

## **Major Depression**

### **MAJOR RECOMMENDATIONS (from National Guidelines Clearinghouse)**

Recommendations are identified as either "evidence-based (A-D, I)" or "consensus-based." For definitions of the levels of recommendations see the end of the "Major Recommendations" field.

#### **I. First-Line Treatment Of Major Depressive Disorder (MDD)**

For patients with mild to moderate Major Depressive Disorder (MDD), use either antidepressant medication or psychotherapy<sup>1</sup> as first-line treatment.

##### ***Evidence-based***

Given the lack of evidence on a clearly superior approach for mild to moderate MDD, treatment decisions should be based on patient and clinician preference, potential side effects, and cost.

##### ***Consensus-based***

For patients with severe or chronic MDD, combined treatment with antidepressants and psychotherapy<sup>1</sup> is recommended as first-line treatment.

##### ***Evidence-based***

If antidepressants are to be used, any class of antidepressant (selective serotonin reuptake inhibitor [SSRI], tricyclic antidepressant [TCA], serotonin norepinephrine reuptake inhibitor [SNRI], norepinephrine reuptake inhibitor [NRI], or dopamine agonist [DA]) can be prescribed as first-line treatment of MDD.

##### ***Evidence-based***

Given the equivalence of therapeutic effect, base the choice of antidepressant on patient's prior response, patient and clinician preference, potential side effects, and cost.

##### ***Consensus-based***

#### **II. St. John's Wort for MDD**

For patients with mild to moderate Major Depression, there is insufficient evidence to recommend for or against hypericum as a treatment alternative. The evidence on hypericum (St. John's Wort) in mild to moderate Major Depression is conflicting and of questionable quality. The balance of benefits, harms, and costs compared with other treatments cannot be fully determined.

##### ***Evidence-based (I)<sup>2</sup>***

For patients with severe Major Depression, hypericum (St. John's Wort) is not recommended.

##### ***Evidence-based***

#### **III. Antidepressants In Patients With MDD Expressing Suicidal Ideation, Intent, Or Plan**

For patients with Major Depression expressing suicidal intent or plan, consultation with specialty behavioral health is recommended.

***Consensus-based***

For patients with suicidal ideation or who have made previous suicide attempts, consult or collaborate with a psychiatrist before prescribing tricyclic antidepressants (TCAs) or venlafaxine.

***Consensus-based***

#### IV. **Second-Line Treatment Of MDD**

For patients with MDD whose symptoms fail to remit after first line treatment, assess adherence to the initial treatment regimen.

***Consensus-based***

For patients with MDD whose symptoms fail to remit after adherence to first-line treatment, second-line treatment options include:

- Combining antidepressants and psychotherapy. ***Evidence-based***
- Increasing the dose of the initial antidepressant. ***Consensus-based***
- Combined treatment with selective serotonin reuptake inhibitors (SSRIs) and low-dose desipramine (monitoring for TCA toxicity). ***Consensus-based***
- Switching to a different antidepressant of the same or different class. ***Consensus-based***
- Augmenting with low dose (300 to 600 mg/day) of lithium (in consultation with psychiatry). ***Consensus-based***
- Switching from psychotherapy to antidepressants or antidepressants to psychotherapy. ***Consensus-based***

For patients whose MDD symptoms fail to remit after adhering to first-line treatment, there is insufficient evidence to recommend the following treatments:

- Right prefrontal transcranial magnetic stimulation (rTMS).
- Folate
- Inositol
- Vagus nerve stimulation

***Evidence-based (I)***

For patients with (non-psychotic) MDD whose symptoms fail to remit after adherence to first-line treatment, augmentation with atypical antipsychotic agents is not recommended.

***Evidence-based***

For patients with MDD whose symptoms fail to remit after adherence to first-line treatment, augmentation with pindolol is not recommended.

***Evidence-based***

**V. Length Of Treatment With Antidepressants In Patients With MDD**

Patients with MDD who achieve **symptom remission** with antidepressants should continue antidepressants at the same dose for at least an additional six to 12 months.

*Evidence-based*

**Patients With One Lifetime Episode of MDD**

Based on patient and provider preference, a trial of antidepressant discontinuation is optional for patients in their first lifetime episode of MDD, who are being treated with antidepressants, achieve remission, and remain asymptomatic for six to 12 months after acute phase treatment.

*Consensus-based*

**Patients with Two or More Lifetime Episodes of MDD**

Patients with two or more lifetime episodes of MDD, who are being treated with antidepressants and remain asymptomatic after acute phase treatment, should be maintained on the medication and dose with which they achieved remission for at least an additional 15 months to five years after acute phase treatment.

*Consensus-based*

**Patients with Chronic MDD or MDD with concurrent Dysthymia**

Patients with chronic MDD (continual symptoms for more than two years) or Double Depression (MDD and dysthymia) who improve with antidepressants during acute phase treatment should continue antidepressants for at least an additional 15 to 28 months after acute phase treatment.

*Evidence-based*

**VI. Follow-Up For Patients In The First Three Months (Acute Phase) Of Treatment For MDD**

For patients who are starting treatment with antidepressants for Major Depression, the minimum recommended follow-up frequency is one patient contact<sup>3</sup> within the first month, and at least one additional patient contact four to eight weeks after the first contact.

*Consensus-based*

Assess for adherence, side effects, suicidal ideation, and patient response during both these visits.

*Consensus-based*

**Follow-Up For Asymptomatic Patients In Continuation Phase (Months Four To 12) Of Treatment Of MDD**

After achieving symptom remission, at least one follow-up contact<sup>4</sup> is recommended during the fifth or sixth month of treatment in patients with Major Depression. Assess for continuing symptom remission and dosage/treatment adjustment during this contact.

*Consensus-based*

Additional patient follow-up is recommended to consider either continuing treatment beyond the continuation phase, or attempting a trial of treatment discontinuation.

*Consensus-based*

**VIII. Follow-Up For Asymptomatic Patients With Major Depression In Maintenance Phase (Beyond 12 Months) Of Treatment Of MDD**

For asymptomatic patients with Major Depression who are continuing on antidepressants beyond 12 months, at least one annual follow-up contact<sup>5</sup> is recommended to assess for continuing symptom remission, the need for ongoing treatment, and dosage/treatment adjustment.

*Consensus-based*

Additional follow-up for asymptomatic patients with Major Depression who are continuing on antidepressants beyond 12 months should be based on patient preference and response.

*Consensus-based*

**IX. Discontinuation Of Antidepressants In Patients With MDD**

Fluoxetine may be discontinued without tapering with a relatively low risk of adverse effects.

*Evidence-based*

Taper other antidepressants (other selective serotonin reuptake inhibitors, tricyclic antidepressants, serotonin norepinephrine reuptake inhibitors, norepinephrine reuptake inhibitors, or dopamine agonists) over a two to four week period.

*Consensus-based*

**X. Treatment Preferences For MDD In Different Ethnic Groups**

Because patient preferences for treatment may vary based on their ethnicity and culture, asking patients from different ethnic groups about treatment preference is recommended when discussing treatment options for MDD.

*Evidence-based*

**XI. Patient Self-Management Strategies For Improving Depressive Symptoms In MDD**

**Exercise** is recommended as an adjunctive strategy (in addition to antidepressants or psychotherapy) for treating the symptoms of MDD.

*Consensus-based*

**Bibliotherapy** is an optional adjunct strategy (in addition to antidepressants or psychotherapy) for treating the symptoms of MDD.

*Consensus-based*

Patient self-help materials on selected **internet-sites**<sup>6</sup> are an optional adjunct strategy (in addition to antidepressants or psychotherapy) for treating symptoms of MDD.

*Evidence-based*

**Befriending** is an optional adjunct to antidepressants or psychotherapy for treating the symptoms of MDD.

*Consensus-based*

Use of **automated telephone programs** is not recommended as adjunctive therapy for MDD.

*Evidence-based*

There is currently insufficient evidence to recommend **light therapy** as a primary or adjunctive treatment for non-seasonal forms of MDD.

*Evidence-based (I)*

There is insufficient evidence to recommend for or against **music therapy** as an adjunct to antidepressants or psychotherapy for treating the symptoms of MDD.

*Evidence-based (I)*

There is insufficient evidence to recommend for or against **life review therapy** as an optional adjunctive depression management strategy for depressed older adult patients who are concurrently receiving regular social services care.

*Evidence-based (I)*

## XII. **Behavioral Health Education Classes (Cognitive Behavioral Skills or Problem-Solving Classes) for Adults with MDD**

For patients with mild to moderate MDD, behavioral health education classes are an adjunctive treatment option, but should not be used in lieu of either antidepressant medication or psychotherapy.

*Evidence-based*

<sup>1</sup> (Interpersonal Therapy, Cognitive Behavioral Therapy, and Problem-Solving Therapy)

<sup>2</sup> Please note that only recommendations approved since the adoption in 2006 of evidence grading will use letters (A, B, C, etc.) to specify the grade of the evidence. Recommendations approved prior to 2006 will not include a letter grade following the statement "evidence-based." For additional information on evidence grading, see Table 1 on page 181 of the original guideline document.

<sup>3</sup> Contact may include in-person visits, phone calls or email between patient and clinician, or phone calls/email between patient and a care manager. The use of email between patients and providers is relatively new, and has not been a widely utilized means of communication to date. However, it is being increasingly advocated as part of a patient-centered, more efficient ("less visit dependent") model of care. At least one member of the Guideline Development Team uses this modality regularly and deems it effective for follow-up contacts.

<sup>4</sup> Contact may include in-person visits, phone calls or email between patient and clinician, or phone calls/email between patient and a care manager.

<sup>5</sup> Follow-up contact may include in-person visits, phone calls or email between patient and clinician, or phone calls/email between patient and a care manager. The use of email

between patients and providers is relatively new, and has not been a widely utilized means of communication to date. However, it is being increasingly advocated as part of a patient-centered, more efficient ("less visit dependent") model of care. At least one member of the Guideline Development Team uses this modality regularly and deems it effective for follow-up contacts.

<sup>6</sup> Evidence at this time is limited to the following internet sites: Blue Pages, Mood GYM, and ODIN.

**Definitions:**

Recommendations are classified as either "evidence-based (A-D, I)" or "consensus-based."

- Evidence-based: sufficient number of high-quality studies from which to draw a conclusion, and the recommended practice is consistent with the findings of the evidence. A recommendation can also be considered "evidence-based" if there is insufficient evidence and no practice is recommended.
- Consensus-based: insufficient evidence and a practice is recommended based on the consensus or expert opinion of the Guideline Development Team.

**Label and Language of Recommendations\***

<b>Label</b>	<b>Evidence-Based Recommendations</b>
<b>Evidence-based (A)</b>	<p><b>Language:</b> <sup>a</sup> The intervention is strongly recommended for eligible patients.</p> <p><b>Evidence:</b> The intervention improves important health outcomes, based on good evidence, and the Guideline Development Team (GDT) concludes that benefits substantially outweigh harms and costs.</p> <p><b>Evidence Grade:</b> Good.</p>
<b>Evidence-based (B)</b>	<p><b>Language:</b> <sup>a</sup> The intervention is recommended for eligible patients.</p> <p><b>Evidence:</b> The intervention improves important health outcomes, based on 1) good evidence that benefits outweigh harms and costs; or 2) fair evidence that benefits substantially outweigh harms and costs.</p> <p><b>Evidence Grade:</b> Good or Fair.</p>
<b>Evidence-based (C)</b>	<p><b>Language:</b> <sup>a</sup> No recommendation for or against routine provision of the intervention. (At the discretion of the GDT, the recommendation may use the language "option," but must list all the equivalent options.)</p>

<b>Label</b>	<b>Evidence-Based Recommendations</b>
	<p><b>Evidence:</b> Evidence is sufficient to determine the benefits, harms, and costs of an intervention, and there is at least fair evidence that the intervention improves important health outcomes. But the GDT concludes that the balance of the benefits, harms, and costs is too close to justify a general recommendation.</p> <p><b>Evidence Grade:</b> Good or Fair.</p>
<b>Evidence-based (D)</b>	<p><b>Language:</b> <sup>a</sup> Recommendation against routinely providing the intervention to eligible patients.</p> <p><b>Evidence:</b> The GDT found at least fair evidence that the intervention is ineffective, or that harms or costs outweigh benefits.</p> <p><b>Evidence Grade:</b> Good or Fair.</p>
<b>Evidence-based (I)</b>	<p><b>Language:</b> <sup>a</sup> The evidence is insufficient to recommend for or against routinely providing the intervention. (At the discretion of the GDT, the recommendation may use the language "option," but must list all the equivalent options.)</p> <p><b>Evidence:</b> Evidence that the intervention is effective is lacking, of poor quality, or conflicting and the balance of benefits, harms, and costs cannot be determined.</p> <p><b>Evidence Grade:</b> Insufficient.</p>
<b>Consensus-based</b>	<p><b>Language:</b> <sup>a</sup> The language of the recommendation is at the discretion of the GDT, subject to approval by the National Guideline Directors.</p> <p><b>Evidence:</b> The level of evidence is assumed to be "Insufficient" unless otherwise stated. However, do not use the A, B, C, D, or I labels which are only intended to be used for evidence-based recommendations.</p> <p><b>Evidence Grade:</b> Insufficient, unless otherwise stated.</p>
<p>For the rare consensus-based recommendations which have "Good" or "Fair" evidence, the evidence must support a different recommendation, because if the evidence were good or fair, the recommendation would usually be evidence-based. In this kind of consensus-based recommendation, the evidence</p>	

Label	Evidence-Based Recommendations
	grade should point this out (e.g., "Evidence Grade: Good, supporting a different recommendation)."

<sup>[a]</sup> All statements specify the population for which the recommendation is intended.

\*Recommendations should be labeled and given an evidence grade. The evidence grade should appear in the rationale. Evidence is graded with respect to the degree it supports the specific clinical recommendation. For example, there may be good evidence that Drugs 1 and 2 are effective for Condition A, but no evidence that Drug 1 is more effective than Drug 2. If the recommendation is to use either Drug 1 or 2, the evidence is good. If the recommendation is to use Drug 1 in preference to Drug 2, the evidence is insufficient.

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