Treatment in Pregnancy: Overview and Discussion

Julia Nardi Riddle, MD
Assistant Profressor
Center for Women's Mood Disorder
University of North Carolina – Chapel Hill

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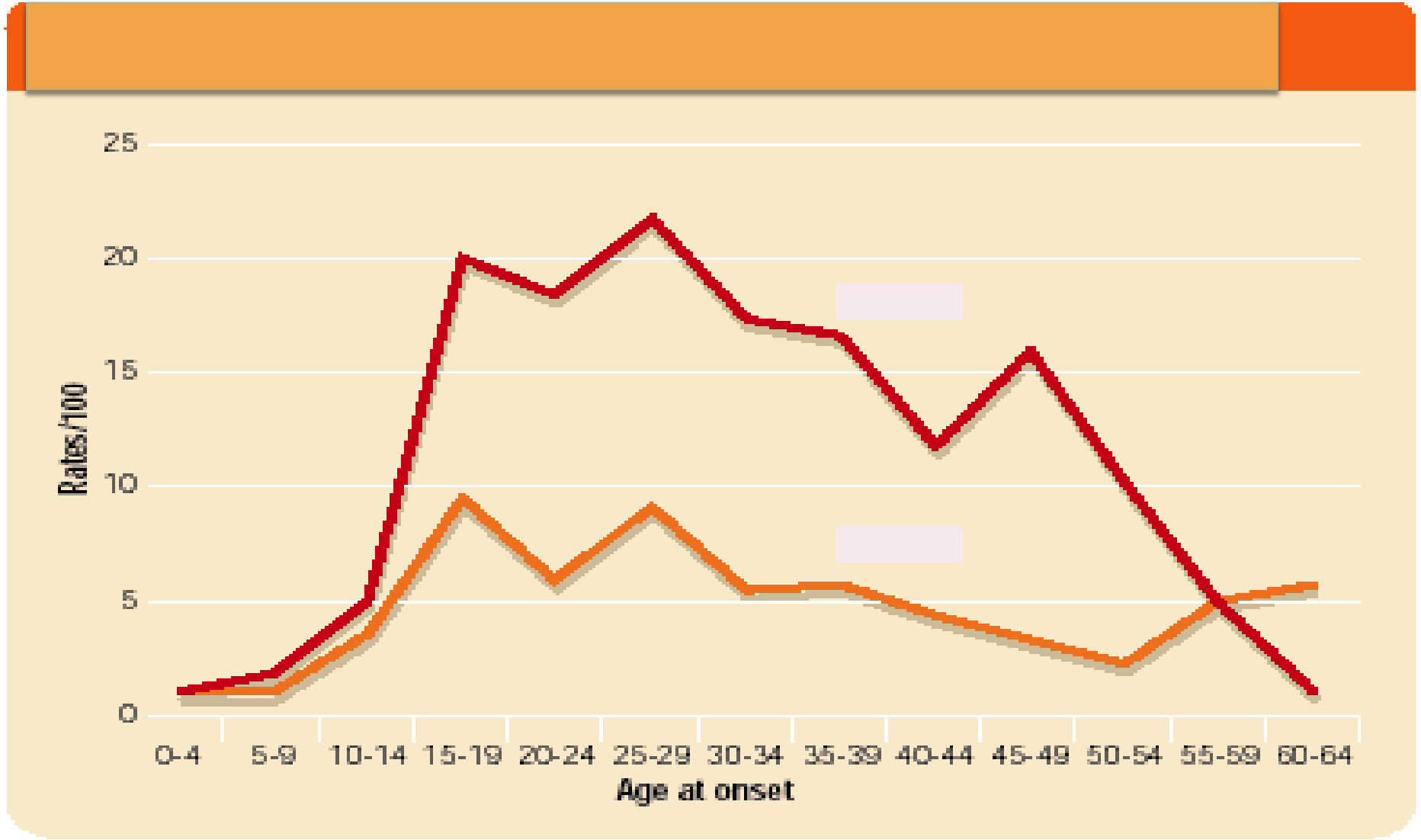
- Financial/COI: None!
- Slides were adapted from talks given by myself and Drs. Lauren Osborne, Lindsay Standeven, and Jennifer Payne
- Slides also utilized information from the National Curriculum for Reproductive Psychiatry (NCRP)

"What conflict of interest?!
I work here in my spare time."

Overview

- Mental Illness during Pregnancy and the postpartum
  - Epidemiology
  - Diagnosis
  - Screening
  - Treatment
- Further Treatment considerations


25
20
15
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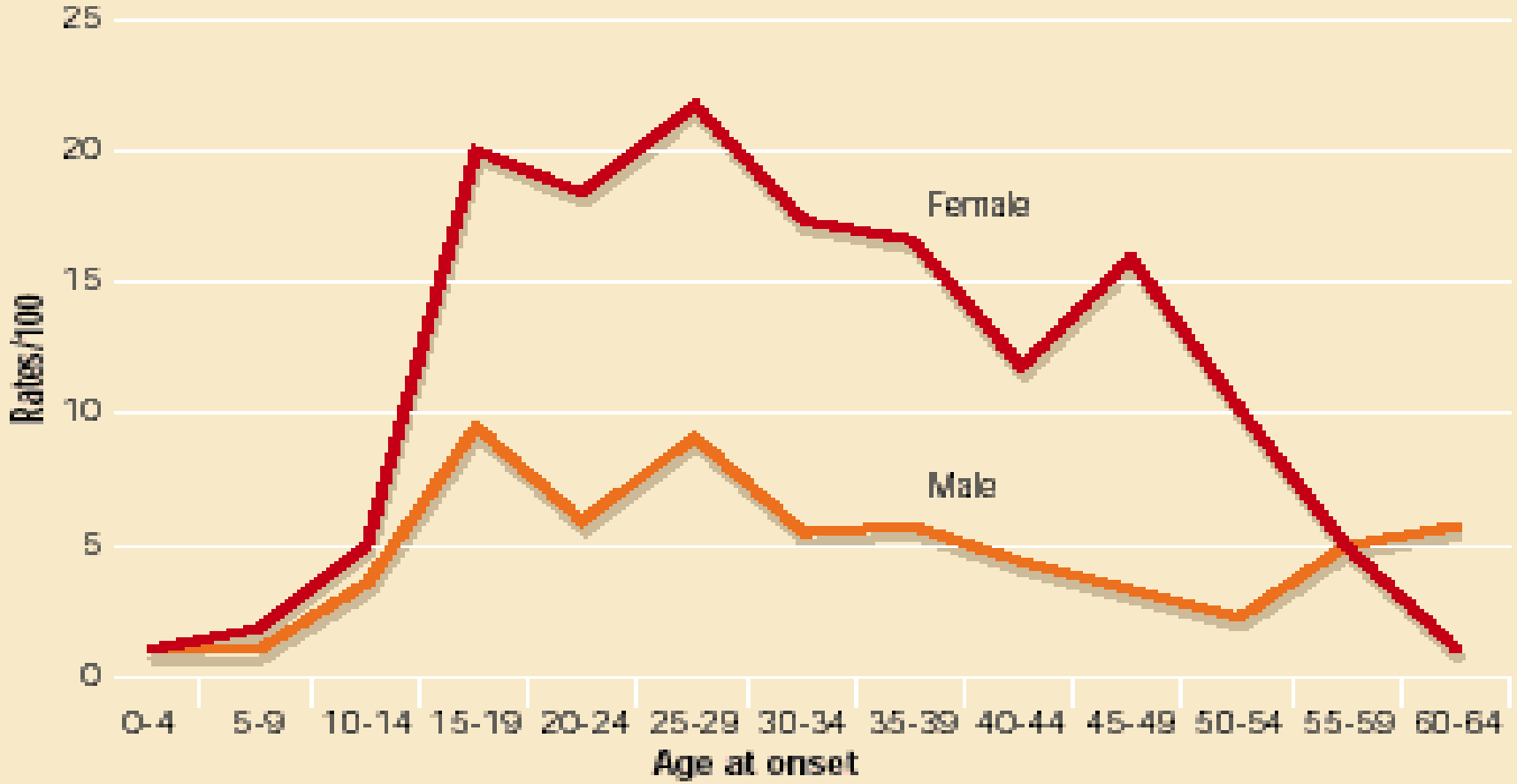
Rates/100
0-4
5-9
10-14
15-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
Age at onset

FIGURE 1. Age-specific rates of major depression in the US



Source: Kessler RC, Zhao S, Blazer DG, et al[11]

Chart shows the steep rise in risk for major depressive disorder just as females enter the fertile period of their lives.

CHANGES TO THE BODY AND MIND DURING PREGNANCY

Physiological and psychological changes in normal pregnancies

Physiological changes

- Weight gain
- **Sleep**
- Endocrine system
- Cardiovascular system
- Hematologic system
- Respiratory system
- Urinary system
- Gastrointestinal system
- Central nervous system

Psychological stages

- Preconception
- First stage (known pregnancy to quickening)
- Second stage (quickening to viability)
- Third stage (viability to delivery)

Sleep

- Most pregnant women (66% to 94%) report alterations in sleep that lead to the subjective perception of poor sleep quality.
- Pregnancy sleep disorder is characterized by insomnia and/or daytime fatigue.
- Abnormal sleep patterns in pregnancy may contribute to certain complications, such as hypertensive disorders and fetal growth restriction.

Gabbe et al., Obstetrics: Normal and Problem Pregnancies, 2017

Sleep

First trimester

- Increased total sleep time: increase in naps
- Increased daytime sleepiness
- Increased nocturnal insomnia

Second trimester

- Normalization of total sleep time
- Increased awakenings

Third trimester

- Decreased total sleep time
- Increased insomnia
- Increased nocturnal awakenings
- Increased daytime sleepiness

Gabbe et al., Obstetrics: Normal and Problem Pregnancies, 2017 Modified from Santiago J, Nolledo M, Kinzler W. Sleep and sleep disorders in pregnancy. Ann Intern Med. 2001;134:396.

Psychological Stages of Pregnancy

Preconception: Early preparation for motherhood starting in childhood (through play)

First stage of pregnancy: realization of pregnancy to feeling baby move

- Primary task: acceptance of pregnancy
- Most common fear: miscarriage
- Common psychological changes:
  - Impaired memory
  - Emotional lability
  - Preoccupation with bodily needs (especially food)
  - Focus on secrecy/privacy of the knowledge of pregnancy

(Stotland and Stewart, Psychological Aspects of Women's Health Care, 2001)

Psychological Stages of Pregnancy

Second stage: Baby movement to third trimester

- Primary tasks:
  - Emotional attachment to fetus
  - Recognizing fetus as separate individual
- Common changes
  - Decrease in uncomfortable physical symptoms -> relative calm
  - Increase in signs of nurturing, such as talking to fetus
  - Increase in anxiety about mothering, and identifying with own mother
  - With increasing awareness of fetus as separate entity, new feelings of ambivalence, resentment
  - As pregnancy begins to show, loss of control over who knows

(Stotland and Stewart, Psychological Aspects of Women's Health Care, 2001)

Psychological Stages of Pregnancy

Third stage: viability to end of pregnancy

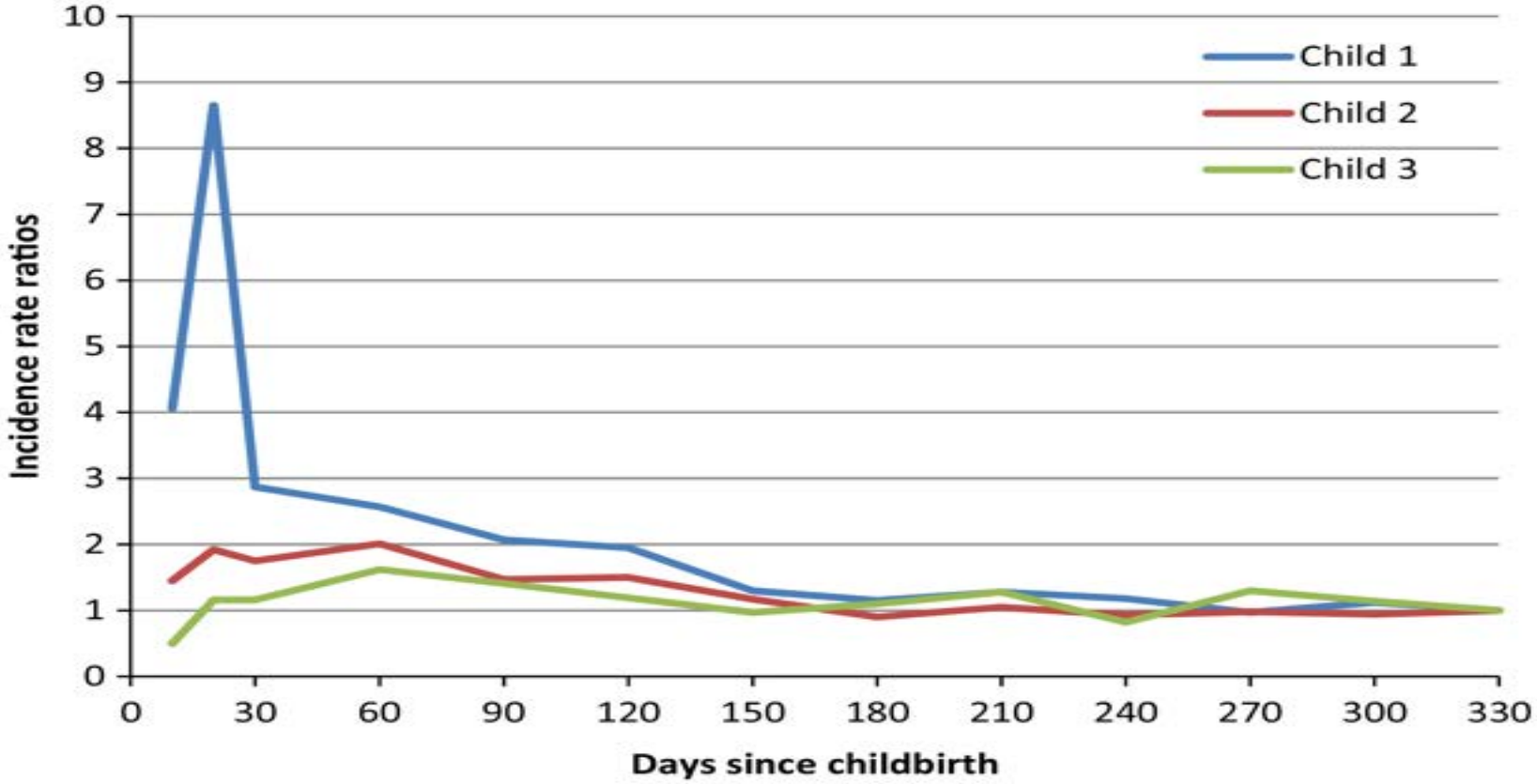
- Maternal-fetal attachment peaks, and at the same time, mother prepares for separation (delivery)
- Major themes:
  - preparation for baby: nesting behaviors
  - somatic concerns and physical discomfort
  - worries about delivery
    - Baby's health
    - Pain
    - Loss of control

(Stotland and Stewart, Psychological Aspects of Women's Health Care, 2001)

MENTAL HEALTH CONDITIONS DURING PREGNANCY

The "Gerber Myth"…

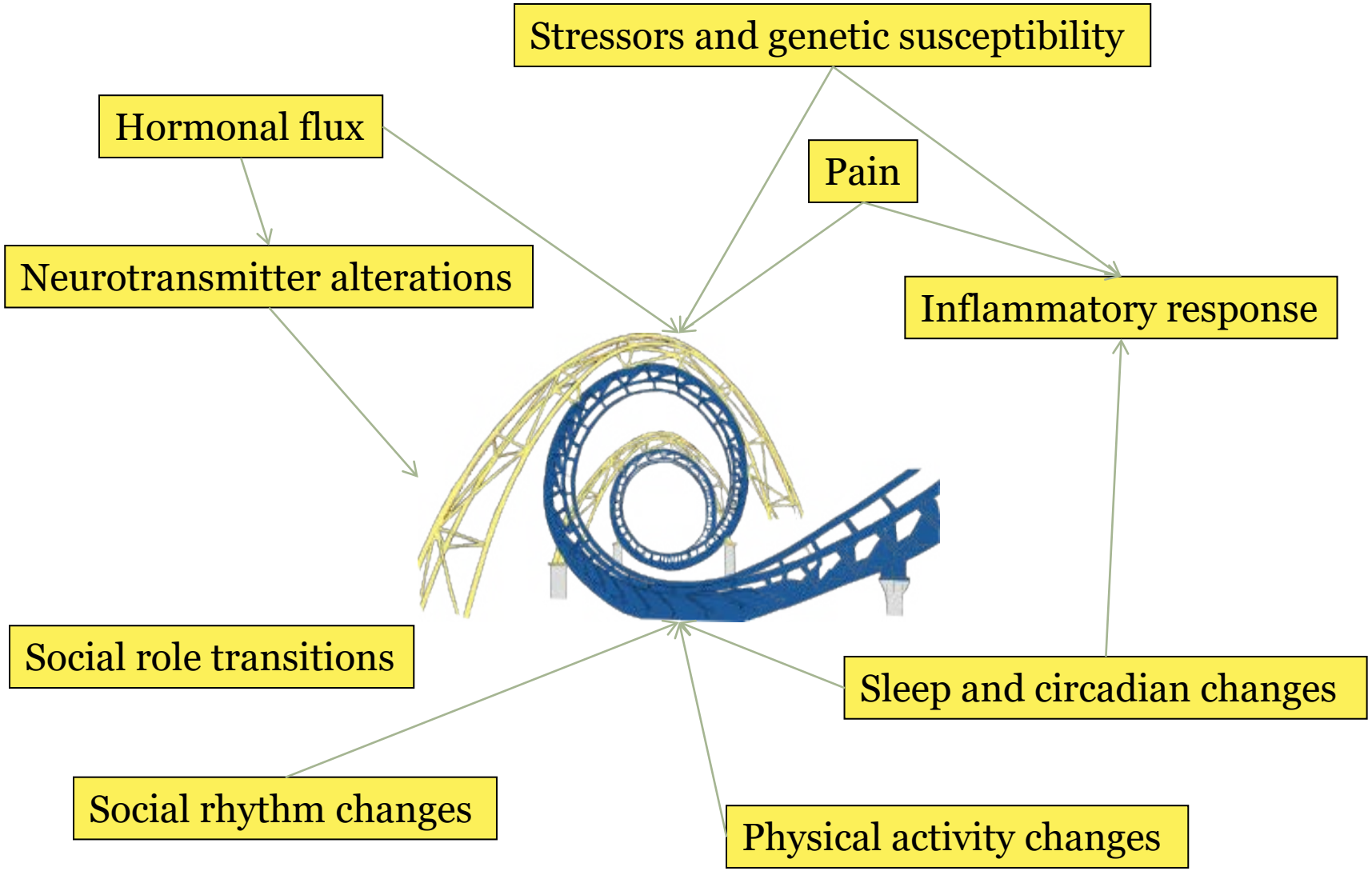
Postpartum vulnerability: First Admission to Psychiatric Hospital



Incidence rate ratios of first admission to a psychiatric hospital 0–12 months after the first, second, or third childbirth. Adjusted for age and calendar period: reference category 300–360 days postpartum after the first, second, or third childbirth, respectively.

Munk-Olsen et al., BIPOLAR DISORDERS, 2013

Contributors to perinatal depression and anxiety



Consequences of perinatal depression

- **Mothers' well-being**
  - Decreased maternal self-efficacy
  - Poor compliance with prenatal care
- **Fathers' well-being**
  - Increased depression & marital stress
  - Increased concern of infants
- **Infant development**
  - Emotion dysregulation
  - Cognitive and language delays
  - Increased risk for psychopathology
- **Mother-infant interaction**
  - Mothers: understimulating or overstimulating
  - Infants: Less responsive, more gaze avoidant, more distress, impaired attachment

Field, 1997; Luomo et al., 2001; Milgrom & McCloud, 1996; Moses, Kolko & Roth, 2004; O'Hara, 1994; Zuckerman et al., 1989

Other effects of perinatal depression and anxiety that mediate outcomes for offspring

- Greater use of alcohol, cigarettes and illicit addictive substances[1]
- Less healthy nutrition[2]
- Higher body mass index[3]
- Less prenatal care[4]
- Increased risk of preterm birth[5]
- Reduced breastfeeding[6]

1. Le Strat Y et al: J Affect Disord 135(1-3):128-38, 2011; 2. Barker ED et al: Br J Psychiatry 203(6):417-21, 2013; 3. McPhie S et al: Midwifery 2014 Jul 19 Epub; 4. Kim HG et al: Arch Womens Ment Health 9(2):103-7, 2006; 5. Grigoriadis S: J Clin Psychiatry 74(4):321-41, 2013; 6. Dennis CL, McQueen K: Pediatrics 123(4):e736-51, 2009

Relationships are the "active ingredients" of early experience

- Crucible of infant experiences are in caregiving relationships
- Nurturing and responsive relationships build healthy brain architecture that provides a strong foundation for learning, behavior, and health.
- When protective relationships are not provided, elevated levels of stress hormones disrupt brain architecture by impairing cell growth and interfering with the formation of healthy neural circuits.

Suicide

- Major cause of maternal death in pregnancy and accounts for up to **20%** of all postpartum deaths
- In countries that track, leading cause of maternal death in first year postpartum

(Shadigian & Bauer, 2005)

How common are these illnesses?

- Depression during pregnancy: 10-15% of women
- Postpartum depression affects up to 20% of women
  - Most common complication of childbirth!
- Women with pre-existing mood disorders at increased risk: 20-50%
- Relapse of Bipolar Illness: 80-100%
- Peripartum Anxiety is under-recognized! Range: 5- 40%
- Prevalence of postpartum anxiety 10-25%
- Intrusive Thoughts in the Postpartum: 100%

Mental Health Conditions in Pregnancy & Postpartum

- Depression and Anxiety During Pregnancy
- Postpartum Depression
- Postpartum Anxiety and OCD
- Post-Traumatic Stress Disorder
- Bipolar Disorder I & II
- Postpartum Psychosis
- ADHD

PERINATAL AND POSTPARTUM DEPRESSION

Baby Blues: Symptoms

WHEN: First 3-5 days postpartum

WHO: Common, 85% of new mothers

SYMPTOMS:

- Weepy
- Mood swings – happy one minute, then sad for no apparent reason

TREATMENT:

- Resolves naturally
- Support groups and family support can help
- Sleep!

Adapted from PSI. www.postpartum.net

Postpartum Depression: Symptoms

WHEN: During Pregnancy and up to a year postpartum, most common in first 3 months postpartum

WHO: 10-15% of women

SYMPTOMS

- Feelings of anger or irritability
- Lack of interest in the baby
- Appetite and sleep disturbance
- Crying and sadness
- Feelings of guilt, shame or hopelessness
- Loss of interest, joy or pleasure in things you used to enjoy
- Possible thoughts of harming the baby or yourself

Adapted from PSI. www.postpartum.net

Postpartum Depression: Risk Factors

- A personal or family history of depression, anxiety, or postpartum depression
- Premenstrual dysphoric disorder (PMDD or PMS)
- Inadequate support in caring for the baby
- Financial stress
- Marital stress
- Complications in pregnancy, birth or breastfeeding
- A major recent life event: loss, house move, job loss
- Mothers of multiples
- Mothers whose infants are in Neonatal Intensive Care (NICU)
- Mothers who've gone through infertility treatments
- Women with a thyroid imbalance
- Women with any form of diabetes (type 1, type 2 or gestational)

Adapted from PSI. www.postpartum.net

Edinburgh Postnatal Depression Scale (EPDS)

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

Treatment for Perinatal/Postpartum Depression

- Therapy
- Medication: SSRIs
- Brexanolone
- ECT
- Self-care: Sleep!

Pregnant Women with Major Depression

- Women with history of Major Depression at greatest risk
- 60-70% of women who stop their antidepressants will relapse into depression

Table 3. Relapse of Major Depression During Pregnancy

Relapse Status	All Women	Medication Status			
		Maintained	Increased	Decreased	Discontinued
No relapse	115 (57.2)	61 (74.4)	11 (55.0)	22 (64.7)	21 (32.3)
Relapse by trimester					
All	86 (42.8)	21 (25.6)	9 (45.0)	12 (35.3)	44 (67.7)
First	44 (51.2)	11 (52.4)	7 (77.8)	5 (41.7)	21 (47.7)
Second	31 (36.0)	9 (42.9)	2 (22.2)	3 (25.0)	19 (43.2)
Third	11 (12.8)	1 (4.8)	0 (0.0)	4 (33.3)	4 (9.1)

ANXIETY DISORDERS IN PREGNANCY AND POSTPARTUM

Epidemiology: Prevalence

	In Peripartum Period	In General Population (Lifetime)	Women in General Population (12 months)
Any anxiety disorder	20.7%	31.1%	23.4%
GAD	9%	5.7%	3.4%
Panic Disorder	1-2%	4.7%	3.8%
OCD	Pre: 0.2-4% Post: 2.3–9%	0.7 - 2.3%	1.8%
PTSD	0.6 - 8%	6.8%	5.2%

Postpartum Anxiety: Symptoms

WHEN: Most common in first 3 months postpartum, can also occur after weaning breastfeeding

WHO: 6-10% of moms in the postpartum

SYMPTOMS :

- Constant worry
- Feeling that something bad is going to happen
- Racing thoughts
- Disturbances of sleep and appetite
- Inability to sit still
- Physical symptoms like shortness of breath, dizziness, hot flashes, and nausea

Adapted from PSI. www.postpartum.net

Perinatal Obsessive Compulsive Disorder (OCD): Symptoms

WHEN: 1 week to 3 months postpartum

WHO: 4% of women, 25% have impairing symptoms though may not meet full criteria

SYMPTOMS

- Obsessions are persistent, disturbing, repetitive thoughts which are often related to the baby
- Compulsions, where the mom may do certain things over and over again to reduce her fears and obsessions. This may include things like needing to clean constantly, check things many times, count or reorder things.
- A sense of horror about the obsessions
- Fear of being left alone with the infant
- Hypervigilance in protecting the infant
- Moms with postpartum OCD know that their thoughts are bizarre and are very unlikely to ever act on them.

Adapted from PSI. www.postpartum.net

Diagnostic Criteria: Key features

- Excessive or uncontrolled worry
- Duration: >1 month during peripartum

GAD

Excessive worry present majority of days

Functional impairment

Worries about a variety of topics that are difficult to control

Feeling keyed-up, mind blanking

Panic Disorder

Recurrent, unexpected panic attacks

Persistent worry about additional panic attacks and their consequences

Panic attack: Abrupt surge of intense fear/discomfort, along with physical symptoms of tachycardia, dizziness, fear of dying

OCD

Presence of obsessions, compulsions or both

Recurrent/persistent thoughts, urges or images experiences as intrusive and unwanted

Compulsions are repetitive behaviors or mental acts that a patient is drive to perform in response to obsession

GAD vs. OCD

The Nature of the Thoughts	
GAD	**OCD**
Anxious thoughts are worries related to real-life, routine matters that bring about apprehension and thought distortions. Thought content tends to shift over time.	Intrusive, repetitive thoughts and/or ritualistic behaviors that are experienced as unwanted.

"what if I have to have a C-section and I have a complication and then I can't work again and am a bad mother?"

"I keep seeing an image that I'm going to drop the baby down the stairs, so now I sit when I go down the stairs or I don't hold the baby at all"

A word about intrusive thoughts and images

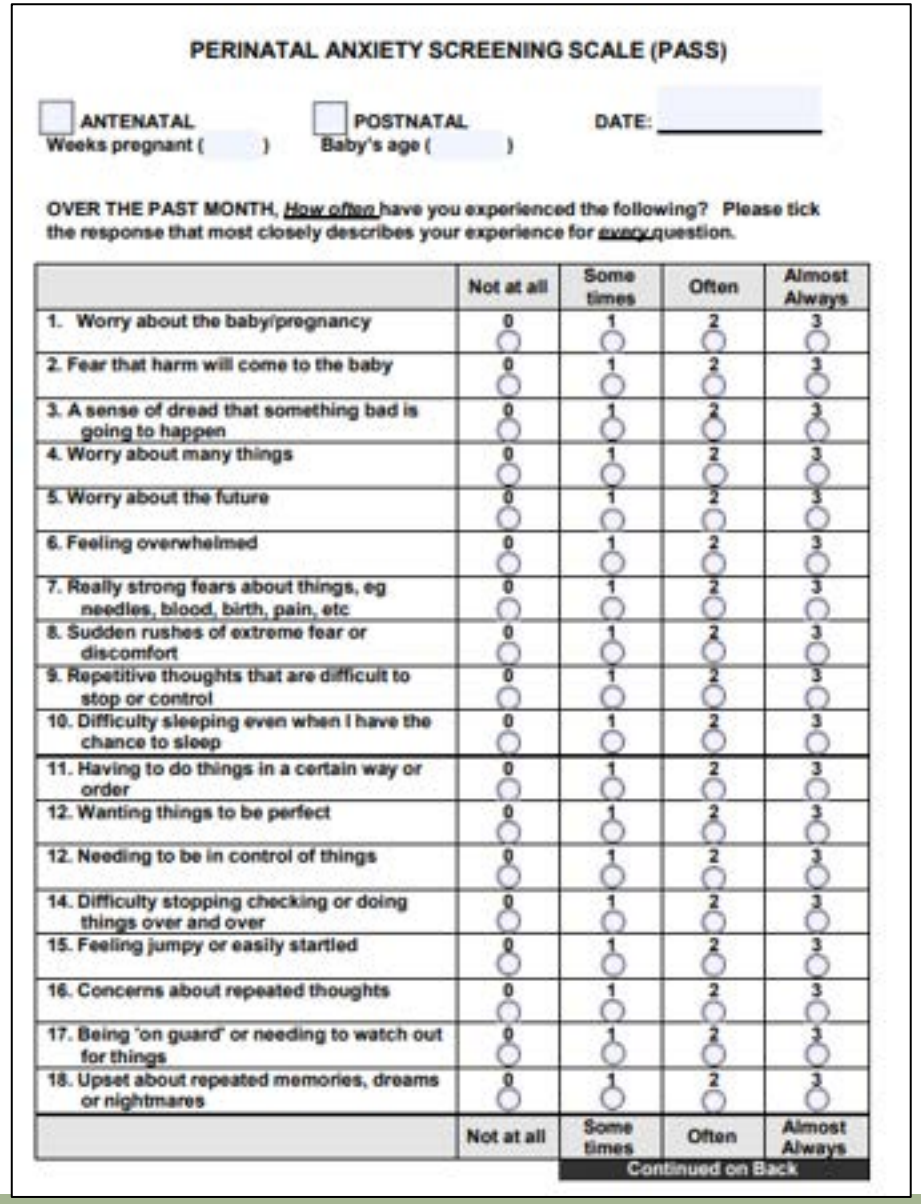
- 100% of new moms (and many dads) will experience intrusive thoughts and/or images of harm coming to the baby. Most of them do not have OCD.
- What are intrusive thoughts and images?
  - Unwanted thoughts, images or urges that cause distress
  - Examples in lecture
- These only become problematic if they change how a mother acts
  - Ie. If you no longer feel like you can care for your baby
  - Ie. You cannot sleep
- These are NOT psychotic symptoms!!!
  - Psychotic delusions of harm coming to the baby do not cause distress – due to illness, they seem like a good idea

Epidemiology: Screening

- Consider using the Perinatal Anxiety Screen Scale (PASS) or GAD-7
  - Preliminary validation shows that the PASS identifies 68% of women with diagnosable anxiety disorder. EPDS anxiety subscale only identified 36% (Somerville et al 2014)
- For OCD: Perinatal Obsessive Compulsive Scale (PCOS) or the Obsessive-Compulsive Inventory – Revised (OCI-R)

- A full assessment of emotional and mental well-being in the postpartum period regardless of prior assessment

The Perinatal Anxiety Screening Scale (PASS)



PERINATAL ANXIETY SCREENING SCALE (PASS)

☐ ANTENATAL Weeks pregnant ( ) ☐ POSTNATAL Baby's age ( ) DATE: _____

OVER THE PAST MONTH, How often have you experienced the following? Please tick the response that most closely describes your experience for every question.

	Not at all	Some times	Often	Almost Always
1. Worry about the baby/pregnancy	0	1	2	3
2. Fear that harm will come to the baby	0	1	2	3
3. A sense of dread that something bad is going to happen	0	1	2	3
4. Worry about many things	0	1	2	3
5. Worry about the future	0	1	2	3
6. Feeling overwhelmed	0	1	2	3
7. Really strong fears about things, eg needles, blood, birth, pain, etc	0	1	2	3
8. Sudden rushes of extreme fear or discomfort	0	1	2	3
9. Repetitive thoughts that are difficult to stop or control	0	1	2	3
10. Difficulty sleeping even when I have the chance to sleep	0	1	2	3
11. Having to do things in a certain way or order	0	1	2	3
12. Wanting things to be perfect	0	1	2	3
12. Needing to be in control of things	0	1	2	3
14. Difficulty stopping checking or doing things over and over	0	1	2	3
15. Feeling jumpy or easily startled	0	1	2	3
16. Concerns about repeated thoughts	0	1	2	3
17. Being "on guard" or needing to watch out for things	0	1	2	3
18. Upset about repeated memories, dreams or nightmares	0	1	2	3
	Not at all	Some times	Often	Almost Always

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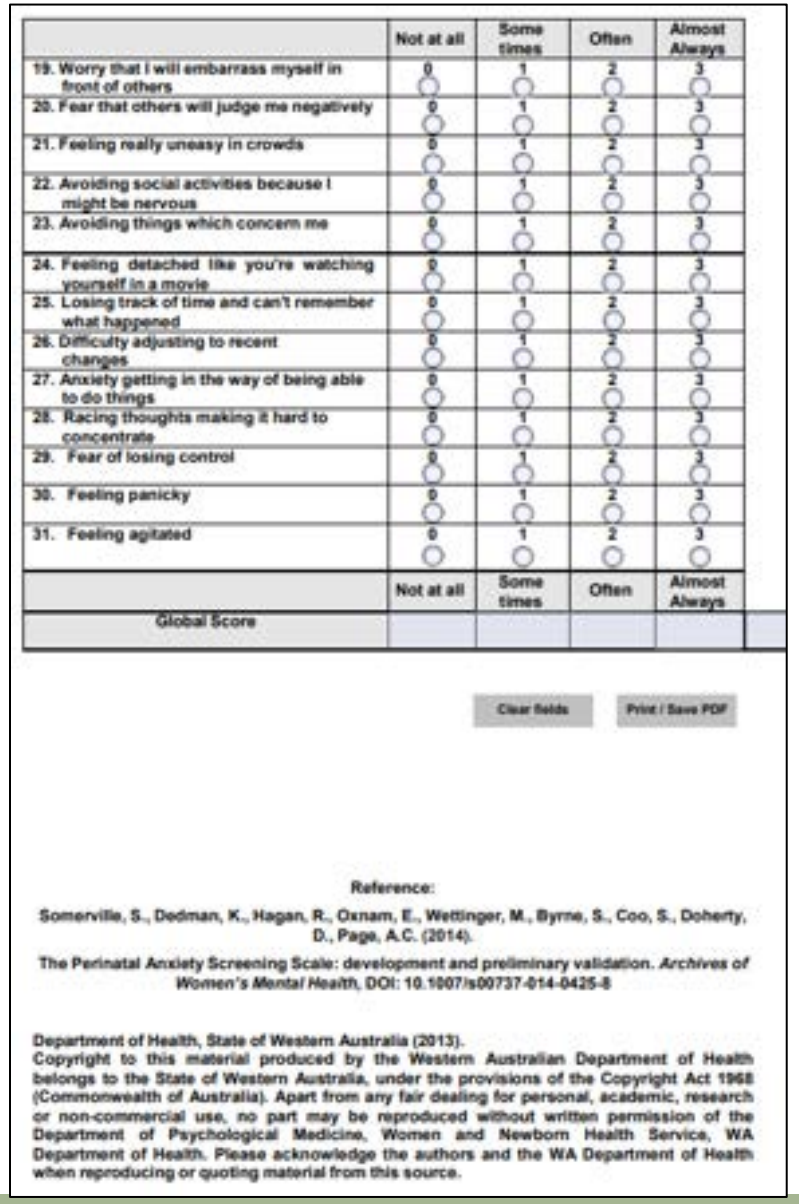

	Not at all	Some times	Often	Almost Always
19. Worry that I will embarrass myself in front of others	0	1	2	3
20. Fear that others will judge me negatively	0	1	2	3
21. Feeling really uneasy in crowds	0	1	2	3
22. Avoiding social activities because I might be nervous	0	1	2	3
23. Avoiding things which concern me	0	1	2	3
24. Feeling detached like you're watching yourself in a movie	0	1	2	3
25. Losing track of time and can't remember what happened	0	1	2	3
26. Difficulty adjusting to recent changes	0	1	2	3
27. Anxiety getting in the way of being able to do things	0	1	2	3
28. Racing thoughts making it hard to concentrate	0	1	2	3
29. Fear of losing control	0	1	2	3
30. Feeling panicky	0	1	2	3
31. Feeling agitated	0	1	2	3
	Not at all	Some times	Often	Almost Always
Global Score				

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Reference:

Somerville, S., Dedman, K., Hagan, R., Oxnam, E., Wettinger, M., Byrne, S., Coo, S., Doherty, D., Page, A.C. (2014).

The Perinatal Anxiety Screening Scale: development and preliminary validation. *Archives of Women's Mental Health*, DOI: 10.1007/s00737-014-0425-8

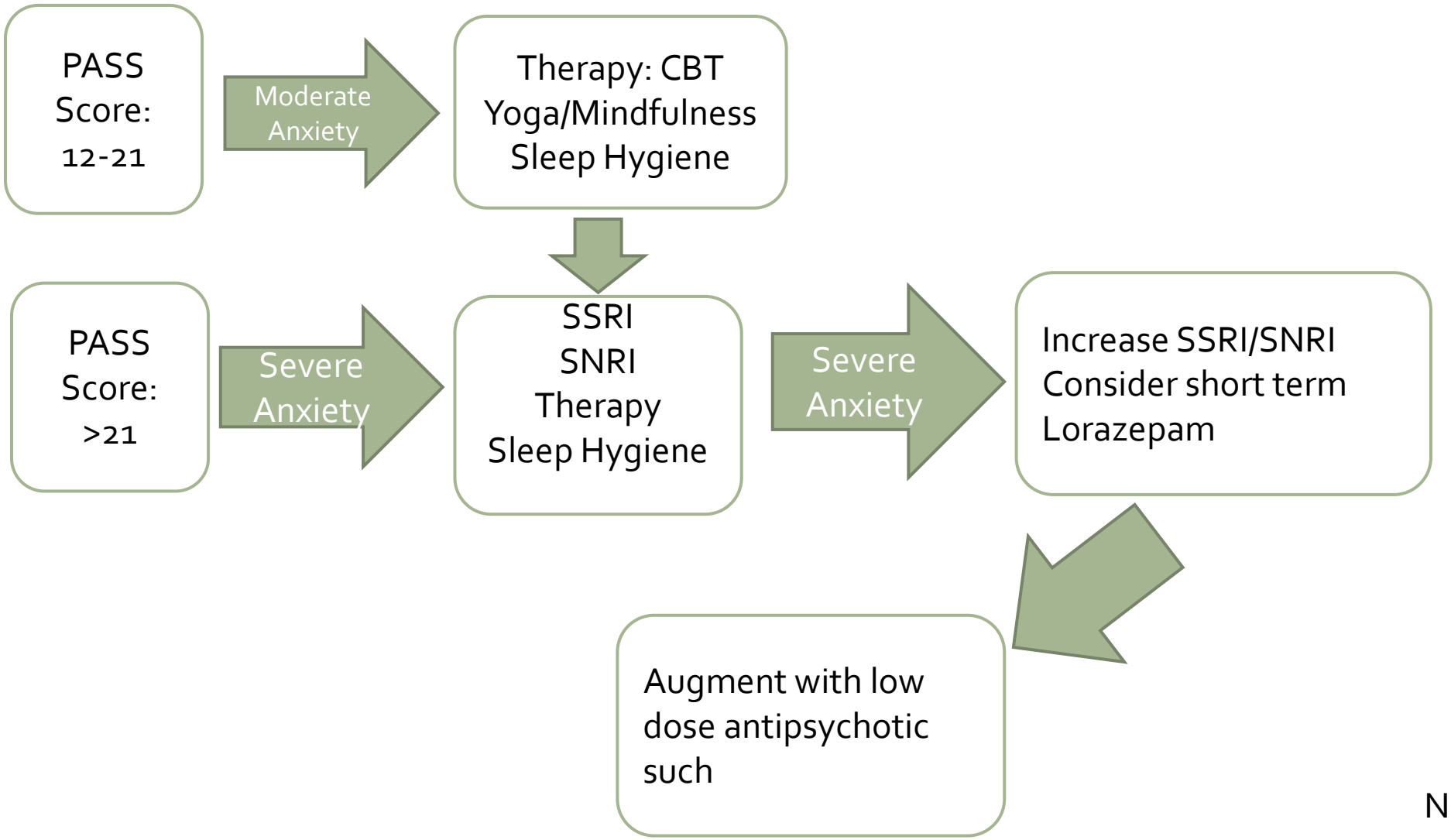
Physiological Symptoms: Mimics

- Physical symptoms may trigger feelings of anxiety/panic in some women
  - Normal physiology of pregnancy: elevated heart rate, shortness of breath
  - Thyroid dysfunction
  - Anemia
  - Preeclampsia
  - Pulmonary embolism
  - Cardiac arrythmia
  - Asthma
  - Infection

Dosages for common SSRIs

	Starting Dose (to mitigate side effects)	Range often needed for MDD/PPD	Range often needed for GAD	Range often needed for OCD
Sertraline	25-50 mg	100 – 200 mg	100-200 mg	200-400 mg
Fluoxetine	10 mg	20 – 60 mg	20-60 mg	40-120 mg
Escitalopram	5-10 mg HS	10-20 mg	20-40 mg	20-60 mg
Citalopram	10 mg	20-40 mg	20-40 mg	20-80 mg
Fluvoxamine	50-100 mg HS	----------	--------	100-300 mg

Treatment: Perinatal General Anxiety Disorder



NCRP x OB

Post-Traumatic Stress Disorder related to childbirth: Symptoms

WHEN: Pregnancy and up to a year postpartum

WHO: Approximately 9% of women experience postpartum post-traumatic stress disorder (PTSD) following childbirth

RISKS

Most often, this illness is caused by a real or perceived trauma during delivery or postpartum:

- Prolapsed cord
- Unplanned C-section
- Use of vacuum extractor or forceps to deliver the baby
- Baby going to NICU
- Feelings of powerlessness, poor communication and/or lack of support and reassurance during the delivery
- Women who have experienced a previous trauma, such as rape or sexual abuse, are also at a higher risk for experiencing postpartum PTSD.
- Women who have experienced a severe physical complication or injury related to pregnancy or childbirth, such as severe postpartum hemorrhage, unexpected hysterectomy, severe preeclampsia/eclampsia, perineal trauma (3rd or 4th degree tear), or cardiac disease.

Adapted from PSI. www.postpartum.net

Post-Traumatic Stress Disorder related to childbirth: Symptoms

SYMPTOMS

- Intrusive re-experiencing of a past traumatic event (which in this case may have been the childbirth itself)
- Flashbacks or nightmares
- Avoidance of stimuli associated with the event, including thoughts, feelings, people, places and details of the event
- Persistent increased arousal (irritability, difficulty sleeping, hypervigilance, exaggerated startle response)
- Anxiety and panic attacks
- Feeling a sense of unreality and detachment

Adapted from PSI. www.postpartum.net

BIPOLAR DISORDERS AND POSTPARTUM PSYCHOSIS

Bipolar 1 Disorder: Symptoms

NOTE: This is not specific to pregnancy and postpartum

SYMPTOMS

- To be considered mania, the elevated, expansive, or irritable mood must last for at least one week and be present most of the day, nearly every day. To be considered hypomania, the mood must last at least four consecutive days and be present most of the day, almost every day.
- Periods of severely depressed mood and irritability
- Mood much better than normal
- Rapid speech
- Little need for sleep
- Racing thoughts, trouble concentrating
- Continuous high energy
- Overconfidence
- Delusions (often grandiose, but including paranoid)
- Impulsiveness, poor judgment, distractability
- Grandiose thoughts, inflated sense of self-importance
- In the most severe cases, delusions and hallucinations

Adapted from PSI. www.postpartum.net

Bipolar 2 Disorder: Symptoms

NOTE: No specific to pregnancy/postpartum

SYMPTOMS

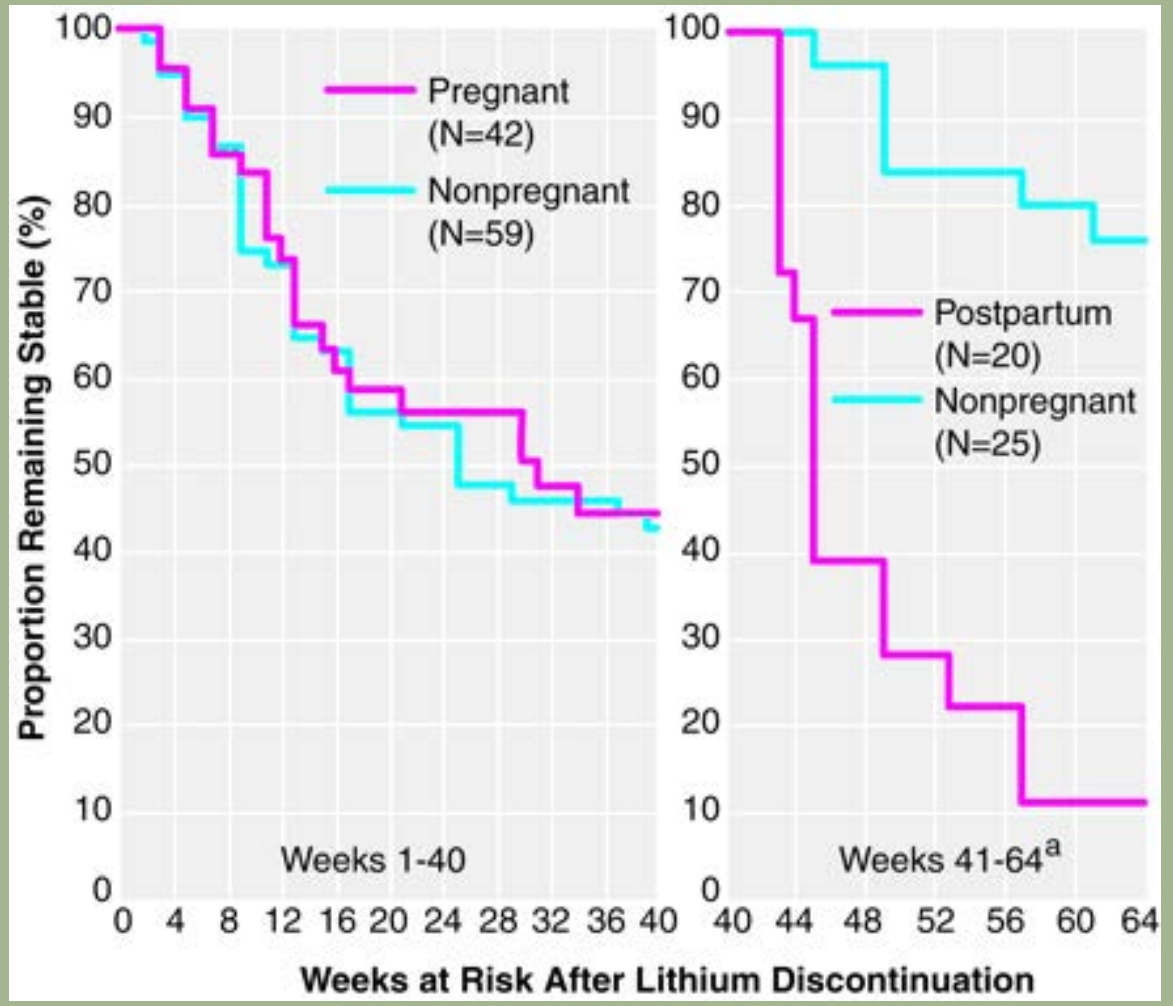
- Periods of severe depression
- Periods when mood much better than normal
- Rapid speech
- Little need for sleep
- Racing thoughts, trouble concentrating
- Anxiety
- Irritability
- Continuous high energy
- Overconfidence

Adapted from PSI. www.postpartum.net

Pregnant Women with Bipolar Disorder

In an initial retrospective study, the relapse rate off of lithium was no different during pregnancy than at any other nine-month period

In contrast, the relapse rate postpartum was 2.9 times greater than for non-pregnant females



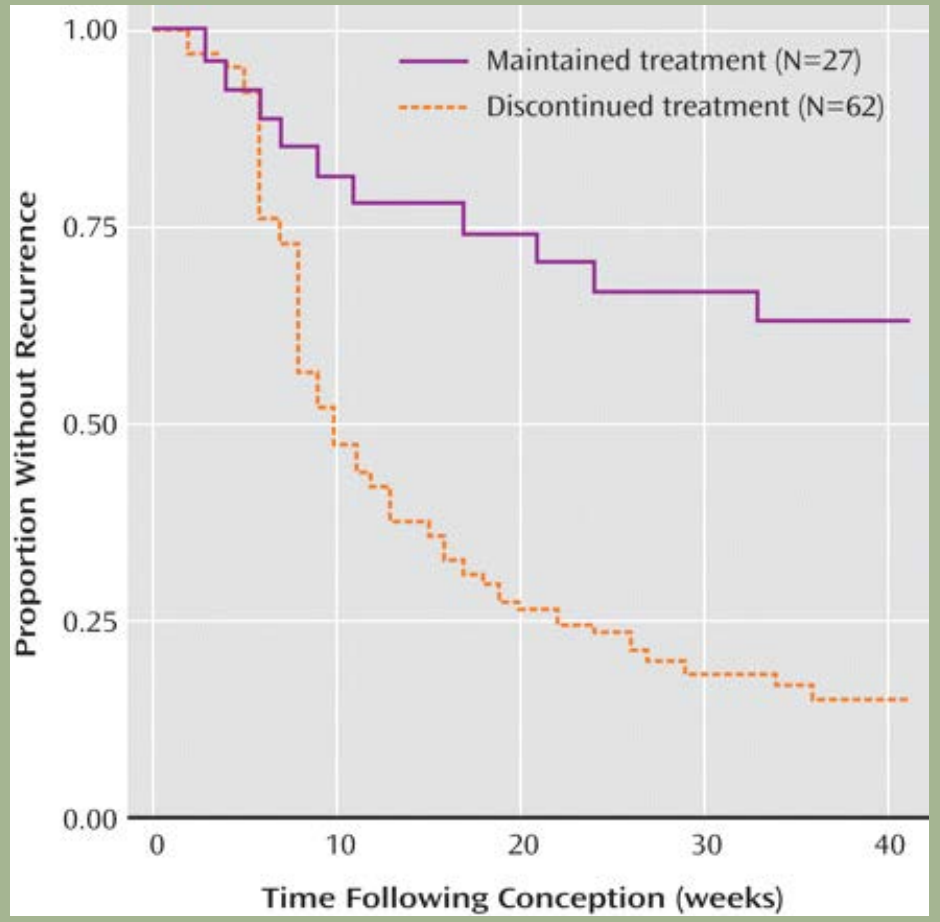
Viguera et al., AJP 2000

Pregnant Women with Bipolar Disorder

In a prospective study….

Discontinuation of mood stabilizers during pregnancy increases the risk of relapse

- 85.5% women who discontinued meds relapsed
  - 40% of pregnancy in illness episode
- 37% of women who continued meds relapsed
  - 8.8% of pregnancy in illness episode



Viguera et al., AJP 2007

Postpartum Psychosis: Symptoms

WHEN: Rapidly after birth, between 2-12 weeks, especially when >48 without sleep – last until treated

WHO: Occurs in .1-.2% of births

NOTE: This is very RARE and VERY SERIOUS (emergency)

RISK FACTOR:

- Personal or family history of bipolar disorder
- Prior postpartum psychosis (80% will reoccur)
- Sleep deprivation
- Stopping medications for bipolar illness

Adapted from PSI. www.postpartum.net

Postpartum Psychosis: Symptoms

SYMPTOMS

- Can fluctuate
- Delusions or strange beliefs, particularly related to the baby or family unit
- Hallucinations (seeing , hearing, feeling things that aren't there)
- Bizarre behaviors
- Feeling very irritated
- Hyperactivity
- Decreased need for or inability to sleep
- Paranoia and suspiciousness
- Rapid mood swings
- Difficulty communicating at times

Postpartum Psychosis: Symptoms

TREATMENT:

- Lithium!! (And antipsychotics)
- Not SSRIs!
- Required immediate psychiatric help
- Often requires hospitalization
- TREATABLE!!

Postpartum Psychosis vs. OCD

The Nature of the Thoughts	
Postpartum Psychosis	**OCD**
More of a manic state with severe and dangerous delusions. Can include confusion or appear similar to delirium. This is a psychiatric emergency. Delusional beliefs ego-syntonic: they are experienced without insight. Mothers likely need urgent hospitalization and the baby needs to be in the care of someone else.	These thoughts are ego-dystonic: extreme distress is experienced with the thoughts. They are unwanted and do not make sense. It is not recommended to separate infants from their mothers but, instead, to pursue treatment and psychoeducation.

"I am on a special mission to save this baby and the only option is for her to go to heaven and be protected by God"

"I keep images on my baby dead in bed from rolling over, so I bought an Owlet and I sleep beside her bed so I can check on her every few minutes"

MCPAP For Moms

Summary of Emotional Complications During Pregnancy and the Postpartum Period

	Baby Blues	Perinatal Depression	Perinatal Anxiety	Posttraumatic Disorder (PTSD)	Obsessive-Compulsive Disorder	Postpartum Psychosis
What is it?	Common and temporary experience right after childbirth when a new mother may have sudden mood swings, feeling very happy, then very sad, or cry for no apparent reason.	Depressive episode that occurs during pregnancy or within a year of giving birth.	A range of anxiety disorders, including generalized anxiety, panic, social anxiety and PTSD, experienced during pregnancy or the postpartum period.	Distressing anxiety symptoms experienced after traumatic events(s).	Intrusive repetitive thoughts that are scary and do not make sense to mother/expectant mother. Rituals (e.g., counting, cleaning, hand washing). May occur with or without depression.	Very rare and serious. Sudden onset of psychotic symptoms following childbirth (increased risk with bipolar disorder). Usually involves poor insight about illness/symptoms, making it extremely dangerous.
When does it start?	First week after delivery. Peaks 3-5 days after delivery and usually resolves 10-12 days postpartum.	Most often occurs in the first 3 months postpartum. May begin after weaning baby or when menstrual cycle resumes.	Immediately after delivery to 6 weeks postpartum. Occasionally begins after weaning baby or when menstrual cycle resumes.	May be present before pregnancy/birth. Can present as a result of traumatic birth. Underlying PTSD can also be worsened by traumatic birth.	1 week to 3 months postpartum. Occasionally begins after weaning baby or when menstrual cycle resumes. May also occur in pregnancy.	Typically presents rapidly after birth. Onset is usually between 2 – 12 weeks after delivery. Watch carefully if sleep deprived for ≥48 hours.
Risk factors	Life changes, lack of support and/or additional challenges (difficult pregnancy, birth, health challenges for mom or baby, twins). Prior pregnancy loss. Dysregulated baby-crying feeding, sleep problems.	Life changes, lack of support and/or additional challenges (difficult pregnancy, birth, health challenges for mom or baby, twins). Prior pregnancy loss. Dysregulated baby-crying feeding, sleep problems.	Life changes, lack of support and/or additional challenges (difficult pregnancy, birth, health challenges for mom or baby, twins). Prior pregnancy loss. Dysregulated baby-crying feeding, sleep problems.	Lack of partner support, elevated depression symptoms, more physical problems since birth, less health promoting behaviors. Prior pregnancy loss. Dysregulated baby-crying feeding, sleep problems.	Family history of OCD, other anxiety disorders. Depressive symptoms. Prior pregnancy loss. Dysregulated baby-crying feeding, sleep problems.	Bipolar disorder, history of psychosis, history of postpartum psychosis (80% will relapse), family history of psychotic illness, sleep deprivation, medication discontinuation for bipolar disorder (especially when done quickly). Prior pregnancy loss. Dysregulated baby-crying feeding, sleep problems.
How long does it last?	A few hours to a few weeks.	2 weeks to a year or longer. Symptom onset may be gradual.	From weeks to months to longer.	From 1 month to longer.	From weeks to months to longer.	Until treated.
How often does it occur?	Occurs in up to 85% of women.	Occurs in up to 19% of women.	Generalized anxiety occurs in 6-8% in first 6 months after delivery. Panic disorder occurs in .5-3% of women 6-10 weeks postpartum. Social anxiety occurs in 0.2-7% of early postpartum women.	Occurs in 2-15% of women. Presents after childbirth in 2-9% of women.	May occur in up to 4% of women.	Occurs in 1-2 or 3 in 1,000 births.
What happens?	Women experience dysphoric mood, crying, mood lability, anxiety, sleeplessness, loss of appetite, and irritability. Postpartum depression is independent of blues, but blues is a risk factor for postpartum depression.	Change in appetite, sleep, energy, motivation, and concentration. May experience negative thinking including guilt, hopelessness, helplessness, and worthlessness. May also experience suicidal thoughts and evolution of psychotics symptoms.	Fear and anxiety, panic attacks, shortness of breath, rapid pulse, dizziness, chest or stomach pains, fear of detachment/doom, fear of going crazy or dying. May have intrusive thoughts.	Change in cognition, mood, arousal associated with traumatic event(s) and avoidance of stimuli associated with traumatic event.	Disturbing repetitive thoughts (which may include harming baby), adapting compulsive behavior to prevent baby from being harmed (secondary to obsessional thoughts about harming baby that scare women).	Mood fluctuation, confusion, marked cognitive impairment. Bizarre behavior, insomnia, visual and auditory hallucinations and unusual (e.g. tactile and olfactory) hallucinations. May have moments of lucidity. **May include altruistic delusions about infanticide and/or homicide and/or suicide that need to be addressed immediately.**
Resources and treatment	May resolve naturally. Resources include support groups, psycho-education (see MCPAP for Moms website and materials for detailed information) and sleep hygiene (asking/accepting other help during nighttime feedings). Address infant behavioral dysregulation -crying, sleep, feeding problems- in context of perinatal emotional complications.	For depression, anxiety, PTSD and OCD, treatment options include individual therapy, dyadic therapy for mother and baby, and medication. Resources include support groups, psycho-education, and complementary and alternative therapies including exercise and yoga. Encourage self-care including healthy diet and massage. Encourage engagement in social and community supports (including support groups) (see MCPAP for Moms website and materials for detailed resources). Encourage sleep hygiene and asking/accepting help from others during nighttime feedings). Address infant behavioral dysregulation -crying, sleep, feeding problems- in context of perinatal emotional complications. Additional complementary and alternative therapies options for depression include bright light therapy, Omega-3, fatty acids, acupuncture and folate.				**Requires immediate psychiatric help. Hospitalization usually necessary.** Medication is usually indicated. If history of postpartum psychosis, preventative treatment is needed in subsequent pregnancies. Encourage sleep hygiene for prevention (e.g. consistent sleep/wake times, help with feedings at night).

[1] Adapted from Susan Hickman, Ph.D., Director of the Postpartum Mood Disorder Clinic, San Diego, Valerie D. Raskin, M.D., Assistant Professor of Clinical Psychiatry at the University of Chicago, IL ("Parents" September 1996)

[2] O'Hara MW, Wisner KL. Perinatal mental illness: Definition, description and aetiology. Best Pract Res Clin Obstet Gynaecol. 2013 Oct 7. pii: S1521-6934(13)00133-8. doi: 10.1016/j.bpobgyn.2013.09.002. [Epub ahead of print]

ADHD
IN PREGNANCY

TREATMENT

Prescribing Sleep

Focus on Self-Care over Self-Sacrifice

Change the message from "A good mother sacrifices for her family" to "Meeting a mother's needs allows her to better care for her family."

Consolidate Sleep

One chunk of 4-5 hours uninterrupted sleep plus another 2-3 hours is better than being woken all night every 2 hours.

Expand the Workforce

Infant night feedings are a job for more than 1 person. Recruit help if possible.

Flex the Breast

Breastfeeding women can pump during the day and have others bottle feed at night. If needed, formula is compatible with breastfeeding.

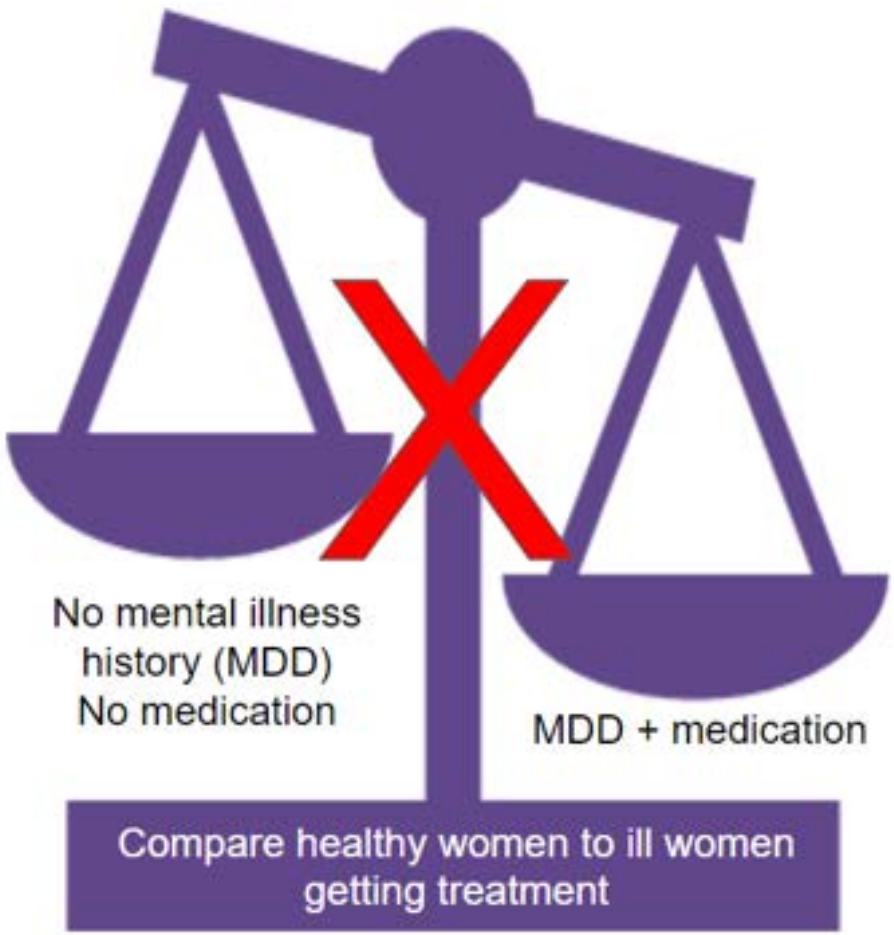
Leistikow N, Baller EB, Bradshaw PJ, Riddle JN, Ross DA, Osborne LM. Prescribing Sleep: An Overlooked Treatment for Postpartum Depression. Biol Psychiatry. 2022 Aug 1;92(3):e13-e15. doi: 10.1016/j.biopsych.2022.03.006. Epub 2022 Mar 16. PMID: 35400485.

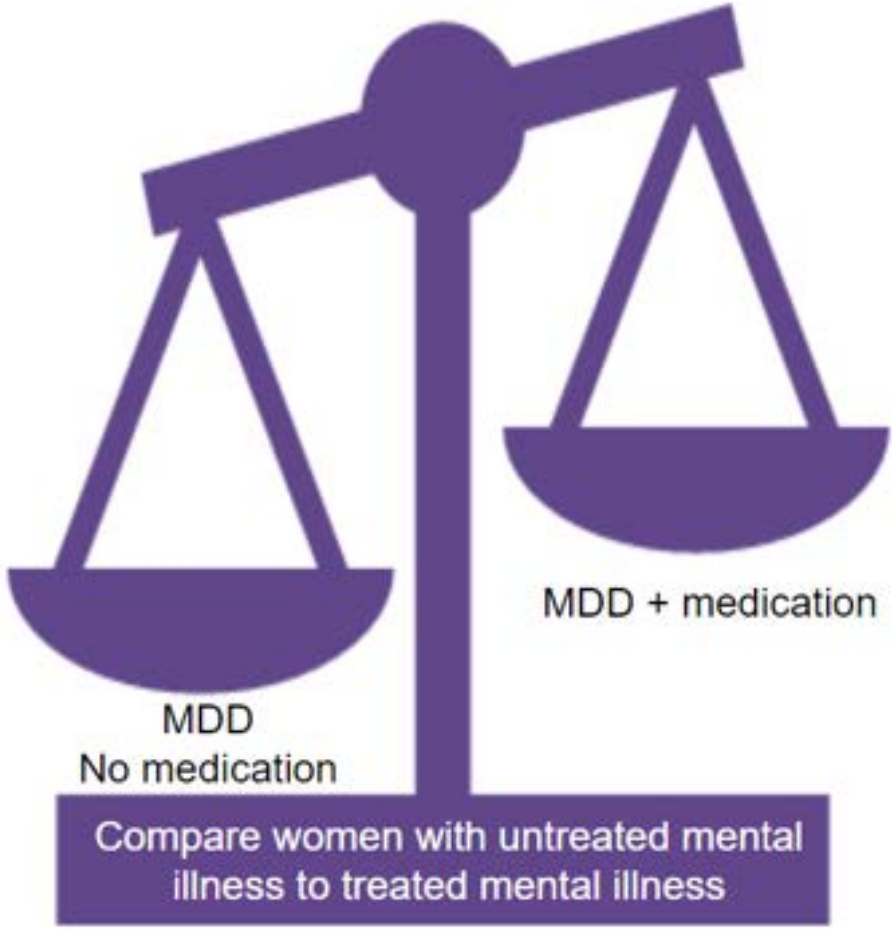
Pharmacological management

- Several trials indicate good efficacy of antidepressants for perinatal depression:
  - SSRIs (sertraline and fluoxetine most safety data)
  - Bupropion
  - SNRIs (chronic pain or migraine)
  - Mirtazapine (good for hyperemesis)
- Antidepressants work comparably for PPD and depression at other points in the life cycle; no one antidepressant class found to be best (Payne, 2007)
- Brexanolone

Risk-risk paradigm

NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY





Risk-risk paradigm

Risks of untreated perinatal depression:

Worse quality of life

More missed days of work

Suicide attempts/completion

Risk of substance use

Hypertensive disorders of pregnancy

Cesarean delivery

Preterm birth

Small for gestational age birth

Insecure attachment patterns

Developmental delays

Risks of medication (SSRI) use in pregnancy:

~~Congenital malformations~~

~~Preterm birth~~

PPHN

Neonatal adaptation syndrome

~~Developmental delays~~

Historically cited risks that have since been disproven with appropriate analysis

NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

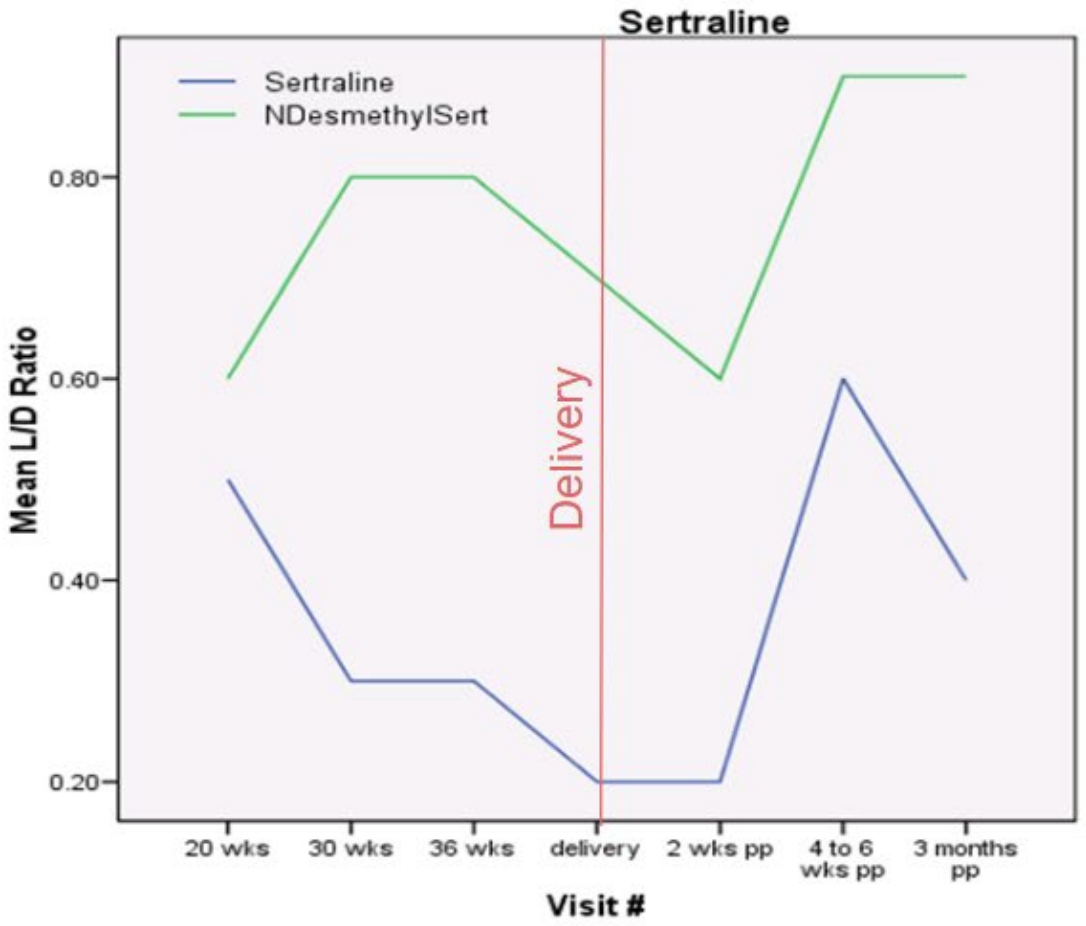
Treatment Pitfalls to Avoid: General

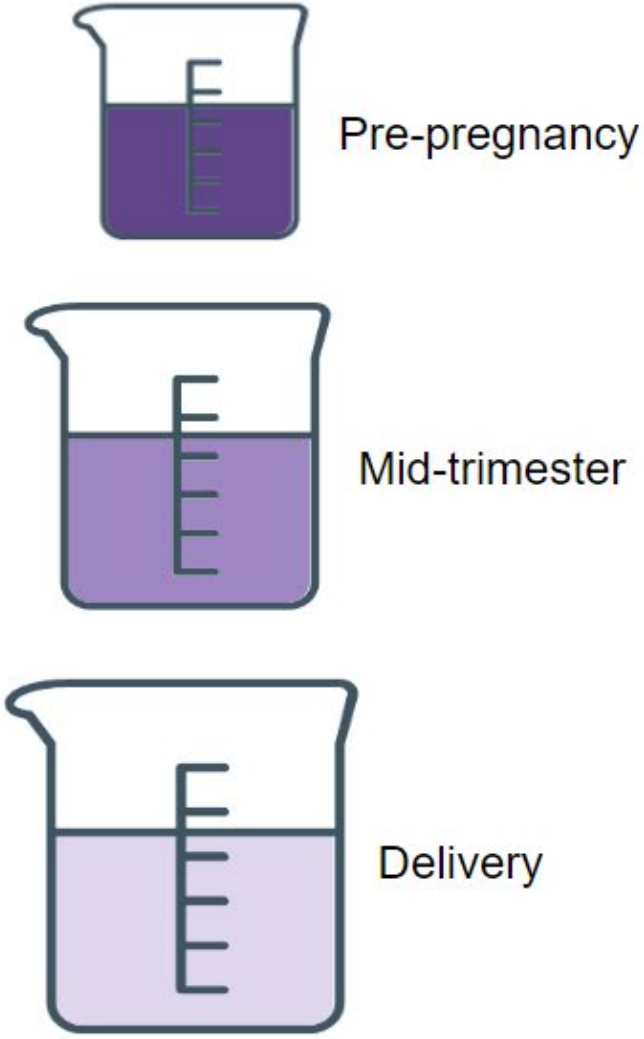
- Stopping treatment abruptly when patients becomes pregnant due exclusively to concerns about medications (and not risk of untreated illness)
- Not optimizing SSRI/SNRIs to target symptoms
- Switching a patient's medication after she is pregnant

Goal: Lowest EFFECTIVE dose (AKA increase!)

- "Lowest dose" or "target dose" does not necessarily mean it's effective
- If the patient is taking medication and is still psychiatrically ill, then the fetus is getting TWO exposures now
- Continue to increase medication until symptom remission
- Optimize non-pharmacological modalities (therapy, exercise, yoga, routine) to maximize outcome

Dose





NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

General Recommendations: Antidepressants

- SSRIs and SNRIs generally considered safe
- Consider tricyclics
- Of the SSRIs, sertraline and fluoxetine have the most evidence for safety
- Paroxetine has been associated with heart defects in some studies with exposure in the 1st trimester
- Less evidence for others including bupropion
- Avoid newer drugs (no data)

Neonatal Adaptation Syndrome

- 20-30% of SSRI-exposed newborns
- May have symptoms of jitteriness, increased muscle tone, rapid breathing – but these are transient, self limited, and not dangerous.
- Risk is not related to dose
- Risk remains even if SSRI is stopped in third trimester

Dosages for common SSRIs

	Starting Dose (to mitigate side effects)	Range often needed for MDD/PPD	Range often needed for GAD	Range often needed for OCD
Sertraline	25-50 mg	100 – 200 mg	100-200 mg	200-400 mg
Fluoxetine	10 mg	20 – 60 mg	20-60 mg	40-120 mg
Escitalopram	5-10 mg HS	10-20 mg	20-40 mg	20-60 mg
Citalopram	10 mg	20-40 mg	20-40 mg	20-80 mg
Fluvoxamine	50-100 mg HS	----------	--------	100-300 mg

Treatment of Anxiety in Pregnancy: Further considerations

- Benzodiazepines
  - Early evidence for association with cleft palate, recent studies do not support this
  - Associated with preterm birth, low birth weight – as is anxiety
  - Floppy baby syndrome and withdrawal if large doses used in 3rd trimester
- Gabapentin
  - Early animal studies showed growth impairment and developmental delay
  - Limited evidence in humans shows no risk
  - Use folic acid 4 mg!

Pregnancy and Mood Stabilizers

- Valproate is a known teratogen
  - 7-10% risk of NTD
  - Cardiac defects, craniofacial abnormalities with 1st trimester exposure
  - Behavioral and cognitive effects
- Carbamazepine
  - 1% risk of spina bifida
  - Associated with craniofacial anomalies and microcephaly

Use folic acid 4mg if use AED during pregnancy

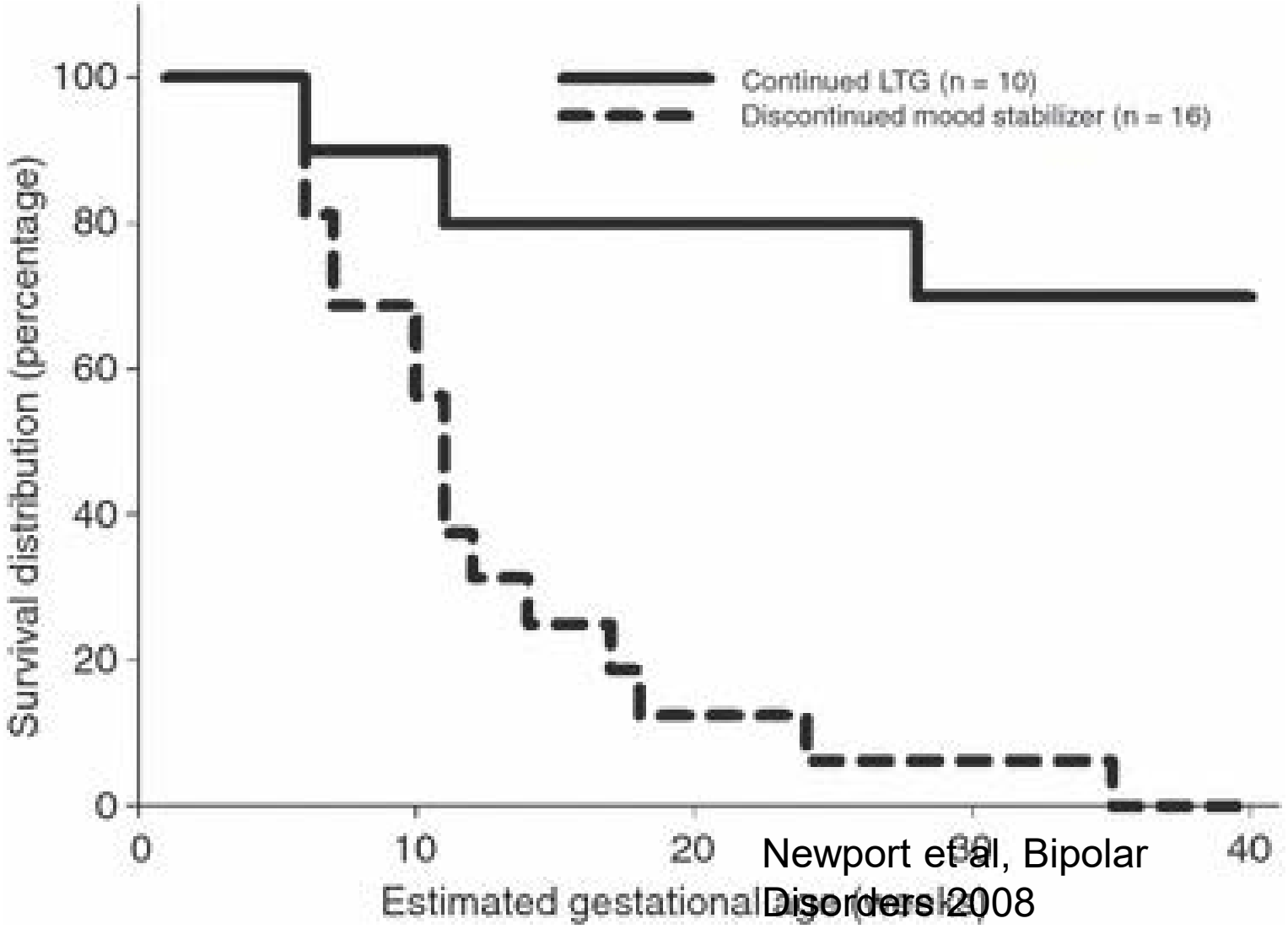
Pregnancy and Mood Stabilizers

- Lithium
  - Originally thought to have a high risk of cardiovascular malformations (Ebstein's Anomaly) based on retrospective reporting
  - Absolute risk now thought to be 1 out of 1000 (0.1%)
  - Advantage: Can monitor lithium level in both mom during pregnancy and in baby postpartum
  - Risks: Floppy baby syndrome with 3rd trimester exposure, rare neonatal hypothroidism, nephrogenic diabetes insipidus
  - 5 year follow-up of babies exposed in utero showed no sequelae

Pregnancy and Mood Stabilizers

- Lamotrigine
  - Pooled risk of major fetal anomalies after 1st trimester exposure: 2.6% (3-4% in general population)
  - Metabolic clearance increases during pregnancy
  - Ideally, measure a level when woman is stable and NOT pregnant – then adjust dosing during pregnancy to maintain that level

Lamotrigine During Pregnancy



Newport et al, Bipolar Disorders 2008

Older Antipsychotics and Pregnancy

- >40 years of experience with older antipsychotics
- No significant teratogenic effect has been shown for chlorpromazine, haloperidol, and perphenazine
- One study of haldoperidol and penfluridol found a higher rate of preterm births and a lower median birth weight (215 grams), though both are also associated with psychiatric illness in pregnancy

Diav-Citrin, O., Shechtman, S., Ornoy, S., Arnon, J., Schaefer, C., Garbis, H., ... & Ornoy, A. (2005). Safety of haloperidol and penfluridol in pregnancy: a multicenter, prospective, controlled study. *Journal of Clinical Psychiatry*, *66*(3), 317-322.

Atypical Antipsychotics and Pregnancy

- Mainly case reports
- More evidence for older atypicals (risperidone, olanzapine)
- Abilify – impacts lactation
- One study of 713 women treated with risperidone showed no teratogenicity, but recent large population study (Huybrechts) showed possible risk of cardiac defects for risperidone only (RR 1.26), but requires more research
- Recommend monitoring for metabolic effects
- Recent summary of 700 cases in registry data – no risks

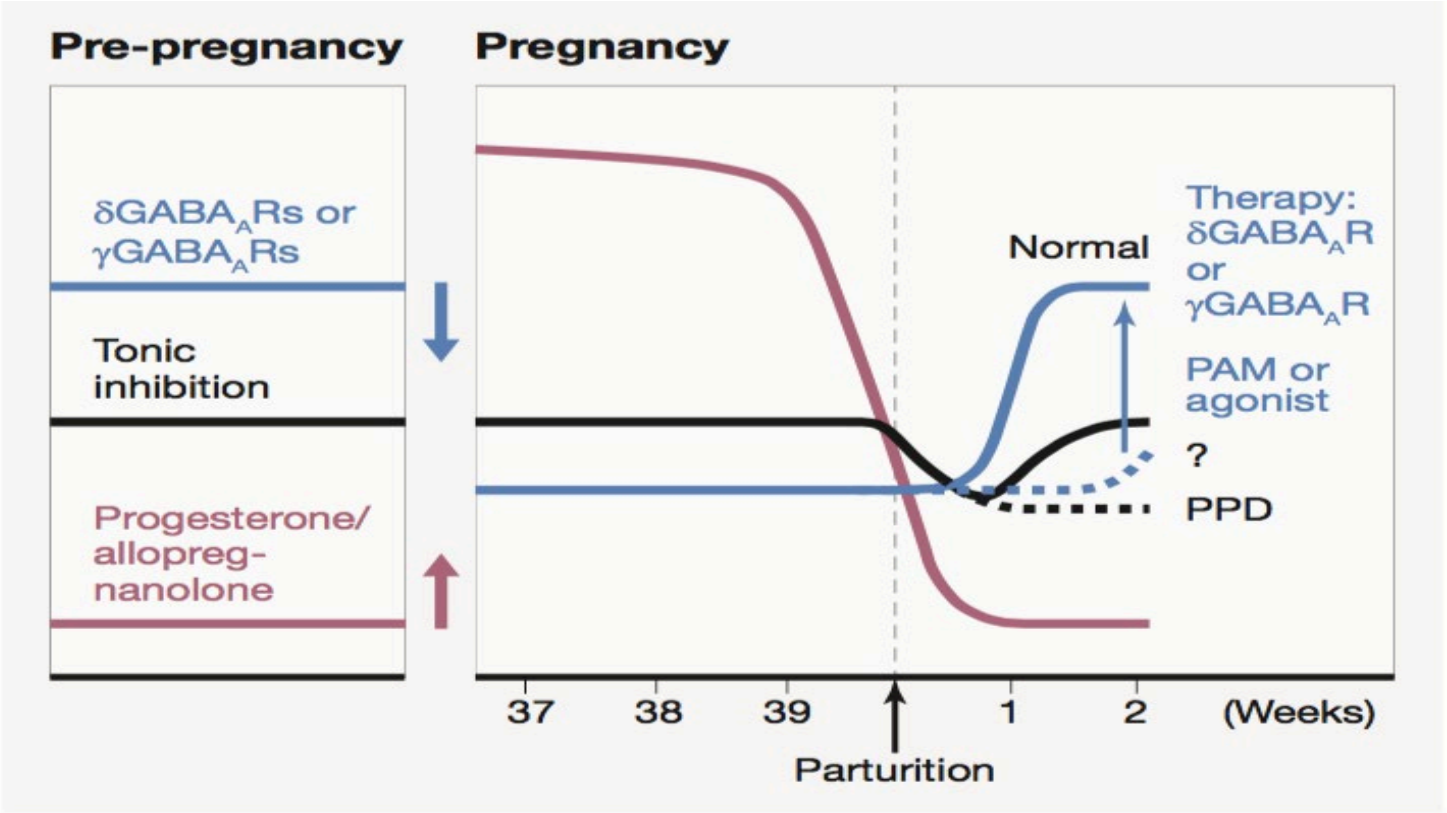
Huybrechts KF, Hernández-Díaz S, Patorno E, Desai RJ, Mogun H, Dejene SZ, Cohen JM, Panchaud A, Cohen L, Bateman BT. Antipsychotic Use in Pregnancy and the Risk for Congenital Malformations. JAMA Psychiatry. 2016 Sep 1;73(9):938-46. doi: 10.1001/jamapsychiatry.2016.1520. PMID: 27540849; PMCID: PMC5321163.

F.D.A. Approves First Drug for Postpartum Depression

The medication works quickly, within 48 hours. But it's an expensive infusion and requires a stay in a medical center.

March 19, 2019

BENCH to BEDSIDE….

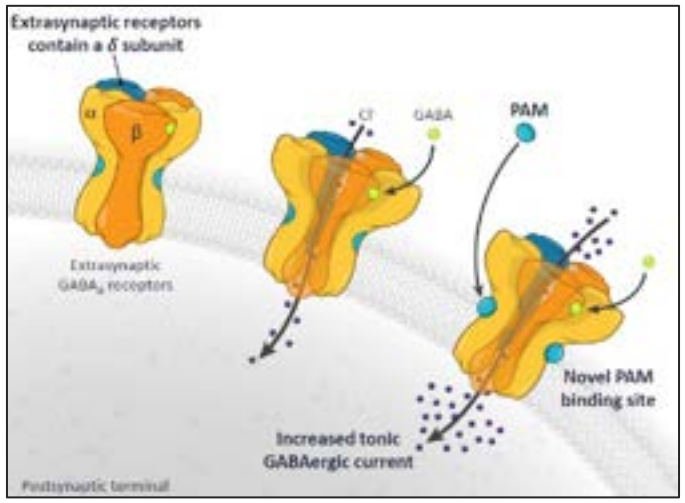


During the postpartum period, the brain's inhibitory GABA$_A$ receptors may not recover in time following their reduced numbers during pregnancy. This is likely the cause of postpartum depression prevalent in ~12% of childbearing women. A new therapy for this condition consists of administering a synthetic neurosteroid during the postpartum period to alleviate the mood disorder.

ZULRESSO™ (Brexanolone) Injection is Hypothesized to Work in PPD by Increasing GABA Function

Brexanolone Injection

- Proprietary iv formulation of allopregnanolone
- Positive allosteric modulator of $GABA_A$ receptors

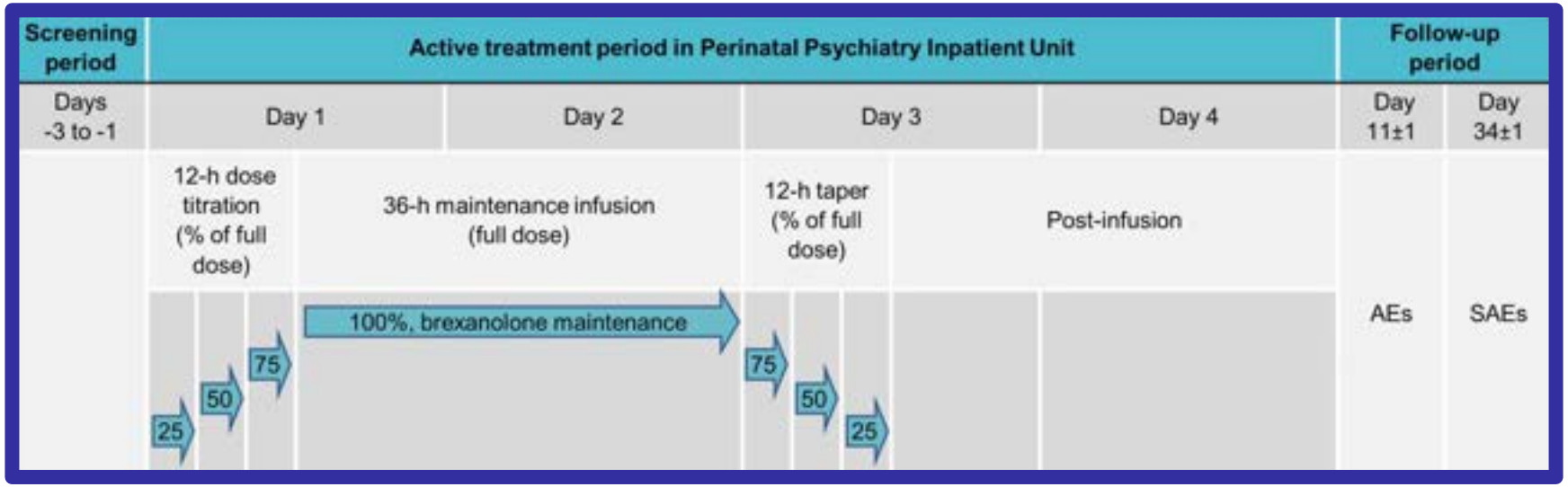


Therapeutic Rationale for Use of Brexanolone Injection

- GABAergic hypofunction has been associated with PPD[1,2,3]
- Brexanolone injection is a positive allosteric modulator of $GABA_A$ receptors[4,5]
- **Therefore, brexanolone injection may have therapeutic potential in PPD by increasing GABAergic function**

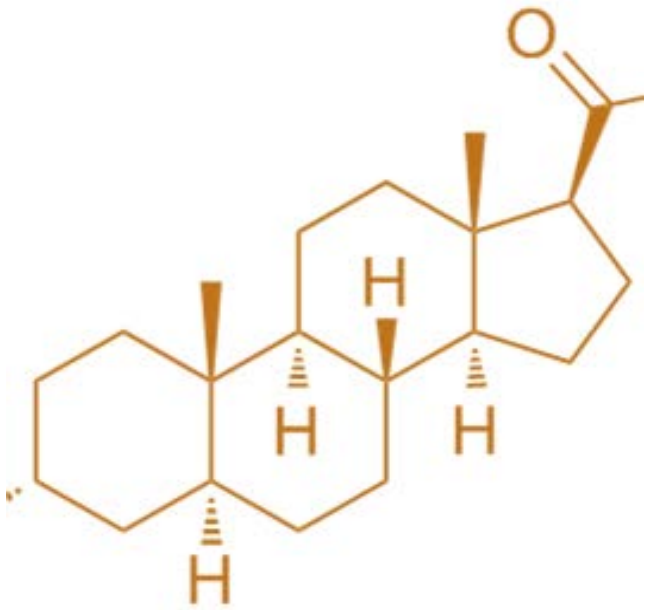
1. Luscher B, et al. *Molecular Psychiatry* 2011; 16(4): 383-406; 2. Deligiannidis KM, et al. *Psychoneuroendocrinology*. 2016;70:98-107; 3. Epperson CN et al *Psychopharmacology* 2006; 186(3): 425-433; 4. Maguire J and Mody I. *Psychoneuroendocrinology*. 2009 Dec;34 Suppl 1:S84-90; 5. Bialer M, et al. *Epilepsy Res* 2015; 11:85-141.

Infusion Plan – 60 HR IV INFUSION



Use of Brexanolone

- Available now!
- Anticipated cost: $34,000
- Insurance coverage: Most major insurances are covering!
- MUST be administered inpatient with monitoring (continuous pulse ox, 1:1).
- Use: Inpatients for fast relief of suicidal ideation, severe symptoms, or treatment resistance.
- Likely does not change standard approaches to perinatal depression but stay tuned….



POSTPARTUM/BREASTFEEDING

Meds in Breastfeeding: Rule # 1

All psychiatric medications enter breast milk

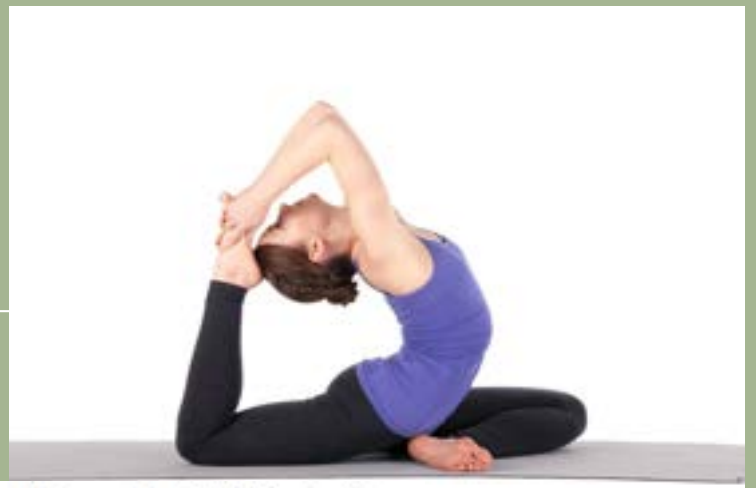
BUT – almost all safe to use

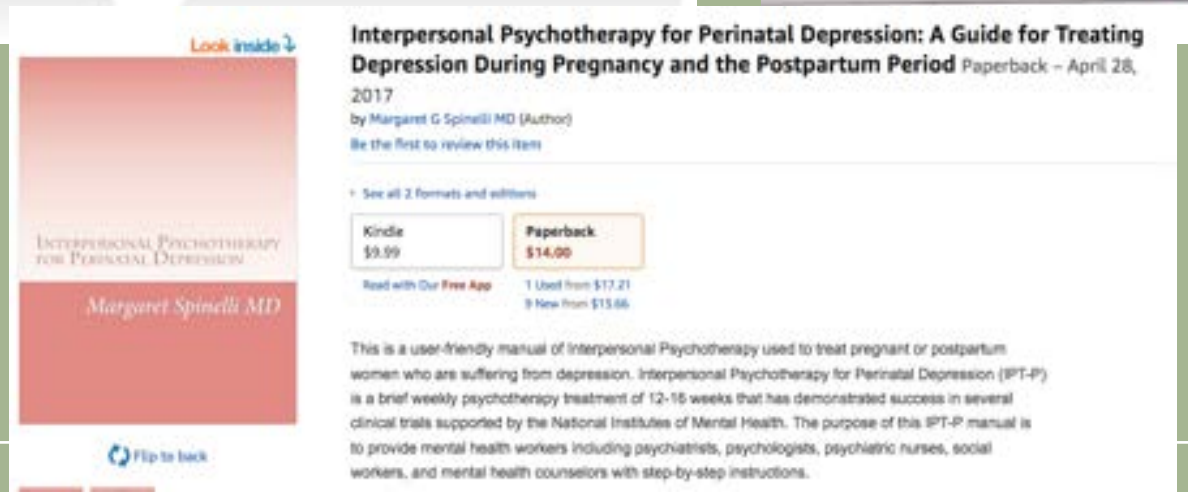
American Academy of Pediatrics <10%

Meds in Breastfeeding: Rule # 2

- If the baby was exposed in utero there is usually no reason to not continue the medication during breast feeding
  - Exceptions: clozapine, or if baby seems to be sedated or having particular side effects
  - Lithium toxicity has occurred in infants- monitor blood levels, TSH and kidney function
  - Large doses of long-acting benzos likely to result in sedation

ARE THERE ALTERNATIVES TO MEDICATIONS?





Psychotherapy

- There have been a number of studies of various types of psychotherapy for depression during and after pregnancy
- Interpersonal Therapy best studied
- Cognitive Behavioral Therapy also shows promise
- Mindfulness Based CBT also shows promise
- Need more well-designed, randomized trials

Exercise

- Exercise was as effective as sertraline in two separate studies. (Blumenthal et al, *Arch Intern Med*. 1999 and *Psychosom Med*. 2007).
- A meta-analysis confirmed efficacy as stand-alone and as adjunctive to medication in MDD (Saeed et al, *Amer Fam Phys.* 2010)
- One study of aerobic exercise during pregnancy that showed reduced depressive symptoms in women without a psychiatric history. (Robledo-Colonia et al, *J. Physiother*. 2012;58(1):9-15).
- No studies in pregnant women with mood disorders, for treatment or prevention

Light Box Therapy

Established therapy for Seasonal Affective Disorder

Has also been shown to be helpful in non-seasonal depression

Three studies have shown that LBT was effective in treating depression in pregnant women with MDD

No studies on prevention

Oren DA et al, *American Journal of Psychiatry* 2002; 159: 666-669
Epperson CN et al, *Journal of Clinical Psychiatry* 2004: 65: 421-425
Wirz-Justice A et al, *Journal of Clinical Psychiatry* 2011; 72 (7): 986-993

Repetitive Transcranial Magnetic Stimulation

- Approved by FDA for adults with MDD who have failed an antidepressant
- Open label study of 10 depressed pregnant women: 70% responded, 30% remitted (Kim, D. R*J Womens Health* 2011; 20(2): 255-261).
- No adverse outcomes for the fetus but no long-term data
- No maintenance studies to date
- Recent review of 12 studies found good response rates (largest studies 40-70%, remission in 20-30%) and no adverse effects (Felipe & Ferrao, Trends Psych Psychother 2016;38(4):190-197)
- More work needs to be done!

Electroconvulsive Therapy

- Articles published on safety and efficacy since 1940s
- Four recent systematic reviews
- 2017 "meta-review" of the systematic reviews (Sinha et al.)
- Findings of most rigorous (Anderson & Reti 2009):
  - Remission 78%
  - Very low rate of adverse effects for mother and fetus reviewed 339 cases, very effective, low rate of adverse effects

. J ECT. 2017 Jun;33(2):81-88. **A Meta-review of the Safety of Electroconvulsive Therapy in Pregnancy.** Sinha P[1], Goyal P, Andrade C. Anderson EL, Reti IM. ECT in pregnancy: a review of the literature from1941 to 2007. Psychosom Med 2009;71:235-242.Leiknes KA, Cooke MJ, Jarosch-von Schweder L, et al. Electroconvulsive therapy during pregnancy: a systematic review of case studies. Arch Womens Ment Health 2015;18:1-39. Pompili M, Dominici G, Giordano G, et al. Electroconvulsive treatment during pregnancy: a systematic review. Expert Rev Neurother 2014;14: 1377-1390. Saatcioglu O, Tomruk NB. The use of electroconvulsive therapy in pregnancy: a review. Isr J Psychiatry Relat Sci 2011;48:6-11

Conclusions

- There is a high relapse rate for mood disorders in women who stop their medications for pregnancy
- Exposure to psychiatric illness in utero is associated with poor outcomes for both mother and child
- The use of psychiatric medications can be safely done but requires an individualized plan based on the woman's history and preferences.

Goal: Healthy Mom, Healthy Baby!

Conclusions

- Treat women in pregnancy and postpartum
- Consider joining networks (PSI, MONA, Reprotox) to get up-to-date information and guidance
- We need much more research!

Resources

- Center for Women's Reproductive Mental Health (East Baltimore): (410) 502-7449: Clinical and Research, MOST insuranc. Brexanolone inpatient. http://www.hopkinsmedicine.org/psychiatry/specialty_areas/moods/patient_information/clinic_women.html
- Perinatal Mood Clinic (Bayview): (410) 550-0104: Clinical Only, BCBS http://www.hopkinsmedicine.org/psychiatry/bayview/medical_services/adult/perinatal_mood.html
- Reprotox: Summary of literature on all meds in pregnancy, subscription service https://reprotox.org/
- Lactmed: Summary of literature on all meds in lactation, free services http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm
- MothertoBaby: Patient-friendly fact sheets on meds: http://mothertobaby.org/
- MGH Center for Women's Mental Health: Best informational website: https://womensmentalhealth.org?doing_wp_cron=1452175286.3503780364990234375000
- Motherrisk: Canadian helpline: http://www.motherisk.org/
- Postpartum Support International: Support group and help finding local resources http://www.postpartum.net/
- MCPAP FOR MOMS, https://www.mcpapformoms.org/

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Marrs et al., Eur J Obstet Gynecol Reprod Biol. (2009);143:127–8.
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Meltzer-Brody et al., Lancet (2018); 392: 1058–70
Osborne et al., Psychoneuroendocrinology. (2017);79:116–21.
Osborne et al., Frontiers in Psychology, in press.
Romeo et al., Am J Psychiatry. (1998);155:910–3.
Schiller et al., Psychopharmacology. (2014);231:3557–67.

Fetal programming

- The fetus is well protected from toxic effects of everyday maternal stress…
  - Maternal HPA axis has reduced baseline activity and reduced responsiveness during pregnancy
  - A placental enzyme (11βHSD2) inactivates some of the circulating maternal glucocorticoids

- But with severe, prolonged stress or depression…
  - Maternal cortisol level can rise enough to overwhelm these defenses (enzyme less effective)
  - This increases methylation at promoter regions of fetal genes that affect glucocorticoid receptors
  - The child's stress response system can become hypersensitive
  - This can lead to enduring behavioral changes

HPA = hypothalamic pituitary adrenal
11βHSD2 = 11β-hydroxysteroid dehydrogenase 2