Treating Mood Disorders Across the Reproductive Years

Kay Roussos-Ross, MD
Professor
Chief, Division Academic Specialist in General Obstetrics and Gynecology
Department of Obstetrics and Gynecology
University of Florida College of Medicine
Gainesville, FL

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Disclosure

I have no financial interests or relationships to disclose.

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Topics of Focus Today

- Premenstrual dysphoric disorder (PMDD)
- Perinatal Depression
- Perimenopausal Depression

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Mood Disorders in Women

- Mood disorders in women arise most frequently between the ages of 18 and 45 years
- Mood disorders tend to be chronic and recurrent, thus, many women of childbearing age experience psychiatric illness

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Mood Disorders and Hormones

- Evidence of worsening of mood disorders during times of hormonal fluctuation
  - Related to menses
  - Related to pregnancy or postpartum
  - Related to menopausal transition

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Pathophysiology of Mood Disorders

- Abrupt changes in hormone levels may alter the equilibrium of neurotransmitters found in the brain thus increasing risk of mood disorders
  - ESTROGEN

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Role of Estrogen in Treatment of Mood Disorders

- Modulates serotonin and norepinephrine
- Increases GABA activity
- Decreases activity of MAO (involved in serotonin degradation)
- Increases tryptophan hydroxylase (involved in serotonin synthesis)
- Selectively increases serotonin receptor density in brain
- Promotes NE availability
- Involved in increasing NE hydroxylation from dopamine

(Soares. Menopause. 2014)

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Role of Progestins in Treatment of Mood Disorders

- Increases concentration of MAO causing decrease in serotonin concentration (Steiner et al. J Affective Disorders. 2003)
  - Opposite effect from estrogen

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What Questions Do We Ask When Screening for Mood Disorders?

- Duration of symptoms?
- Associated symptoms?
- Severity of symptoms?
- What has she tried for treatment thus far?
- What intervention is she willing to try?

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PMDD

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PMDD vs PMS
What Is the Difference?

- Both PMS and PMDD occur in a **cyclic** pattern
  - Symptoms appear in the late luteal phase and resolve with the onset of menstruation
- PMDD is distinguished from PMS by:
  - Severity of symptoms
  - Predominance of mood symptoms
  - Functional impairment

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Epidemiology

- Prevalence of PMS is 3-8% in a 12-month period
- Prevalence of PMDD is 2% in a 12-month period
  - Less common in black women

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Risk Factors for Development of PMDD

- History of depression
- History of trauma
- History of anxiety
- Lower SES
- Hormonal predisposition

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Evaluation of PMDD

- Detailed history
  - Menstrual diary
    - Symptoms begin late luteal phase- approximately 5 days prior to onset of menses
    - Symptoms resolve within 3 days of onset of menses
  - Rule out medical or pharmacologic causes of symptoms
    - Thyroid disorder
    - Worsening of mood with combined contraception (estrogen/progesterone)

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Diagnosis of PMDD

- Symptoms present majority of last year
- 5 + symptoms occurring in late luteal phase and resolving within a few days after onset of menses
- One or more of following physical symptoms
  - Mood swings, sudden sadness, increased sensitivity to rejection, anger, irritability, sense of hopelessness, depressed mood, self-critical thoughts, tension, anxiety, feeling on edge
- One or more of the following affective symptoms
  - Difficulty concentrating, change in appetite, food cravings, decreased interest in usual activity, increased fatigue, decreased energy, feeling overwhelmed or out of control, breast tenderness, bloating, weight gain, or joint/muscles aches, sleeping too much or not sleeping enough

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Treatment Options for PMDD

- Lifestyle modifications
- Psychotherapy
- Pharmacologic management

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Lifestyle Modifications for PMDD

- Exercise
- Stress reduction
  - Cognitive behavioral therapy
- Herbal/Vitamin supplementation (likely not better than placebo)
  - Chasteberry 20-40mg daily
  - B6, Calcium, Magnesium supplementation

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Alternative Medicine

- Acupuncture
  - Shown in some studies to be superior to sham in treatment of PMDD

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Pharmacologic Management Options for PMDD

- SSRI
  - Increase serotonin transmission
- Combined estrogen-progestin oral contraceptives
  - Work by suppressing H-P-O axis

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SSRI

- Effective treatment of PMDD in up to 70% of patients
- Chose as 1st line **IF** the woman does not also require contraception
- Dosing options
  - Continuous
    - Consider this when concern about compliance, low grade mood symptoms outside of PMDD
  - Luteal phase only
    - Prescribe day 14-28 of cycle
  - Symptom onset only
    - Start with symptom onset and stop few days after onset of menses
- If no improvement with SSRI can consider alternative types of antidepressants (SNRI, Atypicals)

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Combined Hormonal Contraceptives

- Use first line in patients who require contraception
- Choose monophasic combined oral contraceptives (COC)
- Remember some patients may have worsening of mood with COC
  - Try a different progestin component
- Only approved COC for PMDD includes drospirenone
- Can dose monthly or continuous
- If unable to tolerate, consider levonorgestrel IUD

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Pharmacologic Management Options

- For severe symptoms, insufficiently improved with monotherapy
  - Consider combination of SSRI/SNRI/Atypical with COC/LNG-IUD

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Perinatal Depression

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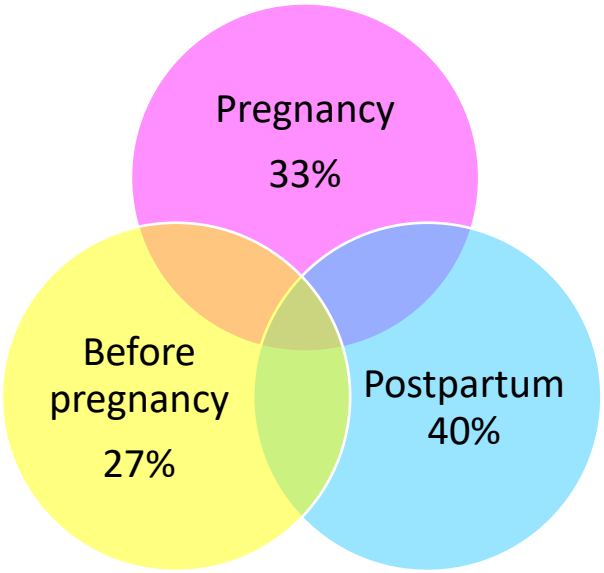
Two-thirds of Perinatal Depression Begins Before Birth



Wisner et al. *JAMA Psychiatry* 2013

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Risk Factors for Perinatal Depression

- Younger age
- Lack of social support
- Living alone
- Having more children
- History of depression
- Family history of depression

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Pregnancy and Mood Disorders

- Mood disorders during pregnancy increase the risk for:
  - Limited prenatal care
  - Gestational hypertension/Pre-eclampsia
  - Placental abnormalities
  - Low birth weight
  - Preterm labor
  - Fetal distress
  - Substance exposures (tobacco, illicit drugs)

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Pregnancy and Mood Disorders

- Mood disorders in the postpartum period increase the risk for:
  - Poor maternal/infant bonding
  - Poor infant attachment
  - Inadequate socialization
  - Learning disabilities
  - Behavioral disorders

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Prevalence of Mood Disorders in Pregnancy

- Up to 20% of women suffer from mood disorders in pregnancy (depression and anxiety)
- Women who discontinue pharmacologic management are 5x more likely to relapse compared to women who continue treatment

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Prevalence of Mood Disorders in Pregnancy

- Untreated depression
  - 50-60% risk of postpartum episode and worsening of the psychiatric condition (Evans et al, 2001)
  - 15% increased risk of suicide (Appleby, 1991)

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How Common Is It Really?

- Depression: 15-20% of pregnancies
- Gestational diabetes: 3-7% of pregnancies
- Hypertensive disorders: 5-8% of pregnancies

WAY MORE COMMON!!!

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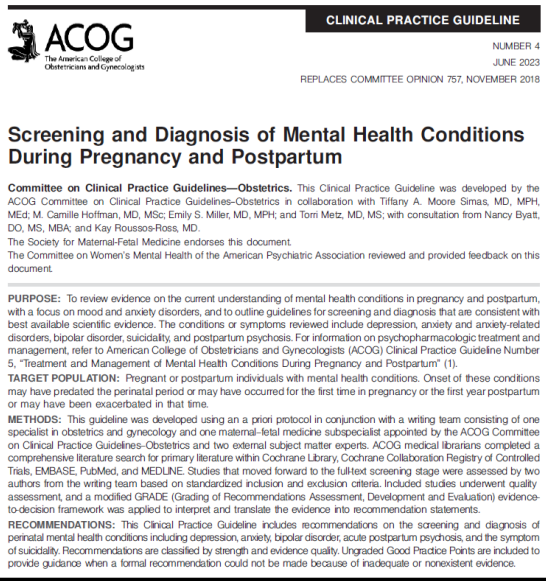
ACOG Guidelines & Recommendations



ACOG
The American College of Obstetricians and Gynecologists

CLINICAL PRACTICE GUIDELINE

NUMBER 4
JUNE 2023
REPLACES COMMITTEE OPINION 757, NOVEMBER 2018

Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum

Committee on Clinical Practice Guidelines—Obstetrics. This Clinical Practice Guideline was developed by the ACOG Committee on Clinical Practice Guidelines–Obstetrics in collaboration with Tiffany A. Moore Simas, MD, MPH, MEd; M. Camille Hoffman, MD, MSc; Emily S. Miller, MD, MPH; and Torri Metz, MD, MS; with consultation from Nancy Byatt, DO, MS, MBA; and Kay Roussos-Ross, MD.

The Society for Maternal-Fetal Medicine endorses this document.

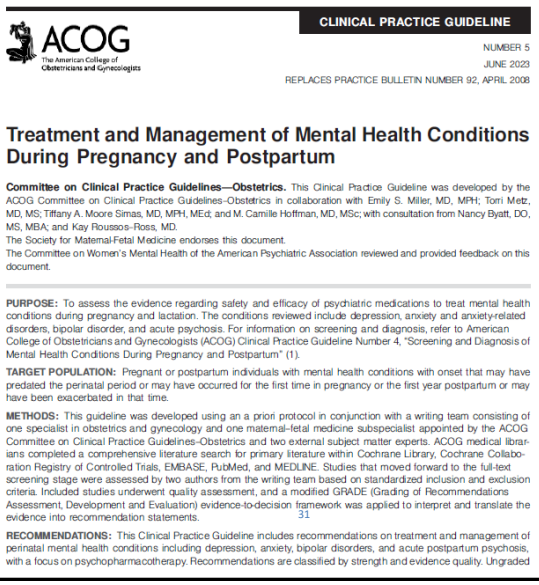
The Committee on Women's Mental Health of the American Psychiatric Association reviewed and provided feedback on this document.

PURPOSE: To review evidence on the current understanding of mental health conditions in pregnancy and postpartum, with a focus on mood and anxiety disorders, and to outline guidelines for screening and diagnosis that are consistent with best available scientific evidence. The conditions or symptoms reviewed include depression, anxiety and anxiety-related disorders, bipolar disorder, suicidality, and postpartum psychosis. For information on psychopharmacologic treatment and management, refer to American College of Obstetricians and Gynecologists (ACOG) Clinical Practice Guideline Number 5, "Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum" (1).

TARGET POPULATION: Pregnant or postpartum individuals with mental health conditions. Onset of these conditions may have predated the perinatal period or may have occurred for the first time in pregnancy or the first year postpartum or may have been exacerbated in that time.

METHODS: This guideline was developed using an a priori protocol in conjunction with a writing team consisting of one specialist in obstetrics and gynecology and one maternal-fetal medicine subspecialist appointed by the ACOG Committee on Clinical Practice Guidelines–Obstetrics and two external subject matter experts. ACOG medical librarians completed a comprehensive literature search for primary literature within Cochrane Library, Cochrane Collaboration Registry of Controlled Trials, EMBASE, PubMed, and MEDLINE. Studies that moved forward to the full-text screening stage were assessed by two authors from the writing team based on standardized inclusion and exclusion criteria. Included studies underwent quality assessment, and a modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) evidence-to-decision framework was applied to interpret and translate the evidence into recommendation statements.

RECOMMENDATIONS: This Clinical Practice Guideline includes recommendations on the screening and diagnosis of perinatal mental health conditions including depression, anxiety, bipolar disorder, acute postpartum psychosis, and the symptom of suicidality. Recommendations are classified by strength and evidence quality. Ungraded Good Practice Points are included to provide guidance when a formal recommendation could not be made because of inadequate or nonexistent evidence.



ACOG
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CLINICAL PRACTICE GUIDELINE

NUMBER 5
JUNE 2023
REPLACES PRACTICE BULLETIN NUMBER 92, APRIL 2008

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The Committee on Women's Mental Health of the American Psychiatric Association reviewed and provided feedback on this document.

PURPOSE: To assess the evidence regarding safety and efficacy of psychiatric medications to treat mental health conditions during pregnancy and lactation. The conditions reviewed include depression, anxiety and anxiety-related disorders, bipolar disorder, and acute psychosis. For information on screening and diagnosis, refer to American College of Obstetricians and Gynecologists (ACOG) Clinical Practice Guideline Number 4, "Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum" (1).

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RECOMMENDATIONS: This Clinical Practice Guideline includes recommendations on treatment and management of perinatal mental health conditions including depression, anxiety, bipolar disorders, and acute postpartum psychosis, with a focus on psychopharmacotherapy. Recommendations are classified by strength and evidence quality. Ungraded

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Perinatal Mood Disorders

- Can occur at any time in pregnancy and up to 1 year postpartum
- ACOG recommends screening for perinatal mood disorders at least once during the perinatal period
  - Ideally screen once in each trimester and again in postpartum

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Perinatal Depression Screening

- Edinburgh Postnatal Depression Scale
  - Self administered
  - 100% sensitivity and 95.5% specificity
  - Can be filled out while women are waiting in the exam room
  - Has 10 screening questions
  - May be used at both pediatric visits as well as perinatal and postpartum visits

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EPDS

I have felt happy:
- ☐ Yes, all the time
- ☒ Yes, most of the time — This would mean: "I have felt happy most of the time" during the past week.
- ☐ No, not very often — Please complete the other questions in the same way.
- ☐ No, not at all

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

Administered/Reviewed by _____ Date _____

[1]Source: Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786 .

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Diagnosis of Major Depressive Disorder

DSM V Diagnostic Criteria (5 symptoms for 2-week period)

- Depressed mood or anhedonia *
- - Changes in **sleep**
- - Loss of **interest**/pleasure
- - **Guilt**/worthlessness
- - Fatigue/loss of **energy**
- - Decreased focus or **concentration**
- – Changes in **appetite** or weight
- – Changes in activity (**psychomotor**)
- – Thoughts of death/**suicide**

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Treatment Options for Depression in Pregnancy

- Psychotherapy
  - Cognitive behavioral therapy (CBT)
  - Interpersonal therapy
- Psychotropic Medication
  - SSRI
  - Zuranolone (postpartum only)
- Alternative Medicine
  - DHA, Omega-3, Primrose oil, Light therapy
  - Acupuncture
- Combined Treatments
  - Psychotherapy and Medication, etc.
- ECT

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Remember:

- Prior to beginning an SSRI for the treatment of perinatal or postpartum depression
  - ALWAYS screen for bipolar disorder
    - If you begin an unopposed antidepressant in a patient with bipolar disorder, you could cause a manic episode with/without associated psychosis

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Mood Disorder Questionnaire (MDQ)

Name: _____ Date: _____

Instructions: Check (✓) the answer that best applies to you. Please answer each question as best you can.

	Yes	No
1. Has there ever been a period of time when you were not your usual self and...		
...you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?	○	○
...you were so irritable that you shouted at people or started fights or arguments?	○	○
...you felt much more self-confident than usual?	○	○
...you got much less sleep than usual and found you didn't really miss it?	○	○
...you were much more talkative or spoke faster than usual?	○	○
...thoughts raced through your head or you couldn't slow your mind down?	○	○
...you were so easily distracted by things around you that you had trouble concentrating or staying on track?	○	○
...you had much more energy than usual?	○	○
...you were much more active or did many more things than usual?	○	○
...you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?	○	○
...you were much more interested in sex than usual?	○	○
...you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?	○	○
...spending money got you or your family in trouble?	○	○
2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time? *Please check 1 response only.*	○	○
3. How much of a problem did any of these cause you — like being able to work; having family, money, or legal troubles; getting into arguments or fights? *Please check 1 response only.* ○ No problem ○ Minor problem ○ Moderate problem ○ Serious problem		
4. Have any of your blood relatives (ie, children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?	○	○
5. Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?	○	○

This questionnaire should be used as a starting point. It is not a substitute for a full medical evaluation. Bipolar disorder is a complex illness, and **an accurate, thorough diagnosis can only be made through a personal evaluation by your doctor.**

Adapted from Hirschfeld R, Williams J, Spitzer RL, et al. Development and validation of a screening instrument for bipolar spectrum disorder: the Mood Disorder Questionnaire. *Am J Psychiatry.* 2000;157:1873-1875.

This instrument is designed for screening purposes only and is not to be used as a diagnostic tool. How to Use The questionnaire takes less than 5 minutes to complete. Patients simply check the yes or no boxes in response to the questions. The last question pertains to the patient's level of functional impairment. The physician, nurse, or medical staff assistant then scores the completed questionnaire.

How to Score Further medical assessment for bipolar disorder is clearly warranted if patient: • Answers Yes to 7 or more of the events in question #1 AND • Answers Yes to question #2 AND • Answers Moderate problem or Serious problem to question #3

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SSRI Dosage

- Fluoxetine 10 mg-40 mg
- Escitalopram 10 mg-20 mg
- Sertraline 50 mg- 150 mg
- Citalopram 10 mg – 40 mg

*treatment of anxiety typically requires higher doses

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ACOG Practice Advisory

- Zuranolone:
  - Depression onset within the third trimester of pregnancy or within 4 weeks postpartum, that is orally administered for 14 days
  - Study showed significantly more improvement in symptoms compared to those in the placebo groups
    - The treatment effect was maintained four weeks after the last dose of zuranolone

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Considerations for zuranolone therapy:

- The daily recommended dose of zuranolone is generally 50 mg. It is taken in the evening with a fatty meal (eg, 400 to 1,000 calories, 25% to 50% fat), for 14 days. Dosage may be reduced to 40 mg if central nervous system (CNS) depressant effects occur. In the case of severe hepatic or moderate to severe renal impairment, dosing should be initiated at 30 mg. Dose adjustments will also be needed if patients are taking medications that are strong CYP3A4 inhibitors and concomitant use with CYP3A4 inducers should be avoided.*
- If an evening dose is missed, take the next dose at the regular time the following evening; do not take extra doses on the same day. Complete 14 days of treatment total.
- Zuranolone can be used alone or as an adjunct to other oral antidepressant therapy like SSRIs and SNRIs.
- Patients should use effective contraception during the 14-day treatment course and for 1-week after the final dose. Zuranolone may cause fetal harm [2]. If pregnancy does occur, there is a registry.**
- Patients should be warned and given precautions about adverse reactions including:
  - Impaired ability to drive or engage in other potentially hazardous activities,
  - CNS depressant effects including somnolence and confusion, and
  - Increased suicidal thoughts and behaviors.
- Patients should not drive or engage in activities requiring complete mental alertness until at least 12 hours after each dose for the duration of the full treatment course. Patients may not be able to accurately assess their own degree of impairment during the treatment cycle.
- Other CNS depressing substances should be avoided (eg, alcohol, benzodiazepines, opioids, tricyclic antidepressants). If unable to avoid, a dose reduction may be necessary.
- The most common side effects include dizziness, fatigue, drowsiness, diarrhea, common cold-like symptoms, and urinary tract infections.
- Zuranolone passes into breast milk, although with a RID lower than that of SSRIs. There are no data on effects on a breastfed infant and limited data on milk production. The patient's clinical need for zuranolone and the developmental and health benefits of breastfeeding should be balanced through a shared decision-making process that considers continuation, pumping and discarding milk through 1-week past treatment completion, and cessation.

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ACOG recommends consideration of zuranolone in the postpartum period (ie, within 12 months postpartum) for depression that **has onset in the third trimester or within 4 weeks postpartum**. The decision to use zuranolone should balance the benefits (eg, significantly improved and rapidly resolved symptoms) with the risks and challenges (eg, potential suicidal thoughts or behavior, sedation that precludes performing some activities of daily living like driving, and lack of efficacy data beyond 42 days)

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Today's Focus: Perimenopausal/Midlife Women

- Midlife women=Menopausal transition (MT)= Perimenopause=Climacteric
- Includes time frame between full reproductive function and menopause (Dell et al. Menopause and Mood. 2000)
  - Time frame typically 4-8 years in length
  - Typically occurs in 45–55-year-old women
    - Average age 47 years old

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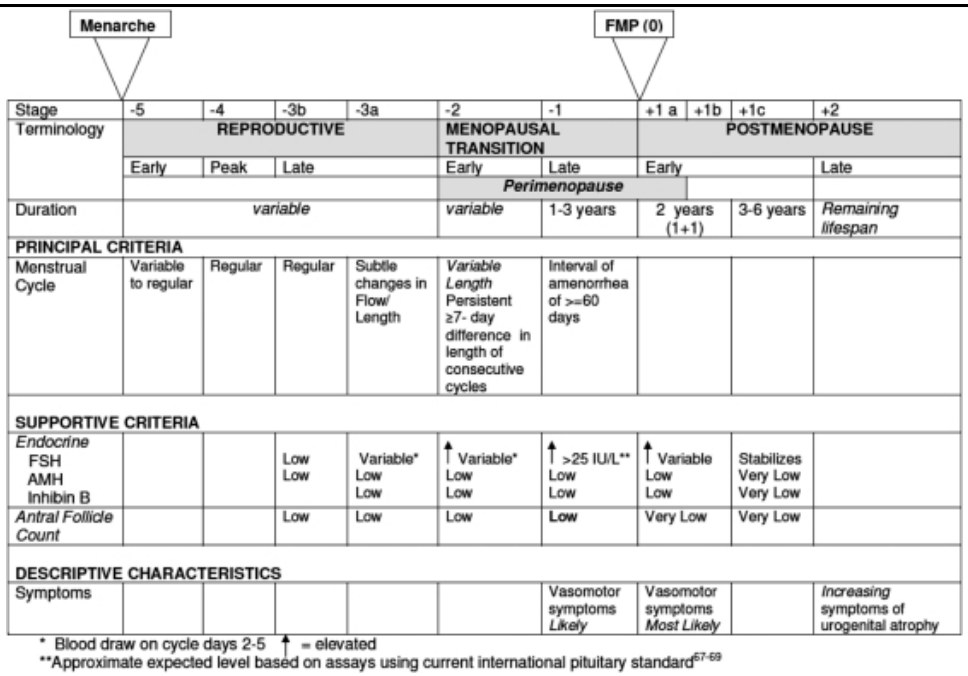

Stage	-5	-4	-3b	-3a	-2	-1	+1 a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	*variable*				*variable*	1-3 years	2 years (1+1)		3-6 years	*Remaining lifespan*
PRINCIPAL CRITERIA										
Menstrual Cycle	Variable to regular	Regular	Regular	Subtle changes in Flow/ Length	*Variable Length* Persistent ≥7- day difference in length of consecutive cycles	Interval of amenorrhea of >=60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable* Low Low	↑ Variable* Low Low	↑ >25 IU/L** Low Low	↑ Variable Low Low		Stabilizes Very Low Very Low	
Antral Follicle Count			Low	Low	Low	Low	Very Low		Very Low	
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms *Likely*	Vasomotor symptoms *Most Likely*			*Increasing* symptoms of urogenital atrophy

* Blood draw on cycle days 2-5 ↑ = elevated
**Approximate expected level based on assays using current international pituitary standard[67-69]

Executive Summary of the Stages of Reproductive Aging Workshop + 10: Addressing the Unfinished Agenda of Staging Reproductive Aging. Harlow et al. J Clin Endocrinol Metab. 2012

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Epidemiology

- Mood disorders are twice as common in women as in men
  - This distinction occurs in adolescence and equalizes after menopause
- 15-50% of women experience depressive symptoms during the menopausal transition (MT) (Toffol et al. Menopause. 2015)
  - 15-30% meet criteria for depressive disorders
  - There is a 2x increased risk of a first episode of depression for women in MT
  - SWAN study showed women 2-4x more likely to experience MDD if they were perimenopausal or early postmenopausal (Bromberger et al. Psychol Med. 2011)
  - Seattle midlife Women's Health Study found a doubling of the rate of depressive symptoms in late MT (Woods et al. Menopause. 2008)

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Risk Factors for Mood Disorders in Midlife

- Prior depressive episode *
  - Especially if related to prior reproductive event (Soares. Menopause. 2014)
  - Majority of women who have perimenopausal depression have had a prior episode of depression
- Significant vasomotor symptoms
- Sleep disturbance
- Psychosocial stressors
  - Financial stress
  - Changes in work-life
  - Divorce, Children leaving for college, Caring for elderly parents
- Health related issues

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Pathophysiology of Mood Disorders in Midlife

- Domino theory
  - Vasomotor symptoms trigger depressed mood due to disruption in sleep and functional impairment (Gordon et al. Curr Psych Rep. 2014)
    - Hot flushes provoke sleep disturbance which affects mood
- Empty Nest Syndrome
  - Women become more aware of their loss of fertility and their maternal role
  - Psychosocial stressors: Changes in family dynamic, changes in work life, changes in financial security occur at the same time as MT and may cause depressive symptoms

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Diagnosis of Major Depressive Disorder

DSM V Diagnostic Criteria (5 symptoms for 2-week period)

- Depressed mood or anhedonia *
- - Changes in **sleep**
- - Loss of **interest**/pleasure
- - **Guilt**/worthlessness
- - Fatigue/loss of **energy**
- - Decreased focus or **concentration**
- – Changes in **appetite** or weight
- – Changes in activity (**psychomotor**)
- – Thoughts of death/**suicide**

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Patient Health Questionnaire (PHQ-9)

Patient Name: _____ **Date:** _____

	Not at all	Several days	More than half the days	Nearly every day
1. Over the *last 2 weeks*, how often have you been bothered by any of the following problems?				
a. Little interest or pleasure in doing things	☐	☐	☐	☐
b. Feeling down, depressed, or hopeless	☐	☐	☐	☐
c. Trouble falling/staying asleep, sleeping too much	☐	☐	☐	☐
d. Feeling tired or having little energy	☐	☐	☐	☐
e. Poor appetite or overeating	☐	☐	☐	☐
f. Feeling bad about yourself or that you are a failure or have let yourself or your family down	☐	☐	☐	☐
g. Trouble concentrating on things, such as reading the newspaper or watching television.	☐	☐	☐	☐
h. Moving or speaking so slowly that other people could have noticed. Or the opposite; being so fidgety or restless that you have been moving around a lot more than usual.	☐	☐	☐	☐
i. Thoughts that you would be better off dead or of hurting yourself in some way.	☐	☐	☐	☐
2. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
	☐	☐	☐	☐

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Treatment Options for Women in MT

- Psychotherapy
  - Cognitive-Behavioral Therapy
- Pharmacologic
  - Antidepressants
    - SNRI
    - SSRI
  - Estrogen
    - Oral
    - Transdermal

Don't forget importance of treating sleep disturbances

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Therapy

- Cognitive-Behavioral Therapy (CBT)
  - CBT offers improvement in hot flushes and night sweats by changing the cognitive appraisal of symptoms (Norton et al. Menopause. 2014)
  - Telephone guided self help CBT improved symptoms of hot flushes and night sweats (Stefanopoulou et al. Maturitas. 2014)
  - Telephone delivered CBT improved sleep-in midlife women with insomnia related to vasomotor symptoms (McCurry et al. JAMA Intern Med 2016)
    - Insomnia associated with increased depression, impaired daytime function

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Complementary Medicine

- Acupuncture
  - No clear evidence of improvement of vasomotor symptoms or mood in perimenopausal women (Cho et al. Menopause. 2009, Dodin et al. Cochrane Data Base Syst Rev. 2013)

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Antidepressants

- Antidepressants
  - SNRI
    - Duloxetine (20-60 mg)
    - Venlafaxine (37.5-225 mg)
  - SSRI
    - Fluoxetine (10-40 mg)
    - Sertraline (50-150 mg)
    - Citalopram (20-40 mg)
    - Escitalopram (10-20 mg)
    - Paroxetine (20-50 mg)

- Side Effects (15-20% of patients)
  - GI symptoms (nausea)
  - Sexual dysfunction (20%)
  - Headache
  - Sleep disturbance

- Should see improvement in symptoms within 1 month

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Antidepressants: SNRI vs SSRI

- In a pooled analysis, SNRIs showed higher remission rates than SSRIs (Entsuah et al. J Clin Psychiatry 2001)
- Good evidence of improvement in symptoms with citalopram, escitalopram, paroxetine, venlafaxine as monotherapy
- Good evidence for using citalopram and mirtazapine as adjunct to estrogen when estrogen alone is insufficient in aiding mood (Joffe et al. J Womens Health Gend Based Med. 2001, Soares et al. J Clin Psychiatry. 2003)
- If a woman has had success in the past with a certain antidepressant should start with that antidepressant as 1st line regardless of class
- If a woman is taking tamoxifen should use SNRI instead of SSRI due to concern about interference with metabolism of tamoxifen with SSRI (Stubbs et al. J Okla State Med Assoc. 2017)
  - CYP2D6 inhibitors- paroxetine, fluoxetine

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Role of Estrogen in Treatment of Mood Disorders in Perimenopausal Women

- Estrogen as treatment
  - Perimenopausal women with MDD treated with estradiol monotherapy have improvement in mood similar to that with antidepressants
  - Transdermal estradiol (50-100 microgram/day) resulted in 60-75% of subjects noting partial or total remission in depressive episodes compared to 20-30% of subjects receiving placebo (Soares et al. Arch Gen Psychiatry. 2001, Schmidt et al. Am J Obstet Gynecol. 2000)
  - Postmenopausal women do not have the same improvement in depressive symptoms with estradiol monotherapy
  - Data shows estradiol may be used as augmentation for women with inadequate response to antidepressants alone
  - Estrogen treatment should show improvement within the 1st month of use

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Treatment Strategies

- How to decide which treatment
  - Mood symptoms and vasomotor symptoms frequently coincide
    - Primary mood symptoms- SNRI, SSRI
    - Primary vasomotor symptoms-Estrogen
      - Oral vs Transdermal formulations
      - If uterus present must still use progesterone
    - Both symptoms equally bothersome- consider dual therapy with antidepressant and estrogen
  - Don't forget to address sleep disturbances

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Other Considerations

- Women in menopause transition may still ovulate
  - Menopausal doses of estrogen and progesterone may not suppress ovulation
    - Irregular bleeding may occur
  - Consider levonorgestrel IUD plus estrogen
  - Consider estrogen-progestin formulations with sufficient dose of progestin to suppress ovulation
    - EE 5 mcg/NETA 1mg
    - E2 1 mg/NETA 0.5mg

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Conclusions

- Mood disorders occur within the reproductive age years
- Many times, they are chronic and recurrent
- Hormone fluctuations are thought to play a role
- Many options for treatment are available

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