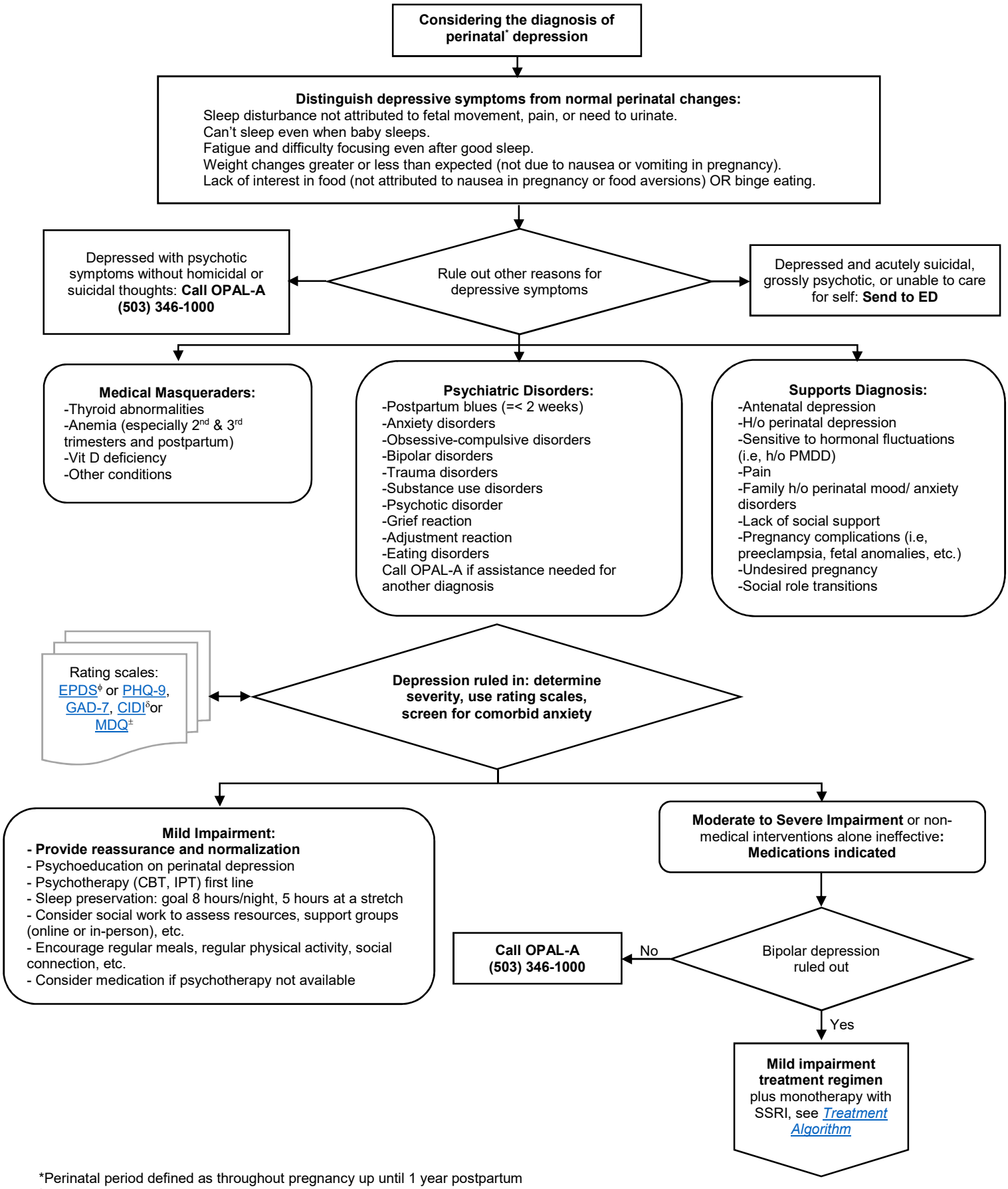
OPAL-A Assessment & Treatment Flow Chart for Perinatal Depression



*Perinatal period defined as throughout pregnancy up until 1 year postpartum

ϕEPDS (Edinburgh Postnatal Depression Scale): gold standard for perinatal period, reduces confounds from normal perinatal changes (eating, sleeping) and screens for anxiety (questions #4,5,6). Note: PHQ-9 is validated during pregnancy and postpartum.

δCIDI 3.0 (Composite International Diagnostic Interview) Screening Scale: screens for bipolar disorder, not diagnostic

±MDQ (Mood Disorder Questionnaire): screens for bipolar disorder, not diagnostic

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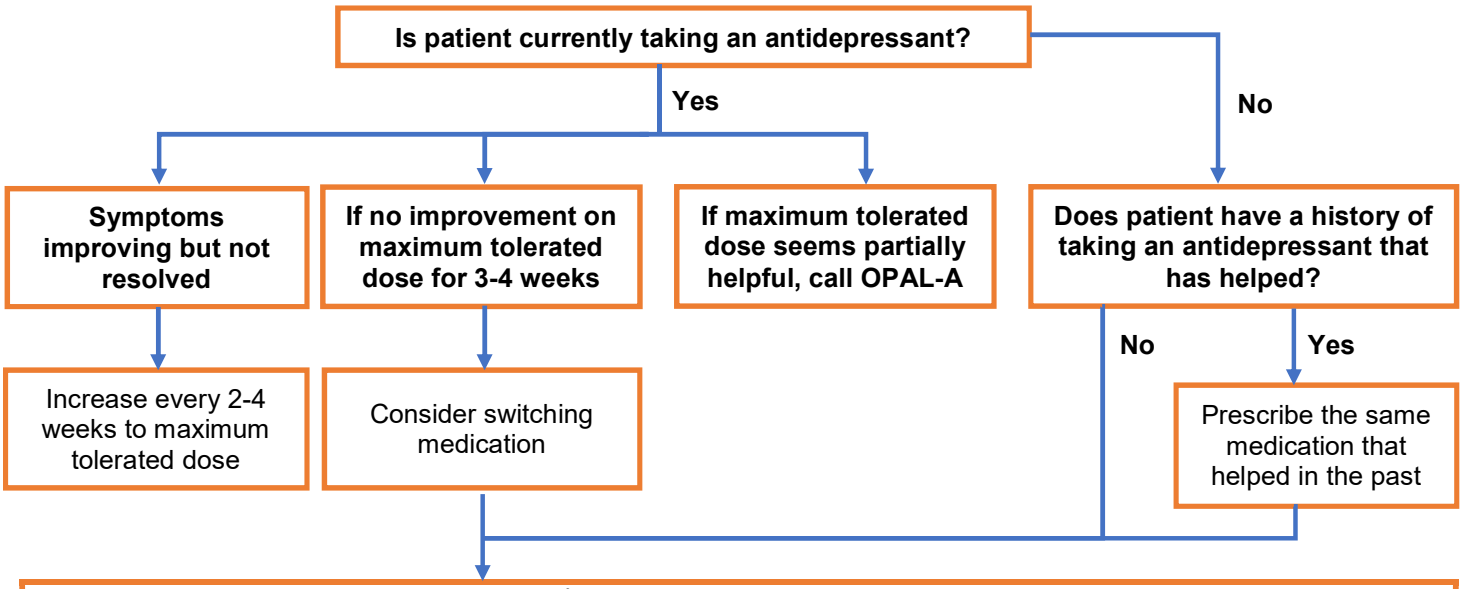
Antidepressant Treatment Algorithm

Treatment recommendations for depression during pregnancy and lactation are essentially the same with only a few exceptions (i.e., avoid starting fluoxetine in lactation – see *OPAL-A Treatment Guidelines for Perinatal Depression in Pregnancy and Lactation*)



Medication	First line treatment† sertraline‡ (Zoloft)	escitalopram (Lexapro)	Other SSRI Options citalopram (Celexa)	fluoxetine (Prozac)
Starting dose	25 mg	5 mg	10 mg	10-20 mg
How to ↑	↑ to 50 mg after 4 days, ↑ to 100 mg after 7 days, then ↑ by 50 mg until symptoms remit	↑ to 10 mg after 4 days, then ↑ by 10 mg up to 20mg until symptoms remit	↑ to 20 mg after 4 days, then ↑by 10mg until symptoms remit	↑ to 20 mg after 4 days, then ↑ by 10 mg until symptoms remit
Therapeutic Range	50 – 200 mg	10 – 20 mg	20 – 40 mg	20 – 60 mg
Target Dose	100 – 200 mg	10 – 20 mg	20 – 40 mg	40 – 60 mg

†If not currently on a medication that is helping

‡First line for both pregnancy and lactation. Lowest passage into breastmilk, fewest reported adverse effects compared to other antidepressants Typically, if an antidepressant has helped, it is best to continue it during lactation

General side effects of medication

Temporary
Nausea
Constipation/diarrhea
Lightheadedness
Headaches

Long-term
Increased appetite/weight gain
Sexual side effects
Vivid dreams/insomnia

Recommend patients take medication with food to decrease side effects

Advise patient to only increase dose if tolerating; otherwise wait until side effects dissipate before increasing

Repeat EPDS every 2-4 weeks and re-evaluate treatment plan via clinical assessment

If no/minimal clinical improvement after 3-4 weeks

If patient has **no or tolerable side effects**, increase dose
If patient has intolerable side effects, switch medication

If clinical improvement and no/tolerable side effects

Reevaluate every month and at postpartum visit

Key Clinical Considerations When Assessing Perinatal Depression

Assessing Suicidal Ideation

Suggests low risk of perinatal suicide:	Suggests increased risk of perinatal suicide:[i]
• Strong social supports • Planned pregnancy • No prior suicide attempts • No suicidal plan or intent. • If present, only passive suicidal ideation • Patient can identify protective factors **Suicide is the leading cause of death in first year postpartum. Suicide risk in perinatal period is est. to be 1.6 to 4.5 per 100,000 live births in US.[ii]**	• Younger maternal age (teen pregnancy) • Unpartnered relationship status / paternity rejection • Unplanned pregnancy • Personal and/or family history of suicide attempt • Postpartum status • Plan with high lethality (i.e., by firearm) • Access to means (medication stores, firearms) • Psychotic symptoms • Bipolar depression[iii]

Assessing Thoughts of Harm to the Baby

COMMON: Thoughts of harming baby are secondary to obsessions/anxiety and are distressing	UNCOMMON: Thoughts of harming baby are secondary to psychosis/non reality-based thoughts and without guilt
• Good insight • Realty-based thoughts • Thoughts are intrusive and scary • No psychotic symptoms • Thoughts cause anxiety **6.5% of first time moms meet criteria for OCD[iv]** ⬇ **Suggests not at risk of harming baby**	• Poor insight • Psychotic symptoms • Delusional beliefs with distortion of reality ⬇ **Suggests at risk of harming baby**

Suggests Medication May Not be Indicated	Suggests Medication Treatment Should be Considered
• Mild depression based on clinical assessment • No suicidal ideation • Engaged in psychotherapy or other non-medication treatment • Depression has improved with psychotherapy in the past • Able to care for self/baby • Strong preference for and access to psychotherapy	• Moderate/severe depression based on clinical assessment • Suicidal ideation • Difficulty functioning or caring for self/baby • Psychotic symptoms present (**call OPAL-A** or refer for emergency department evaluation) • History of severe depression and/or suicide ideation/attempts • Comorbid anxiety symptoms

Other Considerations During Clinical Assessment

- Past history of psychiatric diagnosis
- Previous psychiatric medication trials
- Previous counseling or psychotherapy
- Anxiety or excessive worrying
- Trauma history
- Perceived threat to self or baby during delivery
- Substance use or substance use treatment, past or present
- Domestic violence
- Desired or unplanned pregnancy
- History of prior pregnancy losses
- Complications during pregnancy
- Medical fragility of infant (preterm, hospitalized, congenital anomalies, etc.)
- Breastfeeding status
- Ability to enjoy baby

Recommended Steps before Starting Antidepressant Medication

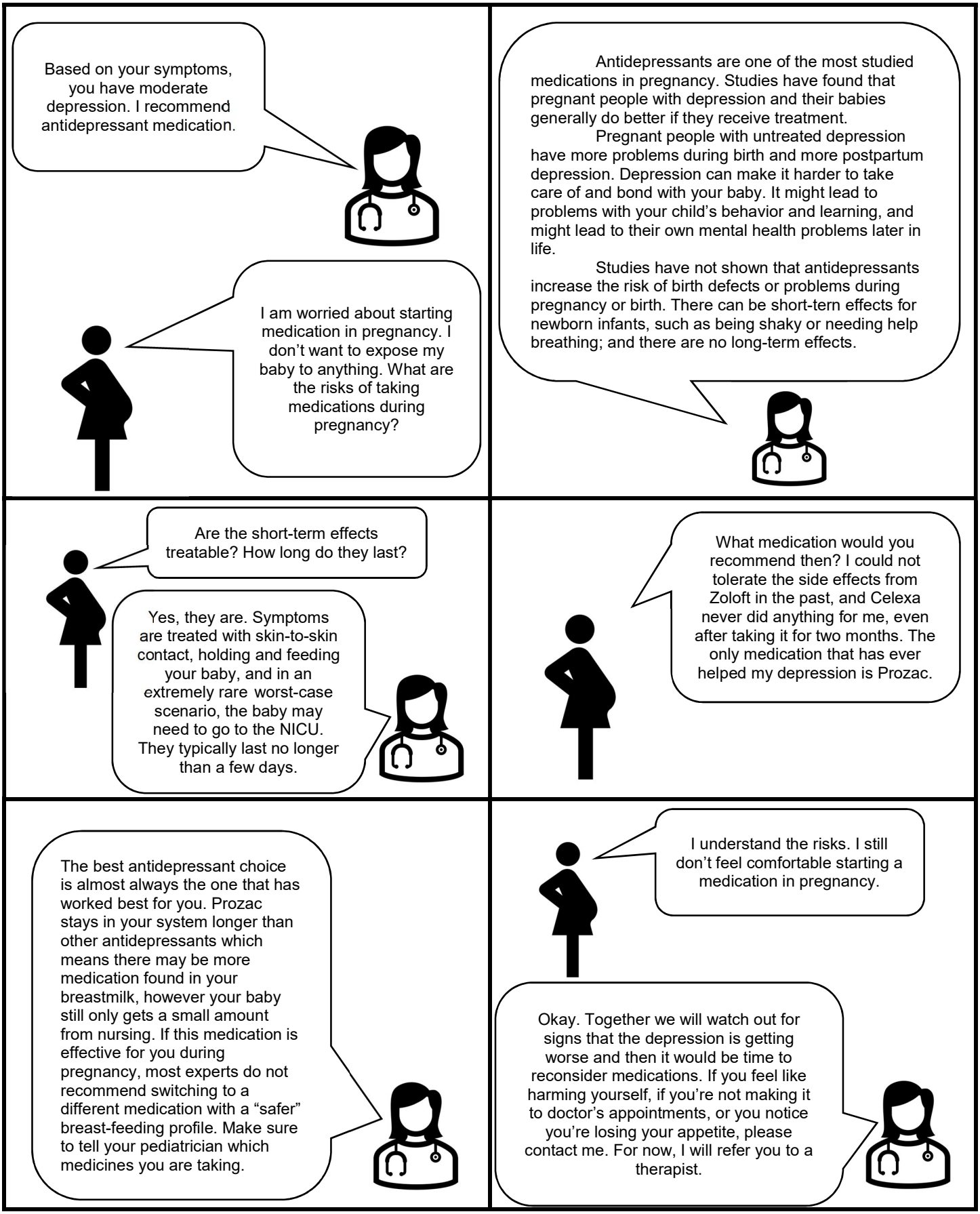
Engage in an Informed Consent and Shared Decision-Making discussion (see example below).
No need to discuss every possible potential risk from medication; summarize major categories of risk.

Counsel patient:

- There is no perfect or risk-free decision regarding whether to use antidepressants during pregnancy.
- Risks of medication exposure must be balanced against the risks of untreated/undertreated depression in pregnancy
- SSRIs are among the best studied medications during pregnancy
- Both medication and non-medication options should be considered
- Encourage non-medication treatments (e.g., psychotherapy, increased social support) in addition to medication treatment or as an alternative when clinically appropriate

Depression during pregnancy:	**Antidepressant use during pregnancy:**
• Increases risk of postpartum depression • Increases risk of birth complications • Can make it harder for moms to take care of themselves and their babies • Can make it harder for moms to bond with their babies • May later negatively affect a child's behavior or development[v]	• Not believed to cause birth defects (including paroxetine[vi]) • Little evidence for birth complications • No long-term neurobehavioral effects on children • Possible transient neonatal symptoms

Shared Decision-Making Discussion Example:



OPAL-A Perinatal Depression Treatment Guidelines

Treatment recommendations for depression during pregnancy and lactation are essentially the same with few exceptions (i.e., fluoxetine initiation de novo in lactation)

Antidepressant Management Guidelines[vii]	
Dosing	• Use lowest effective dose. • Avoid polypharmacy. • Dose increases in 2nd to 3rd trimester may be required due to pharmacokinetic changes in pregnancy, monitor symptoms. • EPDS and GAD-7 can be used to adjust dose to efficacy. • Optimize* medication prior to switching or augmenting.
Initiation	• Sertraline is 1st line in pregnancy and lactation due to lowest concentration in breastmilk and least reported adverse effects. • If sertraline was not tolerated in the past, chose an alternative SSRI such as escitalopram or citalopram. • Fluoxetine may accumulate in breastmilk due to longer half-life; this is not a reason to avoid in pregnancy or lactation if history of proven efficacy for the patient. • The best antidepressant choice is usually the one that has been effective in the past (not necessarily sertraline).
Switching	• Cross-taper or switch antidepressants after the current one has been optimized and/or is not tolerated or is deemed ineffective after an adequate trial (3-4 weeks at a therapeutic dose). • Switching to an antidepressant with a “safer” pregnancy or breastfeeding profile when the patient is already on an effective or partially effective antidepressant is not recommended due to risk of destabilization and the possible additive risks of fetal medication exposures.
Discontinuing	• Do not stop an antidepressant due to an unexpected pregnancy. • Do not stop medication prior to delivery or in the 3rd trimester. • See “Switching” recommendations before discontinuing an antidepressant.
Augmentation	• Consider adding an augmenting agent (e.g. quetiapine, mirtazapine) for depression refractory to an optimized antidepressant. • Call OPAL-A for guidance.
Special Cases	• For **hyperemesis gravidarum**, sertraline may not be tolerated due to GI side effects. Consider mirtazapine, especially if patient has poor oral intake due to nausea. • For **smoking cessation** and/or **ADHD**, consider bupropion, though not first line treatment for depression in pregnancy. • For **severe sleep deprivation** due to anxiety, consider a time-limited course of lorazepam or quetiapine at night. Avoid co-sleeping while on sedating medications.

*Optimize: increased to maximum tolerated dose

Psychosocial Treatment Guidelines

Tailor these interventions to patient's needs. Enlist natural supports and social work, lactation, or nursing services to help meet these goals. Do not chose an intervention that will overwhelm or be an additional stressor to the patient. Collaborate with the patient (and supports) to set realistic goals/interventions.

- **Sleep preservation cannot be overstated for healing**. In postpartum period, enlist supports or postpartum doula to take on night time feeds with goal of 4-5 consecutive hours of sleep and eight hours total sleep per night. This is necessary but not always sufficient for recovery.

- Other self-care: hygiene; healthy diet; regular meals, snacks, and hydration. Encourage the new parent to leave housework and cooking to others. The adage "eat when the baby eats, and sleep when the baby sleeps" is especially useful in the first month after birth.

- Minimize stressors

- Community/social support (including support groups)

- Mindfulness/relaxation techniques and exercises

- Social work assessment

- Increased physical activity, being mindful of pregnancy (e.g., placenta previa) or postpartum (e.g., healing from operative delivery) conditions/limitations

- Increased postpartum bonding with infant (e.g., scheduled skin-to-skin time if lack of motivation a factor)

- Support with dysregulated baby: crying, sleep, feeding problems (support might come from family, friends, or a lactation consult or professional post-partum doula or night nurse)

- Cognitive Behavioral Therapy or Interpersonal Psychotherapy with trained specialist

- Dyadic therapy for mother and baby

Data on Selective Serotonin Reuptake Inhibitors in Pregnancy[viii]

Selective Serotonin Reuptake Inhibitors are the most widely studied and used prescription medications in pregnancy. The risk-benefit analysis includes risks to both mother and baby, and of exposure to illness and/or to medication. Ideally, the fetus will not be exposed to untreated illness which has worse, longer-lasting outcomes than the transient risks of medication exposure.

- SSRIs in the first trimester have been well studied are not believed to be **teratogenic**. This includes paroxetine which past reports suggested an association between first trimester exposure and increased cardiac defects. Independently conducted meta-analyses have not replicated this association.

- **Neurodevelopmental disorders**: Parental psychiatric disorders such as depression, anxiety, ADHD, and Autism Spectrum Disorders (ASD) increase the risk of ASD and ADHD in offspring. When controlled for parental psychiatric disorders and other confounders, medications have not been associated with increased risk of ADHD or ASD.

- Approximately 25% of babies exposed to antidepressants late in pregnancy will experience a **transient neonatal distress syndrome** known as **neonatal adaptation syndrome.** Most commonly reported symptoms include tremor, restlessness, increased muscle tone, and increased crying which appear to be relatively benign and resolve within 1-4 days after birth without any specific medical intervention.

- Long term studies of up to **7 years** show children exposed to antidepressants in utero **do not have long term negative effects** on emotional or cognitive **development**.

- There is a small increased risk of **Persistent Pulmonary HTN of the Newborn** (PPHN). The absolute risk increases from 2/1000 births to 3/1000.

- **Miscarriage** -Although controversial, several studies link increase risk of miscarriage with SSRI use from 8 vs. 12 %. This is also seen in depressed patients who stop their antidepressant prior to conception.

- There may be mild effects on **decreased gestational age** (3-5 days), **Low Birth Weight** (75g lower birth weight) and a small decrease in **APGAR scores** (decrease of 0.5 points on 1- and 5-minute Apgar). However, this is also seen in infants of depressed mothers who are not taking medication.

Antidepressants and lactation

- Sertraline is the most studied new antidepressant and has the lowest excretion into human milk.

- When selecting a medication postpartum, fluoxetine and other antidepressants with longer half-lives may be less desirable due to higher infant serum levels, thereby increasing the risk of adverse effects (most common, but rare, side effects seen in infants include fussiness, sedation, decreased infant weight gain).

- Choosing an antidepressant with known efficacy for the patient may be the best choice, regardless of half-life.

- Patients taking antidepressants may experience increased difficulty with breast/chestfeeding, although this also may reflect their disease state. Maintain a low threshold to refer to a lactation consultant.

- Nursing infants of patients taking an antidepressant during lactation and in the 3rd trimester of pregnancy appear to have a lower risk of poor neonatal adaptation (antidepressant withdrawal) than formula-fed infants. However, withdrawal symptoms may arise from abrupt discontinuation of human milk, particularly when the parent is taking a medication with a shorter half-life (e.g., paroxetine).

Detailed List of Risks of Untreated Depression[ix]

This is the rationale to treat as the risks associated with exposure to illness is greater than exposure to medication.

- Maternal depression increases stress hormone release. These hormones enter the fetal compartment and have been linked with up to two-fold increases in the following antenatal complications:
  - miscarriage
  - birth defects
  - preeclampsia
  - gestational diabetes mellitus
  - babies with low birth weight
  - preterm birth

- Maternal depression is also linked with neurodevelopmental issues in children, including:
  - developmental delays
  - impairment in attachment resulting in dysfunction in the parent-infant dyad, which can have behavioral, cognitive, and psychiatric sequelae
  - mood and psychiatric diagnoses
  - cognitive diagnoses

- During organogenesis in the first trimester, there is a baseline 3-5% risk of birth defects in the general population. Extreme stress and untreated depression have been shown to increase rates of birth defects.

- Infants born to parents with antenatal depression may have:
  - Increased reactivity to pain and stress
  - May spend more time in medical nursery than well-baby nursery
  - More likely to be delivered by cesarean section or operative delivery

Online Information, Support, and other Resources

For clinicians

- Reprotox (paid subscription, accessible through Micromedex) – pharmacological database summarizing evidence based reproductive effects of medications perinatally (pregnancy, lactation, fertility)

- LactMed (free app from National Library of Medicine) – pharmacological database summarizing evidence based reproductive effects of medications in lactation
    - https://www.ncbi.nlm.nih.gov/books/NBK501922/

- Massachusetts General Hospital – information for patients and clinicians
    - http://womensmentalhealth.org/

- Mother to baby – Handouts on each medication in pregnancy
    - https://mothertobaby.org/

- National Curriculum of Reproductive Psychiatry – online, interactive curriculum designed to teach reproductive psychiatry to mental health professionals – either within an educational program or self-guided
    - https://ncrptraining.org/

For patients

- Postpartum Support International, Oregon Chapter
    - 1-800-944-4PPD (4773) in English and Spanish
    - http://www.postpartum.net/Get-Help.aspx

- OHA Maternal Mental Health Website
    - http://public.health.oregon.gov/HealthyPeopleFamilies/Women/MaternalMentalHealth/Pages/index.aspx

- Postpartum Progress – wonderful blog
    - http://www.postpartumprogress.com/

- Postpartum Husbands and Dads
    - http://www.postpartumdads.org/
    - http://www.postpartummen.com/

- Postpartum resources – information for patients and clinicians
    - http://www.mededppd.org/

- Massachusetts General Hospital – information for patients and clinicians
    - http://womensmentalhealth.org/

- Mother to baby – Handouts on each medication in pregnancy
    - https://mothertobaby.org/

- Healthy Birth Initiative – addresses the needs of pregnant African American women
    - https://www.multco.us/children-and-family-health-services/healthy-birth-initiative

Support Groups

- Baby Blues Connection
    - 1 (800) 557-8375
    - https://www.babybluesconnection.org/

- Postpartum Depression Online Support Group
    - http://www.ppdsupportpage.com/

Books

- *Beyond the Blues: A Guide to Understanding and Treating Prenatal and Postpartum Depression* by Shoshana S. Bennett, Ph.D. and Pec Indman, Ed.D., MFT. http://www.beyondtheblues.com/book/home.html

- *This Isn't What I Expected: Overcoming Postpartum Depression* by Karen Kleiman and Valerie Raskin

- *The Pregnancy & Postpartum Anxiety Workbook* by Pamela S. Wiegartz, PhD and Kevin L. Gyoerkow, PsyD

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viii Contributions from Nicole Cirino, MD, Reproductive Psychiatrist, Director, Division of Women's Mental Health and Wellness, Oregon Health & Science University, Portland, Oregon

ix National Curriculum of Reproductive Psychiatry. https://ncrptraining.org/.