Managing Depression in Primary Care

VA

U.S. Department of Veterans Affairs

Veterans Health Administration

PBM Academic Detailing Service

Managing Depression in Primary Care

A VA Clinician's Guide

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Key Facts

Major depressive disorder (MDD) is the most prevalent and disabling form of depression. It is a leading cause of disability and one of the most common mental health disorders in the United States and worldwide.[1,2] This disorder may be graded on its severity from mild to severe and may present as a single episode or recurrent. This guide focuses on managing mild to moderate MDD (or "depression") in the primary care setting.

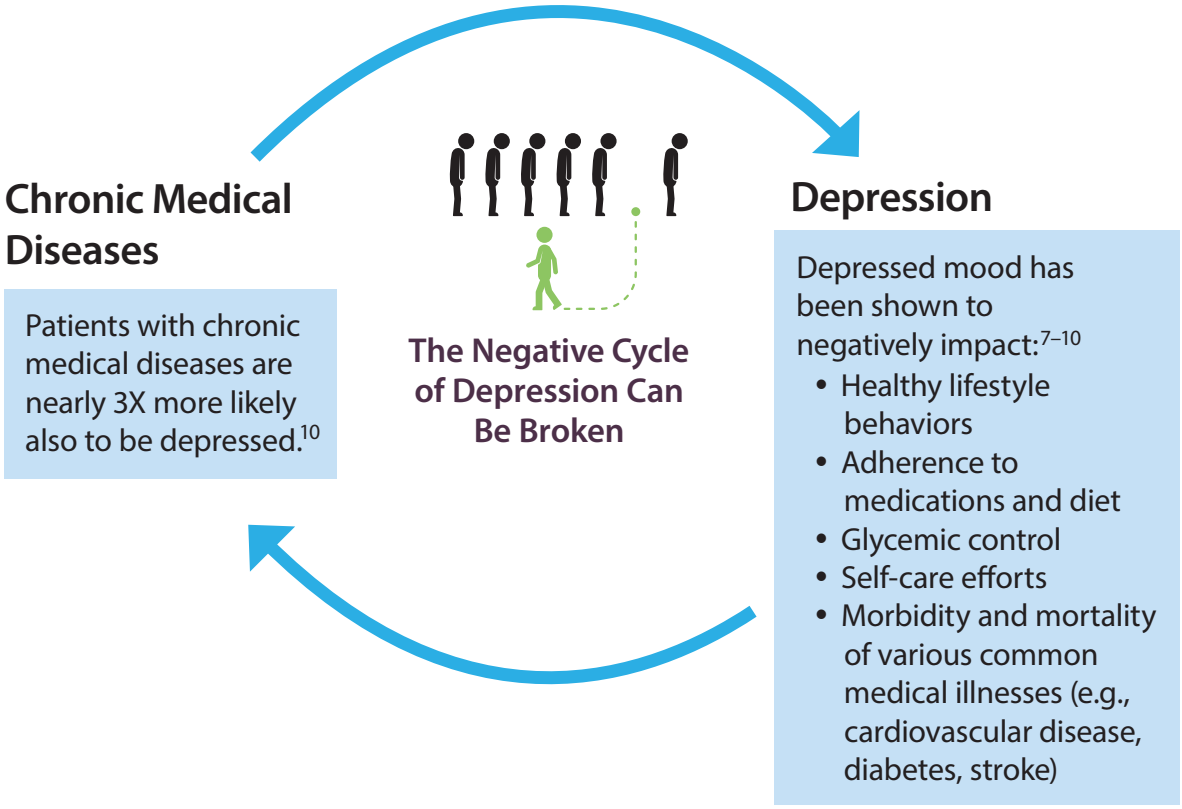
- Depression can result in severe impairments that interfere with or limit the ability to carry out major life activities.

Compared to most patients with general medical conditions, patients with depression struggle more at work, in social situations, and with their families.[3–6]

MDD is a common mental disorder that manifests with depressed mood or loss of interest or pleasure in regular activities. Other symptoms include decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite, poor concentration, and suicidal ideation.

Depression can negatively impact the management of other chronic medical diseases.[7–10]

Figure 1. The Cycle Can Be Broken



Approximately one in three adults with a depressive episode does not receive treatment.[1]

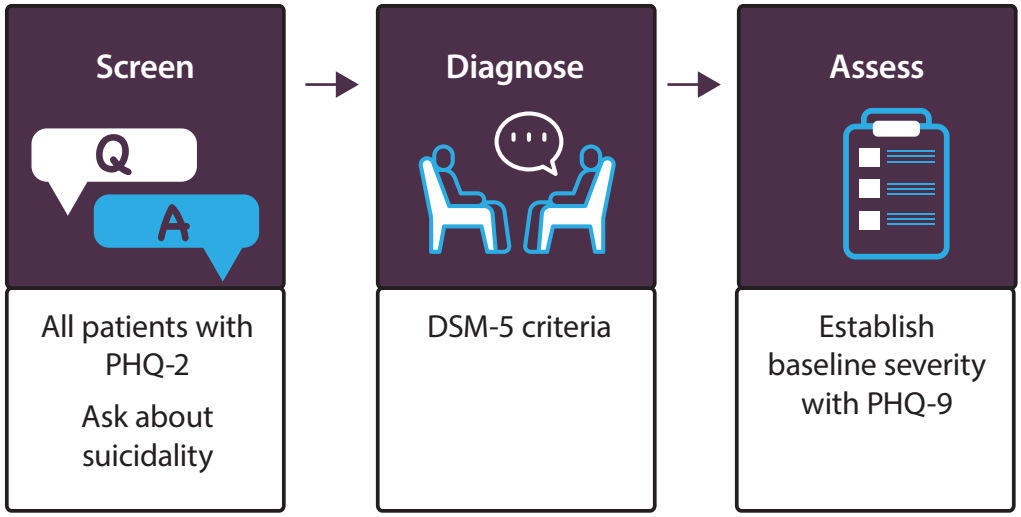
This disorder is under-recognized and under-treated.[9]

Why Manage Depression in Primary Care?

- Primary care practitioners (PCP) are accessible, can provide continuity of care, and foster long-term relationships with the patient.[11]
- A strong therapeutic relationship, along with empathic listening and motivational interviewing skills, have been shown to improve outcomes.[11,12]
- Some Veterans may be resistant to referral to mental health services.

The first step is to identify, diagnose, and assess Veterans suffering from depression.

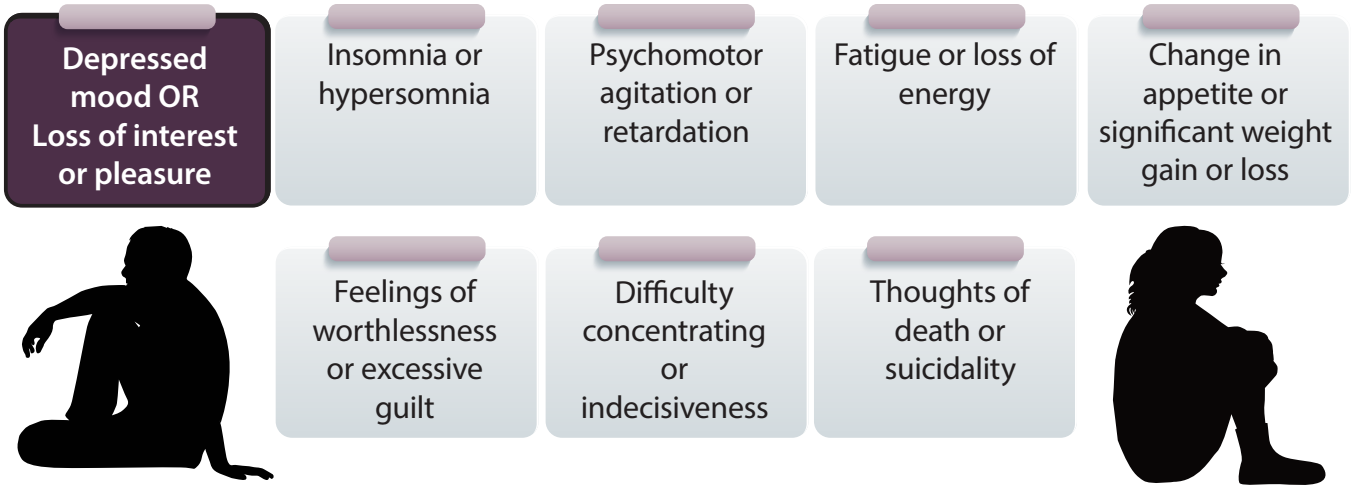
Figure 2. Identifying, Diagnosing and Assessing Depression[6,13,14]



PHQ: Patient Health Questionnaire, 2-and 9-item versions; DSM-5: Diagnostic and Statistical Manual, 5th edition

Depression is characterized by a discrete episode of at least two weeks duration that includes depressed mood and/or a marked loss of interest or pleasure along with at least four additional symptoms.

Figure 3. Symptoms of Major Depressive Disorder[6,15]



Symptoms must be present nearly every day, with the exception of weight change and suicidal ideation.

Did You Know?

Depression in the elderly is frequently characterized by anhedonia.

It's important to distinguish unipolar depression from bipolar depression. Ask about past episodes of mania or hypomania or if they have experienced activation with antidepressants in the past. If present, refer the patient to a mental health provider for further evaluation and treatment.

Past symptoms that may represent mania or hypomania, indicating that a referral is needed, include:[15]

- Elevated, expansive or irritable mood
- Grandiosity
- Decreased need for sleep
- Excessive involvement in activities with potential or painful consequences
- Pressured or increased speech
- Flight of ideas or racing thoughts
- Distractibility
- Increased goal-directed activity
- Psychomotor agitation

When you suspect depression, do an appropriate diagnostic evaluation that includes medical history, past psychiatric history (prior depressive episodes, any history of manic or hypomanic episodes, and treatment history), and relevant family history. It is also important to perform testing that could identify remediable co-occurring conditions or alternative diagnoses.

Examples of medical conditions that can worsen depression or present with symptoms of depression:[6,14]

- Obstructive Sleep Apnea
- Endocrine Disorders (e.g., hypo/hyperthyroidism)
- Drug toxicities and withdrawal (cocaine, anxiolytics, and amphetamines)
- The use of alcohol and hypnotics might mimic and/or induce depression, and comorbidity is common.
- Stroke
- Dementia
- Delirium
- Parkinson's disease
- Infections (e.g., HIV, syphilis, Lyme)
- Metabolic disorders (e.g., anemia, B12 deficiency, electrolyte disturbances)

Primary Care Mental Health Integration (PCMHI) can include consultative advice for the diagnosis and treatment of depression in primary care.

Once a Veteran has been diagnosed with depression, it is important to do an evaluation and determine the best treatment setting.

Patients evaluated and determined to have mild to moderate depression (according to the PHQ-9) can most often be managed in primary care (Figure 4). Even patients with psychiatric comorbidities, if adequately controlled, may not require referral to mental health specialty care.

Identify, diagnose, and offer treatment for mild to moderate depression in the primary care setting.

Some Veterans will not be receptive to specialty mental health referral. The utilization of PCMHI is often helpful in these situations. In many facilities, PCMHI is the first step of mental health treatment. PCMHI consists of mental health providers embedded in the patient aligned care team (PACT) as well as care managers, who provide ongoing patient follow-up, and decision support for PCPs, using the Collaborative Care Model (CoCM).

Table 1. Referral Criteria

Criteria for Referral to Either PCMHI or Specialty Mental Health Care*	
• Complex MDD (severe, chronic, recurrent, treatment-resistant) • Bipolar Disorder (current or prior manic or hypomanic episodes) • Depression with psychosis	• Co-occurring PTSD, SUD, or significant anxiety • Coexisting cognitive impairment • Suicidality (Evaluate patient's safety; see page 19 for more information.)

Chronic is characterized as MDD with a duration of more than two years (DSM-5 eliminated use of "chronic" and combined it with dysthymia to become persistent depressive disorder); recurrent MDD is defined by three or more depressive episodes; treatment-resistant MDD is an episode that does not remit after two or more proven treatments of adequate strength and duration. *Acute interventions may be warranted. PTSD = posttraumatic stress disorder; SUD = substance use disorder

Measurement-Based Care

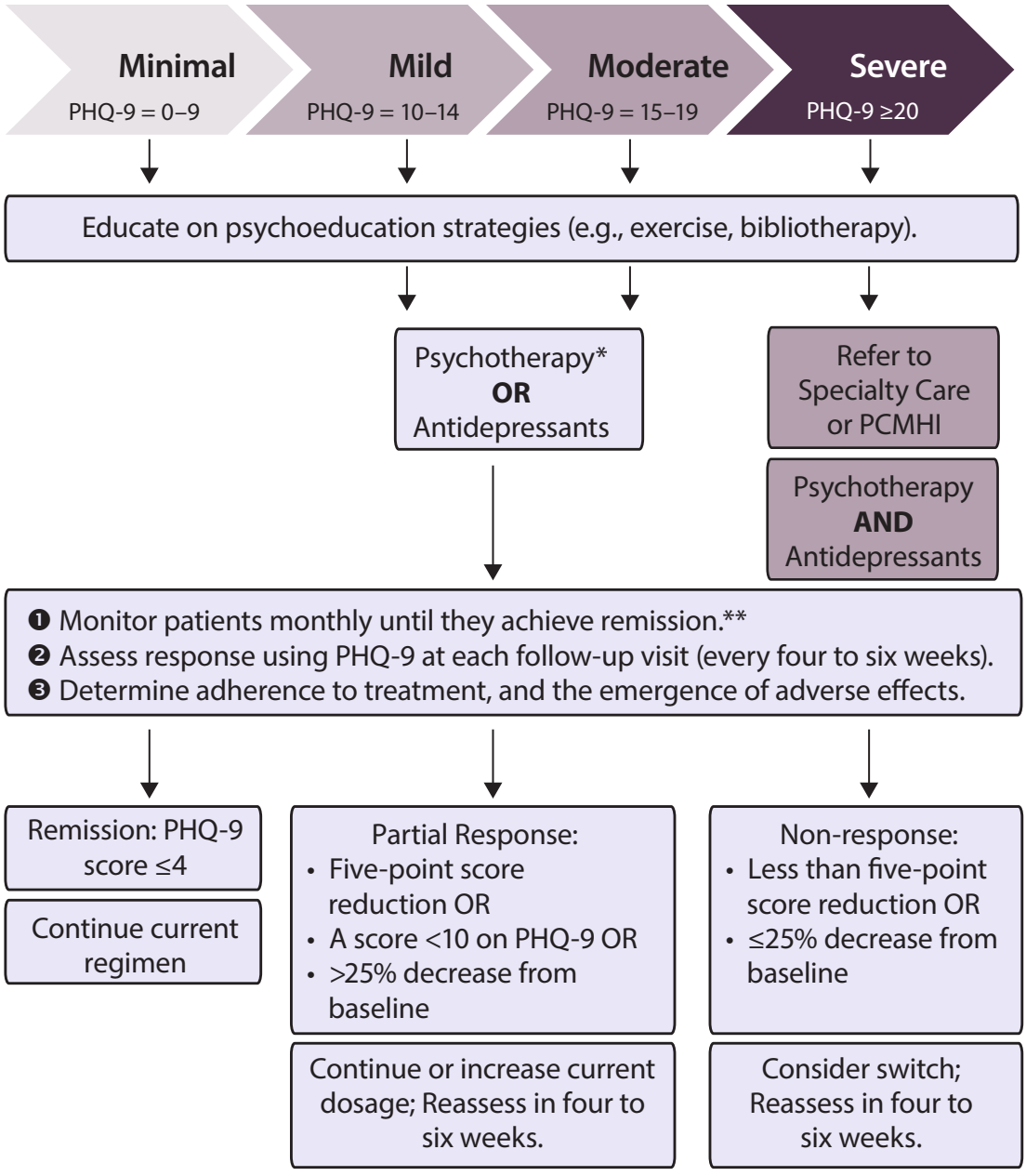
Measurement-based tools provide a consistent and objective measure of a patient's clinical status.[16] Use the PHQ-9 to assess and monitor the Veteran's level of depression.

PHQ-9

- Can be self-administered
- Validated in clinical studies and shown to have excellent reliability[16,17]

- Helps lead to improved outcomes[17,18]
- Can be integrated into primary care workflow in busy clinic settings[17,18]

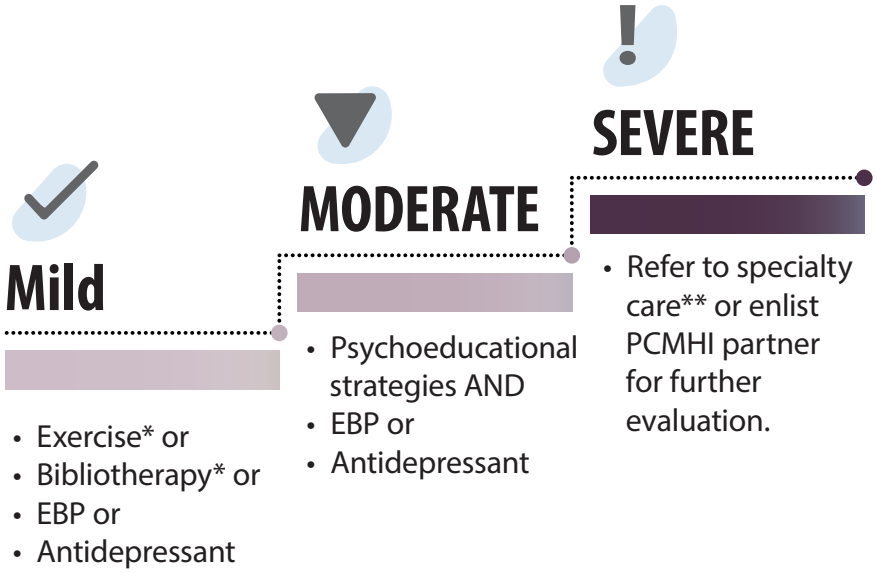
Figure 4. Use the PHQ-9 to Guide Treatment Decisions.[16,19]



Use the PHQ-9 for sensitive, objective measurement of response and to determine if remission was achieved.

*Refer or consult PCMHI partner. Option to utilize computer-based cognitive behavioral therapy as adjunctive, or first-line treatment, based on patient's preference. **Follow-up PHQ-9 and assessment of adherence can be done by PCMHI providers or care managers, nurse or pharmacist, or other identified health care professional, face to face, by telephone, or other virtual modality based on patient severity and clinical judgment.

Figure 5. A Stepwise Approach to Managing Depression Based on Severity



If available, consider utilizing Peer Specialists who are Veterans trained to provide support and guide other Veterans through treatment.

*Exercise and bibliotherapy are psychoeducational strategies with evidence to support their use as monotherapy. Other psychoeducation strategies may still be utilized with EBP or antidepressant treatment. **Some Veterans are unwilling to go to specialty care. In these circumstances, it's important to leverage PCMHI. EBP = evidence based psychotherapy.

Psychoeducational Strategies

These strategies enhance engagement in treatment and should entail systematic monitoring of treatment adherence and responses.

Work with the Veteran to collaboratively select one or two self-management goals.

Figure 6. Self-management Strategies[6,20–27]

Bibliotherapy

- Alternative to pharmacotherapy or psychotherapy for MILD depression if provided with intermittent monitoring and overview of the outcome of treatment by a healthcare professional
- Helps patient understanding of illness and development of self-management skills
- Moderate, mean-weighted effect size (0.69 ($p < 0.01$)) for acute treatment
- Example evidence-based self-help books: Feeling Good: The new mood therapy by David Burns M.D. and Mind over Mood: Change How You Feel by Changing the Way You Think by Dennis Greenberger, PhD and Christine A. Padesky, PhD..

Exercise

Figure 6. Self-management Strategies[6,20–27] *(cont.)*

Exercise

- Excellent self-management and preventive strategy for MILD depression that can be used adjunctively with a first-line evidence-based treatment for moderate to severe depression.
- Recommend at least three moderate-intensity sessions weekly for at least 30–40 minutes.
- Energy expenditure correlates with mood improvement, not type of exercise.
- Cochrane review found moderate (-0.62, 95% CI -0.81 to -0.42) to small (-0.33 95% CI -0.63 to -.0.3) clinical effect based on study strength inclusion criteria.

Sleep Hygiene

- Sleep problems are common (e.g., insomnia, hypersomnia, disturbances in sleep maintenance).
- Information on sleep hygiene should be included for patients exhibiting any sleep disturbances.
- Studies indicate cognitive behavioral therapy for insomnia (CBT-I) significantly reduces depressive symptoms and increases remission rates.

Tobacco, Caffeine, and Alcohol Use

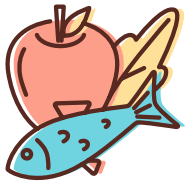
- Tobacco use has been demonstrated to negatively impact the recovery of depression; offer treatment to assist with quitting and refer to the VA Tobacco Quitline 1-855-QUIT-VET (1-855-784-8838).
- Excessive caffeine use may exacerbate some symptoms of depression (e.g., sleep, anxiety).
- Even low levels of alcohol use have been demonstrated to negatively impact recovery from depression; advise to abstain until symptoms remit.

Pleasurable Activities

- Systematic scheduling and monitoring of pleasurable or reinforcing activities has been shown to have significant antidepressant effects.

Nutrition

- Often patients with MDD do not have a balanced diet. Expert opinion suggests that diet should be included in the treatment plan.
- Advise a diet high in fruits and vegetables, whole grains, seeds and nuts, and some lean proteins (e.g., Mediterranean diet).



Several VA Apps are available to assist with self-management strategies: https://mobile.va.gov/appstore/veterans.

Psychotherapies

Mild to moderate depression does not always require medication.

- First-line treatment is either evidence-based psychotherapy or pharmacotherapy.[6]
- Psychotherapy is the preferred treatment in elderly and pregnant women with mild to moderate depression.[6]
- Psychotherapy is time-limited (average of 12 sessions for complete benefit) and has been shown to maintain effectiveness after formal treatment ends.

When provided information about all effective treatment options, patients with depression often choose psychotherapy over pharmacotherapy.[28,29]

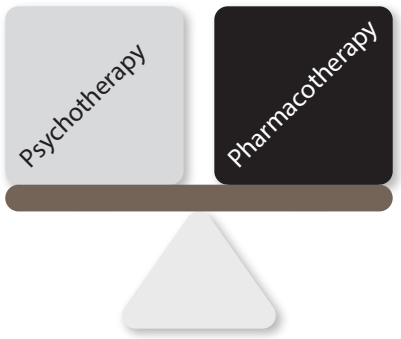
Figure 7. Evidence-based Psychotherapy (EBP) for Depression Reduces the Severity of Depression and Suicidal Ideation.[30–32]

Severity of suicidal ideation decreased by **57%** over the course of EBP for depression.

Veterans participating in EBP for depression experience a **41%** average reduction in depression severity.

Studies show that Evidence-based Psychotherapies are effective for:[30,31,33]

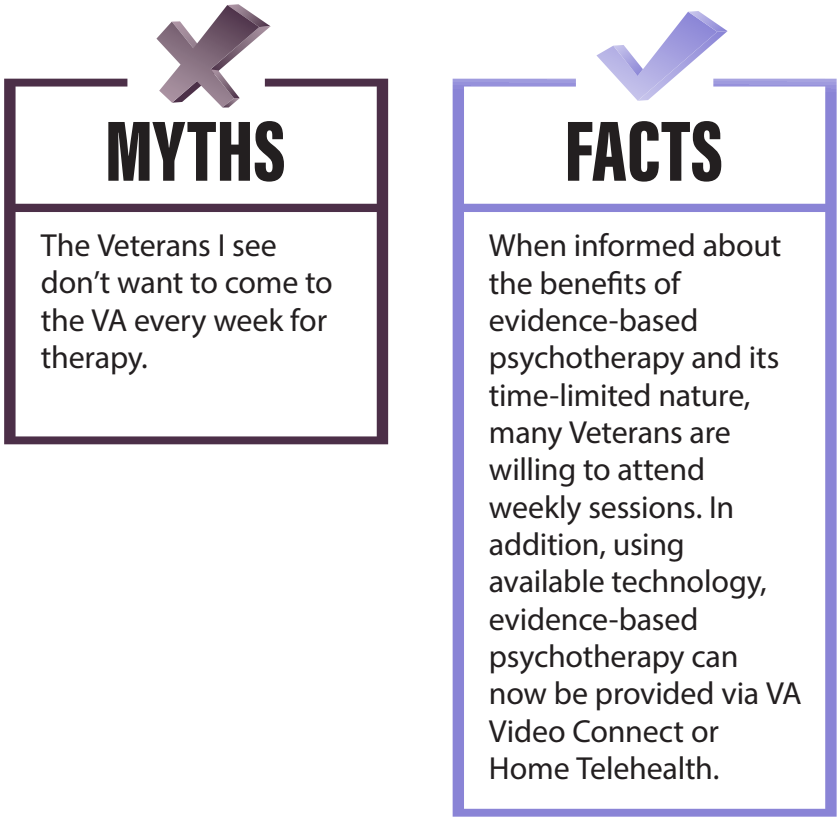
- Reducing symptoms of depression
- Decreasing suicidal ideation
- Improving the quality of life
- Promoting recovery



Direct comparisons between pharmacotherapy and psychotherapy have generally demonstrated no differences in outcomes for mild to moderate depression.[6] An important advantage of psychotherapy is the absence of medication side effects or drug interactions.[6]

Evidence-based Psychotherapies are Time-limited and have Lasting Effects.[6]

Figure 8. Veterans Participate in Time-limited Weekly Therapy Sessions.



When the Veteran prefers psychotherapy, one of the following evidence-based interventions can be offered based on Veteran preference and availability:

- Acceptance and commitment therapy (ACT)*
- Cognitive behavioral therapy (CBT)*
- Interpersonal therapy (IPT)*
- Behavioral therapy/behavioral activation (BT/BA)
- Mindfulness-based cognitive therapy (MBCT)
- Problem-solving therapy (PST)

*EBPs for depression disseminated by the VA National EBP Training Program

PCMHI offers an array of brief psychotherapy treatments that are suitable for the management of depression in patients in primary care.

Refer Veterans to evidence-based psychotherapy for depression.

Pharmacotherapy

There is no evidence to suggest that one antidepressant drug class is superior to another. In recent meta-analyses, all antidepressants have been found to be more effective than placebo in achieving response or remission in adults with moderate to severe depression.[6,34]

When selecting initial pharmacotherapy, it is important to consider other comorbid conditions, past response to medication (in the Veteran or a family member), and contraindications (e.g., drug interactions, allergies).

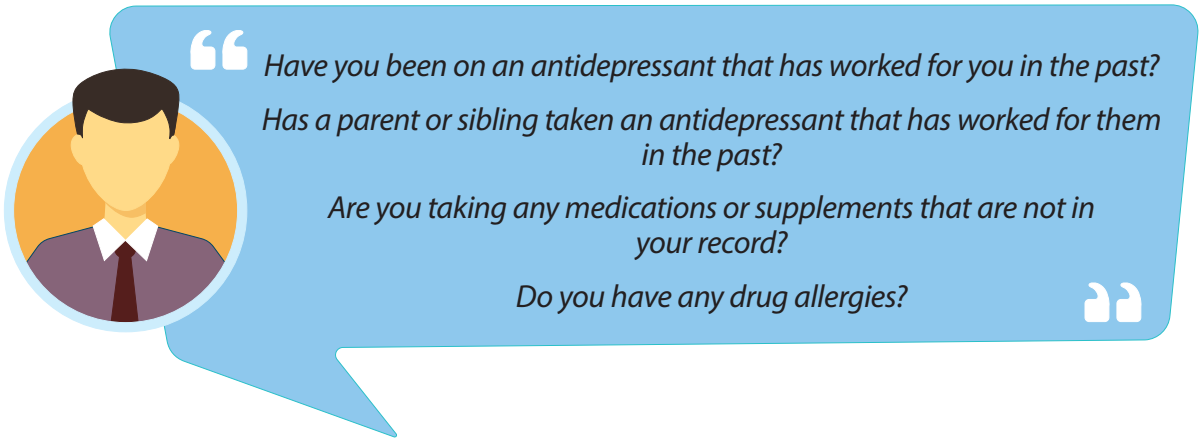


Table 2. Comparison of Commonly Used Antidepressants[6,35]

Drug	Starting dose (mg)	Therapeutic dose (mg)	Safety*					
			Anti-Ach	Sedation	GI	Withdrawal	Drug interactions	OD risk
Selective Serotonin Reuptake Inhibitors (SSRI)								
Citalopram⁺	20	20–40	+	+	N ++	++	++	++
Escitalopram	5–10	10–20	+	+	N ++	++	+	++
Fluoxetine	20	20–80	+	+	N ++	+	+++	+
Paroxetine	20	20–50	++	++	N,D ++	+++	+++	+
Sertraline	25–50	50–200	+	+	N,D ++	++	++	+

*Data compiled from package inserts; **May have less anticholinergic and hypotensive side effects than other TCAs; ⁺If >60 y/o, hepatic impairment, poor CYP2C19 metabolizer, or on cimetidine the maximum dose is 20 mg daily; Initial doses in elderly should be lower than those in healthy adults. Maximized pharmacotherapy is defined as an antidepressant dose advanced to either the FDA maximum recommended dose and/or maximum dose tolerated by the patient for a minimum of four to six weeks. Anti-ach = anticholinergic; GI = gastrointestinal; OD = overdose; C = constipation, D = diarrhea, N = nausea/vomiting.

\+ = less common ++ = intermediate +++ = more common

Table 2. Comparison of Commonly Used Antidepressants[6,35] *(cont.)*

Drug	Starting dose (mg)	Therapeutic dose (mg)	Safety*					
			Anti-Ach	Sedation	GI	Withdrawal	Drug interactions	OD risk
Serotonin Norepinephrine Reuptake Inhibitors (SNRI)								
Duloxetine	20–30	60	+	+	N ++	+++	++	++
Venlafaxine ER	75	75–225	+	+	N ++	+++	++	++
Tricyclic Antidepressants (TCA)								
Amitriptyline	25	100–300	+++	+++	C ++	++	++	+++
Nortriptyline**	25–50	75–150	++	++	C ++	++	++	+++
Norepinephrine and Dopamine Reuptake Inhibitor								
Bupropion XR	150	300–450	+	+	+	+	++	++
Noradrenergic Antagonist								
Mirtazapine	15	30–45	++	+++	+	++	++	+

*Data compiled from package inserts; **May have less anticholinergic and hypotensive side effects than other TCAs; +If >60 y/o, hepatic impairment, poor CYP2C19 metabolizer, or on cimetidine the maximum dose is 20 mg daily; Initial doses in elderly should be lower than those in healthy adults. Maximized pharmacotherapy is defined as an antidepressant dose advanced to either the FDA maximum recommended dose and/or maximum dose tolerated by the patient for a minimum of four to six weeks. Anti-ach = anticholinergic; GI = gastrointestinal; OD = overdose; C = constipation, D = diarrhea, N = nausea/vomiting.

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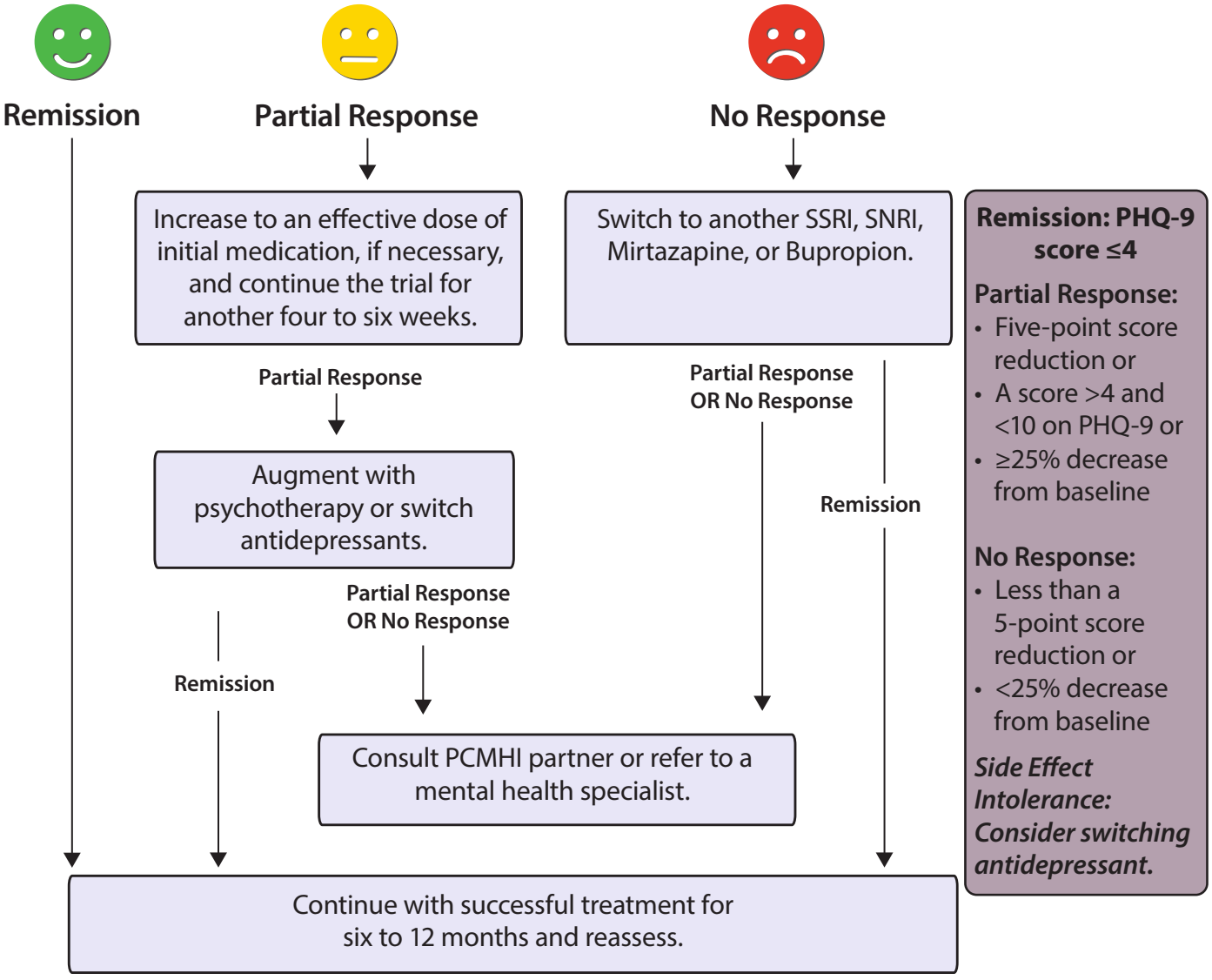
Table 3. Special Considerations for Select Antidepressant Medications[6,36–38]

Medication Examples	Treatment Considerations
Bupropion XR	• May assist with tobacco cessation. • Minimal sexual side effects. • Avoid in patients with a history of seizure or eating disorders. • Abrupt discontinuation of alcohol or benzodiazepines can increase risk of seizures.
Duloxetine	• Can be used to treat pain. • Avoid in patients with a creatinine clearance <30 mL/min or hepatic impairment.
Escitalopram	• Minimal drug interactions. • Starting dose may be an effective dose. • Supratherapeutic (30 mg/day) doses associated with QT prolongation. Use with caution in patients with multiple risk factors for QT prolongation.

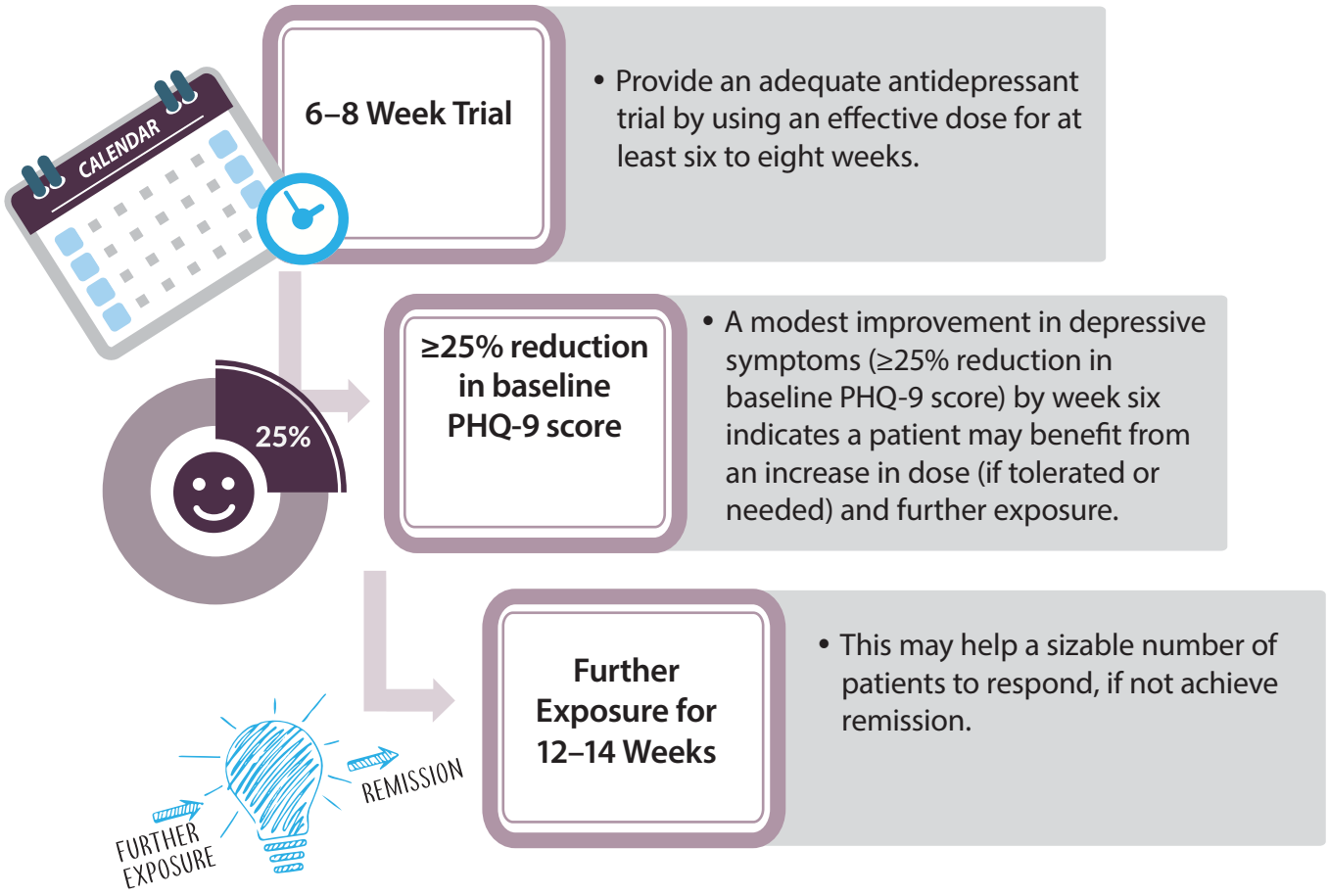
Table 3. Special Considerations for Select Antidepressant Medications[6,36–38] *(cont.)*

Medication Examples	Treatment Considerations
Fluoxetine	• No need to taper with discontinuation; good for poor adherence. • Higher rates of drug interactions.
Mirtazapine	• Sedating, so may help with sleep problems (doses >15 mg may be less sedating). • Minimal sexual side effects. • May increase appetite and cause weight gain.
Sertraline	• Medication of choice for pregnant and/or breastfeeding patients.

Figure 9. Prescribe an Antidepressant, Titrate to a Therapeutic Dose, Continue for Four to Six Weeks, and Assess Response.[6,36–38]



Provide a six to eight-week antidepressant trial and if a modest improvement in depressive symptoms (≥25% reduction in baseline PHQ-9 score) is noted by week six, continue for an additional 6–8 weeks (total trial 12–14 weeks).[18,36]



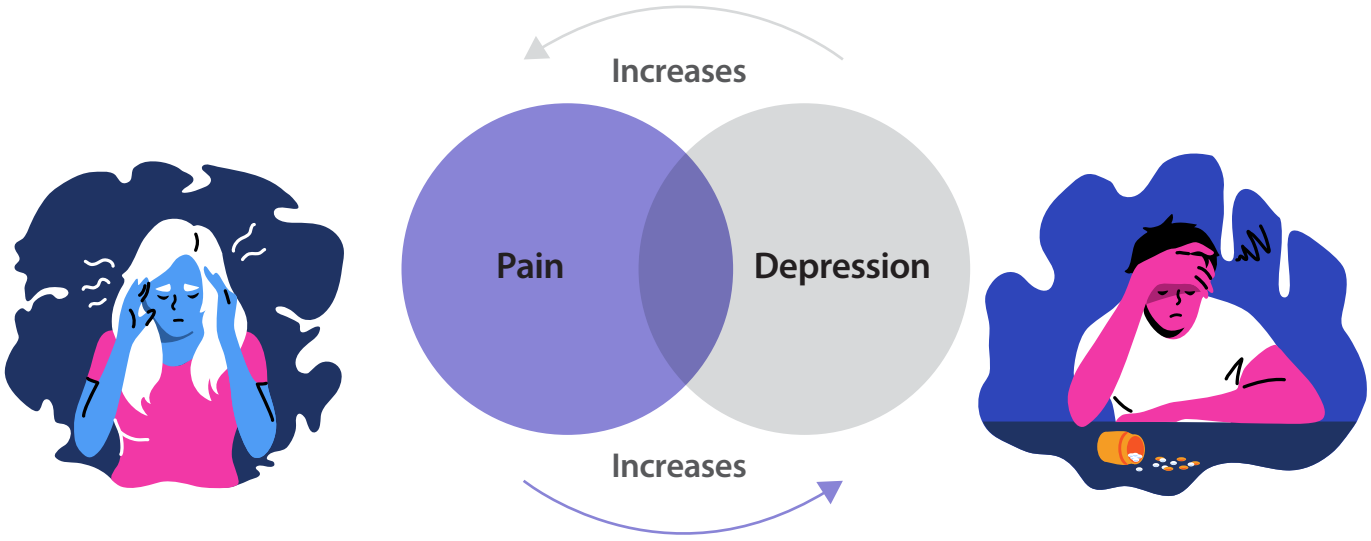
Remember to leverage your local resources like the PCMHI providers and/or care managers to assist with assessment of symptoms, response to medication, and to provide feedback about possible medication titrations.

Treat depression with a therapeutic dose of an antidepressant for an adequate duration to increase odds of remission.

Depression and Pain Management

Depression and chronic pain are frequently comorbid conditions.[40] Also, a longer duration of opioid utilization has been associated with an increased risk of developing depression.[41] Antidepressants have analgesic effects that are independent of their effect on depression, and the effective treatment of depression can lessen chronic pain in some patients.[40,42,43]

Figure 10. Pain and Depression Often Co-occur, Exacerbate One Another, and Display Overlapping Symptoms.[39]



Antidepressant classes have differences in analgesic effectiveness.[40,42]

- Evidence supports the use of tricyclic antidepressants and serotonin norepinephrine reuptake inhibitors (venlafaxine, duloxetine).[43,44]
- There is inconsistent and limited evidence for selective serotonin reuptake inhibitors.[40,43,44]

Onset of analgesia typically is faster than antidepressant effects and occurs at lower doses.[43,45]

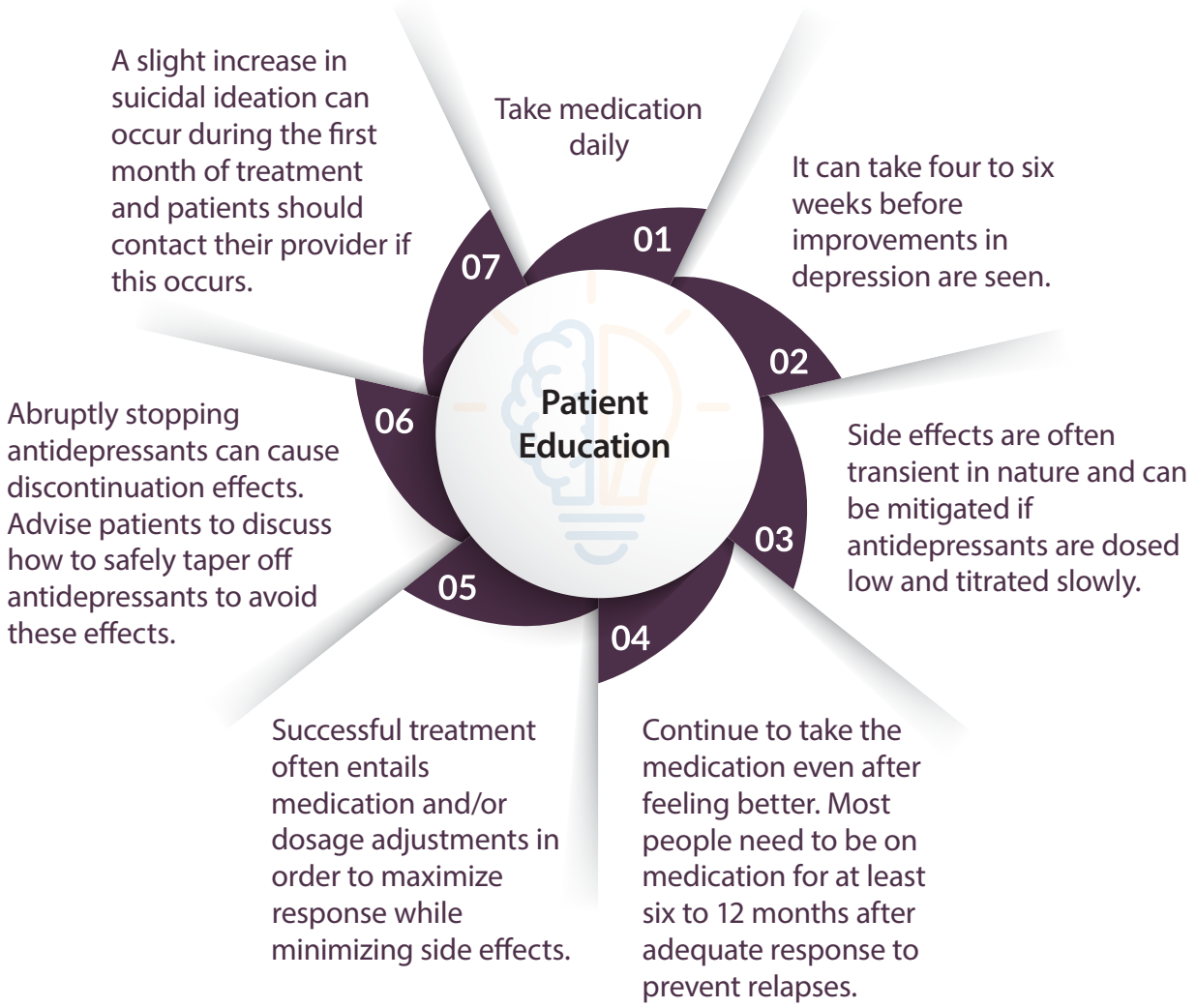
Table 4. Antidepressants with Evidence for Use in Chronic Pain Conditions[40,43,46–48]

Pain Syndrome	Chronic Low Back Pain	Fibromyalgia	Migraine Headache Prophylaxis	Neuropathic Pain	Osteoarthritis
Antidepressant with evidence for use	Duloxetine	Amitriptyline* Duloxetine SSRIs	Amitriptyline* Nortriptyline Venlafaxine	Duloxetine Venlafaxine TCAs	Duloxetine

*Largest body of evidence supports amitriptyline; however, amitriptyline has more anticholinergic effects than nortriptyline or desipramine, which may be considered for treatment. SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants

Beyond pharmacotherapy, Veterans with pain and depression can benefit from psychotherapeutic approaches, such as cognitive behavioral therapy and acceptance and commitment therapy.[44]

Figure 11. Patient Education that Can Enhance Adherence to Medication:[6]



Setting Expectations and Referral to Specialty Care

After an initial treatment course, 50% of patients will respond to the first antidepressant, and 33% will become symptom-free.[18] Consider referring to specialty care those patients with depression that does not remit after two separate treatment trials.[36]

Approaches that may be recommended by a psychiatrist include:

- Combination with another antidepressant
- Augmentation with other medications such as lithium, liothyronine (T3), buspirone, antipsychotics, esketamine, or ketamine
- Electroconvulsive therapy (ECT) or transcranial magnetic stimulation (rTMS)

Examples of Antidepressant Combinations[49–51]

- SSRIs + bupropion
- SSRIs or SNRIs + mirtazapine
- SSRIs + TCAs*

*Caution should be used with this combination; prior to use, consider consultation with mental health.
SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin and norepinephrine reuptake inhibitor; TCA =tricyclic antidepressant

Once a Veteran is stabilized on maintenance treatment or in remission from depression, accepting Veterans back for management of depression in primary care will increase access for the more chronically and severely depressed Veterans to be managed by specialty care.

Maintenance Pharmacotherapy

Figure 12. Antidepressants Should Be Continued for At Least Six Months After Remission is Achieved.[6,16,35]

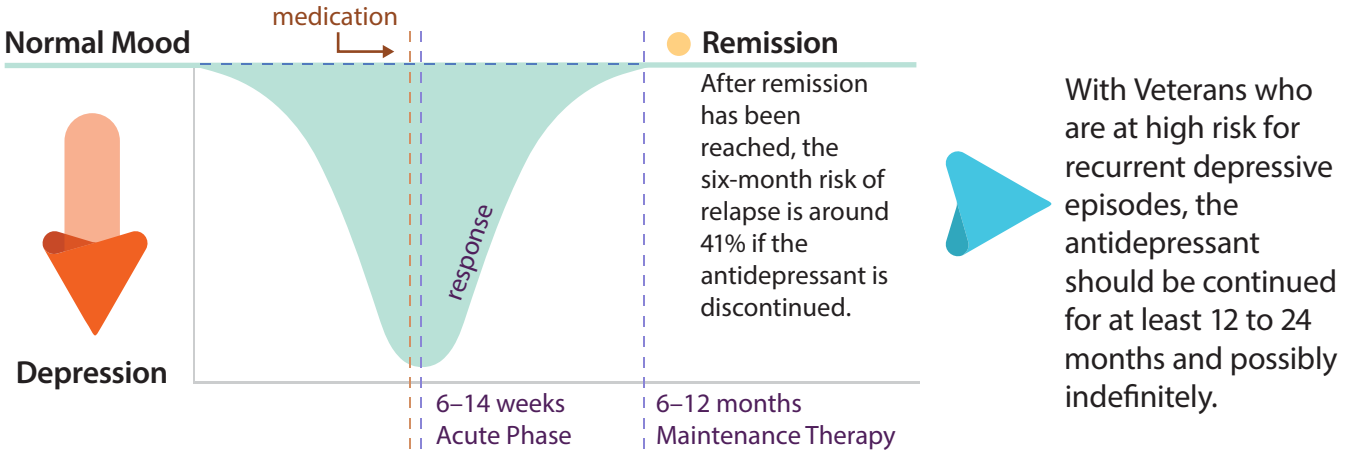
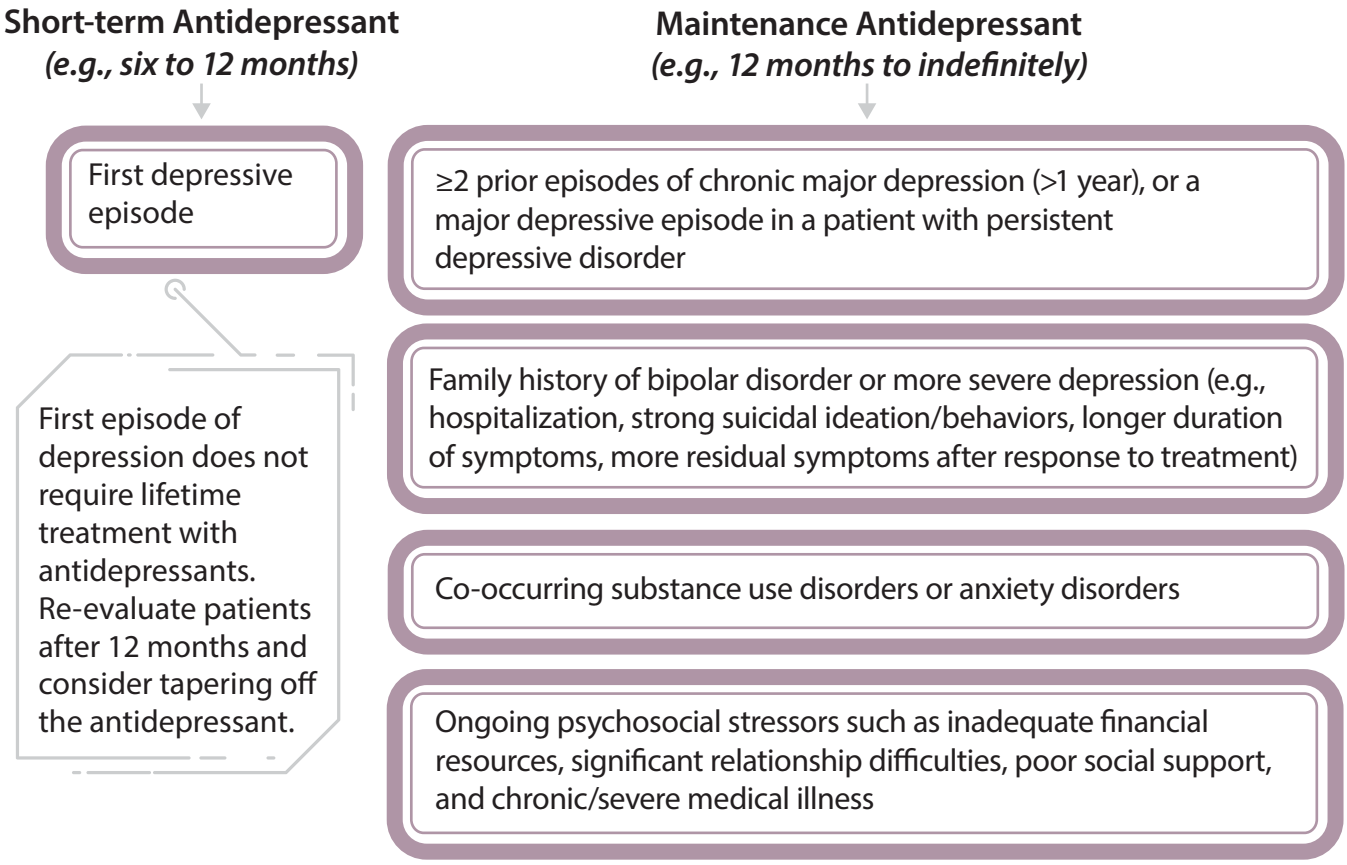


Figure 13. Maintenance Pharmacotherapy Recommendations[6,35]



Discontinuation of Pharmacotherapy

If antidepressants are discontinued abruptly, there is a risk of discontinuation syndrome.

> **!** Antidepressants should be tapered over a four-week period or longer to avoid discontinuation syndrome.

Risk of discontinuation syndrome is increased with:[35]

- Shorter half-life medications (e.g., paroxetine, venlafaxine)
- Treatment duration of eight weeks or longer
- Anxiety experienced when antidepressant initiated
- Previous discontinuation syndrome experienced
- Concurrent centrally-acting medications (e.g., antihypertensives, antihistamines, antipsychotics).

Common Discontinuation Symptoms[35]

- Dizziness
- Flu-like symptoms
- Electric shock-like sensations
- Insomnia
- Excessive (vivid) dreams
- Irritability
- Crying spells

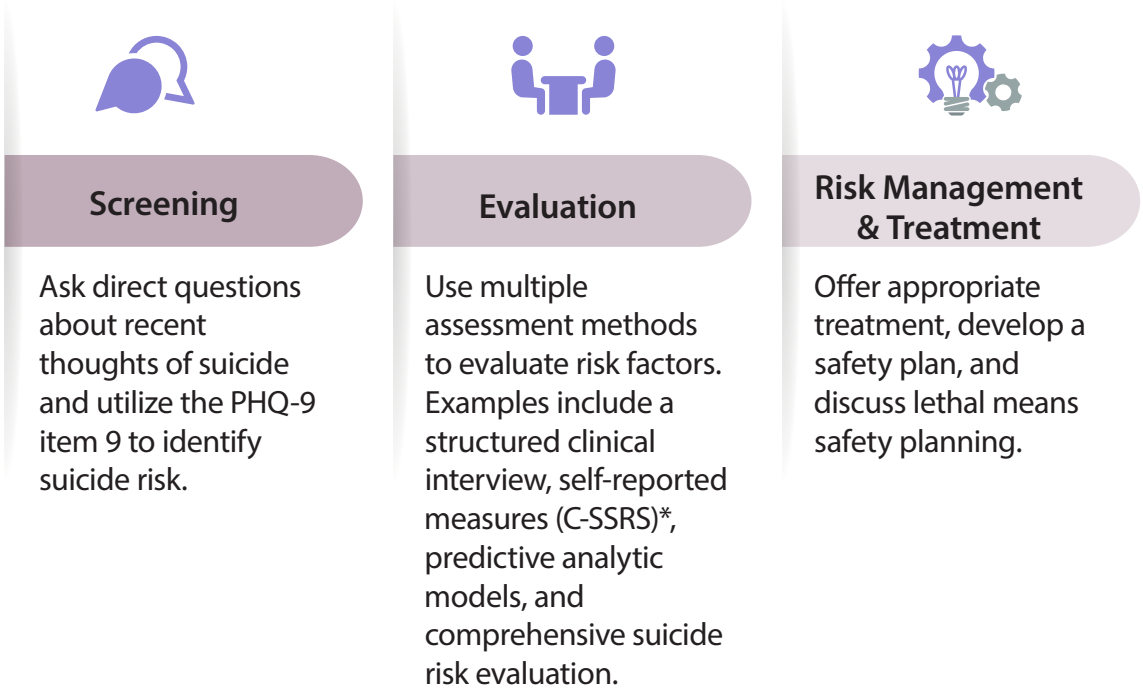
Identifying Suicidal Thoughts

All Veterans with a presumed diagnosis of MDD need to be assessed for acute safety risks (e.g., harm to self or others). Asking about suicide intentions does not increase the risk of suicide and should be done using non-judgmental, direct-questioning.[54]

A significant number of patients who die by suicide were seen by their primary care clinician in the month prior to their death.[52,53]

Primary care providers play important roles in identifying and assessing suicide risk. By taking the time to determine a Veteran's level of suicide risk, you can more confidently determine an individualized care plan for the Veteran. Not all Veterans with suicidal ideation will need to be admitted or even referred to a behavioral health clinician immediately.

Figure 14. Suicide Prevention Strategies[55]

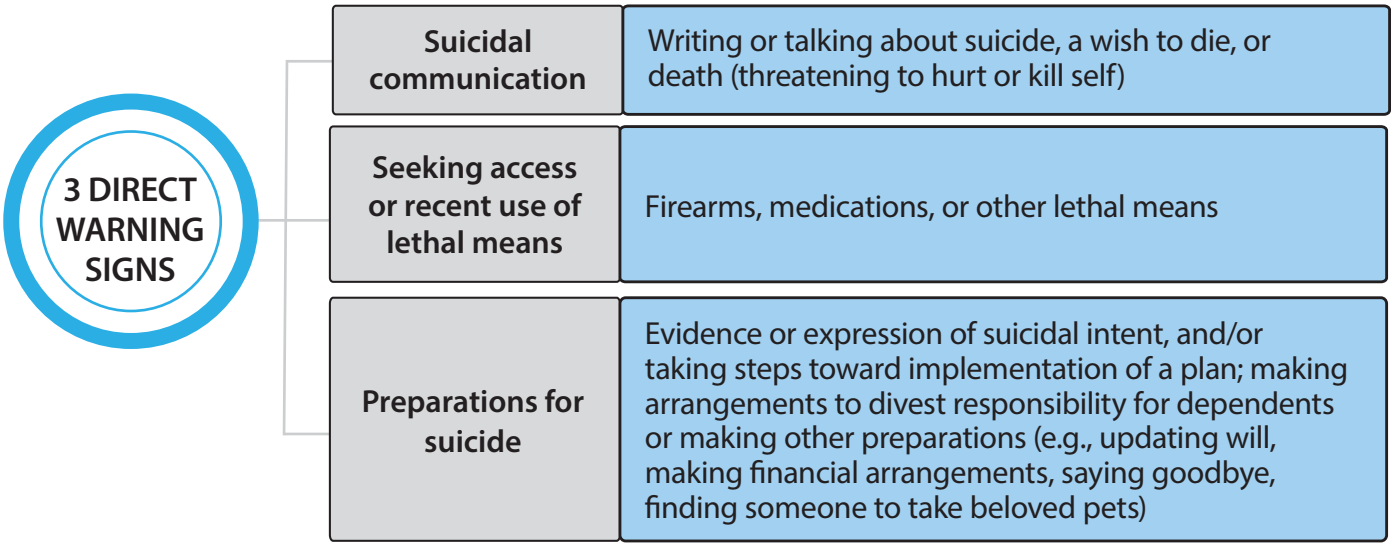


C-SSRS = Columbia-Suicide Severity Rating Scale; *Must be completed if PHQ-9 item 9 is positive.

Three direct warning signs (Figure 15) indicate the highest likelihood of suicidal behaviors occurring in the near future.

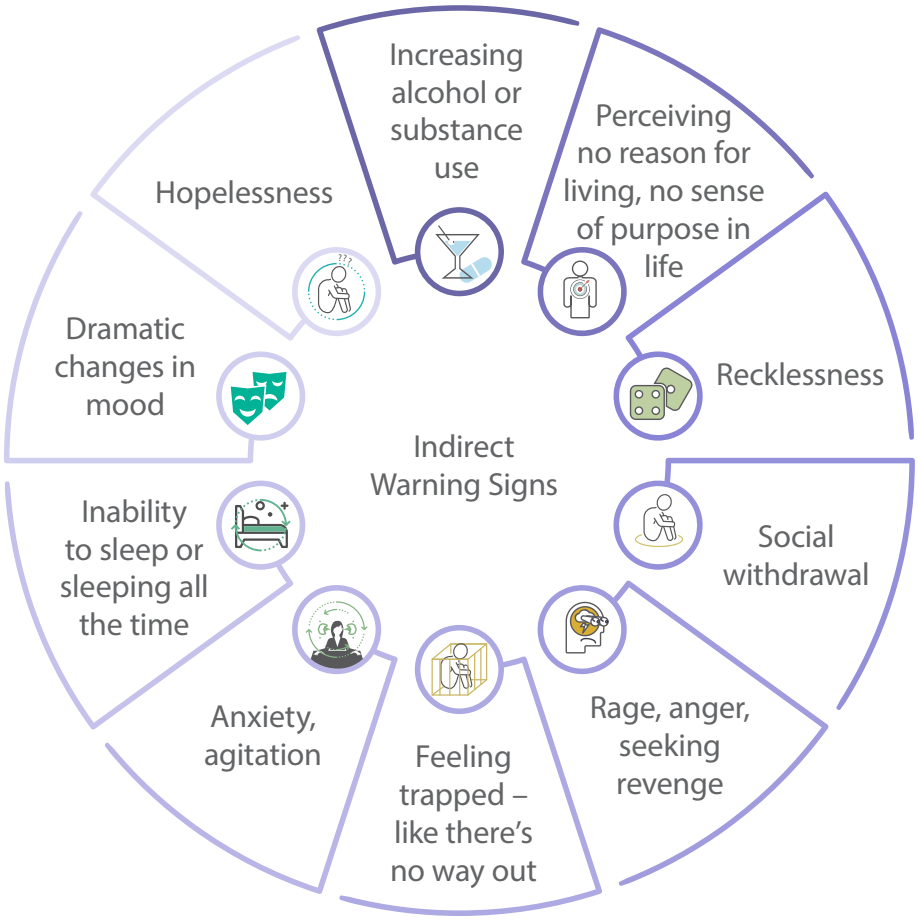
- Observing these warning signs warrants immediate attention (mental health evaluation, referral, or consideration of hospitalization) to ensure the safety, stability, and security of the individual.
- These signals may indicate an even more dangerous situation if the person has previously attempted suicide, has a family history of suicide, or intends to use and has access to a method that is lethal.

Figure 15. 3 Direct Warning Signs



Indirect warning signs are more subtle and they may indicate an increased risk for suicide and urgency to address.

Figure 16. Indirect Warning Signs



Recognize the presence of warning signs among Veterans.

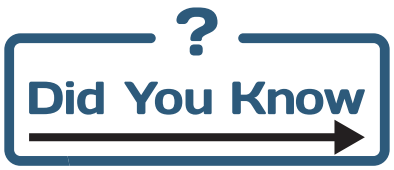
★ High Risk Individuals

Some high-risk individuals may not explicitly express or may attempt to conceal suicidal ideation, plans, or preparatory behavior no matter how we ask.

In situations like this, you may need to rely on objective observations, demonstrated behaviors, or consultation with a mental health professional (such as your local suicide prevention coordinator).

Lethal Means Safety Counseling

Help the Veteran understand that the risk for suicide sometimes escalates rapidly and can be triggered by any stressor (e.g., death of a family member, job loss, fight with a friend or family member). Not having access to lethal means quickly reduces bad outcomes in volatile situations.



The most common means for suicide among Veterans is a firearm.

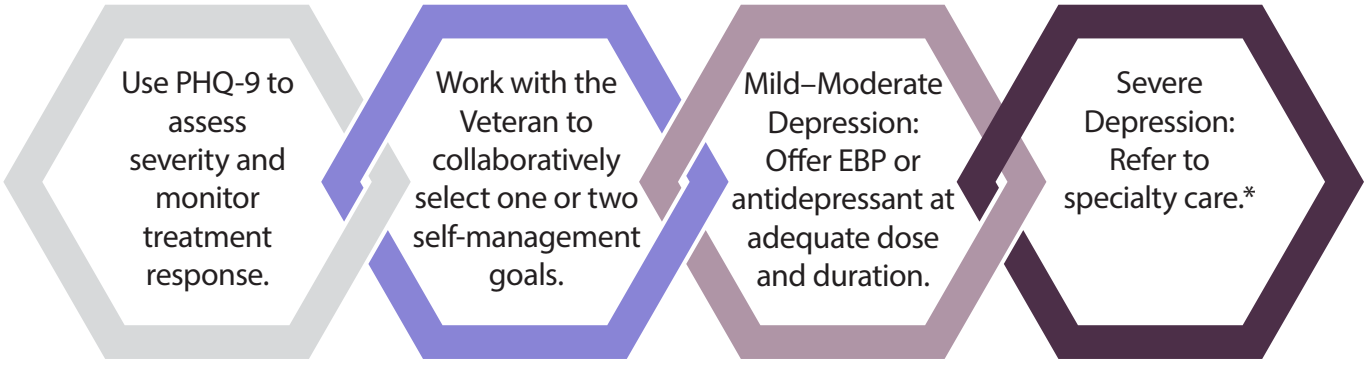
Lethal means counseling involves two primary actions:

- Identifying whether the Veteran has access to firearms or other lethal means
- Collaborating with the Veteran to limit their access until they are no longer feeling suicidal; You may need to encourage the Veteran to involve friends or family members to help limit access.

Screen, evaluate, and manage suicide risk in patients with depression.

Summary

- After diagnosing depression, offer treatment with psychotherapy and/or an antidepressant based on patient preference and severity of depression.
- Screen, evaluate, and manage suicide risk in patients with depression.



*Some Veterans are unwilling to go to specialty care. In these circumstances, it's important to leverage PCMHI.

This summary was written by:

Sarah J. Popish, Pharm.D., BCPP
Daina L Wells, Pharm.D., MBA, BCPS, BCPP
Julianne Himstreet, Pharm.D., BCPS

We thank our expert reviewers:

Bruce P. Capehart, MD
John F. Chardos, MD
Matthew A. Fuller, Pharm.D., BCPP, FASHP
Paul E. Holtzheimer, MD
Shawn Kohlhaas, Pharm.D., BCPP
Scott Pawlikowski, MD
Kimberly R. Schnacky, Pharm.D., BCPS, BCACP
Anna E. White, Pharm.D., BCPP
Ilse Wiechers, MD

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