VA/DoD clinical practice guideline for the management of major depressive disorder.

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Department of Veterans Affairs (VA) | Department of Defense (DoD) | Veterans Health Administration (VHA)

Management of Major Depressive Disorder Working Group. VA/DoD clinical practice guideline for the management of major depressive disorder. Version 4.0. Washington (DC): Department of Veterans Affairs, Department of Defense; 2022 Feb. 159 p. [229 references]

View Original Guideline

Overview

Guideline Objective

To provide an evidence-based framework for evaluating and managing care for adults (≥18 years) who have a Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) or International Classification of Diseases (ICD-9 or 10) diagnosis of major depressive disorder (MDD), including those with mild, moderate, and severe MDD, as well as those with chronic major depression diagnosed per DSM-5 criteria and those with persistent depressive disorder/chronic major depression per DSM-5 criteria

Patient Population

Adults (≥18 years) who have a DSM or ICD-9 or ICD-10 diagnosis of MDD who are eligible for care in the VA or DoD healthcare delivery systems

Note: This clinical practice guideline (CPG) also includes adults with MDD who have either partially responded or not responded to treatment for depression. This CPG does not address patients at risk for suicide or patients with post-stroke depression or bipolar disorder I/II, as recommendations for managing these patient populations are included in the *VA/DoD CPG for the Assessment and*

Management of Patients at Risk for Suicide, *VA/DoD CPG for the Management of Stroke Rehabilitation*, and the *VA/DoD CPG for the Management of Bipolar Disorder*.

Recommendations

Recommendation Statements

Screening

1. We suggest that all patients not currently receiving treatment for depression be screened for depression. (**Weak For; Not reviewed, Amended**)

   The Work Group's confidence in the quality of the evidence was **low**.

Monitoring Outcomes

2. For patients with major depressive disorder (MDD), we suggest using a quantitative measure of depression severity in the initial treatment planning and to monitor treatment progress at regular intervals to guide shared treatment decision making. (**Weak For; Reviewed, New-replaced**)

   The Work Group's confidence in the quality of the evidence was **very low**.

Treatment Setting

3. For patients with MDD who are being treated in the primary care setting, we recommend the use of collaborative/integrated care models. (**Strong For; Reviewed, Amended**)

   The Work Group's confidence in the quality of the evidence was **moderate**.

4. For patients with MDD, there is insufficient evidence to recommend for or against the use of a team-based model in specialty mental health care settings. (**Neither For nor Against; Reviewed, New-added**)

   The Work Group's confidence in the quality of the evidence was **very low**.

5. For patients with MDD, there is insufficient evidence to conclude that interventions delivered by clinicians using telehealth are either superior or inferior to in-person treatment. (**Neither For nor Against; Reviewed, New-added**)

   The Work Group's confidence in the quality of the evidence was **very low**.

Treatment of Uncomplicated MDD

6. We recommend that MDD be treated with either psychotherapy or pharmacotherapy as monotherapy, based on patient preference. Factors including treatment response, severity, and chronicity may lead to other treatment strategies such as augmentation, combination treatment, switching of treatments, or use of non-first line treatments (see Recommendations 17, 18, and 20, below). (**Strong For; Reviewed, New-replaced**)

   The confidence in the quality of evidence for specific treatment modalities was **very low** when looking at the range of outcomes considered in this evidence review (e.g., symptom improvement, remission rates).

7. When choosing psychotherapy to treat MDD, we suggest offering one of the following interventions (not rank ordered):

   - Acceptance and commitment therapy
   - Behavioral therapy/behavioral activation
   - Cognitive behavioral therapy
   - Interpersonal therapy
   - Mindfulness-based cognitive therapy
   - Problem-solving therapy
   - Short-term psychodynamic psychotherapy

   (**Weak For; Reviewed, New-replaced**)

   The confidence in the quality of the evidence was **very low**.

8. For patients who select psychotherapy as a treatment option, we suggest offering individual or group format based on patient preference. (**Weak For; Reviewed, Not changed**)

The Work Group's confidence in the quality of the evidence was **moderate**.

9. There is insufficient evidence to recommend for or against combining components from different psychotherapy approaches. (**Neither For nor Against; Reviewed, New-added**)

   The Work Group's confidence in the quality of the evidence was **very low**.

10. For patients with mild to moderate MDD, we suggest offering clinician-guided computer/internet-based cognitive behavioral therapy either as an adjunct to pharmacotherapy or as a first-line treatment, based on patient preference. (**Weak For; Reviewed, New-replaced**)

    The Work Group's confidence in the quality of the evidence was **low**.

11. When choosing an initial pharmacotherapy, or for patients who have previously responded well to pharmacotherapy, we suggest offering one of the following (not rank ordered):

    - Bupropion
    - Mirtazapine
    - A serotonin-norepinephrine reuptake inhibitor
    - Trazodone, vilazodone, or vortioxetine
    - A selective serotonin reuptake inhibitor

    (**Weak For; Reviewed, New-replaced**)

    The Work Group rated the quality of the evidence as **very low**.

12. When choosing an initial pharmacotherapy, we suggest against using:

    - Esketamine
    - Ketamine
    - Monoamine oxidase inhibitors
    - Nefazodone
    - Tricyclic antidepressants

    (**Weak Against; Reviewed, New-added**)

The Work Group rated the quality of the evidence as **very low**.

13. There is insufficient evidence to recommend for or against pharmacogenetic testing to help guide the selection of antidepressants. (**Neither For nor Against; Reviewed, New-added**)

    The Work Group's confidence in the quality of the evidence was **very low**.

14. For patients with mild to moderate MDD who decline pharmacotherapy and who decline or cannot access first-line evidence-based psychotherapies (either in-person or virtually), we suggest considering non-directive supportive therapy. (**Weak For; Not reviewed, Amended**)

    The Work Group's confidence in the quality of the evidence was **low**.

Treatment of MDD that is Severe or has a Partial or Limited Response to Initial Treatment

15. We suggest offering a combination of pharmacotherapy and evidence-based psychotherapy for the treatment of patients with MDD characterized as:

    - Severe (e.g., PHQ-9 >20)
    - Persistent major depressive disorder (duration greater than two years)
    - Recurrent (with two or more episodes)

    (**Weak For; Not reviewed, Amended**)

    The Work Group's confidence in the quality of the evidence was **very low**.

16. For patients with MDD who have demonstrated partial or no response to an adequate trial of initial pharmacotherapy, we suggest (not rank ordered):

    - Switching to another antidepressant (including tricyclic antidepressants [TCAs], monoamine oxidase inhibitors [MAOIs], or those in Recommendation 12)
    - Switching to psychotherapy
    - Augmenting with a psychotherapy
    - Augmenting with a second-generation antipsychotic

(**Weak For; Reviewed, Amended**)

The Work Group's confidence in the quality of the evidence was **low**.

17. For patients who have demonstrated partial or no response to two or more adequate pharmacologic treatment trials, we suggest offering repetitive transcranial magnetic stimulation for treatment. (**Weak For; Reviewed, Amended**)

    The Work Group's confidence in the quality of the evidence was **very low**.

18. There is insufficient evidence to recommend for or against theta-burst stimulation for the treatment of MDD. (**Neither For nor Against; Reviewed, New-added**)

    The Work Group's confidence in the quality of the evidence was **very low**.

19. For patients with MDD who have not responded to several adequate pharmacologic trials, we suggest ketamine or esketamine as an option for augmentation. (**Weak For; Reviewed, New-replaced**)

    The Work Group's confidence in the quality of the evidence was **low**.

20. We recommend offering electroconvulsive therapy (ECT) with or without psychotherapy for patients with severe MDD and any of the following conditions:

    - Catatonia
    - Psychotic depression
    - Severe suicidality
    - A history of a good response to ECT
    - Need for rapid, definitive treatment response on either medical or psychiatric grounds
    - The risks associated with other treatments are greater than the risks of ECT for this specific patient (i.e., co-occurring medical conditions make ECT the safest MDD treatment alternative)
    - A history of a poor response or intolerable side effects to multiple antidepressants

    (**Strong For; Reviewed, Not changed**)

    The Work Group's confidence in the quality of the evidence was **very low**.

Relapse Prevention/Continuation Phase (All Severities and Complexities)

21. For patients with MDD who achieve remission with antidepressant medication, we recommend continuation of antidepressants at the therapeutic dose for at least six months to decrease risk of relapse. (**Strong For; Not reviewed, Not changed**)

    The Work Group's confidence in the quality of the evidence was **moderate**.

22. For patients with MDD at high risk for relapse or recurrence (e.g., two or more prior episodes, unstable remission status), we suggest offering a course of cognitive behavioral therapy, interpersonal therapy, or mindfulness-based cognitive therapy during the continuation phase of treatment (i.e., after remission is achieved) to reduce the risk of subsequent relapse/recurrence. The evidence does not support recommending one of these three evidence-based psychotherapies over another. (**Weak For; Not reviewed, Amended**)

    The Work Group's confidence in the quality of the evidence was **low**.

Recommendations for Specific Populations

23. For individuals with mild to moderate MDD who are breastfeeding or pregnant, we recommend offering an evidence-based psychotherapy as a first-line treatment (see Recommendation 7, above). In patients with a history of MDD prior to pregnancy who responded to antidepressant medications, and are currently stable on pharmacotherapy, weigh risk/benefit balance to both mother and fetus in treatment decisions. (**Strong For; Not reviewed, Amended**)

    The Work Group's confidence in the quality of the evidence was **low**.

24. For older adults (≥65 years) with mild to moderate MDD, we suggest offering a first-line psychotherapy (see Recommendation 7, above). Patient preference and the additional safety risks of pharmacotherapy should be considered when making this decision. (**Weak For; Not reviewed, Amended**)

    The Work Group's confidence in the quality of the evidence was **low**.

25. For patients with mild to moderate MDD and significant relationship distress, we suggest offering couples-focused therapy. (**Weak For; Not reviewed, Amended**)

    The Work Group's confidence in the quality of the evidence was **low**.

26. For patients with mild to moderate MDD with or without a seasonal pattern (formerly seasonal affective disorder), we suggest offering light therapy. (**Weak For; Reviewed, New-replaced**)

    The Work Group's confidence in the quality of the evidence was **low**.

Self-help, Complementary, and Alternative Treatments

27. For patients with MDD, we suggest exercise (e.g., yoga, tai chi, qi gong, resistance, aerobics) as an adjunct. (**Weak For; Reviewed, New-replaced**)

    The Work Group's confidence in the quality of evidence was **very low**.

28. For patients with MDD, we suggest CBT-based bibliotherapy as an adjunct to pharmacotherapy or psychotherapy, or as an alternative when patients are unwilling or unable to engage in other treatments. (**Weak For; Reviewed, Amended**)

    The Work Group's confidence in the quality of the evidence was **low**.

29. For patients with mild MDD who are not pregnant or breastfeeding and who prefer herbal treatments to first-line psychotherapy or pharmacotherapy, we suggest standardized extract of St. John's wort as monotherapy. (**Weak For; Not reviewed, Amended**)

    The Work Group's confidence in the quality of the evidence was **moderate**.

30. For patients with MDD, there is insufficient evidence to recommend for or against acupuncture as an adjunct. (**Neither For nor Against; Reviewed, New-replaced**)

    The Work Group's confidence in the quality of the evidence was **low**.

31. For patients with MDD, there is insufficient evidence to recommend for or against the addition of biofeedback. (**Neither For nor Against; Reviewed, New-added**)

    The Work Group's confidence in the quality of the evidence was **very low**.

32. For patients with MDD, there is insufficient evidence for or against the use of meditation as an adjunct. (**Neither For nor Against; Reviewed, New-added**)

    The Work Group’s confidence in the quality of the evidence was **very low**.

Other Treatments with a Recommendation Against Use

33. For patients with MDD, we suggest against using vagus nerve stimulation outside of a research setting. (**Weak Against; Reviewed, Amended**)

    The Work Group's confidence in the quality of the evidence was **very low**.

34. For patients with MDD, we recommend against using deep brain stimulation outside of a research setting. (**Strong Against; Reviewed, Not changed**)

    The Work Group's confidence in the quality of the evidence was **low**.

35. Given the limited information on the safety and efficacy of psilocybin, MDMA, cannabis, and other unapproved pharmacologic treatments, we recommend against using these agents for MDD outside of a research setting. (**Strong Against; Reviewed, New-added**)

    The Work Group's confidence in the quality of the evidence was **very low**.

36. We suggest against using omega-3 fatty acids or vitamin D for treatment of MDD. (**Weak Against; Not reviewed, Not changed**)

    The Work Group's confidence in the quality of the evidence was **low**.

Evidence Rating Scheme

Quality of Evidence and Definitions*

High quality: Further research is very unlikely to change our confidence in the estimate of effect

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very low quality: Any estimate of effect is very uncertain

***** Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ, GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008 Apr 26;336(7650):924-6.

Recommendation Rating Scheme

The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework (refer to the original guideline), which incorporates the four domains. A *Strong* recommendation generally indicates *High* or *Moderate* confidence in the quality of the available evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient values and preferences, and understood influence of other implications (e.g., resource use, feasibility).

In some instances, there is insufficient evidence on which to base a recommendation for or against a particular therapy, preventive measure, or other intervention. For example, the systematic evidence review may have found little or no relevant evidence, inconclusive evidence, or conflicting evidence for the intervention. The manner in which this is expressed in the CPG may vary. In such instances, the Work Group may include among its set of recommendations a statement of insufficient evidence statement for an intervention that may be in common practice even though it is not supported by clinical evidence, and particularly if there may be other risks of continuing to use it (e.g., high opportunity cost, misallocation of resources). In other cases, the Work Group may decide to not include this type of statement about an intervention. For example, the Work Group may remain silent where there is an absence of evidence for a rarely used intervention. In other cases, an intervention may have a favorable balance of benefits and harms but may be a standard of care for which no recent evidence has been generated.

Using these elements, the Work Group determines the strength and direction of each recommendation and formulates the recommendation with the general corresponding text.

Recommendation Strength and Direction	**General Corresponding Text**
Strong For	"We recommend..."
Weak For	"We suggest..."
Neither For nor Against	"There is insufficient evidence to recommend for or against..."
Weak Against	"We suggest against..."

Recommendation Strength and Direction	General Corresponding Text
Strong Against	"We recommend against..."

It is important to note that a recommendation's strength (i.e., *Strong* versus *Weak*) is distinct from its clinical importance (e.g., a *Weak* recommendation is evidence-based and still important to clinical care).

Recommendation Categories and Definitions

Recommendation categories were used to track how the previous CPG's recommendations could be reconciled. These categories and their corresponding definitions are similar to those used by the National Institute for Health and Care Excellence (NICE). The table below lists these categories, which are based on whether the evidence supporting a recommendation was systematically reviewed, the degree to which the previous CPG's recommendation was modified, and whether a previous CPG's recommendation is relevant in the updated CPG. Refer to Appendix A of the original guideline for further details on recommendation categorization.

Evidence Reviewed	Recommendation Category	Definition
Reviewed[a]	New-added	New recommendation
	New-replaced	Recommendation from previous CPG was carried and revised
	Not changed	Recommendation from previous CPG was carried forward but not changed
	Amended	Recommendation from previous CPG was carried forward with a nomial change
	Deleted	Recommendation from previous CPG was deleted

Not reviewed[b]	Not changed	Recommendation from previous CPG was carried forward but not changed
	Amended	Recommendation from previous CPG was carried forward with a nomial change
	Deleted	Recommendation from previous CPG was deleted

Adapted from: The guidelines manual. London (UK): NICE; 2012 & Martinez Garcia L, et al. Updated recommendations: An assessment of NICE clinical guidelines. Implement Sci. 2014;9:72.

a The topic of this recommendation was covered in the evidence review carried out as part of the development of the current CPG.

b The topic of this recommendation was not covered in the evidence review carried out as part of the development of the current CPG.

Related Content

Supporting Documents

No supporting documents available.

Implementation Tools

- Provider Summary; 2022 Feb.
- Pocket Card; 2022 Feb.
- The Original Guideline includes the following:
    - Module A: Initial Assessment and Treatment (p. 17)
    - Module B: Advanced Care Management (p. 21)
    - Appendix I: Quick Guide to the Patient Health Questionnaire in Clinical Practice (p. 127)
    - Appendix J: Pharmacotherapy (p. 132)
    - Appendix K: Definitions of Major Depressive Disorder and Treatments (p. 140)

Patient Education

- Patient Summary; 2016 Apr.
- Understanding Depression: A Resource for Providers and Patients; 2016 Dec.
- Depression: Facts for Families; 2016 Dec.

Note: This patient information is intended to help patients better understand their health and their diagnosed disorders. Patients and their representatives should still consult with a licensed health care professional for evaluation of treatment options as well as answers to their personal medical questions.

Disclaimer

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ECRI's Guideline Profiles are designed to provide information and assist decision-making. Variations in practice will inevitably, and appropriately, occur when clinicians take into account the needs and preferences of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional using these Guideline Profiles is responsible for evaluating the appropriateness of applying them in a clinical setting.

TRUST Scorecard

Composition of Guideline Development Group (GDG)

Multidisciplinary GDG Members	**Yes**
Methodologist Involvement	**Yes**
Incorporation of Patient and Public Perspective	★★★★★

Systematic Review of Evidence

Literature Search	★★★★★
Study Selection	★★★★★
Evidence Synthesis	★★★★★

Foundations for Recommendations

Strength of Evidence Grade	★★★★★
Description of Benefits and Harms of Recommendations	★★★★★
Summary of Evidence Supporting Recommendations	★★★★★
Strength of Recommendations Rating	★★★★★
Clear Articulation of Recommendations	★★★★☆

Funding Source — **Yes**

Disclosure and Management of Financial Conflicts of Interests — ★★★★★

External Review — ★★★★☆

Updating — ★★★★★

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