**Sidebar 1: Risk Assessment and Work-up**

- Functional status, medical history, past treatment history, and relevant family history
- Consider administration of PHQ-9
- Evaluate for suicidal and homicidal ideation and history of suicide attempts, and consult the VA/DoD Assessment and Management of Patients at Risk for Suicide CPG, as appropriate
- Rule out depression secondary to other causes (e.g., hypothyroidism, vitamin B-12 deficiency, syphilis, pain, chronic disease)
- Incorporate MBC principles in the initial assessment

**Sidebar 2: DSM-5 Criteria**

**Criterion A:** Five or more of the following symptoms present during the same 2-week period; at least one of the symptoms is either (1) depressed mood or (2) loss of interest/pleasure:
- Depressed mood most of the day, nearly every day
- Markedly diminished interest or pleasure in almost all activities most of the day, nearly every day
- Significant weight loss when not dieting or weight gain
- Insomnia or hypersomnia nearly every day
- Fatigue or loss of energy every day
- Feelings of worthlessness or excessive inappropriate guilt
- Diminished ability to think, concentrate, or indecisiveness, nearly every day
- Recurrent thought of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

**Criterion B:** The symptoms cause significant distress or functional impairment

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

**Sidebar 3: Factors to be Considered in Treatment Choice**

- Prior treatment response
- Severity (e.g., PHQ-9)
- Chronicity
- Comorbidity (e.g., substance use, medical conditions, other psychiatric conditions)
- Suicide risk
- Psychosis
- Catatonic or melancholic features
- Functional status

**Sidebar 4: Considerations in Treatment of Uncomplicated MDD**

- For initial treatment, select pharmacotherapy, psychotherapy, or both based on SDM
- If previous treatment was successful, consider restarting this approach
- Based on patient preferences, consider self help with exercise (e.g., yoga, tai chi, qi gong, resistance, aerobics), light therapy, patient education, and bibliotherapy
- Include patient characteristics (e.g., treatment of co-occurring conditions, pregnant patients, geriatric patients) in SDM
- Consider collaborative care in primary care for appropriate patients

Access to the full guideline and additional resources is available at: [https://www.healthquality.va.gov/](https://www.healthquality.va.gov/).
Sidebar 5: Treatment Options for Patients Who Have Not Responded to Adequate Treatment Trials*

Consider the following treatment options:
- Consider other pharmacotherapy options (e.g., MAOIs, TCAs) (see Recommendation 16)
- ECT (see Recommendation 20)
- rTMS (see Recommendation 17)
- Ketamine/esketamine (see Recommendation 19)

*Patients who have demonstrated partial or no response to initial pharmacologic monotherapy (maximized) after a minimum of four to six weeks of treatment

Sidebar 6: Treatment Options for Switching or Augmenting

Consider the following treatment options:
- Adding psychotherapy or pharmacotherapy
- Switching to a different treatment (e.g., switch between psychotherapy or pharmacotherapy, switch to a different focus of psychotherapy or different antidepressant)
- Augmenting with a different class of medication (e.g., adding an SGA)

Abbreviations: CBT: cognitive behavioral therapy; CPG: clinical practice guideline; DoD: Department of Defense; DSM-5: Diagnostic and Statistical Manual of Mental Disorders, 5th edition; ECT: electroconvulsive therapy; MAOI: monoamine oxidase inhibitor; MBC: measurement-based care; MDD: major depressive disorder; MH: mental health; PHQ-9: Patient Health Questionnaire-9; rTMS: repetitive transcranial magnetic stimulation; SDM: shared decision-making; SGA: second-generation antipsychotics; TCA: tricyclic antidepressant; VA: Department of Veterans Affairs