebo 9.0 (6.0); effect size = 1.2, (95% CI = 2.3, 0.1), $p = 0.037$) and anxiety scores (HN001 12.0 (4.0), placebo 13.0 (4.0); effect size = 1.0 (-1.0, -0.2), $p = 0.014$) than those in the placebo group. Rates of clinically relevant anxiety on screening (score ≥ 15) were significantly lower in the HN001 treated mothers (OR = 0.44 (0.26, 0.73), $p = 0.002$).
Interpretation: Women who received HN001 had significantly lower depression and anxiety scores in the postpartum period. This probiotic may be useful for the prevention or treatment of symptoms of depression and anxiety postpartum.
Funding Source: Health Research Council of New Zealand (11318) and Fonterra Co-operative Group Ltd.
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1. Introduction

Major depression in pregnancy and after birth occurs in 10–15% of women in New Zealand, a rate comparable to other western countries

(Abbott and Williams, 2006). Postnatal depression (PND) is associated with persistent depression, and even, in a few cases each year, death from suicide (PMNBC, 2014). This disorder may affect a mother's ability to care for and bond with her new infant, as well as her quality of life and daily functioning (Da Costa et al., 2006). In addition, maternal depression can produce long-lasting effects on children's cognitive, social-emotional and health outcomes (Trockick and Reck, 2005; Grace

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NC MATTERS: What are our goals?

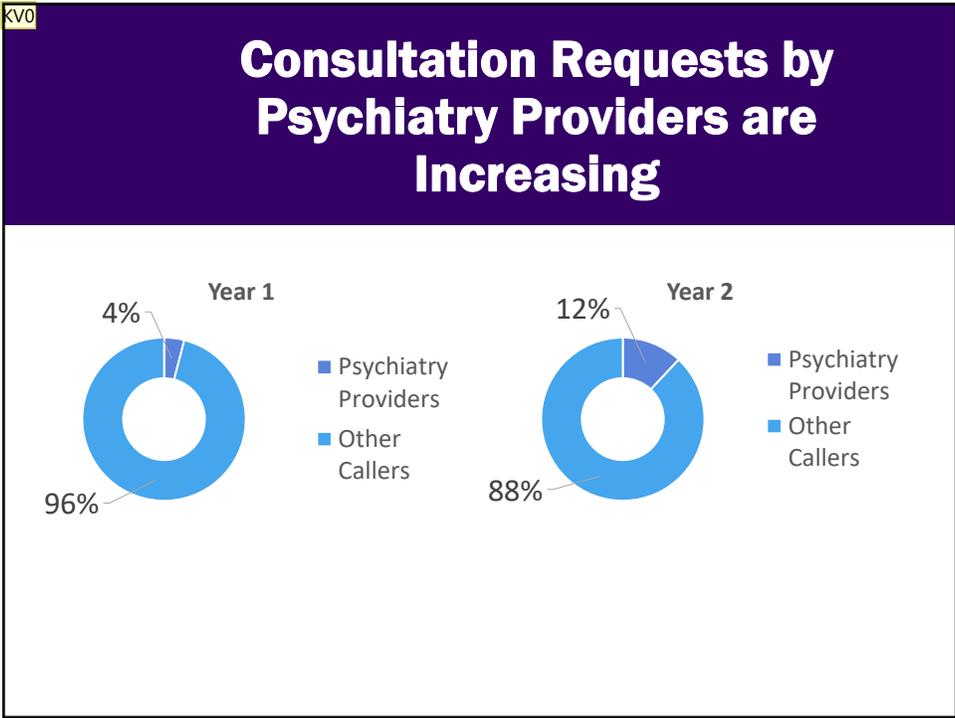
Patients	Providers	Health Care Systems
<ul style="list-style-type: none">• Receive screening during and after pregnancy• Have timely access to mental health services• Continue care in their medical homes	<ul style="list-style-type: none">• Increase confidence addressing perinatal mental health and substance use• Provide satisfactory interprofessional collaboration model	<ul style="list-style-type: none">• Reduce unnecessary referrals & missed appointments• Integrate care with other health conditions and SDOHs• Reduce immediate need for a higher level of care

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NC MATTERS: What do we do?

	Education <ul style="list-style-type: none">• Training for providers and staff• Screening and treatment algorithms
	Consultation <ul style="list-style-type: none">• Real-time psychiatric consultation for health care professionals
	Telepsychiatry <ul style="list-style-type: none">• One-time psychiatric assessments for perinatal patients at no cost
	Resource & Referral <ul style="list-style-type: none">• Linkages with community-based mental health resources

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Slide 48

KV0 Mary can you adjust the key to better explain the provider vs. non-ob? The two bar graphs may be confusing

Katrina Velasquez, 2022-05-24T17:46:15.371

NC Maternal Mental Health MATTERS

NC Maternal Mental Health MATTERS
 We help health care providers support the behavioral health needs of their pregnant and postpartum patients.
 Have a question? Call our consult line!

(919) 681-2909
 ext. 2

Please have on hand:

- Patient Name
- Patient DOB
- Patient Zip Code
- Patient Insurance



ncmatters.org

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Thank you!

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 Karen_Burns@med.unc.edu

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 919-681-2909 x 2

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**Healthy Mom is Critical to
Healthy Baby (and also
because she deserves to be
Healthy too)**

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