Mass General Brigham

Mood and Anxiety Disorders in Pregnancy and Postpartum

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HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

MAGNET RECOGNIZED AMERICAN NURSES CREDENTIALING CENTER

No Conflicts to Report

Will discuss off-label use of medications

Objectives:

- To provide an overview of the epidemiology of Major Depressive Disorder in women
- To discuss the clinical presentation and general approach to the management of Major Depressive Disorder in women during the perinatal period
- To provide an overview of the epidemiology of Anxiety Disorders in women
- To discuss the clinical presentation and general approach to the management of Anxiety Disorders in women during the perinatal period

Major Depressive Disorder

- 21 million adults in the USA have had at least 1 episode of MDD, this represents 8.3% of the U.S. adults
- Prevalence of MDD is higher in adult females than males, 10.3% vs 6.2%

https://www.nimh.nih.gov/health/statistics/major-depression as of 05/2024

Perinatal Depression

www.acog.org

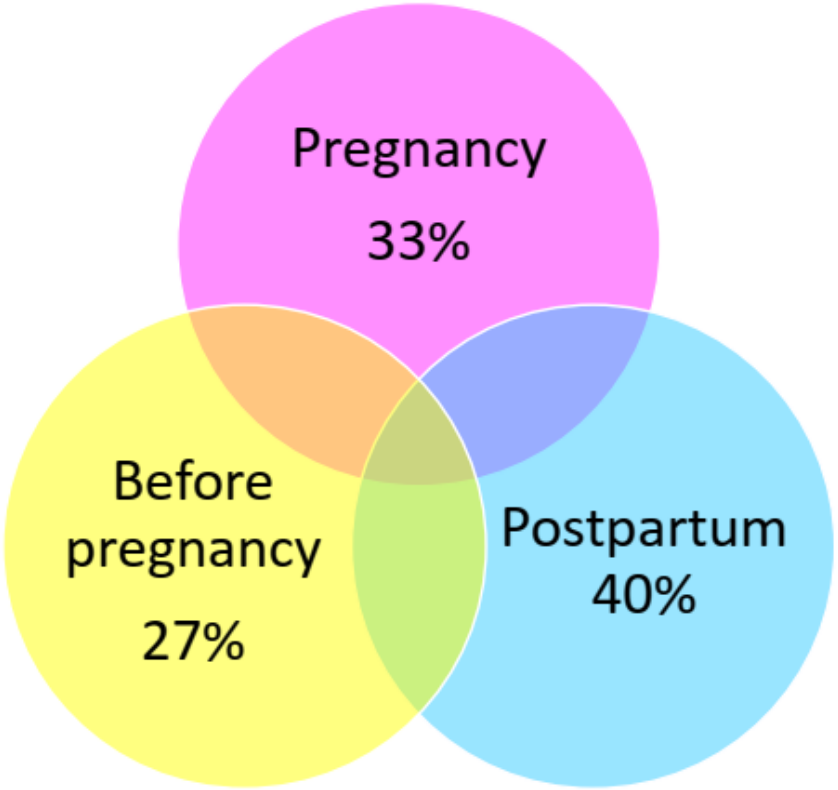
Perinatal Depression

- DSM V defines 'postpartum onset' as within 4 weeks of delivery while many research studies use 6-12 months
- Perinatal depression is the most common complication of pregnancy
- Suicide accounts for about 20% of postpartum deaths

Gavin et al, Obs&Gyn, 2005;106

Lindahl et al, Arch of Women's Mental Health, 2005

Perinatal Depression



Wisner et al, JAMA Psych 2013

- Prior depression is the largest risk factor for perinatal depression
- Reproductive risk factors
  - Personal hx of PPD
  - Family hx of PPD
  - Hx of mood changes related to hormonal changes
- General risk factors
  - Younger age
  - Hx of trauma
  - Hx of sexual abuse
  - Psychosocial stressors
  - IPV
  - Chronic medical conditions
  - Race

Melville et al OBGYN 2010 ; Meltzer-Brody et al, Arch Women MH2013

Perinatal depression affects patient and family---risks to patient and pregnancy

- Poor participation in prenatal care
- Increased rates of substance use
- Increased rates of preeclampsia, gestational HTN
- Maternal suicide

Bodnar et al. J Clin Psych 2009. Cripe et al. Pedi &Perinatal Epid 2011. Forman et al. Dev & psych 2007

Perinatal depression affects patient and family---Epigenetics

- Maternal cortisol can affect fetal HPA axis
- Maternal depression is associated with increased methylation affecting glucocorticoid receptor gene expression
- Elevated placental CRH leads to thinning of selective cortical regions & commensurate cognitive and emotional deficits in childhood

Glover et al. Psychoneuroendorcinology 2009; Oberlander et al Epigenetics 2008; Gunnar AJP 2018

Perinatal depression affects patient and family---risks to offspring

- Newborn: excessive crying, increased NICU admission, inconsolable
- Babies: poor growth, increased risk of infection, sleep difficulties
- Children: difficult temperament, autism, higher rates of depression, behavioral disturbance, lower IQ

Marcus et al. Can J Clin Pharmacol 2009; Li et al. Hum Reprod 2009; Henrichs et al. Psychol Med 2010; Zuckerman et al. J Dev Behav Pediatr 1990; Huot et al AnnN Y Acad Sci 2004; Muzik 2009; Bodnar et al. Journal of Clin Psych 2009; Cripe et al. Pedi and Perinatal Epidemiology 2011; Forman et al Dev and Psych 2007; Brennan et al Dev Psychol 2000; Hay et al J Child Psychol Psychiatry 2008

Treatment

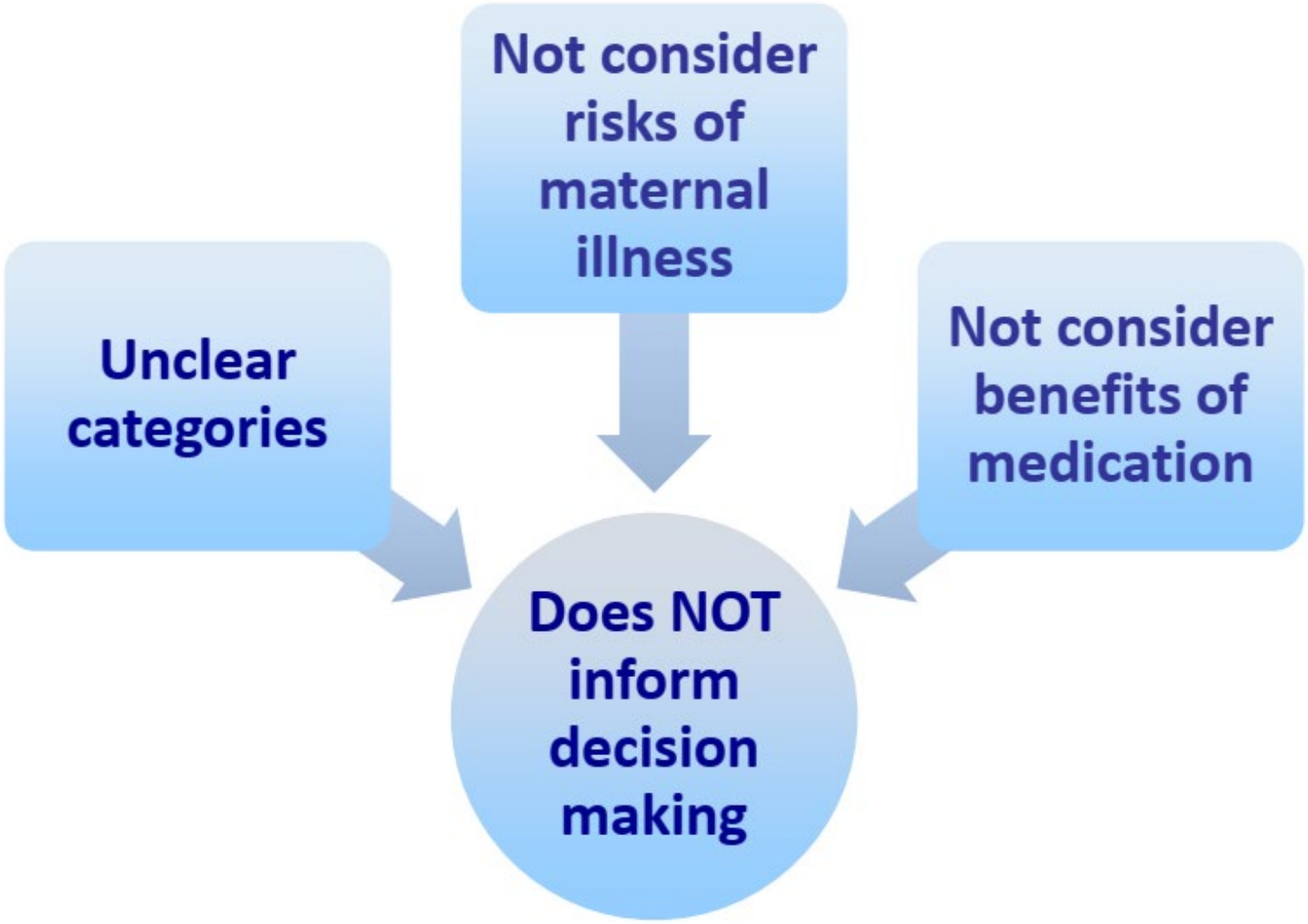
- When possible, preconception counseling and planning is key
- Clarify the diagnosis
- Optimize non-pharm options
- Awareness of need to balance risks of medication treatment vs risks of untreated illness
- There are no risk-free choices!

Treatment

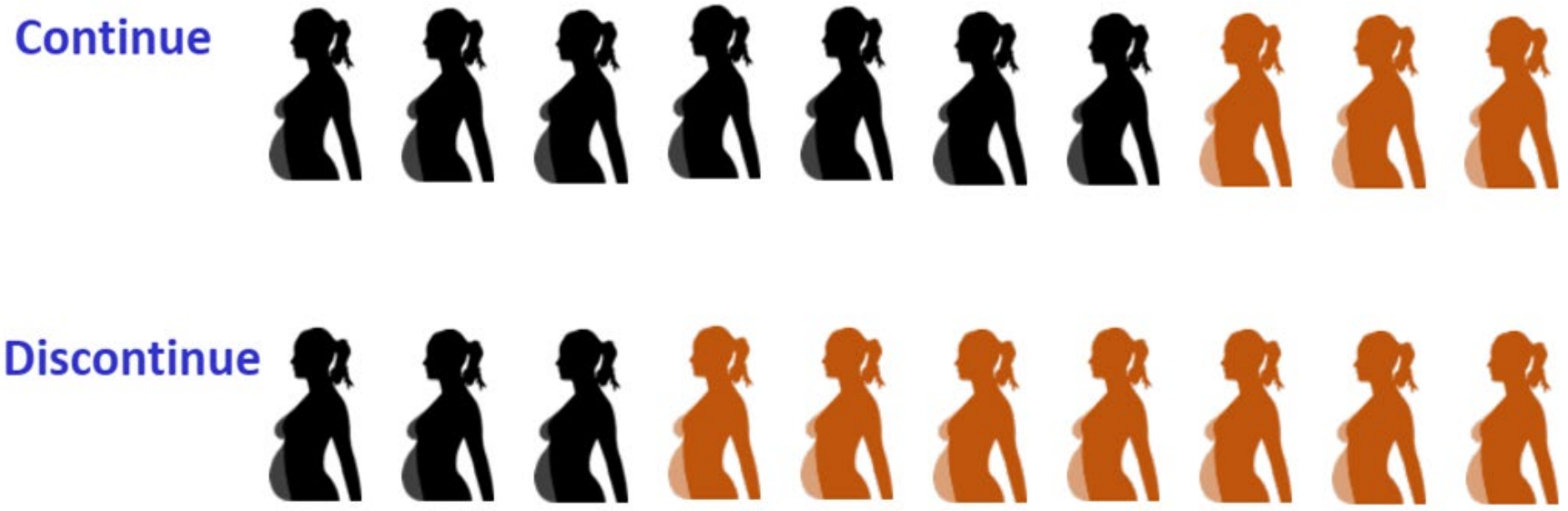
- When in pregnancy is the patient?
  - 1st trimester—physical teratogenicity
  - 2nd & 3rd –behavioral, altered mental functioning. Altered pharmacokinetics
  - 3rd and beyond —neonatal side effects, growth, timing of labor, withdrawal, breastfeeding plans
- Med management: lowest effective dose of the fewest medications
  - What has worked in the past?
  - Monotherapy when possible
  - Minimize switching
  - Lowest EFFECTIVE dose

McAllister-Williams et al J Psychopharm 2017

U.S FDA pregnancy risk categorization



Risk of relapse during pregnancy in women who discontinue antidepressants preconception



Cohen et al. JAMA 2006, Yonkers et al Epidemiology 2011

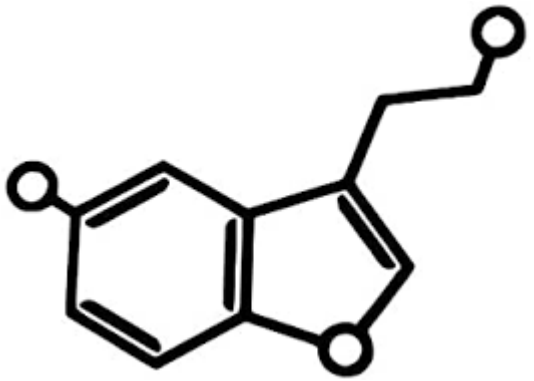
Behavioral measures to reduce PPD

- Early morning sun light exposure
- Light exercise
- Nutritious diet (Ω-3 fatty acids, FA, B-12, Fe, D, Ca)
- Adequate sleep (including unbroken sleep)
- Psychotherapy

Jeste et at Psychiatric Clinics of North America 2011

SSRI in pregnancy

- No major malformations consistently found
- No consensus on developmental issues, latest data reassuring
- May increase SAB
- Smaller size (in gm)
- Early labor (3-4 days)
- PPHTN
- Preeclampsia
- Neonatal adaptation syndrome
  - Lasts 1-2 days
  - Respiratory distress, irritability, tremor, jitteriness, restlessness, changes in muscle tone, poor sleep, eating difficulties, Sz, prolonged QT
  - Affects about 30% of newborns
  - Taper does not appear to reduce risk



Moses-Kolko et al. Jama 2005; Huybrect et al. PLoS ONE 2014; Byatt et al. Acta Psych Scand 2013

Atypical antidepressants

Bupropion:

- Less data than SSRIs, but increasing and reassuring data in the past few years
- Not associated with higher risk of major malformations, preterm birth, low birth weight, or neurodevelopmental changes
  - Exception: possible small increase in LVOT obstructions

Turner et al 2019, Einarson 2009

Atypical antidepressants

Mirtazapine

- Less data than SSRIs, but increasing and reassuring data in the past few years
- Not associated with higher risk of major malformations, pregnancy loss, or neonatal death
- Less data around neurodevelopmental outcomes
- May be particularly favored in cases of nausea/emesis

Ostenfeld 2022

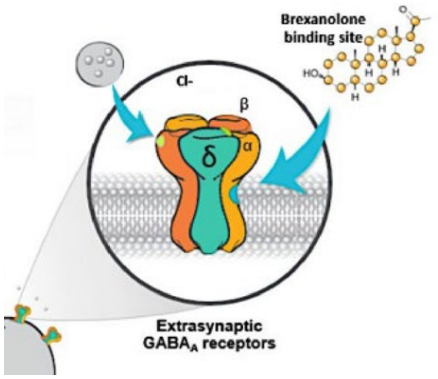
Breastfeeding generally should not preclude treatment with antidepressants

New treatments—Brexanolone and Zuranolone

- Allopregnanolone, a neurosteroid that acts at $GABA_A$ receptors which are reduced in PPD
- In trials shows rapid reduction in depressive symptoms compared to placebo
- Indicated for moderate to severe PPD

Maguire J and Mody I, *Neuron*, 2008; Meltzer-Brody et al, *Lancet,* 2018,

Deligiannidis et al 2023 AmJPsych



Anxiety

Women Have Higher Rates of Anxiety Disorders

Increased prevalence in women

- Panic disorder
- Social anxiety
- GAD
- Most phobias
- PTSD

Similar Prevalence in men and women

- OCD

Women are more likely to have comorbid anxiety and depression

Kessler, Arch Gen Psychiatry, 1995; Altemus et al, Front Neuroendocrinol, 2014

Perinatal Anxiety

- Can have PPD, PPA, or both
  - PPA affects at least 1 in 10 women
- OCD:
  - Vast majority of perinatal women have intrusive thoughts
  - High-risk time period for onset or worsening of OCD
- Risks to mom and baby
  - Not as well studied as a separate entity, but overall similar to risks from depression

Dennis et al 2017, Labad et al 2005; Kingston 2014, Dubber 2014

Risk of harm to baby when mother has thoughts of harming baby

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

Anxiety treatments

SSRIs–see above

Benzos

- Not associated with major malformations or neurodevelopmental changes
- Possible increased risk of:
  - Low birth weight
  - Neonatal withdrawal syndrome/sedation, rare risk of floppy infant
  - Miscarriage in the first trimester
- Guidelines:
  - Fewer active metabolites (lorazepam > clonazepam)
  - Not hepatically metabolized (lorazepam > alprazolam)
  - Avoid longer acting if possible (e.g. diazepam)

…but it's always risk v risk!

Szpunar et al 2022, Wang et al 2022, Lin-Chieh et al 2023

Summary:

- Maternal mental health affects the patient, child, and family
- Roughly 30-50% of pregnancies in the USA are unplanned
- Assume that all women of reproductive age can become pregnant at any time in treatment
- Screening for mood disorders is essential
- Consider the risks of untreated psychiatric illness when making treatment plan
  - Don't reflexively stop or switch!

Resources:

- **MCPAP for Moms Mcpapformoms.org**
- **MGH Center for Women's Mental Health Womensmentalhealth.org**
- **Reprotox Reprotox.org**
- **Postpartum Support International Postpartum.net**
- **Lactmed toxnet.nlm.nih.gov/newtoxnet/lactmed.htm**
- **MotherToBaby https://mothertobaby.org/**