



Adult Depression - Clinical Practice Guideline

05/2018

Diagnosis and Screening

Diagnostic criteria

- Please refer to Attachment A

Screening

- The United States Preventative Services Task Force (USPSTF) recommends screening for depression in the general adult population, including pregnant and postpartum women. Screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up.

USPSTF, 2016

Treatment Plan

Acute Phase Treatment:

The choice of initial treatment modality for patients with major depression include depression focused psychotherapies and pharmacotherapy. Patients should be provided with information on the various treatment options including the strengths and limitations of each.

Psychotherapy avoids potential side effects, safety issues and drug interactions of medications but requires regular attendance (generally weekly), availability of reliable transportation and availability of therapists to see patients within a reasonable amount of time (within several weeks). Psychotherapy may be particularly helpful for patients with significant psychosocial stressors and patients with more chronic, severe depression.

Pharmacotherapy may be more convenient for patients with transportation difficulties or limitations in therapy availability. However, pharmacotherapy requires good adherence to be effective and may cause side effects.

Severity of the current episode is another consideration when discussing treatment modalities with your patient. For mild or moderate depression, pharmacotherapy *or* psychotherapy monotherapy is appropriate. However, for severe depression a combination of psychotherapy and pharmacotherapy is recommended. Psychotherapy should not be the only modality in severe depression. On the PHQ-9, a severity of severe would correspond to a score of ≥ 20 .

Severity of Depression per PHQ-9	Pharmacotherapy Alone	Psychotherapy Alone	Combination of Pharmacotherapy and Psychotherapy
Mild to Moderate	Yes, antidepressant	Yes	Optional
Severe without Psychotic Features	Yes, antidepressant	No	Yes
Severe with Psychotic Features	Yes, antidepressant + antipsychotic	No	Yes

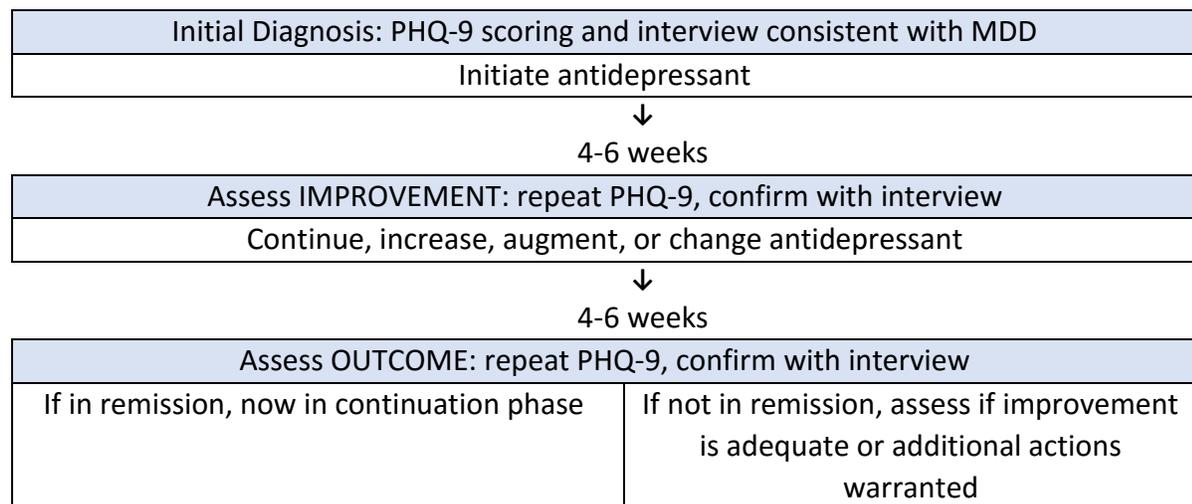
Adapted from American Psychiatric Association (APA) Treatment Guidelines (2010)

Psychotherapy Options

For patients with mild depression, exercise alone is a reasonable initial intervention for a few weeks. If there is no significant improvement, psychotherapy or an antidepressant should be recommended.

There is no differences in depression outcomes, between different therapy theories and approaches; differences in outcome are shown to be related to the strength of the therapeutic alliance.

Improvement from antidepressants can be seen as early as 1-2 weeks but allow for 4-6 weeks before assessing improvement. Patients continue to accrue benefit for an additional 4-6 weeks so allow 8-12 weeks before concluding on the outcome of an antidepressant trial. The following is a visual summary of a typical antidepressant trial:



IMPROVEMENT after 4-6 weeks (assuming adequately dosed and adherent) using the PHQ-9

PHQ-9 score drop from baseline	Improvement	Antidepressant Plan	Psychotherapy Plan*
≥ 5 points	Adequate	Continue current dose	No change
2-4 points	Probably Inadequate	Consider ↑ Dose vs Augment* OR Switch if not tolerating	Consider adding antidepressant if not taking already
1 point or increase	Inadequate	↑ Dose vs. Augment** OR Switch if not tolerating	Strongly consider taking antidepressant if not already taking. Contact therapist re: PHQ-9 score
* Reasonable time to improvement may vary depending on the type of psychotherapy **Augment is defined as adding an additional agent to the regimen			

Research suggests that psychotherapy and pharmacology treatment interventions have a 20-30% placebo effect. The expectation of benefit is therefore an important component, and should be maximized.

Potential reasons for inadequate improvement

- Inaccurate diagnosis
- Nonadherence to treatment
- Unaddressed co-occurring medical, psychiatric, or substance use disorders
- Inadequate dose of medication or frequency of therapy
- Inadequate duration of treatment
- Pharmacokinetic/pharmacodynamic factors affecting medication action
- Complicating psychosocial or psychological factors

Factors favoring augmentation vs. switch of pharmacology

AUGMENT	<ul style="list-style-type: none"> ○ Partial response on target dose ○ Minimal side effects ○ Patient okay with two medications
SWITCH	<ul style="list-style-type: none"> ○ No response on target dose ○ Intolerable side effects ○ Patient hesitant about two medications
AUGMENTATION OPTIONS	Another Antidepressant with different mechanism of action <ul style="list-style-type: none"> ○ SSRI + Bupropion ○ SSRI or SNRI + Mirtazapine

	<p>Non Antidepressant augmentation</p> <ul style="list-style-type: none"> ○ Buspirone (BusPar) ○ Second Generation Antipsychotics <ul style="list-style-type: none"> ○ Aripiprazole (Abilify)* ○ Quetiapine (Seroquel)* ○ Lithium ○ Thyroid Hormone (Triiodothyronine) <p>* FDA approved options</p>
SWITCH OPTIONS	<p>If the initial antidepressant was a SSRI, there is no compelling evidence that would favor changing to a different SSRI, versus switching to a different class of antidepressant. Important to consider if there is a co-morbid anxiety disorder since serotonergic antidepressants are more likely to be effective for co-morbid anxiety and depression.</p>

OUTCOME after 8-12 weeks (assuming adequately dosed and adherent) using the PHQ-9

Patient Condition	PHQ-9	Antidepressant Management
Remission	Total PHQ-9 score ≤ 5	At GOAL! Continue AD and/or PT
Response	>50% drop from baseline, but not remission	Continue AD vs Augment*
Partial Response	25-49% drop from baseline	Consider \uparrow dose vs Augment*
No Response	<25% drop from baseline	Switch*

The goal of treatment is remission. Remission is defined as the absence or near absence of symptoms for at least 3 weeks. On the PHQ-9, this would correspond to a score of < 5 and a rating of “not difficult at all” on the function question.

*For patients with significant psychiatric and or medical co-morbidity, or ongoing severe psychosocial stressors, complete remission may take longer or be difficult to achieve.

Treatment Monitoring

The baseline PHQ-9 score or < 10 on the PHQ-9 may be reasonable goals of treatment. The decision to escalate treatment intensity in such settings is one made between provider and patient in alignment with goals defined by the patient. During active treatment, the frequency recommendation of PHQ-9 administration is monthly.

Continuation Phase

Patients who have recovered from an acute major depressive episode should continue pharmacotherapy of the same dose and frequency for an additional 4-9 months to prevent relapse.

At the end of the continuation phase, patients should be considered for proceeding into the maintenance phase versus discontinuation of treatment. Factors in favor of proceeding to the maintenance phase include:

- Persistence of subthreshold depressive symptoms
- History of ≥ 3 episodes of major depressive disorder
- Greater severity of initial and any subsequent episodes
- Earlier age at onset
- Presence of a co-occurring psychiatric condition
- Presence of a chronic general medical disorder
- Family history of psychiatric illness, particularly mood disorder
- Ongoing psychosocial stressors or impairment
- Negative cognitive style
- Persistent sleep disturbances

Maintenance Phase

Patients proceeding to the maintenance phase are generally continued on the same pharmacotherapy and at the same dose as in the acute and continuation phases. If there are side effects at this dose, attempts should be made to at least remain at the lowest known therapeutic dose of the medication.

Patients in psychotherapy proceeding to the maintenance phase may reduce the frequency of therapy from approximately once weekly to once monthly (depending on the type of psychotherapy).

Discontinuation of Treatment

Patients proceeding to discontinuation of pharmacotherapy after the continuation phase should be monitored closely after treatment discontinuation as the highest risk of relapse is in the first two months. Early signs of relapse should be reviewed with the patient and if possible, with a family member. A plan should be developed and agreed upon in case of depressive relapse.

Discontinuation of pharmacotherapy should be done over several weeks or longer depending on the dose of the medication. If that patient is on multiple medications for depression, they should be tapered one at a time.

Medication Management

The effectiveness of antidepressants is comparable between and within classes. Therefore, consideration between antidepressants is largely determined by patient preference, cost, safety, side effect profile, potential drug interactions, co-occurring psychiatric or general medical conditions and history of previous response to an antidepressant. Based on these considerations, the following antidepressants and classes of antidepressants are optimal initial options for most patients: Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), Bupropion, and Mirtazapine.

In addition to the usual information on when and how often to take the medication and common side effects, it is important to review the following with patients:

- The medication will need to be taken for several weeks before beneficial effects may be noticed.
- Antidepressants need to be taken even if they are feeling better and not to “double up” on days they are feeling worse. In other words, they are not “as needed” medications

Dosing and properties of preferred initial first-line antidepressants:

SSRI's	Starting Dose (mg)	Therapeutic Dose Range (Max dose)	P450 Enzyme Inhibition	Notes	Side Effects
Fluoxetine (Prozac)	20 daily	20-40 daily (max 60)	Strong 2D6 Mod 1A2	long half-life, slightly activating Lowest risk of discontinuation syndrome among SSRI's	<p>Common: initial activation, nausea, diarrhea and headaches. (if anxious, start with ½ starting dose x 1-2 weeks)</p> <p>Can also cause decreased libido, erectile dysfunction, insomnia, akathisia, increased risk of falls.</p> <p>Increase GI bleed risk with NSAIDs</p>
Paroxetine (Paxil)	20 bedtime	20-40 bedtime (max 60)	Strong 2D6	Weight gain, sedating, greatest risk of discontinuation syndrome among SSRI's	
Citalopram (Celexa)	20 daily	20-40 daily (max 40)	--	No drug interactions	
Escitalopram (Lexapro)	10 daily	10-20 daily (max 20)	Mild 2D6	S-enantiomer of citalopram	

Sertraline (Zoloft)	50 daily	50-200 daily (max 200)	Mild 2D6	Take with food	
SNRI's	Starting Dose (mg)	Therapeutic Dose Range (Max dose)	P450 Enzyme Inhibition	Notes	Side Effects
Venlafaxine ER (Effexor XR)	37.5 daily	75-150 daily (max 375)	--	Discontinuation syndrome risk similar to paroxetine	Same as SSRI + dry mouth, activation, constipation, tachycardia and elevated blood pressure, especially at doses > 150 daily
Duloxetine (Cymbalta)	30 daily	60 daily (max 120)	Mod 2D6	Also approved for fibromyalgia, diabetic peripheral neuropathy	Same as SSRI + dry mouth, activation, constipation, tachycardia and elevated blood pressure, especially at doses > 60 daily

Dopamine Reuptake Inhibitors	Starting Dose (mg)	Therapeutic Dose Range (Max dose)	P450 Enzyme Inhibition	Notes	Side Effects
Bupropion, SR, XL (Wellbutrin SR, ER)	150 morning	SR: 150 morning and midday (max 400) XL/ER: 300 morning (max 450)	Strong 2D6	Avoid with history of seizures or eating disorder No decrease in libido or erectile dysfunction.	Activating, constipation, dry mouth, irritability, insomnia, headache
Nonadrenergic Antagonist	Starting Dose (mg)	Therapeutic Dose Range (Max dose)	P450 Enzyme Inhibition	Notes	Side Effects
Mirtazapine (Remeron)	15 bedtime	15-30 bedtime (max 45)	--	No decrease in libido or erectile dysfunction. Monitor cholesterol	Sedation, weight gain, dry mouth

Adapted from APA treatment Guidelines (2010)

Note: Some antidepressants can be started at the target dose without titration while other antidepressants are titrated to the target dose over 1-2 weeks. This will depend on the development of side effects and co-occurring medical or psychiatric conditions, especially very anxious patients. Also, older patients and those with a decreased ability to metabolize or clear antidepressants should be started on a lower initial dose and titrated to 50% of the usual therapeutic dose.

When to Refer to a Specialist

- PCPs and other practitioners are responsible for identifying, diagnosing, and treating patients' behavioral health conditions within their scope of practice.
- Patients presenting with complex or mixed psychiatric symptomatology that makes the diagnosis uncertain must be referred to a licensed behavioral health practitioner for assessment and diagnosis.
- Certain behavioral health conditions, when combined with functional impairments and/or multiple psychiatric issues, are generally beyond the PCP's scope of practice and require a referral to a Behavioral Health practitioner for evaluation, diagnosis, and treatment.

Lifestyle Management and Member Education

- Engage patients in conversations regarding mental health by screening for depression on a routine basis
- Be patient and continue to show care/concern during visits. Patients are listening. As the relationship strengthens, trust builds, and adherence often increases.
- Place signs in waiting/exam rooms inviting patients to ask about depression
- Encourage patients to have a well-balanced diet, live a healthy lifestyle, and stay active.
- Recommend that the patients seek support from family, friends, or support groups.
- Encourage patients to try a variety of coping methods such as: meditation, relaxation, creative activities, or exercising.

References and Resources:

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Attachment A:

Diagnostic Criteria

Major Depressive Disorder

1. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly attributable to another medical condition.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (*Note:* In children and adolescents, can be irritable mood.)
 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation.)
 3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (*Note:* In children, consider failure to make expected weight gain.)
 4. Insomnia or hypersomnia nearly every day.
 5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
 6. Fatigue or loss of energy nearly every day.
 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
 9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
2. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
 3. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Note: Criteria A-C represent a major depressive episode.

Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence

of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the context of loss.

4. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic episode or a hypomanic episode.

Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

Specify:

With anxious distress

With mixed features

With melancholic features

With atypical features

With mood-congruent psychotic features

With mood-incongruent psychotic features

With catatonia.

With peripartum onset

With seasonal pattern (recurrent episode only)

Persistent Depressive Disorder (Dysthymia)

1. Depressed mood for most of the day, for more days than not, as indicated by either subjective account or observation by others, for at least 2 years.

Note: In children and adolescents, mood can be irritable and duration must be at least 1 year.

2. Presence, while depressed, of two (or more) of the following:
 1. Poor appetite or overeating.
 2. Insomnia or hypersomnia.
 3. Low energy or fatigue.
 4. Low self-esteem.
 5. Poor concentration or difficulty making decisions.
 6. Feelings of hopelessness.
3. During the 2-year period (1 year for children or adolescents) of the disturbance, the individual has never been without the symptoms in Criteria A and B for more than 2 months at a time.
4. Criteria for a major depressive disorder may be continuously present for 2 years.

5. There has never been a manic episode or a hypomanic episode, and criteria have never been met for cyclothymic disorder.
6. The disturbance is not better explained by a persistent schizoaffective disorder, schizophrenia, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder.
7. The symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hypothyroidism).
8. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Note: Because the criteria for a major depressive episode include four symptoms that are absent from the symptom list for persistent depressive disorder (dysthymia), a very limited number of individuals will have depressive symptoms that have persisted longer than 2 years but will not meet criteria for persistent depressive disorder. If full criteria for a major depressive episode have been met at some point during the current episode of illness, they should be given a diagnosis of major depressive disorder. Otherwise, a diagnosis of other specified depressive disorder or unspecified depressive disorder is warranted.

Specify if:

With anxious distress

With mixed features

With melancholic features

With atypical features

With mood-congruent psychotic features with mood-incongruent psychotic features with peripartum onset

Specify if:

In partial remission

In full remission *Specify if:*

Early onset: If onset is before age 21 years. Late onset: If onset is at age 21 years or older.

Specify if (for most recent 2 years of persistent depressive disorder):

With pure dysthymic syndrome: Full criteria for a major depressive episode have not been met in at

least the preceding 2 years.

With persistent major depressive episode: Full criteria for a major depressive episode have been met throughout the preceding 2-year period.

With intermittent major depressive episodes, with current episode: Full criteria for a major depressive episode are currently met, but there have been periods of at least 8 weeks in at least the preceding 2 years with symptoms below the threshold for a full major depressive episode.

With intermittent major depressive episodes, without current episode: Full criteria for a major depressive episode are not currently met, but there has been one or more major depressive episodes in at least the preceding 2 years.

Specify current severity:

Mild

Moderate

Severe

Source: Diagnostic and Statistical Manual of Mental Disorders: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition