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Psychiatry and Addictions Case Conference

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PSYCHOTROPICS IN PREGNANCY AND LACTATION

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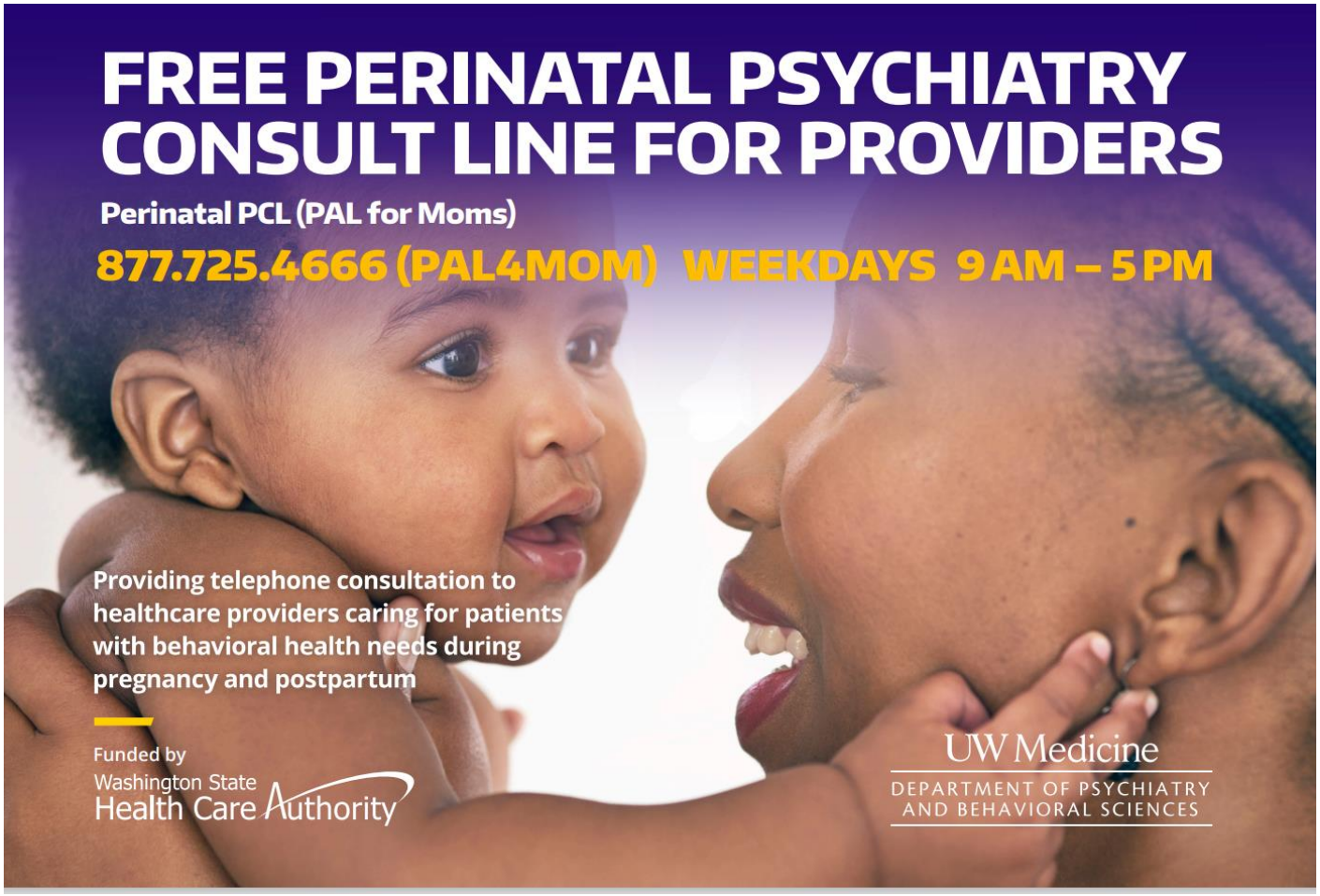
SPEAKER DISCLOSURES



OBJECTIVES

1. Describe risks of untreated mental disorders during pregnancy and postpartum
2. Compare the risks of untreated perinatal psychiatric disorders with the risks of psychotropic medication use during pregnancy and lactation
3. Summarize the principles of prescribing commonly used psychotropics in the perinatal period

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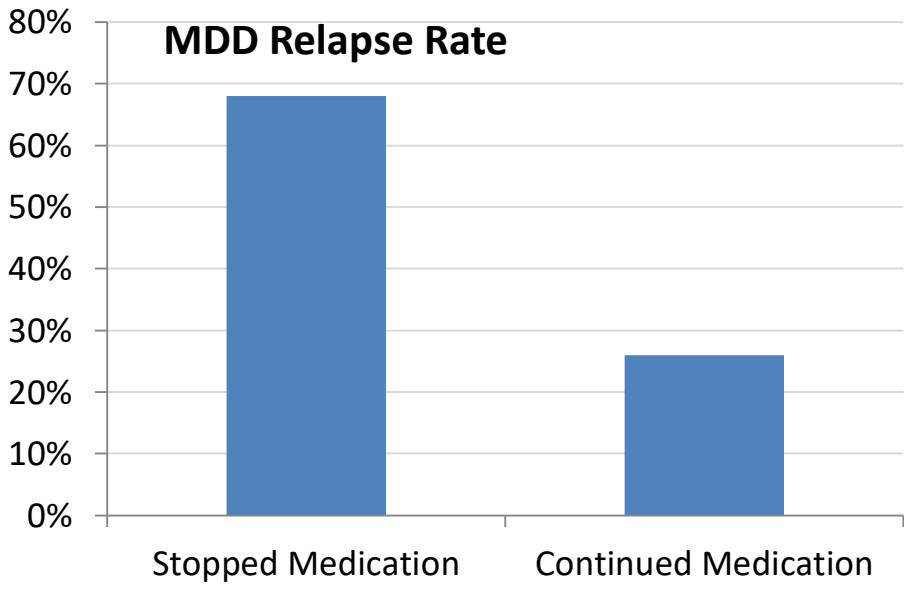
CASE

29 yo with recurrent MDD responded well to citalopram in the past, and as she had been symptom free for over a year and is planning pregnancy, under your supervision tapered and stopped medication. Symptoms returned a month after stopping medication. She is continuing CBT, exercise and light therapy but continues to have symptoms (middle insomnia, panic attacks, low motivation although she forces herself to go to work) 6 months later.

Substances – No; Social support – Husband, parents

h/o severe depression leading to hospitalization 2 years ago, lactation failure, responded to citalopram

RISK OF RELAPSE



- Risk of relapse higher with:
  - > 4 episodes
  - Chronicity
  - Past SA
- Antidepressant discontinuation during pregnancy associated with increased risk of psychiatric emergency (HR = 1.25, 95% CI: 1.00 to 1.55, p = 0.048)

Cohen et al, 2006; Bayrampour et al, 2020; Liu et al 2022

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RISK – RISK ASSESSMENT

Untreated Depression

- Suicide
- Comorbidities
- PTB, LBW
- Internalizing and externalizing disorders in children
- Depression and antisocial behavior in adolescence

Antidepressants

- No congenital malformations (? paroxetine)
- Neonatal adaptation syndrome (30%)
- PPHN (sertraline may have lowest risk)

Alternatives

Jarde et al, 2016; Grote et al, 2010; Lahti et al, 2017; Pawlby et al, 2011; Masarwa et al, 2018

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ALTERNATIVES TO MEDICATION

- For depression:
  - Interpersonal Therapy
  - Cognitive Behavior Therapy
  - Behavioral Activation
  - Mindfulness Based Cognitive Therapy
  - Light therapy

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COMPLEMENTARY AND ALTERNATIVE TREATMENTS

- 20 RCTs, 1092 women
- Acupuncture reduced the number of women diagnosed with antenatal depression (RR 1.68, 95% CI 1.06–2.66, 1 trial)
- Massage reduced the severity of antenatal depression in one trial of 149 women (SMD –0.73, 95%CI –1.07––0.39)
- No evidence of a reduction in depression and anxiety from relaxation, yoga, mindfulness and fish oils.

Smith et al, 2019

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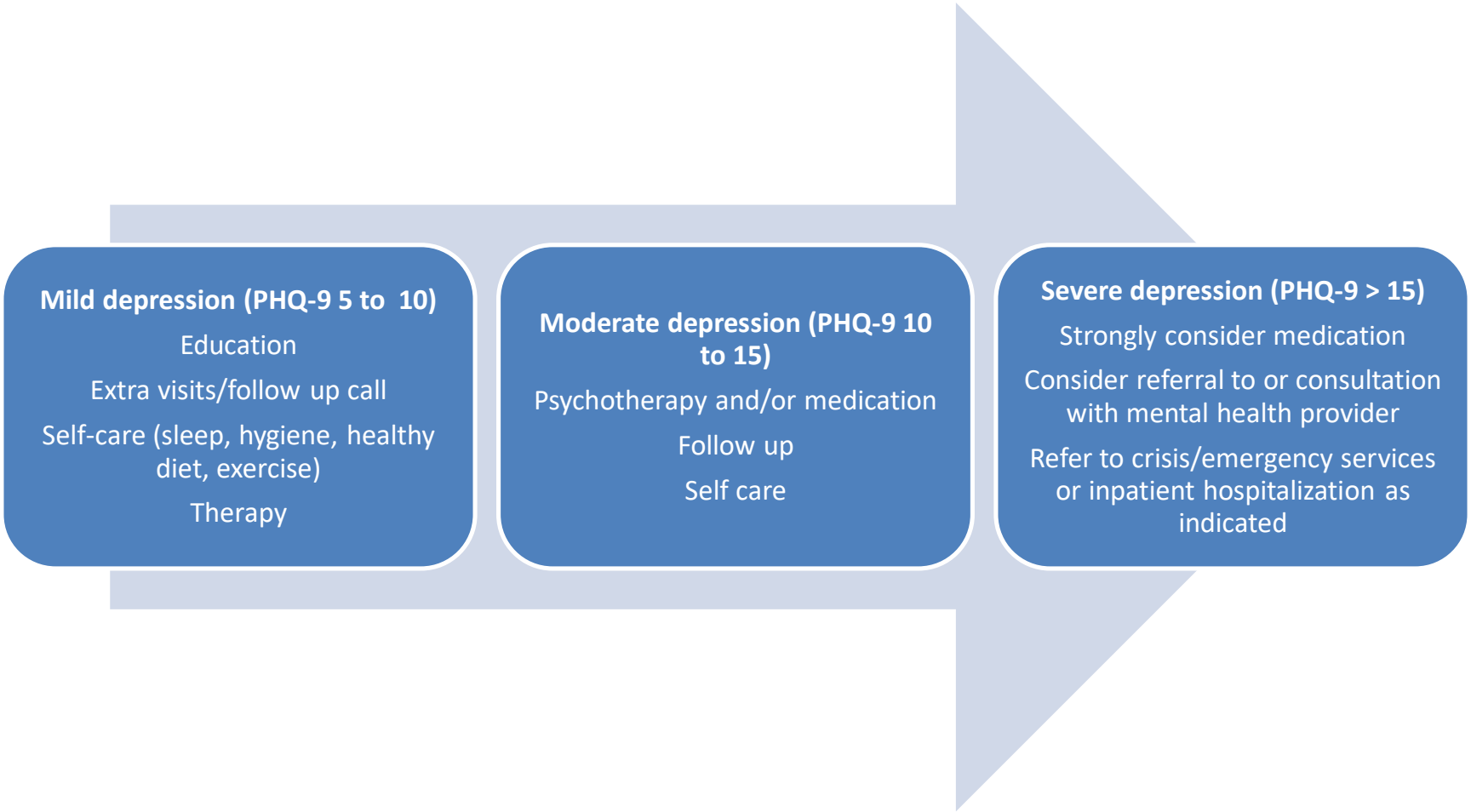
PERINATAL DEPRESSION TREATMENT RECOMMENDATIONS



https://www.integration.samhsa.gov/images/res/STABLE_toolkit.pdf

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POSTPARTUM BLUES

- Mood lability, irritability, tearfulness, anxiety, sleep and appetite disturbance
- Within days of delivery, peaks at day 4-5, resolves by about day 10
- Occurs in 30-75% of women postpartum
- Treatment is reassurance and support
- Closely monitor those with history of depression

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POSTPARTUM DEPRESSION

- Symptoms of major depression within the first month postpartum
- Risk factors:
  - depression or anxiety during pregnancy (50%)
  - prior MDD (30%)
  - prior postpartum depression (50-60%)
  - poor social support, marital problems, intimate partner violence
  - family history
  - life events
  - complicated delivery, emergency C-section
  - infant illness/problems
- Health disparities
  - higher rates, less screening and treatment in BIPOC individuals
- 20% of women with positive postpartum depression screens have bipolar disorder

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A NOTE ON POSTPARTUM PSYCHOSIS

Osborne et al 2018

- A psychiatric emergency, prevalence 0.1%
- Presentation - bizarre thoughts and/or behavior, alterations of consciousness, and mood fluctuation.
- Risk factors - personal history of bipolar disorder, family history, sleep disturbance, ?pre eclampsia, parity
- Differential diagnosis - OCD, Delirium, Autoimmune encephalitis, Sheehan syndrome, Intoxication, Medication reaction (i.e., steroid-induced mania)
- Management – inpatient treatment, medication management
- Risk management – risk of suicide, infanticide

TREATMENT OF DEPRESSION AND ANXIETY IN PREGNANCY AND LACTATION

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TYPES OF FETAL RISK

- Malformations
- Adverse pregnancy outcomes
- Neonatal toxicity
- Neurobehavioral effects

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TIMING OF RISKS

- Up to 32 days – neural tube defects
- 21-56 days – cardiac defects
- 42-63 days – lip and palate
- Craniofacial anomalies can occur after first trimester
- NOTE
  - Methodological issues of studies
  - Base rate of 3% for major malformations

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SSRIS IN PREGNANCY – NEONATAL ADAPTATION SYNDROME

- 30% of SSRI-exposed babies
- High-pitched cry, sleep disturbance, tremor, hypertonicity/myoclonus, tachypnea, gastrointestinal symptoms, seizures
- Peaks within 2 days after birth, resolves in about 4 days
- Worse with SSRI + benzodiazepine
- Reducing dose in 3rd trimester does not prevent PNAS

Moses Kolko 2005, Warburton 2010

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SSRIS IN PREGNANCY – PERSISTENT PULMONARY HYPERTENSION

- Meta-analysis, 11 studies, 156,978 exposed women
- 1.8/1000
- 2.9/1000 with SSRI exposure
- NNH = 1000
- Lowest risk - sertraline

SSRI	Placental Passage	P Score
Sertraline	30%	0.83
Escitalopram	50%	0.69
Paroxetine	-	0.49
Citalopram	70%	0.21
Fluoxetine	65%	0.16

Masarwa, 2018

SSRIS IN PREGNANCY – OTHER CHILD OUTCOMES

- Physical outcomes (5 studies - asthma, cancer, BMI, epilepsy): conflicting associations for BMI.
- Neurodevelopmental outcomes (18 studies - cognition, behavior, IQ, motor development, speech, language, and scholastic outcomes): no consistent associations
- Psychiatric outcomes (11 studies: ASD, ADHD, affective disorders): associations with affective disorder

Rommel et al, 2018

OTHER ANTIDEPRESSANTS IN PREGNANCY

Venlafaxine and Duloxetine

- Similar risks as SSRIs but fewer data
- No increased risk of major malformations
- PNAS similar to SSRIs

Mirtazapine

- No increase risk in major fetal malformations, limited data
- Conflicting reports of increase in spontaneous abortion, preterm birth and low birth weight
- Good choice for severe hyperemesis gravidarum

BUPROPION

Less studied than SSRIs

No increased rate of malformations (?LVOTO)

Possible elevated risk of attention deficit disorder in offspring

Exacerbates anxiety disorders

Case reports of neonatal seizures during lactation

Do not use in women with bulimia, seizure disorders

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BREXANOLONE (ZULRESSO)

- Approved by the FDA 3/19/19 for postpartum depression in adult women
- Allosteric modulator of GABAA receptors; Formulation of allopregnanolone
- 60-hour IV infusion
- Risk Evaluation and Mitigation Strategy (REMS)
  - Pulse oximetry
  - Certified health care facility

Meltzer – Brody et al, 2018

ANTIDEPRESSANTS IN LACTATION

- Most SSRIs RID < 10; Sertraline safest
- Isolated adverse events:
  - colic, irritability, poor feeding, sedation
- Higher levels in breastmilk:
  - Citalopram, fluoxetine, venlafaxine
- Monitor newborn and preterm infants:
  - sedation and adequate weight gain

PRIORITIZE SLEEP!!!

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TREATMENT OF BIPOLAR DISORDER IN PREGNANCY AND LACTATION

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UNTREATED BIPOLAR DISORDER IN PREGNANCY

- 50% of women with bipolar disorder who interrupt treatment become symptomatic; 70% risk in PP
- 2 fold greater recurrence risk, shorter time to recurrence, increased time of illness burden
- Risks for mother - Increased substance use during pregnancy, poor prenatal care, increased substance use
- Risks for child - Microcephaly, SGA, prematurity, low Apgar, increased NICU admissions

Tosato et al, 2017; Hogan et al 2016

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SECOND GENERATION ANTIPSYCHOTICS IN PREGNANCY

- Need for metabolic monitoring
- Congenital malformations
  - No increased risk: Aripiprazole, Olanzapine, Quetiapine
  - Minor increased risk: Risperidone, Paliperidone
  - Insufficient data: Amisulpiride Asenapine, Lurasidone, Sertindole

FDA warning re neonatal EPS, "withdrawal symptoms" (sedation, agitation, tremor, inc or dec muscle tone, breathing/feeding difficulties)

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ANTIPSYCHOTICS IN LACTATION

- Most data available for olanza quetiapine
- Low levels found in breastmilk dosages upto 40 mg / 400 mg
- Watch for sedation
- Ask about co sleeping

PRIORITIZE SLEEP!!!

MOOD STABILIZERS IN PREGNANCY

Mood Stabilizer	Dose / day	Rate of congenital malformation	Neurodev outcomes
Valproate	<700 mg	5.6%	Autism and neurodev delay
	700 – 1500	10.4%	
	≥ 1500	24.2%	
Carbamazepine	< 400 mg	3.4%	Autism and neurodev delay
	400 - 1000	5.3%	
	≥ 1000	8.7%	
Oxcarbazepine		2.4 - 3%	Autism and neurodev delay
Lamotrigine	< 300 mg	2.0%	No adv neurodev outcomes
	≥ 300	4.5%	

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LAMOTRIGINE

Lamotrigine – safest mood stabilizer for use during pregnancy

Prospective study from teratology service (median dose 200 mg/d): No increase in MCM. No cases of oral cleft

29% needed dose increase during pregnancy.

No neurodevelopmental disorders in children exposed to in utero lamotrigine (up to 6 years)

Diav Citrin 2017; Dolk 2016 ; Pariente 2017

OTHER PSYCHOTROPICS IN PREGNANCY AND LACTATION

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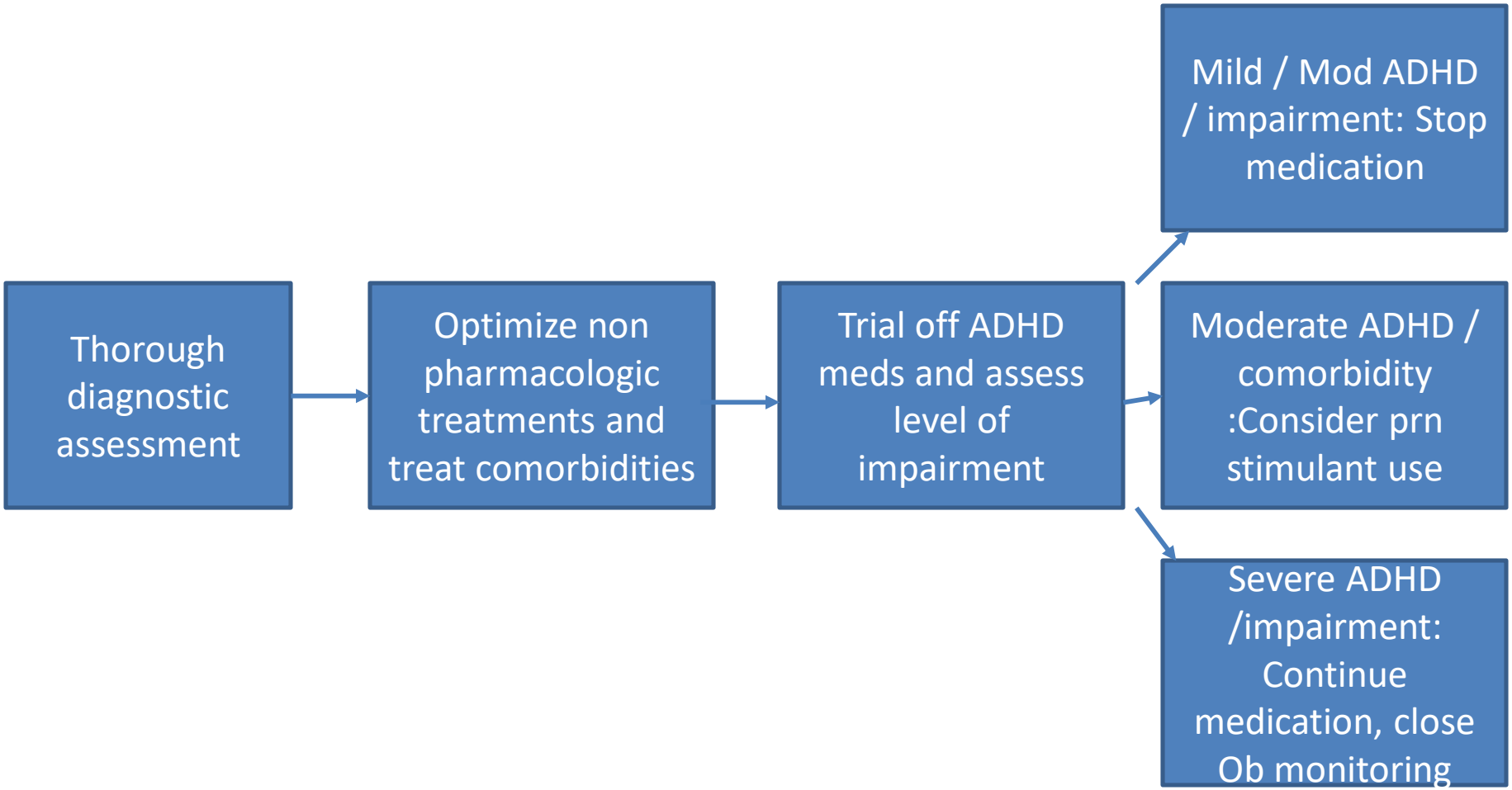
BENZODIAZEPINES IN PREGNANCY AND LACTATION

- Pregnancy
  - No increased rate of malformations with BZs alone; ? Increase with antidepressant + BZ
  - Dose response relationship - SA
  - Neonatal “floppy infant” – hypotonia, hypothermia, low APGAR scores, lethargy
  - Withdrawal – hypertonia, tremors, hyperreflexia
- Tapering benzodiazepines in pregnancy
  - Withdrawal symptoms with rapid taper
  - Case reports of panic attacks, miscarriage
- Lactation
  - Sedation, poor feeding
  - Lorazepam – short-acting, lower transmission into breast milk

ALGORITHM FOR MANAGEMENT OF ADHD



Baker et al, 2018

RISKS OF STIMULANTS IN PREGNANCY

- More studies on stimulant abuse
- No e/o increase in congenital malformations (? Methylphenidate and Cardiac defects)
- Increase in rates of
  - Gestational HTN (5.6%vs 3.2%)
  - Pre eclampsia (6.8% vs 2.9% RR 1.3)
  - PTB (23.4% vs 8.9%; 7.9% vs 4.2% RR 1.3)
  - NICU admissions (16.3% vs 8.3% aOR 1.5)
  - CNS disorders (1% vs 0.3% aOR 1.9)
  - Fetal death (1.4% vs 0.3% / no increased risk)

Gorman et al, 2014; Huybrechts et al 2017; Norby et al, 2017; Baker et al, 2018

RISKS OF STIMULANTS IN BREASTFEEDING

- Methylphenidate: Infant levels <1% of maternal levels
- Amphetamines: Infant levels upto 15% maternal levels
- No adverse effects in babies

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TREATMENT OF ADHD DURING LACTATION

- How old is the baby? Is the baby exclusively breastfeeding?
- Maternity leave?
- Immediate release vs sustained release

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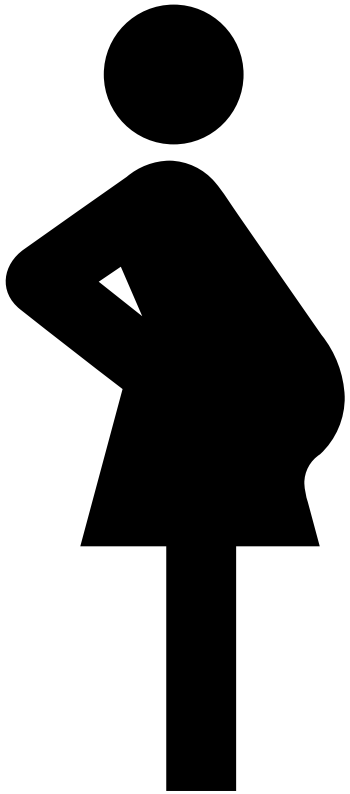
REMEMBER!



- Anyone of childbearing potential could be or could become pregnant; 50% of pregnancies are unplanned.
- In people with childbearing potential:
  - Test for pregnancy
  - Document birth control method
  - Document discussion of risks with exposure during pregnancy and lactation
  - Discourage use of alcohol, tobacco, caffeine
  - Vitamin, folate supplementation (800 mcg folate/day, or 4-5 mg/day with anticonvulsants)

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RULES OF THUMB IN PRESCRIBING FOR PERINATAL MENTAL HEALTH DISORDERS

- Thorough diagnostic evaluation including an understanding of patients responses to previous treatments
- Understanding patient's treatment goals, concerns and constraints (financial, time)
- Prescribe only when clearly indicated and with a strong evidence base
- Changes to meds to be made before pregnancy if possible
- Ideally patient should be psychiatrically stable for at least three months before attempting to conceive
- Use medications with more safety information
- Minimize number of exposures
- Use a team approach
- Be supportive if the patient goes against your recommendations
- Recommend folic acid prenatally.
- Don't forget non – medication factors!

Chisolm et al 2016

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RESOURCES

Patients

- Perinatal Support of Washington - 1-888-404-7763 http://perinatalsupport.org/
- Patient information brochure https://www.nimh.nih.gov/health/publications/perinatal-depression/index.shtml
- MotherToBaby fact sheets: https://mothertobaby.org/fact-sheets/

Partners

- http://www.postpartum.net/family/overview/
- http://www.nimh.nih.gov/health/publications/postpartum-depression-facts/postpartum-depression-brochure_146657.pdf

Providers

- Perinatal PCL 877 – 725 – 4666 (PAL4MOM): https://www.mcmh.uw.edu/ppcl
- UW PAL for Moms Care Guide https://www.mcmh.uw.edu/care-guide
- Reprotox: www.reprotox.org
- Lactmed: https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm
- MGH Center for Women's Mental Health: https://womensmentalhealth.org/

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QUESTIONS?

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