First-Line Treatment of MDD

- For patients with mild to moderate Major Depressive Disorder (MDD), use either antidepressant medication or psychotherapy* as first-line treatment.
  * (Interpersonal Therapy, Cognitive Behavioral Therapy, or Problem-Solving Therapy)

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

- For patients with severe or chronic MDD, combine antidepressant use and psychotherapy* as first-line treatment.

- If antidepressants are used, any class of antidepressant (SSRI, TCA, SNRI, NRI, or DA) may be prescribed as first-line treatment.

- 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.

Hypericum (St. John’s Wort)

- Do not use hypericum (St. John’s wort) as treatment for severe MDD.

- In patients with mild to moderate MDD there is fair evidence of effectiveness of hypericum in this population. However, due to lack of consistency of preparation oversight and dosage across trials, and concerns about lack of FDA oversight and consistency of hypericum preparations, the balance of benefits, harms, and costs compared with other treatments cannot be determined.

Suicidal Ideation, Intent, or Plan

- For patients with MDD expressing suicidal intent or plan, consult with specialty behavioral health.

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

Second-Line Treatment of MDD

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

- For patients with MDD whose symptoms fail to remit after adherence to first-line treatment, the following treatments are options:
  - Combining antidepressants and psychotherapy,
  - Increasing the dose of the initial antidepressant,
  - Switching to a different antidepressant of the same or different class,
  - Switching from psychotherapy to antidepressants or antidepressants to psychotherapy,
  - Combined pharmacologic treatment (monitoring for toxicity, side effects and drug interactions) with SSRIs and:
    - low-dose TCAs, or
    - bupropion, or
    - buspirone, or
    - mirtazepine, or
    - lithium, or
    - liothyronine (T3).

- There is insufficient evidence for or against providing folate or inositol to patients whose MDD symptoms fail to remit after adhering to first-line treatment.

- There is insufficient evidence for or against providing atypical antipsychotics to primary care patients with (nonpsychotic, nonbipolar) MDD whose symptoms fail to remit after adherence to first-line treatment.

There is fair evidence of short-term effectiveness for use of atypical antipsychotic agents to augment antidepressants in patients with nonpsychotic, nonbipolar MDD who fail to remit after initial treatment. However, due to lack of longer-term data, known cardiometabolic risks of treatment with these medications, and lack of comparison data against other strategies, the balance of benefits, harms and costs compared with other treatments cannot be determined.

- Do not provide augmentation with pindolol for patients with MDD whose symptoms fail to remit after adherence to first-line treatment.
Length of Treatment With Antidepressants

Patients Who Achieve Symptom Remission

• 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.

Patients With One Lifetime Episode of MDD

• A trial of antidepressant discontinuation is an option, based on patient and provider preference, 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.

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.

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.

Acute Phase (First Three Months) Follow-up

• For patients who are starting treatment with antidepressants for MDD, the minimum follow-up frequency is one patient contact* within the first month, and at least one additional patient contact four to eight weeks after the first contact.

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

Continuation Phase (Months Four To 12) Follow-up

• After achieving symptom remission, conduct at least one follow-up contact* during the fifth or sixth month of treatment in patients with MDD. Assess for continuing symptom remission and dosage/treatment adjustment during this contact. Additionally, consider either continuing treatment beyond the continuation phase, or attempting a trial of treatment discontinuation.

Maintenance Phase (Beyond 12 Months) Follow-up

• For asymptomatic patients with MDD who are continuing on antidepressants beyond 12 months, conduct at least one annual follow-up contact* to assess for continuing symptom remission, the need for ongoing treatment, and dosage/treatment adjustment.

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

* 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.

Discontinuation of Antidepressants

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

• Other antidepressants (other SSRIs, TCAs, SNRIs, NRIs, and DAs) should be tapered over a two to four week period.

Treatment Preferences

• Because patient preferences for treatment may vary based on their ethnicity and culture, ask patients from different ethnic groups about treatment preference when discussing treatment options for MDD.
Patient Self-Management Strategies

Exercise
• Exercise is an adjunctive strategy (in addition to antidepressants or psychotherapy) for treating MDD.

Internet Resources
• Selected internet-based patient self-help materials may be used as an optional adjunct strategy (in addition to antidepressants or psychotherapy) for treating MDD.

Bibliotherapy
• Selected bibliotherapy† may be used as an optional adjunct strategy (in addition to antidepressants or psychotherapy) for treating MDD.
† Bibliotherapy: Advising people to read specific written material based on cognitive-behavioral approaches to depression treatment.

Befriending
• Befriending‡ is an optional adjunct strategy to antidepressants or psychotherapy for treating MDD.
‡ Befriending: Consists of a designated befriender who meets the depressed person to talk and socialize with for at least one hour per week.

Patient-Initiated Combined Phone/Computer Programs
• There is insufficient evidence for or against using patient-initiated combined phone/computer programs in the treatment of MDD.

Light Therapy
• There is insufficient evidence for or against using light therapy as a primary or adjunctive treatment for non-seasonal forms of MDD.

Music Therapy
• There is insufficient evidence for or against using music therapy in the treatment of MDD.

Life Review Therapy
• There is insufficient evidence for or against using life review therapy in the treatment of MDD.

Behavioral Health Education Classes
• For patients with mild to moderate MDD, behavioral health education classes are an adjunctive treatment option; however, these classes should not be used in lieu of either antidepressant medication or psychotherapy.

Pregnancy
• Do not start paroxetine in women who are pregnant.
• Use caution in starting other selective serotonin re-uptake inhibitors (SSRIs) in women who are pregnant.
  – Discuss risks to the mother and fetus of untreated maternal depression, as well as the risk of fetal adverse effects from antidepressants.
• If drug therapy is a consideration for treatment of maternal MDD during pregnancy and/or breastfeeding, then:
  – Individualize according to patient history and need for medication, and
  – Discuss the benefits and harms of the various treatment options with the patient.
• If MDD is in remission and a woman becomes pregnant while taking antidepressants during the continuation or maintenance phase of treatment, then:
  – Discuss the risks to the mother and fetus of untreated maternal depression or depression relapse after antidepressant discontinuation, as well as the risk of fetal adverse effects from continuing antidepressants, and
  – Monitor for first trimester fetal malformations if taking paroxetine. Consult OB/GYN for considerations on fetal malformation screening.

Breastfeeding
• Do not start fluoxetine and/or citalopram in breastfeeding women in most circumstances. If used, they should be used with caution, and only in patients who had good results with these medications during pregnancy or a previous depression episode.
• In women taking antidepressants during pregnancy whose depression is in remission and who desire to breastfeed:
  – Discuss the risks to the mother and fetus of untreated maternal depression or depression relapse after antidepressant discontinuation and the risk of adverse effects in the nursing newborn of mothers continuing antidepressants, and
  – Consider changing the treatment for depression if the newborn shows potential antidepressant-related adverse effects.