KAISER PERMANENTE®

Perinatal Depression Screening, Diagnosis, and Treatment Guideline

Last guideline approval: December 2018

Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

Major Changes as of December 2018

New	Previous
Fluoxetine is no longer recommended in pregnancy due to risk of congenital malformations.	Previously, fluoxetine was recommended as a second-line antidepressant in pregnancy.
The first-line antidepressant in both pregnancy and lactation is sertraline and second-line is escitalopram. Fluoxetine is not recommended.	Previously, sertraline was first-line and citalopram and fluoxetine were second-line antidepressants for pregnancy and lactation. Escitalopram was not on the preferred list.
For pregnant and postpartum women, we now recommend using the Maternal Behavioral Health Screening tool.	Previously, depression screening for all adults was done by a standalone PHQ-9 tool with additional depression questions on the back page.
Recommendations for women who are pregnant, postpartum, or currently on antidepressants and considering becoming pregnant are now presented in a standalone guideline.	Previously, recommendations for pregnant and postpartum women were included in the KPWA Adult and Adolescent Depression Guideline.

Target Population

The recommendations in this guideline apply to

- Pregnant women.
- Postpartum women from childbirth through the first year of the baby's life.
- Women who are already taking antidepressant medications and are considering becoming pregnant.

Behavioral Health Integration/Maternal Behavioral Health

Kaiser Permanente Washington has integrated behavioral health into all primary care clinics. The goal of Behavioral Health Integration (BHI) is to create a welcoming environment for patients to address common problems—alcohol and substance use disorders as well as depression—with their primary care teams. A major element of BHI has been transitioning primary care social workers to a new role of integrated behavioral health specialist, in which they work as "provider extenders" to address patient needs without disrupting patient flow and team cycle time. Social workers offer consultation to providers, brief interventions, or short-term (4–6 visits) counseling for individuals with mild to moderate depression and alcohol or substance use disorders.

Maternal Behavioral Health (MBH) Screening is part of the BHI initiative that focuses on pregnant and postpartum women through an infant's first year of life. Recent research demonstrates that pregnancy and the first year of the infant's life pose increased risks to the mother's mental health and well-being, including depression, anxiety, and domestic violence. MBH screening tools and processes are similar to those used in BHI, but they are tailored for maternal health and include questions about domestic violence.

Screening and Diagnosis

Routine screening using the Maternal Behavioral Health (MBH) Screening questionnaire is recommended for all pregnant and postpartum women. MBH screening is optimally performed at four visits during the pregnancy and four times through the infant's first year, at the following routine visits:

Pregnancy care (In Women's Health or Family Practice)	**Pediatric care** (In Pediatrics or Family Practice)
• First prenatal visit • 16-week visit • 32-week visit • Postpartum	• 7–14-day well baby visit • 4-month well baby visit • 6-month well baby visit • 12-month well baby visit

MBH screening has been integrated into the OB and Well Child Visit SmartSets. The MBH incorporates the Patient Health Questionnaire (PHQ-9), the Generalized Anxiety Disorder (GAD-2) questionnaire, and questions about substance abuse and domestic violence. A job aid provides details about MBH visit content and documentation (staff intranet).

Note: Pregnant and postpartum women who have a current diagnosis of depression—whether made prior to pregnancy or during the perinatal period—should be followed with the Maternal Behavioral Health Screening questionnaire at the same set of routine visits.

Severity assessment

The first nine questions on the MBH questionnaire comprise the PHQ-9. The PHQ-9 score is the sum of these responses.

Depression severity is correlated with PHQ-9 scores as follows:

20–27: Severe major depression
15–19: Moderately severe major depression
10–14: Moderate major depression
5–9: Indeterminate or mild depression. People with this score could have had major depression that is now improved, chronic mild depression (dysthymia), or transient mild depression. The PHQ-9 cannot distinguish among these. Use clinical judgment to determine appropriate next steps.

Screening for suicidal ideation

Suicidal ideation is assessed by question 9 on the PHQ-9.

> Over the past 2 weeks, how often have you been bothered by any of the following problems: thoughts that you would be better off dead, or hurting yourself in some way?

If the patient scores 2 or 3 on this PHQ-9 question (or otherwise expresses suicidal thoughts, exhibits suicidal behaviors, or has suicide risk factors), administer the Suicide Risk Assessment (SRA). (Also available as an Epic Flowsheet.)

The SRA is scored by adding the "yes" answers together.

6: Acute risk for suicide
3–5: Moderate risk
0–2: Low risk

SRA score of 3 or higher
Requires completion of a crisis response plan and lethal means removal. While the patient is still in the room, obtain immediate consultation with a behavioral health professional through:

- Warm patient hand-off to clinic social worker/integrated behavioral health specialist, or
- Behavioral Health Services (BHS) Mind Phone

SRA score of 0–2
Arrange a follow-up appointment with Behavioral Health through:

- Epic order Urgent referral to BHS, or
- Warm patient hand-off to integrated behavioral health specialist

Psychiatric comorbidities and other life stressors

The remaining questions on the Maternal Behavior Health Screen (questions 10–21) are designed to assess for other mental health conditions and life stressors. Consider consultation or referral to BHS for more definitive diagnosis and management if any of these factors are present.

Table 1. Mental health conditions or life stressors to consider in pregnant and postpartum women

Mental health condition or life stressor	MBH screening question	Next steps
Anxiety disorders, including generalized anxiety disorder, obsessive-compulsive disorder, and panic disorder	**GAD-2** Over the last 2 weeks, how often have you been bothered by the following problems? • MBH #10: Feeling nervous, anxious, or on edge • MBH #11: Not being able to stop or control worrying	If score of 3 or higher, follow with the GAD-7. (Available in Epic.)
Alcohol misuse	**AUDIT-C** • MBH #13: How often did you have a drink containing alcohol in the last 3 months? • MBH #14: How many drinks containing alcohol did you have on a typical day when you were drinking in the last 3 months? • MBH #15: How often did you have 4 or more drinks on one occasion in the last 3 months?	See the Adult Unhealthy Drinking Guideline.
Marijuana misuse	• MBH #16: In the last 3 months, have you used marijuana?	If daily or almost daily, use the Substance Use Symptom Checklist in Epic.
Drug misuse	• MBH #17: In the last 3 months, have you used an illegal drug or used a prescription medication for non-medical reasons?	If yes, use the Substance Use Symptom Checklist in Epic.
Abuse/violence	• MBH #19: Are you currently in a relationship where your partner hits, slaps, kicks, or hurts you? • MBH #20: Does your partner control where you go or make you feel afraid? • MBH #21: Have you had a partner who physically hurt or threatened you?	If yes, follow up with open-ended, non-leading questions to encourage self-disclosure. Consider referral to Social Work.

Treatment: Overview of Options

Treatment recommendations are based on the patient's PHQ-9 score and may include psychotherapy, antidepressants, or both. On average, antidepressant medication and psychotherapy have similar effectiveness. Supportive care is recommended for *all* patients receiving care for depression.

The goals of treatment are to achieve complete remission and prevent relapse or recurrence of depression. Remission is defined as a PHQ-9 score of < 5.

20–27: Severe major depression

For patients with severe major depression, **combined antidepressant medication and psychotherapy** is the preferred treatment recommendation. Antidepressant medication alone is an alternative recommendation. Psychotherapy alone is *not* recommended for these patients.

Moderately severe (15–19) and moderate (10–14) major depression

For patients with moderately severe or moderate major depression, **shared decision making** around treatment options—antidepressants, psychotherapy, and combination therapy— is recommended. For patients with moderately severe depression (PHQ-9 score of 15–19), combining psychotherapy and antidepressants may be more effective than using either treatment alone.

5–9: Indeterminate or mild depression

For patients with indeterminate or mild depression, treatment with antidepressants or psychotherapy is usually not recommended. Supportive care, including patient education and emotional support and guidance, is recommended.

Supportive care

Support and education in the primary care setting are critical and contribute to the likelihood of good follow-through on treatment. Supportive care is recommended for *all* patients receiving care for depression.

Patient education should include:

- The cause, symptoms and natural history of major depression
- Shared decision making about treatment options
- Information on what to expect during treatment
- Follow-up (office visits, e-mail, and/or telephone)

In addition to patient education, supportive care includes emotional support and guidance. Providers can engage in behavioral activation by encouraging patients to consider and adopt some self-management responsibilities, such as writing in a journal or reading self-help books, scheduling pleasant activities, spending time with people who support them, and engaging in physical activity. Patients who are receiving supportive care but are not prescribed medications should be encouraged to follow up with a member of their clinical team within 2–4 weeks of diagnosis, as early behavioral activation may improve patients' self-efficacy and continued investment in treatment (Cuijpers 2014). If possible, schedule follow-up at the time of diagnosis.

Psychotherapy

Psychotherapy often involves a series of structured sessions in which a provider helps the patient identify and change behaviors (isolation, inactivity, avoidance of problem-solving) and cognitions (negative rumination, magnification of bad news, minimization of good news). Behavioral Health Specialty offers therapy for major depression and other severe persistent mental illness (SPMI). Social workers are available in every primary

care clinic to offer brief interventions and short-term counseling (4–6 weeks), which is better suited to patients with mild to moderate depression (PHQ-9 score 5–14).

Group therapy is an alternative or adjunct to individual therapy. Patients may be referred to group therapy to learn skills and to lessen isolation. Depression and anxiety (DAG) groups are currently offered in 11 primary care clinics and will be expanding to additional clinics in the coming months. Emotional regulation groups are also being offered in several BHS specialty clinics.

Online cognitive behavioral therapy (CBT) may be an attractive option as access to in-person psychotherapy may be a significant barrier to care. Kaiser Permanente offers a free online CBT-based program—**Thrive**—which offers modules on behavioral activation, cognitive restructuring, and social skills training, and uses interactive tools and branching logic to create a personalized curriculum for each patient.

Combination therapy

For some patients, particularly those with severe depression (PHQ-9 score of 15 or higher), combining psychotherapy and antidepressants may be more effective than using either treatment alone.

Antidepressants

Pregnant and postpartum women considering antidepressants need to be informed of the risks and benefits of pharmacologic treatment through a shared decision making process.

SSRIs have the most data for use during pregnancy and lactation. Assessing the benefits and risks of taking an antidepressant during pregnancy and lactation is challenging because the evidence is limited to observational studies that are subject to confounding and bias. The potential risks of medication exposure must be balanced with the potential harms of untreated maternal depression. The benefits of breast feeding seem to outweigh the potential side effects of SSRIs.

Untreated maternal depression has been associated with miscarriage, increased preterm birth, low birth weight, increased rates of cigarette, alcohol and other substance misuse, and poor prenatal care. In the postpartum period there is a greater risk of disturbance in the development of the maternal-infant bond in severely depressed mothers; in addition, postpartum depression has been associated with lower IQ, slower language development, increased risk of ADHD and an increased risk of psychiatric illness in the child.

Shared Decision Making: Treating Depression in PREGNANT Women

Assessing the benefits and risks of taking an antidepressant during pregnancy and lactation is challenging because the evidence is limited to observational studies that are subject to confounding and bias. There are no good studies about the long-term effects of SSRI exposure in pregnancy. Only small, less rigorous studies are available and seem to indicate no effect on the child's behavioral, language, or IQ development.

Table 2. Shared decision making: treating depression with SSRIs DURING PREGNANCY
Use SmartPhrase .ssrisandpregnancy

	Treatment with SSRIs	No treatment with SSRIs
Advantages	• Decreased risk of depression relapse (26%) • Decreased risk of low birth weight and postnatal complications • Similar risk of birth defects as for women who don't take SSRIs during pregnancy (about 3–5%)	• No exposure of baby to SSRIs • Decreased risk of preterm birth (4%)
Risks to mother	• Depending on which SSRI is used, increased risk of GI distress, weight gain, insomnia, or sexual issues	• High risk of depression relapse (68%) • Increased risk of cigarette, alcohol, and other substance misuse • Decreased social support and poor prenatal care
Risks to baby	• Increased risk of preterm birth (8%) • Withdrawal symptoms at birth in up to 30% of babies, including jitteriness or irritability, tremors, or trouble feeding • Increased risk of congenital malformations during the first trimester, especially with fluoxetine and paroxetine • Small risk (< 1%) of developing persistent pulmonary hypertension, which may require care in specialty care nursing	• Increased risk of postnatal complications • Increased risk of crying and difficulty being consoled • If depression occurs postpartum: increased risk of lower IQ, slower language development, ADHD, psychiatric illness, and suicidal behavior

Key Points: Treating Depression in BREASTFEEDING Women

- The benefits of breastfeeding generally seem to outweigh the potential side effects of SSRIs.
- In severely depressed postpartum women, the risks of taking SSRIs are generally considered lower than the risk of disturbing the development of the maternal-infant bond.
- Infant drug exposure is generally higher through placental passage than through breast milk. Thus, if a woman has taken an antidepressant during pregnancy, it generally makes sense to continue with the same antidepressant during breastfeeding to minimize the number of medications the infant is exposed to.
- There is weak evidence (e.g., from case studies) linking antidepressant use in breastfeeding mothers with mild adverse events in infants, but because the reported adverse effects were non-specific (e.g., irritability, sedation, and "colic"), it is unclear whether they were directly related to the medication exposure.
- The risk of drug accumulation and associated toxicity may be higher in premature infants or in infants with signs of compromised hepatic metabolism.
- To minimize the risk to the baby, use the minimum medication dose that provides adequate control of the mother's symptoms.
- There does not appear to be any benefit to altering the timing of nursing, or selectively discarding portions of the breast milk, to minimize the drug exposure to the baby.

Pharmacologic Options for Pregnant and Breastfeeding Women

In a patient who is not currently receiving drug therapy, sertraline is the drug of first choice because literature supports its use during preconception, throughout pregnancy, and during breastfeeding. However, if the patient previously failed an adequate dose and duration or experienced intolerable side effects on the first-line option, then any of the medications where literature supports use (green-shaded areas of Table 3 on the following page) are reasonable alternatives. Paroxetine is associated with an increased risk of congenital malformations when taken in the first trimester and is therefore **contraindicated** during pregnancy. Fluoxetine is not recommended due to increased risk of major birth defects during early pregnancy.

In a patient who is on well-established, effective therapy, it is reasonable to continue any of the medications where literature supports use (green-shaded areas) or where absolute risks are likely small (yellow-shaded areas), as the benefits of continuing therapy likely outweigh the risks of switching. However, consideration should be given to switching therapy if the patient is taking a medication for which there is possible evidence of harm (red-shaded areas).

For patient-specific consultations, refer to BHS or OB/GYN or call the Mind Phone.

Table 3. Summary of antidepressant use prior to conception and during pregnancy and lactation [1]

☺ = Current literature supports use
😐 = Caution but absolute risks likely small
☹ = Possible evidence of harm

	Preconception	1st trimester	3rd trimester	Postpartum & lactation	Estimated percentage of maternal dose to baby via breast milk [2]
Sertraline	☺	☺	😐	☺	0.4%–2.3%
Sertraline is a preferred SSRI during pregnancy and lactation because of its short half-life and the relatively low drug levels found in cord blood and breast milk. For women stable on fluoxetine or citalopram during pregnancy, the possible benefits of switching to sertraline for breastfeeding must be balanced against the possible disruption of switching medication.					
Escitalopram	☺	☺	😐	😐	3.9%–7.9%
Based on limited data, escitalopram appears to be preferable to citalopram during pregnancy and breastfeeding. Escitalopram shows lower drug levels in breast milk and a general lack of adverse reactions in breastfed infants.					
Citalopram	😐	😐	😐	😐	0.7%–9.0%
Citalopram is excreted into human breast milk. Compared with other SSRI antidepressants, the relative dose to the infant from citalopram was comparable to fluoxetine but higher than that for sertraline and paroxetine. If citalopram is required by the mother, it is not a reason to discontinue breastfeeding.					
Paroxetine	☹	☹	😐	☺	0.1%–4.3%
Paroxetine is contraindicated in early pregnancy due to the risk of congenital malformations. Paroxetine has low drug levels in breast milk and is a reasonable option if the drug is started after the 2nd trimester or in the postpartum period.					
Fluoxetine	☹	☹	😐	😐	1.2%–12.0%
Recent data shows a statistically significant increased risk of major birth defects when fluoxetine is taken in early pregnancy. Also, the average amount of drug in breast milk is higher with fluoxetine than with most other SSRIs, and the long-acting, active metabolite norfluoxetine is detectable in the serum of most breastfed infants during the first 2 months postpartum and in a few thereafter. Adverse effects such as colic, fussiness, and drowsiness have been reported in some breastfed infants.					
Venlafaxine	☺	☺	😐	😐	3.5%–8.1%
Bupropion	😐	😐	😐	😐	0.2%–2.0%
Venlafaxine and bupropion While data is limited and evidence for use of these medications during pregnancy and lactation is less clear than for other antidepressants, it is reasonable to consider continuing their use in women who are responding to them. The American Academy of Pediatrics classifies bupropion and venlafaxine as drugs whose effect on the nursing infant is unknown but may be of concern.					

[1] See reference list for Table 3 on page 12.
[2] Estimates are weight-adjusted and include the agent and its active metabolites.

Table 4. Recommended antidepressant dosing for PREGNANT OR BREASTFEEDING WOMEN

For women starting or continuing antidepressants during or after pregnancy, use SmartPhrases
.avspregdepressionmedstart
.avspregdepressionmedcont
.avsdepressionbreastfeeding
.avspregdepressionpostpartum
.avsdepmaternalcareplan

Line	Medication	Initial dose	Titration schedule If unsatisfactory clinical response after 2–4 weeks, then:	Usual therapeutic dose range
1st	**Sertraline**	50 mg daily x 7 days, then increase to 100 mg daily.	Increase by 50 mg increments at 4-week intervals.	50–200 mg
2nd	Escitalopram	5 mg daily x 7 days, then increase to 10 mg daily.	Increase to 20 mg daily.	10–20 mg

Other treatment options

Herbal supplements

The safety and efficacy of herbal supplements for depression treatment in pregnant and breastfeeding women was not evaluated, as few animal or human studies have been conducted. Due to the lack of evidence and uncertainty in product quality, women who are pregnant, contemplating pregnancy, or lactating should generally be discouraged from using herbal treatments.

Bright light therapy

Moderate evidence suggests that the use of bright light therapy is not effective for perinatal depression.

Follow-up

See the KPWA Adult and Adolescent Depression Guideline for follow-up recommendations. The Behavioral Health Monitoring Tool should be used at every follow-up visit for depression after the baby's first birthday. The SmartPhrase .smdepfollowup may be used when scheduling follow-up visits.

Evidence Summary

This guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

What is the effectiveness and safety of antidepressants in pregnant women with major depressive disorder?

- Pharmacological treatment vs non-pharmacological treatment: The review identified one meta-analysis (van Ravesteyn 2017) and two randomized trials (Forsell 2017, Van Ravesteyn 2018) that compared non-pharmacological treatment versus usual care, psycho-education, or counseling. No pharmacological trials were identified, and harms were not assessed. Although the evidence shows that non-pharmacological treatment might be more effective in reducing depressive symptoms, there is a lack of direct evidence to evaluate the comparative effectiveness and safety of pharmacological and non-pharmacological treatment in pregnant during pregnancy and the postpartum period.
- Antidepressants for preventing postnatal depression: There is insufficient evidence for or against the use of antidepressants to prevent postnatal depression.
- Treated versus untreated major depression on pregnancy outcomes: One systematic review without meta-analysis (Mitchell 2018) was identified. No differences or comparable findings between antidepressant-treated women and untreated women were reported in terms of risk of low birth weight and related outcomes, or gestational lengths. Evidence regarding spontaneous abortion, however, is insufficient to draw conclusions.
- Untreated depression: Compared with pregnant women without depression, moderate evidence shows that the risks of preterm birth (< 37 weeks) and low birth weight (< 2500 g) are significantly higher in pregnant women with untreated depression. Concerning maternal risks of untreated depression, observational studies show that untreated maternal depression is associated with harms to the mother and her offspring (conclusion of 2017 KPWA guideline evidence review).
- Safety of antidepressants during pregnancy: The 2017 KPWA guideline evidence review concluded that antidepressant use during pregnancy is associated with maternal and fetal risks. In the current review, six meta-analyses assessed the risk of autism. Low evidence shows a significant association between antidepressant exposure during pregnancy and the risk of autism spectrum disease. In addition, fluoxetine is associated with congenital malformations (major malformations, cardiovascular malformations, septal defects, and non-septal defects).

What is the effectiveness of bright light therapy in patients aged 12 years and over with major depressive disorder?

Four meta-analyses (Al-Karawi 2016, Chiu 2017, van Ravesteyn 2017, Holvast 2017) were considered for the review. Patients with depression or postpartum depression and pregnant women with major depressive disorder were included. Some studies included patients who received antidepressants. Treatment lasted up to 8 weeks. Comparators consisted of dim light therapy, red yellow light, placebo light exposure (250 lux), dim red light (< 5 lux), and usual indoor light (150–200 lux).

Bright light therapy (BLT) alone was significantly effective in reducing depression symptoms. No evidence of efficacy was found for BLT as an adjunct to antidepressants. BLT was not effective during pregnancy or in perinatal depression. Both high-intensity and low-intensity BLT are effective; however, in one meta-analysis, high-intensity BLT was found to be significantly more effective than low-intensity BLT (Chiu 2017). The strength of the evidence is moderate. Moderate evidence supports the use of bright light therapy alone in patients with major depressive disorder.

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Guideline Development Process and Team

Development process

The guideline team developed the Perinatal Depression Guideline using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in December 2018.

Team

The Perinatal Depression Guideline development team included representatives from the following specialties: adolescent medicine, behavioral health, family medicine, nursing operations, obstetrics/gynecology, pediatrics, and pharmacy.

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Disclosure of conflict of interest

Kaiser Permanente requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care–related products and/or services relevant to the content of the guideline.

Team members listed above have disclosed that their participation on the Perinatal Depression Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.