



Depression Management Adult, Ambulatory Clinical Practice Guideline

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Guideline Contact for Content/Document Changes:

knowledge.map@hitchcock.org

Guideline Authors:

This guideline is adopted from the University of Wisconsin “Diagnosing and Treating Depression Adult Ambulatory Clinical Practice Guideline”¹ which is a synthesis of guidelines from the [Institute for Clinical Systems Improvement \(ICSI\)](#)² and the [American Psychiatric Association \(APA\)](#).³

D-H Review and Adoption Committee:

Behavioral Health-Primary Care

Integration Team:

Mark McGovern, PhD (Lebanon)
Jennifer Raymond (Lebanon)
Cara Baskin, MPH (Lebanon)

Primary Care:

James Stahl, MD, MPH (Lebanon)
Jonathan Thyng, MD (Nashua)
Andrew Tremblay, MD (Keene)
Timothy Burdick, MD (Manchester)
Virginia Alvord, MD (Lebanon)
Pushkala Muralitharan, MD (Concord)

Psychiatry:

Matthew Duncan, MD (Lebanon)
William Torrey, MD (Lebanon)
Joanne Wagner, MSR (Lebanon)

Approval Body: D-H Knowledge Map™

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EXECUTIVE SUMMARY:

1. Identify Patients

- Physical complaints are extremely common in depression and are often the primary manifestation of the illness. It is important to recognize somatic manifestations of depression, as well as biological, psychological and environmental risk factors.
- Screening for depression is recommended by the US Preventive Services Task Force. Initial screening should be completed using the PHQ-2 at new patient visits, annual preventive visits, and at any visit if not done in previous 90 days (D-H Expert Opinion). A PHQ-2 score of ≥ 3 triggers a full PHQ-9.
- A PHQ-9 score of 10 points or greater indicates the need for clinical evaluation and documentation of a follow-up plan.

2. Establish Diagnosis

- Determine that DSM-5 criteria have been met, other psychiatric or medical conditions have been identified, and that patient functioning has been assessed.
- Differential diagnosis of depression includes certain medical conditions, medication side effects, and other psychiatric conditions or co-morbidities.

3. Initiate Treatment

- The use of psychotherapy, pharmacotherapy, or both should be based on depression severity, comorbid conditions, insurance coverage and patient preferences.
- Selection of a particular medication is based on coexisting conditions (appendix 5), side effect profile (appendix 6), concurrent medications and cost issues.
- All patients with depression in primary care should be enrolled in the Collaborative Care Model (CoCM), in which a care manager (supervised by a psychiatrist) proactively tracks patient symptoms and promotes adherence to the treatment plan.

4. Follow-up Care and Treat to Target

- The goal of treatment is to resolve all signs and symptoms of depression (as assessed by the PHQ-9) and to restore psychological and occupational functioning. Contact (telephone or in-person, by clinician and/or care manager) should occur 1 week after diagnosis and initiation of treatment, and then every 2-4 weeks until there is remission (PHQ $<$ 5) or response (defined as a 50% or greater reduction in symptoms as measured by the PHQ-9).
- Side effects can often be managed by a gradual titration up to the full dose. Sedation or restlessness and sexual side effects can persist, and may require dose or medication adjustment. Bupropion can help lethargy, low motivation or trouble concentrating, while mirtazapine can help insomnia or lack of appetite and neither has the sexual side effects common with SSRIs/SNRIs.
- If the patient does not demonstrate a response to pharmacotherapy (alone or in combination with psychotherapy) within 6 weeks of initiation (4 weeks in severely ill), or responds only partially by 12 weeks, other treatment options should be considered using a stepped care approach.
- Continue pharmacotherapy for 4-9 months following remission of symptoms. Continue maintenance medication indefinitely after a third episode of depression, or after a second episode in the setting of severe or persistent symptoms, strong family history, or significant ongoing stressors. Prior to discontinuation and tapering of treatment, patients should be informed of the potential for relapse and a plan should be established to seek treatment if symptoms reoccur.

5. Referrals

- All patients with significant symptoms should be followed by a CoCM case manager.
- Psychiatric consultation is recommended for diagnostic uncertainty, significant psychiatric co-morbidity, or lack of improvement after initial trials of therapy.

D-H GUIDELINE ENDORSEMENT STATEMENT

Scope:

This guideline is intended to support primary care clinicians and behavioral health clinicians embedded in primary care in their efforts to optimally identify, assess, triage and manage adult patients with depression in a Collaborative Care Model in the ambulatory setting and to clarify D-H clinical standards for this work.

This guideline is adapted from the University of Wisconsin's (UW) Diagnosing and Treating Depression Adult Ambulatory Clinical Practice Guideline. The scope of the D-H guideline adoption statement does not include adolescent, pregnant or post-partum depression management outlined in the UW document.

Introduction

Major depression is the leading cause of disability worldwide,⁴ and commonly co-exists with and worsens outcomes in chronic medical conditions. Primary care physicians are in a unique position to provide initial assessment and diagnosis, as well as initial and ongoing management. The Collaborative Care Model (CoCM) is recommended for all patients with depression in primary care, as it has been shown to improve access, reduce fragmentation, lower care costs, increase patient and clinician satisfaction, and improve both behavioral and physical health outcomes (ICSI High quality evidence, strong recommendation).⁵⁻⁸ Essential elements of this model are:⁹

- **Team driven care**- adding the new roles of care manager (RN or behavioral health clinician) and consulting psychiatrist to the primary care team.
- **Population-based care**- in which care teams share a defined group of patients tracked in a registry. Care managers proactively track patient symptoms and promote adherence to the treatment plan.
- **Measurement-based treatment to target** (or stepped care) where each patient's treatment goals and outcomes are clearly identified and routinely measured by validated tools, such as the PHQ-9. If no improvement is seen, treatments are actively modified until the expected result or outcome is achieved.
- **Evidence Based Care**- use of a standardized approach based on the scientific literature.

Further detail on the CoCM can be found in the [D-H Knowledge Map™ "Behavioral Health Integration into Primary Care Model Guideline"](#)

Identify Patients

Depression may be suspected based on either the patient presentation or the results of screening.

Patient Presentation and Risk Factors

Physical complaints are extremely common in depression and are often the primary manifestation of the illness. Somatic manifestations of depression include fatigue, insomnia, anorexia, weight loss, gastrointestinal disturbances, and a variety of pain complaints. Anxiety and agitation are common as secondary symptoms. It is important that clinicians keep in mind that patients who have depression or any mental illness are often stigmatized and may be at risk of not having medical complaints adequately addressed. Common presentations of patients with depression may include:^{5,10,11}

- multiple patient-initiated office visits (more than five per year)
- numerous unexplained symptoms
- work or relationship dysfunction
- sleep disturbance
- multiple worries and distress
- fatigue
- irritable bowel syndrome

Table 1. Risk Factors in Adults^{5,10-12}

Biological	<ul style="list-style-type: none"> • Personal history of depression • Family history of depression (first-degree relative) • Female gender • Medical co-morbidity 	<ul style="list-style-type: none"> • Postpartum period • Peri/postmenopausal period • Chronic medical condition • Men over age 65 are at a higher risk of suicide
Psychological	<ul style="list-style-type: none"> • Negative thinking styles (i.e., “nothing will ever work out”) • Feelings of hopelessness 	
Environmental	<ul style="list-style-type: none"> • Lack of social support • Loss of relationship (i.e., being widowed, death of family member, romantic relationship, friendship) • Substance use 	<ul style="list-style-type: none"> • Major life change (i.e., job change, financial difficulties) • Traumatic event (i.e., accident, physical or sexual abuse)

Risk factors are often intertwined and related, and may vary based upon patient age and experiences. Patients with chronic illnesses such as diabetes, cardiovascular disease, and chronic pain are at a higher risk for depression.⁵ Older adults, especially white men over age 65 years, are at a higher risk of suicide.¹²

Screening

Depression screening in adults and adolescents is recommended by the U.S. Preventive Services Task Force when systems are in place to ensure accurate diagnosis, psychotherapy, and follow-up (USPSTF Grade B).¹³ Although an optimal interval for screening is currently unknown, it is recommended to be done at least annually. Initial screening should be completed using the Patient Health Questionnaire-2 (PHQ-2).¹⁴

Table 2. Patient Health Questionnaire-2 (PHQ-2)

Patient Health Questionnaire-2 (PHQ-2)	
Population	All non-pregnant patients 12 years or older
Number of Questions	2
Administrator	Self-administered by patient
Scoring:	
Max Score	6 points
Positive Threshold (At-Risk)	3 points or greater

A total score of 3 points or greater on the PHQ-2 constitutes a positive screen and need for assessment using the PHQ-9.¹⁴⁻¹⁶ Assessment using the PHQ-9 may also be completed at any time based upon patient presentation or risk and symptomology in adults (ICSI Low quality evidence, strong recommendation).⁵

Table 3. Patient Health Questionnaire-9 (PHQ-9)

Patient Health Questionnaire-9 (PHQ-9)	
Population	All patients 18 years or older
Number of Questions	9
Administrator	Self-administered by patient
Scoring:	
Max Score	27 points
Positive Threshold (Need for clinical evaluation)	10 points or greater
Positive Threshold (Suicide Risk)	Affirmative response to Question 9
Scoring Interpretation:	
None	0-4 points
Mild depressive symptoms; disorder is unlikely	5-9 points
Moderate depressive symptoms; disorder is possible	10-14 points
Moderately severe depressive symptoms; disorder is likely	15-19 points
Severe depressive symptoms; disorder is very likely	20-27 points

Follow-up Plan Documentation

A score of 10 points or greater on the PHQ-9 indicates the need for clinical evaluation and documentation of a follow-up plan.¹⁴⁻¹⁶ This plan should contain one or more of the following:

- Additional evaluation for depression
- Suicide Risk Assessment
- Referral to a practitioner who is qualified to diagnose and treat depression
- Pharmacological interventions
- Other interventions or follow-up for the diagnosis or treatment of depression.

Establish Diagnosis

To diagnose a depressive disorder, the clinician should determine that criteria outlined within the Diagnostic and Statistical Manual of Mood Disorders, Fifth Edition (DSM-5) have been met using a detailed clinical interview (ICSI Low quality evidence, strong recommendation).^{5,10,11} The diagnostic DSM-5 criteria for major depressive disorder are listed below.

DSM-5 Diagnostic Criteria:¹¹

A. 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.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, and hopeless) or observation made by others (e.g., appears tearful).
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.
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.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

D. 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 (not attributable to substance use or a medical condition).

Interview for Key Symptoms

Patients should receive a thorough evaluation in order to establish a diagnosis of major depressive disorder, identify other psychiatric or medical conditions that may require attention, assess functioning, and develop a treatment plan. This evaluation may include:^{5,17}

History of present illness and current symptoms

Psychiatric history including past symptoms of mania, hypomania, or mixed episodes and responses to previous treatments

General medical history

Personal history including information about psychological development and responses to life transitions and major life events

Social, occupational, and family history including mood disorder and suicide

Review of prescribed and over-the-counter medications

Older adults may be less likely to endorse low mood and worthlessness; rather loss of interest and pleasure may be core symptoms of depression. Questions asked during the clinical interview should elaborate on answers provided on the initial assessment (i.e., PHQ-9), and assess for suicidal or homicidal intent, plan, and access to means. Suicidality can be assessed with the Suicide Assessment Five-Step Evaluation and Triage Card ([SAFE-T](#)).

Consider a Differential Diagnosis

Many other psychiatric disorders, physical conditions or medications can cause depressive symptoms. In evaluating patients with symptoms of depression, the primary care practitioner should determine if the depression is a primary process or whether it is a symptom of other medical conditions.

Medical Conditions: Screening for other medical conditions should be based on clinical judgment. Many medical conditions (i.e. hypothyroidism, hyperthyroidism, cancer, coronary artery disease, diabetes mellitus, cerebral vascular accident, chronic pain, HIV, Parkinson's disease, multiple sclerosis) are risk factors for depression.⁵ If a patient presents with prominent symptoms of low energy or hypersomnia, consider an evaluation for sleep apnea.¹⁸ In patients who are at risk for low levels of B12 (i.e., vegetarians, poor diet, heavy alcohol use, or are elderly), B12 measurement may be considered. Repletion of B12 in deficient patients can improve mood and increase the efficacy of antidepressant medications. Consider obtaining a TSH value, especially in women over age 50.¹⁷ Older patients may also be screened for cognitive impairment through clinical assessment or use of a validated tool(s) such as the [mini-cog](#) with the [Montreal Cognitive Assessment](#) (MoCA) as follow-up (see [D-H Knowledge Map™ Cognitive Impairment Adult, Ambulatory Clinical Practice Guideline](#)).

Medications: Some medications may cause depressive symptoms:

Table 4. Alternatives to Drugs Causing Depression

Drug Causing Depression	Potential Alternatives
Clonidine, Methyldopa, Reserpine	Other antihypertensive agent (diuretics, ACE-I, CCB, ARB, etc.)
Lipophilic beta blockers (propranolol)	Use lowest effective dose (atenolol or metoprolol). For heart rate control consider non-dihydropyridine calcium channel blocker.
Corticosteroids	Minimize dose as allowed
Benzodiazepines, sedative hypnotics, alcohol	Minimize use/taper off
Estrogens/Progesterones	Addition of Vitamin B6, use lower progestin
Anti-Parkinson Medications	No alternatives
Anti-convulsants (especially levetiracetam, phenytoin, topiramate, primidone/phenobarbital)	Consider lamotrigine and other alternative anti-epileptic drugs
Interferons (Hep C, MS)	No alternatives
Isotretinoin	No alternatives
Opioids	Minimize/taper off opioids or use NSAIDS

Psychiatric Conditions:

Bipolar disorder is important to recognize, as treatment is different and antidepressants may precipitate mania. Symptoms of mania include: inflated self-esteem or grandiosity, decreased need for sleep, pressured speech, flight of ideas or experience of racing thoughts, distractibility, protracted irritability, increase in goal-directed activity or psychomotor agitation, and involvement in risky activities.

Anxiety disorders commonly co-exist with depression, and can impact treatment approach.

Grief/Bereavement is considered a normal response to a significant loss, and usually resolves without treatment. Depression can follow or co-exist with grief, and should be suspected if there is persistent anhedonia or dysphoria, guilt or low self-esteem.

Substance use disorders can co-exist with and complicate the diagnosis and treatment of depression. Alcohol, depressant drugs, and withdrawal from stimulant drugs can all cause symptoms of depression, and substances can be used by patients to “self-medicate” their depression. Ongoing substance use during depression increases risk of suicide and interferes with adherence to treatment and follow-up. Patients should be advised to stop substance use, monitored for withdrawal, and have their substance use disorder addressed through medication assisted therapy and counseling, as appropriate. ([See KM Unhealthy Alcohol and Drug Use guideline](#)).

Seasonal Affective Disorder may be present if there is a seasonal pattern to recurrent depression.

Postpartum depression needs to be differentiated from “baby blues”, which are milder depressive symptoms that typically peak 3-5 days after delivery and resolve by the 10th postnatal day.

Initiate Treatment

The objectives of treatment are:

Reduction and ultimately resolution (remission) of all signs and symptoms of the depressive syndrome. This may be assessed objectively through administration of the PHQ-9, with remission defined as a PHQ-9 score < 5.

Restoration of psychosocial and occupational function to that of the baseline asymptomatic state.

Reduction of the likelihood of relapse or recurrence.

Clinicians should develop a treatment plan together with patients, using a shared decision making approach where appropriate. The CoCM is recommended for all patients with depression in primary care (ICSI High quality evidence, strong recommendation).⁵⁻⁸

Factors to consider in making treatment recommendations (Table 5) are the severity of symptoms, presence of psychosocial stressors, presence of co-morbid conditions, insurance coverage, pregnancy status, and patient preferences or prior treatment experiences.^{15,17}

Treatment Modalities

Psychotherapy: The following therapies have demonstrated efficacy in treating major depressive disorder.¹⁷

- **Behavioral Activation:** A therapy that encourages behavioral changes using motivational interviewing. Recommend increase in activities such as adding 20 minutes of exercise 3-4 times per week, improving diet, increase social activities, engage in enjoyable activities, stress reduction (mindfulness practice, relaxation) and sleep hygiene.^{10,17}

- **Cognitive-behavioral Therapy (CBT):** A therapy founded on the perspective that irrational beliefs and distorted attitudes towards the self, environment, and future perpetuate depressive affects and compromise

functioning. The goal of CBT is to reduce depressive symptoms by challenging and reversing these beliefs and attitudes and encourage patients to change their maladaptive preconceptions and behaviors.¹⁷

• **Interpersonal Psychotherapy (IPT):** A therapy which focuses on current life changes including loss, role disputes and role transition (i.e., becoming a new mother, divorce, primary caretaker for an elderly family member), social isolation, deficits in social skills, and other interpersonal factors that may interact with the development of depression. The goal of IPT is to intervene by identifying the current trigger for the depressive episode, facilitating mourning in the case of bereavement, promoting recognition of related affects, resolving role disputes, and transitions, and building social skills.¹⁷

Pharmacotherapy:

For essentially all patients, the clinician who provides the medication also provides support, advice, reassurance, instills optimism as well as medication monitoring. This “clinical management” is critical with depressed patients whose pessimism, low motivation, low energy, and sense of social isolation or guilt lead them to give up, not comply with treatment, or to drop out of treatment.

Selection of a particular medication should take into consideration the following:^{5,17}

- Prior positive/negative response to medication (personal or family history)
- Clinician experience with specific antidepressants
- Patient preference
- Other health conditions (i.e., ADHD, smoking cessation) (see Appendix 5)
- Side effect profiles (see Appendix 6)
- Safety in overdose (i.e., 10 days of a tricyclic can be a lethal overdose)
- Concurrent medications that make selected medications more or less risky
- History of first degree relatives’ responses to medication
- Cost and insurance coverage

Drug information on antidepressant therapies is included in Appendix 6.

Many drug interactions occur with antidepressant therapy; many of these occur with medications commonly prescribed in primary care.

Patient education on depression is important for adherence with therapy. For antidepressant medications, adherence with a therapeutic dose is more important than the specific drug selected.

- Take medicine as prescribed.
- Depression medicine must be taken for 2-4 weeks before benefits are noticeable.
- Understand potential medicine side effects. Many side effects go away after 1-2 weeks.
- Continue to take medication even if you are feeling better, your depression is more likely to return if you take medication for less than 6 months.
- Do not stop taking depression medicine without first discussing plan with your clinician. Some antidepressants may have uncomfortable withdrawal symptoms.
- Contact your provider if you have questions about your medicine.
- Be sure to make and keep follow-up appointments. This is important to ensure you’re getting the best treatment to fully resolve your depression.
- Depression medicine is not addictive and will not change your personality. Depression alters brain function and medicine helps restore healthy patterns, so you eat and sleep more normally, think more clearly and have more energy.
- The medicine should help make psychotherapy more effective.
- Alcohol should be avoided as it can worsen depression, anxiety, and insomnia. In addition, alcohol can lessen the effect of antidepressants and some medications can increase the sedative effect of alcohol.

Patients with Substance Abuse and Use of Antidepressants

Detoxifying patients before initiating antidepressant medication therapy is advisable when possible.¹⁹

Antidepressants may be used to treat depressive symptoms following initiation of abstinence if symptoms do not improve over time. It is difficult to identify patients who should begin a regimen of antidepressant medication therapy soon after initiation of abstinence, because depressive symptoms may have been induced by intoxication and/or withdrawal of the substance. A family history of major depressive disorder, a history of major depressive disorder preceding alcohol or other substance abuse, or a history of major depressive disorder during periods of sobriety raises the likelihood that the patient might benefit from antidepressant medication, which may then be started early in treatment. Comparing the temporal pattern of symptoms with the periods of use and abstinence of the substance may help to clarify the patient's diagnosis. Repeated, longitudinal assessments may be necessary to distinguish substance-induced depressive disorder from co-occurring major depressive disorder, particularly because some individuals with substance use disorders reduce their substance consumption once they achieve remission of a co-occurring major depressive disorder. Benzodiazepines and other sedative-hypnotics carry the potential for abuse or dependence and should rarely be prescribed to patients with co-occurring substance use disorders, except as part of a brief detoxification regimen.

Electroconvulsive Therapy (ECT): ECT may be administered unilaterally or bilaterally (using a bitemporal or bifrontal electrode placement). This therapy is typically administered 2-3 times per week for 6-12 treatments or until symptoms have remitted.¹⁷

Light Therapy: Light therapy is an FDA approved treatment for seasonal depression and is covered by most insurance companies.¹⁰

Table 5. Suggested Treatment Modalities Based on Depression Severity or Other Factors

Factors		Treatment Options
Symptom Severity (based on total PHQ-9 scores)	Mild (5-9 pts.)	<ul style="list-style-type: none"> • Psychotherapy and/or Behavioral Activation alone • Pharmacotherapy usually not indicated
	Moderate (10-14 pts.)	<ul style="list-style-type: none"> • Psychotherapy alone (CBT, IPT) • Pharmacotherapy alone
	Moderately severe (15-19 pts.)	<ul style="list-style-type: none"> • Combination therapy (medications and psychotherapy)
	Severe (20-27 pts.)	<ul style="list-style-type: none"> • Pharmacotherapy alone • Pharmacotherapy in combination with psychotherapy (preferred) • Electroconvulsive therapy
Psychosocial Stressors		<ul style="list-style-type: none"> • Psychotherapy and/or Behavioral Activation
Patient is Pregnant		<ul style="list-style-type: none"> • Psychotherapy and/or Behavioral Activation • Discuss risks and benefits of pharmacotherapy
Seasonal episodes		<ul style="list-style-type: none"> • Light therapy

Making a Treatment Plan (see algorithm within Appendix 2)

Clinicians should provide antidepressant medications and/or referral to psychotherapy as treatment for major depression (ICSI Low quality evidence, strong recommendation).⁵ Treatment decisions may be made through a shared-decision making process which considers the patient's willingness to invest time in psychotherapy, the presence of psychosocial stressors, disease severity, and patient preference. Use of a decision aid (e.g. [Option Grid](#)) can facilitate this process. Mild to moderate levels of depression in adults have been treated as effectively with psychotherapy as with pharmacotherapy.⁵ Psychotherapy in combination with antidepressant medication may be needed for severe depression or if any of the following symptoms are present: severe insomnia, severe anxiety, marked anhedonia, or thoughts of suicide.⁵ Medication may also be the preferred method of treatment in

individuals who decline psychotherapy, or who have required medication to treat depression in the past. Medication class may be determined through a discussion with the patient using the medication information and concurrent conditions outlined in Appendix 4 and Appendix 5, respectively. When prescribing medications in adults age 65 years or older, careful consideration should be taken of how the drug metabolism may be affected by physiologic changes, comorbid illnesses, and/or concomitant medications (ICSI Low quality evidence, strong recommendation).⁵ Antidepressants should be initiated in older adults at ½ (or even ¼) of the usual starting doses.¹⁷ It is important to keep in mind renal and hepatic status of a patient when choosing antidepressant doses, as well as to consider drug-drug interactions (including the risk of serotonin syndrome).¹⁷

ECT is most commonly recommended for adults with severe depression accompanied by psychosis, suicidal intent, or refusal to eat (APA Grade I).¹⁷ It may be tried when medications are not tolerated or other forms of therapy haven't proved effective (APA Grade I), by patient preference, or in patients who have had a previously positive response to ECT (APA Grade II).¹⁷ A full psychiatric assessment is recommended before considering this treatment method.^{2,17}

Use of a light box (10,000 lux for 30 minutes every morning) in the dark months of the year (September–March) can be considered as a treatment option, especially in patients who suffer from seasonal depressive episodes (APA Grade III).¹⁷

Special Considerations

Older Adults (65 years or older): are more likely to experience the side effects such as falls, sedation or cognitive impairment (with tricyclics).²⁰ In adults age 65 and older SSRI's and SNRI's may cause hyponatremia. A plasma sodium should be checked at baseline, 2-3 weeks after initiation, and 2-3 weeks after each titration. Patients should be educated about the symptoms of hyponatremia.²¹ Citalopram should not be prescribed at doses higher than 40 mg per day due to a risk of QT prolongation. In patients 60 years and older the maximum dose is 20 mg per day.

Young Adults (18-24): the FDA requires a "black box" warning that antidepressants may sometimes increase suicidal ideation. Patients should be monitored closely during the initial few months of drug therapy or with dose changes. Engage parents as appropriate.

Pregnancy or breast feeding: psychotherapy, exercise, and light therapy are first line treatments for mild to moderate depression, but antidepressants should be used if depression is severe or impairing function. Citalopram, escitalopram, sertraline, and fluoxetine are generally considered safe, and sertraline and escitalopram have the lowest levels in breast milk. Paroxetine has been less commonly used in pregnancy because older data raised concerns regarding cardiac malformations; newer data do not consistently support this link. In general, women who have previously responded well to a particular antidepressant should be treated with the previously effective medication rather than switched to a different medication. The lowest effective dose of the smallest number of medications should be used to achieve remission of symptoms.

Follow-up Care and Treat to Target

Acute phase of treatment (first 6-12 weeks) aims to resolve all signs and symptoms of the current episode of depression and to restore psychological and occupational functioning (a remission).¹⁷ Patient non-adherence is high with depression, and the team must assertively engage the patient in follow-up care and assessments. Proactive follow-up contacts based on the Collaborative Care model can significantly decrease depression severity.⁵⁻⁸ Contact (telephone or in-person, by clinician and/or care manager) should occur 1 week after diagnosis and initiation of treatment, and then every 2-4 weeks until there is remission (PHQ<5) or response (defined as a 50% or greater reduction in symptoms as measured by the PHQ-9). Patients with severe depression or complex social situations may require more frequent contacts and closer observation. All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy or at times of dose changes, either increases or decreases.

Assessing Treatment Response

Treatment response should be assessed using the PHQ-9 within 4-6 weeks of initiation in patients on drug therapy (alone or in combination with psychotherapy) (APA Grade II).¹⁷ Most patients respond partially to medication within 2-3 weeks and full effect is typically seen in 6-8 weeks.¹⁷ Patients receiving psychotherapy alone should be assessed using the PHQ-9 within 6-12 weeks of initiation, depending on the expectation of the given type of therapy.¹⁷ Patients who demonstrate remission or a response should move into the continuation phase.⁵ Treatment response should be assessed using the PHQ-9 within 4-8 weeks following any change in treatment, particularly if the change was due to a lack of response to previous therapy (APA Grade I).¹⁷

Adjusting Treatment if Insufficient Response- Stepped Care Approach

Treatment in the acute phase should not be discontinued prematurely in patients who do not fully respond at the initial assessment (APA Grade I). If the patient does not demonstrate a response to pharmacotherapy (alone or in combination with psychotherapy) within 6 weeks (4 weeks in severely ill) of initiation, or responds only partially by 12 weeks, other treatment options should be considered (APA Grade I) including:¹⁷

- Assess medication adherence
- Continue medication at a corrected dose
- Change medication (APA Grade II)
- Augment with a second medication (not advised until initial trial adequate in time and dosage)
- Refer for professional psychotherapy. Most patients receiving time-limited psychotherapy respond partially by 5-6 weeks and fully by 10-12 weeks.
- Obtain a Behavioral Health consultation

Patients receiving psychotherapy alone who do not respond initially to treatment should consider augmentation with pharmacotherapy, assessing the frequency of sessions and whether the type of therapy or therapeutic alliance is addressing the patient's needs (APA Grade I).¹⁷

Managing Medication Side Effects

Side effects are common with antidepressants but can be managed for most patients. See Appendix 6 for a list of common side effects and alternative options. To minimize GI distress, headache, and agitation associated with starting an SSRI or SNRI, start at half of the target dose for 1 week then increase to the full amount. If the patient complains of side effects, you can recommend cutting the dose in half and titrating even more slowly (e.g., starting with 5 mg of citalopram, increasing to 10, then 15, then 20 mg). Taking at bedtime with a little food will also minimize nausea. If slow titration is not effective in minimizing these side effects, (GI distress, agitation, or headache), you may need to consider using another SSRI, SNRI, bupropion, mirtazapine, duloxetine, or a TCA instead. Mirtazapine is particularly helpful for patients who experience akathisia, or intense restlessness that causes them to pace.²²

While the above side effects usually go away with time, sedation and sexual side effects of SSRIs and SNRIs persist and are dose dependent. For sedation, switching to escitalopram, venlafaxine, or bupropion is often helpful, as these are the least sedating antidepressants. An initial strategy for reducing sexual side effects can be lowering the dose by 25-50% if the depression is well controlled. Alternatively, bupropion can be added to an SSRI to minimize sexual side effects by as much as 80%. A dose of 300 mg a day is recommended— lower doses are not as effective. Bupropion may also be helpful for patients who complain of lethargy, low motivation, tobacco dependence, or poor concentration. A final option is to add buspirone to the SSRI/SNRI. This is the best choice when the patient has comorbid anxiety that might worsen with bupropion. Start with 5 mg BID for 1 week then increase by 10 mg a week to a target dose of 30-60 mg a day. The dose-limiting side effect for most people is dizziness, which can be managed by giving a higher dose at night than in the morning.^{23,24}

The chronic side effects of bupropion are similar to the effects of caffeine: jitteriness, anxiety, sleeplessness, and tremor. Short term side effects include decreased appetite, and nausea. If a person becomes too stimulated with bupropion, you can either lower the dose or change to another medication.¹⁷

Mirtazapine's two persistent side effects are sedation and weight gain. There is little that can be done to minimize these, although the daytime sedation does improve with time; therefore, switching to another medication is warranted if these side effects are problematic.¹⁷

Venlafaxine should be started at 37.5 mg and titrated by this amount every 4-5 days to a target dose of 75-150 mg. A more abrupt titration will almost always cause agitation. It does not become an "SNRI" (add norepinephrine effect to serotonin) until at least 112.5 mg – so if it is being used for this purpose, it is best to increase to a target dose of 150 mg at the start of treatment.¹⁷ Duloxetine has SNRI effects at all doses.

In patients who are sensitive to most medication (prone to side effects/intolerance), duloxetine or escitalopram are often well tolerated when started at the lowest possible dose (2.5 mg for escitalopram and 20 mg for duloxetine) and titrated very slowly.

Continuation phase (4 - 9 months beyond response/remission) is intended to prevent relapse by continuing the treatment of antidepressants, psychotherapy, or other therapies (i.e., ECT). Given the significant risk of relapse during the continuation phase, it is essential to assess depressive symptoms, functional status, and quality of life using the PHQ-9 (APA Grade II).¹⁷ Following remission or a response, patients should be contacted every 1-3 months during the continuation phase to monitor for relapse.⁷

Therapy should be advanced until remission is achieved. It is strongly recommended that adult patients on pharmacotherapy continue therapy for 4-9 months following successful acute phase treatment (APA Grade I).¹⁷ Continuation of psychotherapy such as CBT is also recommended (APA Grade I).¹⁷ Patients who continue psychotherapy should be reassessed every 3-4 months to ensure adequate improvement.¹⁷

Once the patient has been asymptomatic for at least 4 to 9 months following a depressive episode, recovery from the episode is declared. At recovery, treatment may be stopped unless the patient is considered at high risk for recurrence. Maintenance therapy should be considered in high risk patients experiencing three or more prior major depressive episodes (APA Grade I), or two prior episodes and any of the following risk factors (APA Grade II):¹⁷

- Chronic major depressive disorder (severe prior episodes)
- Presence of residual symptoms
- Ongoing psychosocial stressors
- Early age at onset
- Family history of mood disorders
- Age over 70

Prior to discontinuation of treatment, patients should be informed of the potential for relapse and a plan should be established to seek treatment if symptoms reoccur (APA Grade I).¹⁷ The discontinuation of antidepressant therapy should be tapered over at least several weeks (APA Grade I). It is important to notify patients receiving psychotherapy of discontinuation, well in advance of the last session (APA Grade I).¹⁷

Maintenance phase (1 year to lifetime beyond continuation therapy) is aimed at preventing new or future depressive episodes. Adult patients who have had three or more episodes of depression or are at high risk for recurrence should be considered for long-term antidepressant therapy (APA Grade I).¹⁷ Patients should be contacted throughout the maintenance phase every 3-12 months if stable.⁵

Referrals

All patients with significant symptoms should be followed by a CoCM case manager. Psychiatric consultation is recommended when there is:⁵

- possibility of bipolar disorder
- significant psychiatric co-morbidity (for example, substance abuse, anxiety, obsessive compulsive disorder, or eating disorders)
- concern regarding the possibility of suicide and/or homicide
- psychosis with the depression
- no improvement with medications prescribed by the primary prescriber despite multiple dose adjustments and trials of different medication classes
- significant or prolonged inability to work and care for self and/or family
- diagnostic uncertainty

RECOMMENDATIONS FOR D-H IMPLEMENTATION

Implementation Tools:

1. Clinician Dissemination:

- a. Clinical practice guidelines posted on Knowledge Map intranet site and sent to D-H clinicians via email
- b. Updating existing Preventive Care clinical practice guideline with recommendations for behavioral health screening tools, including frequency and score cut-offs
- c. A primary care clinician "Behavioral Health Playbook" that synthesizes the roles, tasks, workflows and treatment algorithms for depression

2. Clinical Support:

- a. A "one stop" website to support clinicians in addressing behavioral health issues

3. Patient Education and Resources:

- D-H internet web-page that summarizes information, self-help strategies, self-help groups, counseling resources, etc. for depression (including resources below)

- [Healthwise resources on D-H internet site](#): dozens of topics available

- Other web resources

- Information
 - www.nimh.nih.gov/health/topics/depression/index.shtml
 - www.psychiatry.org/patients-families/depression
 - www.suicidepreventionlifeline.org
- Finding a therapist
 - <https://therapists.psychologytoday.com>
- CBT based self-management
 - <http://www.moodjuice.scot.nhs.uk>
 - <https://moodgym.anu.edu.au/welcome>
 - <http://www.beatingtheblues.co.uk/patients/>

- Apps

- Pacifica- anxiety, stress and depression relief
- MoodKit- CBT for depression, anxiety, anger management

- Books

- The Cognitive Behavioral Workbook for Depression- William Knauss, EdD

4. Behavioral Health Clinician/Case Manager/Nurse-supported Behavioral Health Care:

- a. Care pathway
- b. Training for nurses without mental health care delivery experience

5. eDH (EHR) Tools:

- a. PHQ-2 triggering PHQ-9 already exists in the Lebanon AWW and PC questionnaires done before yearly preventive visits. Behavioral health screening can also be tied to an annual preventive visit at other sites. Will add cueing logic to ensure PHQ-2 to 9 is done at any visit in which it hasn't been done in the previous 3 months. For depression follow-up, it should be done at each visit.
- b. Best practice advisories to alert clinicians to positive screens and offer guidance and resources

6. Clinical Performance Measures:

- a. Process Measures: Percent of eligible patients screened (HEDIS), Number of psychiatric eConsults submitted, Percent of patients with PHQ-9 \geq 10 with: documented follow up plan (HEDIS), % with diagnosis enrolled in collaborative care and electronic clinical data system (ECDS/registry) (HEDIS), receiving follow-up PHQ-9 within 7 months (HEDIS); Of patients not responding at 8 weeks, what % had at least one psychiatric consultation between weeks 8-12, Percent of patients how remain on antidepressant at 12 weeks and 6 months (Bao- 2 essential tasks).

- b. Outcome Measures: percent of patients with PHQ-9 \geq 10 with response within 7 months (HEDIS), percent of patients with PHQ-9 \geq 10 with remission within 7 months (HEDIS);

Qualifying Statements

Pathways & Guidelines: Clinical Practice Guideline and pathways are designed to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

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Pertinent Links

D-H Depression Management Pocket Guide

http://one.hitchcock.org/intranet/docs/default-source/d-h-knowledge-map-documents/dep_pocketguide_final.pdf

D-H Depression Management Brief

http://one.hitchcock.org/intranet/docs/default-source/d-h-knowledge-map-documents/depression_brief-final.pdf

D-H Unhealthy Alcohol and Drug Use Guideline

http://one.hitchcock.org/intranet/docs/default-source/d-h-knowledge-map-documents/uadu-guideline-final_2017.pdf

D-H Behavioral Health Integration into Primary Care Model Guideline

<http://one.hitchcock.org/intranet/docs/default-source/d-h-knowledge-map-documents/behavioral-health-integration-guideline-final.pdf>

APPENDIX 1: Depression Screening Instruments

Initial Screening Instrument	Frequency
PHQ-2 ²⁵	New patient visits Annual Preventive visits At any visit if not done in previous 90 days
Secondary Screening Instrument	
PHQ-9	Screening PHQ-2 score ≥ 3 triggers PHQ-9 Full PHQ-9 is done

The PHQ-2 consists of the first 2 questions of the PHQ-9²⁶

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME: _____ DATE: _____

Over the last 2 weeks, how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. 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	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3

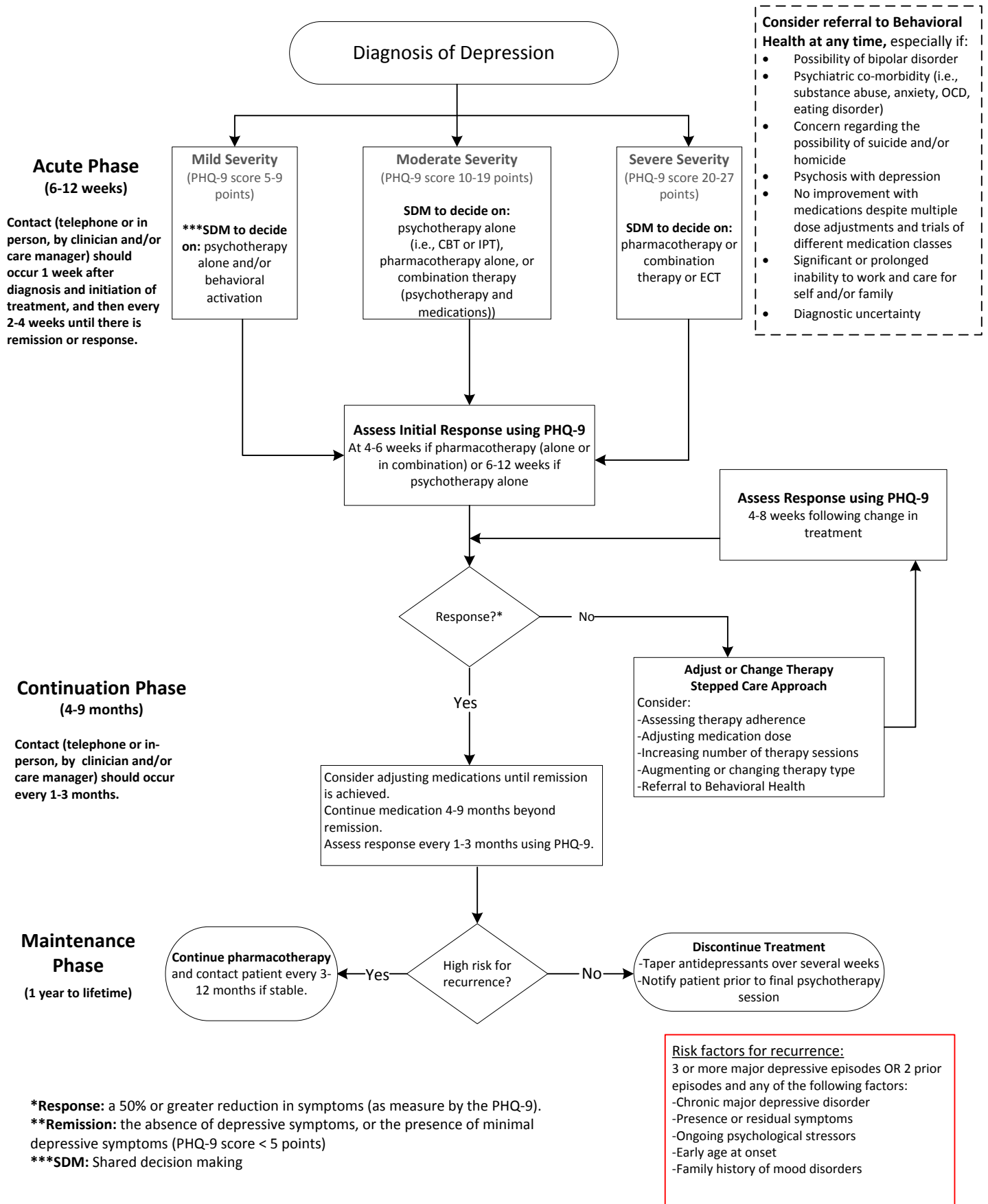
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(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL:

10. If you checked off any problems, 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	_____

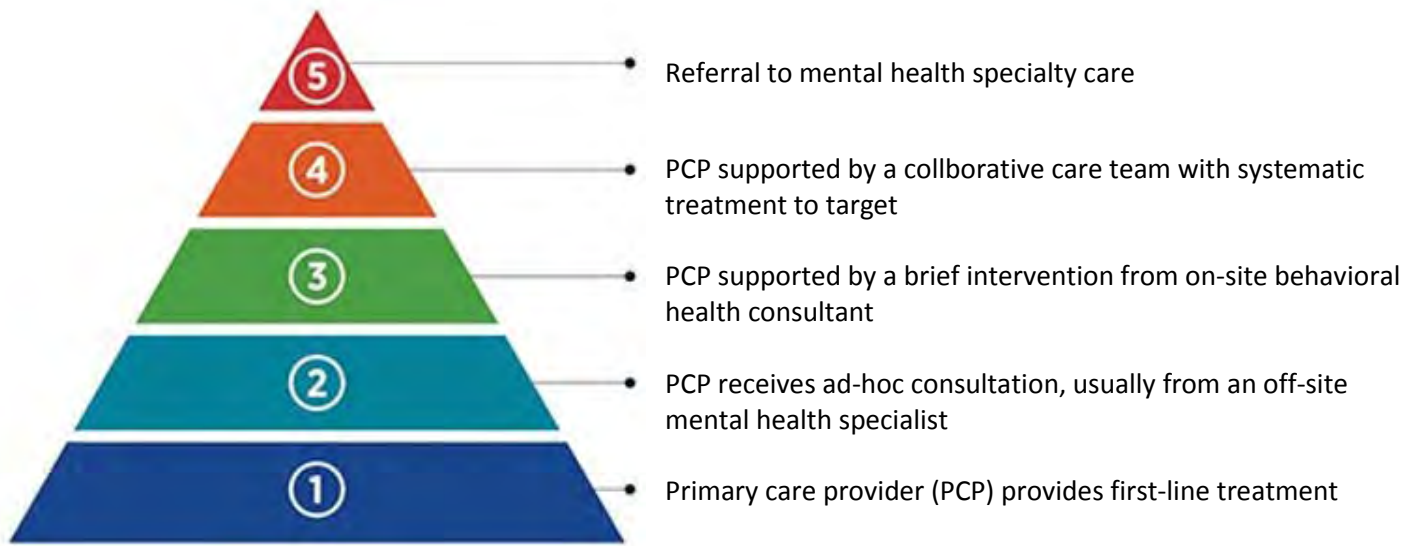
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APPENDIX 2: Depression Treatment in Adults Algorithm



APPENDIX 3: Stepped Care Model²⁷

Stepped Model of Integrated Behavioral Health Care



Source: AIMS Center, University of Washington. 2016

APPENDIX 4: Product and Dosage Chart

Product	How Supplied	Dosage Ranges	Generic? **
SELECTIVE SEROTONIN REUPTAKE INHIBITORS			
Citalopram (Celexa)	10, 20, 40mg scored tab 10mg/4mL soln	20-40mg daily	Yes
Escitalopram (Lexapro)	5mg unscored, 10 and 20mg scored tab 5mg/ 5mL	10-20mg daily	Yes
Fluoxetine (Prozac)	10, 20, 40 cap 90mg delayed release cap 10mg, 20mg tab 20mg/5mL soln	10-80mg daily or 90mg weekly	Yes
Paroxetine (Paxil, Paxil CR)	10, 20mg scored tab 30, 40mg tab 10mg/5mL susp 12.5, 25mg, 37.5mg CR	10-60mg IR daily or 25-62.5mg CR daily	Yes (includes CR)
Sertraline (Zoloft)	25, 50, 100mg scored tab 20mg/mL concentrate	50-200mg daily	Yes
SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITORS			
Desvenlafaxine (Pristiq)	50, 100mg tab	50 daily	Yes
Duloxetine (Cymbalta)	20, 30, 60mg cap	40-60mg daily	Yes
Levomilnacipran (Fetzima)	20, 40, 80, 120mg ER capsules	40-120mg daily following 20mg X2day titration	No
Venlafaxine (Effexor, Effexor XR)	25, 37.5, 50, 75, 100mg IR tab 37.5, 75, 150, 225mg ER tab 37.5, 75, 150mg ER cap	75-225mg IR daily in divided doses 37.5-75mg ER daily	Yes (Includes ER)
ATYPICAL ANTIDEPRESSANTS			
Bupropion (Wellbutrin, Aplenzin)	75, 100mg IR tab 100, 150, 200mg SR tab 150, 300mg XL tab 174, 348, 522mg ER tab	100-150 mg IR TID 150-200mg SR BID 150-450mg XL daily (hydrochloride salt) 174-522mg ER daily (hydrobromide salt)	Yes (Includes ER & XL but not Aplenzin products)
Mirtazapine (Remeron)	7.5, 15, 30, 45mg tab 15, 30, 45mg ODT	15-45mg daily	Yes (includes ODT)
Trazodone* (Oleptro)	50, 100, 300mg IR tab ER 150, 300mg	150-600mg IR daily in divided doses 150 mg ER daily	Yes
Vilazodone (Viibryd)	10, 20, 40mg tablets	20-40mg once daily	No
Vortioxetine (Brintellix)	5, 10, 15, 20mg tablets	5-20mg once daily	No
TRI-CYCLIC ANTIDEPRESSANTS*			
Amitriptyline	10, 25, 50, 75, 100, 150 mg tab	50-150mg daily at bedtime or in divided doses	Yes
Amoxapine	25, 50, 100, 150mg tab	50mg BID-TID	Yes
Desipramine	10, 25, 50, 75, 100, 150mg tab	100-300mg daily in divided or single doses	Yes
Doxepin	10, 25, 50, 75, 100, 150mg cap 10mg/mL conc	25-300mg daily in divided or single doses	Yes
Imipramine	10, 25, 50mg tab 75, 100, 125, 150mg cap	75-200mg daily	Yes
Maprotiline	25, 50, 75mg tab	75-150mg daily in divided or single dose	Yes
Nortriptyline	10, 25, 50, 75mg cap 10mg/5mL soln	75-150mg daily in divided or single doses	Yes

*For TCA'S and trazodone, there are therapeutic blood levels that should be done if patient does not respond to therapeutic dose. **Insurance coverage varies. Patients are less likely to take their medication if they cannot afford it.

APPENDIX 5: Consideration of Concurrent Conditions

Depression With	First-Line Therapeutic Options*	May be Problematic
No Additional Comorbid Conditions	Fluoxetine, Citalopram, Escitalopram, Paroxetine, Sertraline, Trazodone, Mirtazapine, Venlafaxine, Desvenlafaxine, Bupropion	TCA-side effect profile less desirable Nefazodone-hepatotoxicity
Pregnancy	Sertraline, Citalopram, Fluoxetine, TCA	Paroxetine, Venlafaxine, Duloxetine
Elderly patients		Fluoxetine, Paroxetine
Alcohol Use		Duloxetine=Liver injury, as manifested by ALT and total Bilirubin elevations, with evidence of obstruction have occurred with coadministration of alcohol and Duloxetine.
Anxiety or Panic Disorder	Paroxetine, Fluoxetine, Mirtazapine, Sertraline, Citalopram, Escitalopram Venlafaxine, Desvenlafaxine	Bupropion-may increase anxiety
Cardiac Condition	Sertraline	TCA Venlafaxine Desvenlafaxine, Bupropion (increases blood pressure). Mirtazapine (increases cholesterol), Citalopram
Chronic Pain	TCA, SNRI such as Duloxetine	
Decreased Appetite	TCA, Mirtazapine	Venlafaxine Desvenlafaxine SSRI
Dementia	Bupropion, Mirtazapine, Citalopram	
Dementia, Head Injury, Post-Stroke Patients	Citalopram, Escitalopram, Sertraline	TCAs, Paroxetine, Mirtazapine, Bupropion
Diabetes	Fluoxetine, Citalopram, Escitalopram, Paroxetine, Sertraline	TCAs, Mirtazapine (may increase carbohydrate cravings), Duloxetine (causes slowed gastric emptying), Paroxetine
Eating Disorders (anorexia, bulimia)	Fluoxetine, Paroxetine, Sertraline	Bupropion, Mirtazapine
Fibromyalgia	Duloxetine, Venlafaxine	
Glaucoma	Fluoxetine, Citalopram, Escitalopram, Sertraline, Bupropion	TCA, Paroxetine, Duloxetine, Venlafaxine, Desvenlafaxine
Lactation	Sertraline, Paroxetine	Fluoxetine
Liver Disease	Sertraline, Venlafaxine (use at low dose) , Desvenlafaxine (use at low dose)	TCAs, Fluoxetine, Paroxetine, Citalopram, Escitalopram, Trazodone, Mirtazapine, Nefazodone, Duloxetine
Obsessive Compulsive Disorder	Fluoxetine, Citalopram, Escitalopram, Sertraline, Paroxetine	
Parkinson's Disease	Bupropion, Trazodone, Desipramine, Amoxapine, Nortriptyline, Protryptiline	SSRIs, Venlafaxine, Desvenlafaxine, Nefazodone, Mirtazapine
Pheochromocytoma		Selegiline patch
Renal Disease	Fluoxetine, Citalopram, Escitalopram, Sertraline	Mirtazapine, Paroxetine, Venlafaxine, Desvenlafaxine, TCA-levels not predictive
Seizures/Seizure Disorder	Fluoxetine, Citalopram, Escitalopram, Sertraline, Paroxetine	Bupropion, Maprotiline, TCA (in overdose), Duloxetine, Venlafaxine Desvenlafaxine
Symptoms of: insomnia, weight loss, or overstimulation	Mirtazapine, Trazodone, TCAs, Paroxetine	Venlafaxine, Desvenlafaxine, SSRI, Bupropion
Symptoms of: oversatiation, weight gain, or lethargy	Bupropion, Venlafaxine, Desvenlafaxine	Mirtazapine, TCA, Trazodone, Fluoxetine, Sertraline, Citalopram, Escitalopram, Paroxetine
*Prior to selecting an individual agent for therapy, prescribers should screen for other medications and supplements that may cause problematic effects for the patient.		

APPENDIX 6: Depression Side Effect Profiles

Side effects may be observed early in pharmacotherapy treatment and improve over time. If side effects persist, alternatives may be considered.¹⁷

Presenting Symptom	First Line Therapeutic Options	May Be Problematic
Agitation/Insomnia	Mirtazapine, TCA	Selegiline Patch, Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Bupropion, Venlafaxine, Desvenlafaxine
Anticholinergic Side Effects (dry mouth, blurred vision, constipation, urinary retention)	Citalopram, Escitalopram, Fluoxetine, Sertraline, Venlafaxine, Desvenlafaxine, Bupropion	TCA, Mirtazapine, Paroxetine, Duloxetine, Selegiline Patch
GI Sensitivity	Bupropion, TCA, Mirtazapine	Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Nefazodone, Venlafaxine, Desvenlafaxine, Duloxetine (20% pts nausea)
Headache	TCA, Mirtazapine	Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Nefazodone, Venlafaxine, Desvenlafaxine, Bupropion, Selegiline Patch
Orthostatic Hypotension	Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Venlafaxine, Desvenlafaxine, Bupropion	TCA, Mirtazapine, Trazodone, Selegiline Patch
Sedation	Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Venlafaxine, Desvenlafaxine, Bupropion	TCA, Nefazodone, Trazodone, Mirtazapine, Selegiline Patch, Paroxetine
Sexual Dysfunction	Bupropion, Mirtazapine	Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Venlafaxine, Desvenlafaxine, Bupropion, Trazodone
Weight Gain	Fluoxetine, Sertraline, Citalopram, Escitalopram, Venlafaxine, Desvenlafaxine, Bupropion	TCA, Paroxetine, Mirtazapine, Trazodone
Special Considerations for Older Adults (age 65 years or older) ^{5,56,58}		
Poor sleep/Insomnia	Mirtazapine	Benzodiazepines, Paroxetine
Weight loss	Mirtazapine	
Anxiety	SSRIs, SNRIs	
Hypersomnia and low energy	Bupropion	

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