Optum

Optum Behavioral Health Solutions
Evidence-Based Practices

Major Depressive Disorder

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Major Depressive Disorder Description

Major Depressive Disorder is characterized by discrete episodes of at least a 2-week duration (although most episodes last considerably longer) involving clear-cut changes in affect, cognition, and neurovegetative functioning and inter-episode remissions. A diagnosis based on a single episode is possible, although the disorder is a recurrent one in the majority of cases. Careful consideration is given to the delineation of normal sadness and grief from a major depressive episode. Bereavement may induce great suffering, but it does not typically induce an episode of major depressive disorder.

More than 40 percent of patients who recover from an initial episode will experience a recurrence within two years. After two episodes, the risk of recurrence within five years is approximately 75 percent. Response to the treatment of depression is often described in phases. Response is the reduction of symptoms by a clinically meaningful, specified amount usually defined as an improvement score of fifty percent using a specific rating scale. Partial response (30-50%), non-response (less than 30%), remission (cut-off according to rating scale scores), recovery (symptom remission 8-24 weeks), relapse (return of symptoms) and recurrence (new episode) are also considered response phases of treatment. The acute, continuation and maintenance phases of treatment impacting response are addressed in evidence-based interventions.

Depressive disorders rank 13th worldwide as a cause of disability and mortality, with a lifetime prevalence of 12 percent. In the United States, major depression ranks 2nd among all diseases and injuries as a cause of disability. Most adults with clinically significant depression visit a primary care clinician rather than a psychiatrist, and 50 percent of patients are not screened or assessed for depression by their health care providers. Focused screening and evaluation is necessary to identify major depressive disorder.

Evaluation and Diagnosis

Evaluation

Clinical evaluation should consider the following:

- The history of the present symptoms should be obtained from the patient and may often involve others such as family members or other clinicians. Issues of patient confidentiality and consent must be recognized when sources other than the patient are considered.
- The presence of depressive symptoms in context should be established:
    - Depressed mood most of the day
    - Loss of interest or pleasure in most or all activities

- Insomnia or hypersomnia
- Significant weight loss or weight gain (e.g., 5 percent within a month) or decrease or increase in appetite nearly every day
- Psychomotor retardation or agitation nearly every day that is observable by others
- Fatigue or low energy
- Decreased ability to concentrate, think, or make decisions
- Thoughts of worthlessness or excessive or inappropriate guilt
- Recurrent thoughts of death or suicidal ideation, or a suicide attempt

- Determine the chronology of the current depressive symptoms and any prior history of depressive episodes and their course and treatment.
- Determine the impact of the depressive episode upon occupational and interpersonal functioning.
- Elicit contributing factors, including stressful life events and social or occupational circumstances.
- Assessment of comorbid psychiatric and medical conditions that are common in combination or in place of major depressive disorder.
    - Depressed children may be more likely to suffer comorbid ADHD and separation anxiety disorder, whereas depressed adolescents appear to be more vulnerable to substance use disorders.
    - Include questions about a history of mania or hypomania. Bipolar disorder often presents initially with depression rather than mania or hypomania, and multiple episodes of bipolar depression may occur prior to the first lifetime episode of mania/hypomania.
- A careful and ongoing evaluation of suicide risk is necessary for all individuals with major depressive disorder regarding ideation and behavior.
    - Ask about the specific nature of the ideation, intent, plans, available means (e.g., firearms), and actions.
    - Assess the patient for risk factors for suicide, including prior history of suicide attempts, comorbid psychiatric and general medical illnesses, and family history of suicidal behavior.
    - Develop a safety plan for further evaluation and treatment that depends upon the level of risk and may range from continued primary care follow-up alone to outpatient psychiatric or emergency room psychiatric evaluation.
- Given the potential for general medical conditions (spanning all organ systems) and drugs to cause or contribute to depressive episodes, the assessment should address all current and significant past general medical illnesses.
- A family history may confer increased risk for disorders or suicide; thus, the patient should be asked about a family history of depression, suicide, psychosis (e.g., delusions and hallucinations), and bipolar disorder.
- The evaluation includes interpersonal, occupational, or financial stressors and the context for the clinical presentation (which may impact treatment); in addition, the social history may identify possible sources of support that may be enlisted for treatment.
- Assessment of family functioning is often useful in understanding the context of the presenting disorder and possible need for family therapy.
    - In children and adolescents academic and social impacts from depression reinforce depression once an episode begins increasing the risk of future episodes (e.g., academic failure, interpersonal dysfunction, social withdrawal).
- Baseline measurement using clinician and/or member-administered rating scales have demonstrated their validity and reliability in research studies and may be useful in the initial evaluation and ongoing clinical monitoring of depression.
- Commonly used quantitative instruments that measure the presence and severity of depressive symptoms include:
    - Patient Health Questionnaire-9 (PHQ-9);
    - PHQ-9 Modified for Teens
    - Beck Depression Inventory (BDI)
    - Hamilton Depression Rating Scale (HDRS; HAM-D)
    - Montgomery-Asberg Depression Rating Scale (MADRS)
    - Inventory of Depressive Symptomatology (IDS; QIDS)
    - Mood Disorders Questionnaire (MDQ)
    - Geriatric Depression Scale
    - Kutcher Adolescent Depression Scale-6-item for children and adolescents
- Differential diagnosis for major depressive disorder (MDD) includes:

- Manic episodes with irritable mood or mixed episodes;
- Mood disorder due to another medical condition;
- Substance/medication-induced depressive or bipolar disorder;
- Attention-deficit/hyperactivity disorder;
- Adjustment disorder with depressed mood;
- Sadness and grief

Diagnostic Criteria

- A. Five (or more) of the following symptoms have been present during the same two-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

  NOTE: Do not include symptoms that are clearly attributable to another medical condition.

  - Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observations made by others (e.g., appears tearful). (NOTE: In children and adolescents, can be irritable mood.)
  - Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
  - Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month) or decrease or increase in appetite nearly every day. (NOTE: In children, consider failure to make expected weight gain.)
  - Insomnia or hypersomnia nearly every day.
  - Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
  - Fatigue or loss of energy nearly every day.
  - Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
  - Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by their subjective account or as observed by others).
  - Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The episode is not attributable to the direct physiological effects of a substance or to another medical condition.

  NOTE: Criteria A through C represent a major depressive episode.
  NOTE: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgement based on the individual's history and the cultural norms for the expression of distress in the context of loss.
- The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
- There has never been a manic or hypomanic episode.
  NOTE: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.
- Specify:

  - With anxious distress
  - With mixed features
  - With melancholic features
  - With atypical features
  - With psychotic features
  - With catatonia

- With peripartum onset
- With seasonal pattern

- Patients who are initially and correctly diagnosed with major depressive disorder may eventually manifest new or modified symptoms warranting reevaluation and a change in diagnosis.

Evidence-Based Interventions

Phases of Treatment

Treatments for Major Depressive Disorder typically occur in three phases (acute, continuation and maintenance). Treatment choice in any of these phases involves medications, psychotherapy, or a combination of the two. The goals of treatment are symptom remission and restoration of baseline function. Treatment selection should be driven by symptom severity (mild, moderate, severe), patient preference, as well as the findings from the clinical evaluation. The following outlines the typical course of treatment followed be evidence-based treatment options.

Acute Phase

The goal of the acute phase is to achieve remission of depressive symptoms and return of the patient to baseline functioning. . Individuals and symptoms vary; however, the duration of the acute phase is generally 6-12 weeks and treatment strategies include:

- Pharmacotherapy considerations include first line antidepressants starting with SSRIs due to their favorable side effect profile, adjusting based on efficacy and tolerability.
- Psychotherapy considerations include CBT, IPT and Behavioral Activation.
- Combination therapy often produce better outcomes.

Continuation Phase

The goal of the continuation phase is to prevent relapse of depressive symptoms. The duration of the continuation phases is generally 4-9 months after the acute phase remission. Patients are usually seen every two to four weeks in this phase and treatment strategies include:

- Continued pharmacotherapy maintaining the effective dose on the antidepressant used in the acute phase.
- Continued psychotherapy with regular sessions to reinforce coping strategies and address lingering issues.
- Monitoring with regular follow-ups to monitor symptoms, medication adherence, and side effects.
- Encourage lifestyle modifications such as regular exercise, health diet and sleep hygiene.
- Determine if treatment discontinuation is possible especially in patients with a first depressive episode.

Maintenance Phase

The goal of the maintenance phase is to prevent recurrence of future depressive episodes. The duration of the maintenance phase can last up to one year or can be longer-term in individuals with recurrent major depressive disorder. Treatment strategies include:

- Maintenance pharmacotherapy with the continued use of antidepressants at the most effective dose.
- Maintenance psychotherapy with periodic sessions to maintain gains and provide ongoing support.
- Psychoeducation about the signs of relapse and the importance of treatment adherence.
- Continued emphasis and lifestyle modifications.
- Regular check-ins to assess mood, medication, and early signs of relapse.
- Determine if discontinuing treatment is possible.

Treatment Selection

- Antidepressants
    - Treatment with medications is a shared-decision between the doctor and the patient, centered on the doctor's recommendation(s), symptom severity, and patient preference.
    - Selective serotonin reuptake inhibitors (SSRIs, including fluoxetine, citalopram, sertraline, paroxetine, and escitalopram), serotonin-norepinephrine reuptake inhibitors (SNRIs, including venlafaxine and duloxetine), bupropion, and mirtazapine are common antidepressant choices because they have a better side effect profile than older classes of antidepressants, such as tricyclics, monoamine oxidase inhibitors (MAOIs), and tetracyclic medications.

- The use of MAOIs should be restricted to individuals with resistance to other treatments due to the side effects and dietary restrictions
- Numerous forms of medication exist across these antidepressant classes, and each has different side effects
- For individuals with MDD that is moderate or severe, most second-generation antidepressants are the initial treatment. For individuals with mild depressive symptoms, the initial treatments include psychoeducation and psychotherapies
- For individuals who have limited or no response to initial medication monotherapy with a maximum medication dose, after at least four to six weeks of treatment; the recommendation is switching to another monotherapy (medication or psychotherapy) or adding a second medication or psychotherapy.
- Once remission has been attained, individuals enter the continuation and maintenance phases of depression management. Patients should continue antidepressant treatment for at least six months from the time they attain remission.
- Individuals who do not respond or have only a partial response to treatment at four weeks should undergo assessment of potential reasons for nonresponse and have a time-limited trial of continued treatment with the same agent before proceeding to next-step treatment.

- Psychotherapies
  - Commonly used initial psychotherapy strategies for depression include
    - Interpersonal Therapy (IPT), IPT is also generally a short-term therapy, lasting around 12 to 16 sessions over a period of 3 to 4 months. Like CBT, the duration may vary depending on the patient's needs and progress.
    - Cognitive Behavioral Therapy (CBT), CBT is often structured as a short-term treatment, typically lasting between 12 to 20 sessions over the course of 3 to 6 months. In some cases, it may be extended if the individual's symptoms are more severe or if progress is slower.
    - Acceptance and Commitment Therapy for Depression (ACT-D),
    - Mindfulness-Based Cognitive Therapy (MBCT), This is often delivered in a structured format over 8 weeks, with weekly sessions. MBCT is particularly used to prevent relapse in individuals who have experienced recurrent depression. and
    - Problem-Solving therapy (PST)
    - Behavioral Activation Therapy, Individual treatment generally consists of 8 to 24 weekly sessions that each last 50 minutes, a review of 25 studies found that the median number of sessions was eight.
  - CBT shows equal efficacy as second-generation antidepressants (SGAs) as initial treatment in alleviating mild to severe MDD symptoms for adult outpatients
  - A meta-analysis of 575 participants revealed that psychotherapy provided in addition to medication yielded a decrease in self-reported symptoms of depression

- Measurement of Progress
  - Many clinician and/or member-administered rating scales have demonstrated their validity and reliability in research studies and may be useful in the initial evaluation and ongoing clinical monitoring of depression. These should be administered across the course of treatment.
  - Commonly used quantitative instruments that measure the presence and severity of depressive symptoms include:
    - Patient Health Questionnaire-9 (PHQ-9);
    - Beck Depression Inventory (BDI);
    - Hamilton Depression Rating Scale (HDRS; HAM-D);
    - Montgomery-Asberg Depression Rating Scale (MADRS);
    - Inventory of Depressive Symptomatology (IDS; QIDS).
- Switching/Augmenting the Course of Treatment
  - Clinicians should carefully reevaluate patients with depression that have not responded to initial treatment including:
    - Adherence to the treatment plan;
    - That an adequate dose of medication has been given for an adequate duration with a minimum of 4-8 weeks and/or;
    - That psychotherapy has been or is being conducted over an appropriate period of time with an adequate frequency of visits such as at least 8 visits of 30 minutes each;

        - Consider if the patient is a rapid metabolizer of antidepressants.
    - If a patient has not responded to initial treatment, it may suggest a need to reconsider the accuracy of that diagnosis.
    - Treatment switching or augmentation may be reasonable options for those patients with depression who do not respond to initial therapy.
    - The Veterans Affairs (VA, 2015) conducted the trial, Augmentation and Switching Treatments for Improving Depression Outcomes (VAST-D), that examined alternate approaches for outpatients with nonpsychotic MDD and poor antidepressant outcomes. Comparisons were completed for switching to bupropion-SR or augmenting with either bupropion-SR or aripiprazole. The results indicated that switching to the antipsychotic aripiprazole resulted in modest statistical significance with improvement in remission rates compared with switching or augmenting with an antidepressant, although greater side effects were noted.
    - On March 5, 2019, the Food and Drug Administration (FDA) approved esketamine nasal spray for treatment resistant depression. The FDA approval includes a risk valuation and mitigation strategy (REMS) intended to help safeguard proper clinician training in administration and careful candidate selection. According to the FDA (2019), esketamine nasal spray is to be prescribed in combination with a newly initiated oral antidepressant.

- Other treatments for Treatment Resistance
    - Treatment resistant depression may require alternative strategies such as switching medications, augmenting with another antidepressant or mood stabilizer, or using ECT or TMS. Addressing comorbid conditions and patient preference should always be considered when there is a lack of response to treatment.
    - Brain stimulation such as electroconvulsive therapy (ECT) may be a treatment option in individuals with severe depression when there is a history of poor response to medications and when there is a need for a rapid, definitive response due to the severity of the condition (e.g., imminent risk of suicide, signs or symptoms of psychosis, substantial cognitive impairment as a result of the depression).
    - Brain stimulation such as transcranial magnetic stimulation (TMS) may also be considered in individuals who have not responded to prior antidepressant therapy.

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Revision History

Date	Summary of Changes
08/2024	Version 1