

Depression: Risk Factors, Diagnosis, and Current Treatment Approaches

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Abstract

Depression is one of the leading causes of disability worldwide, affecting people across all age groups and socioeconomic backgrounds. Major Depressive Disorder (MDD) is characterized by persistent sadness, loss of interest, impaired cognitive functioning, and physical symptoms that interfere with daily life. The etiology of depression is multifactorial, involving genetic, biological, psychological, and environmental factors. Accurate diagnosis requires comprehensive clinical assessment supported by validated screening tools. Treatment generally combines psychotherapy, pharmacotherapy, lifestyle modification, and, in severe or treatment-resistant cases, advanced interventions such as electroconvulsive therapy (ECT), repetitive transcranial magnetic stimulation (rTMS), or ketamine/esketamine therapy. This paper reviews current evidence regarding risk factors, diagnosis, and treatment approaches for depression while demonstrating the organization of a scholarly research paper.

Keywords

Depression, Major Depressive Disorder, Risk Factors, Diagnosis, Treatment, Psychotherapy, Antidepressants.

1. Introduction

Depression is a common mental disorder that significantly affects quality of life, occupational performance, interpersonal relationships, and physical health. According to the World Health Organization (WHO), depression affects hundreds of millions of individuals globally and contributes substantially to the global burden of disease.

Depression extends beyond normal sadness and typically persists for at least two weeks, causing significant impairment in social and occupational functioning. Untreated depression increases the risk of suicide, chronic medical illnesses, and reduced life expectancy. Early identification and evidence-based treatment are therefore essential.

2. Risk Factors for Depression

Depression develops through the interaction of multiple risk factors rather than a single cause. Genetic factors play an important role in the development of depression, although they do not solely determine whether an individual will experience the disorder. Family, twin, and adoption studies have consistently demonstrated that depression has a moderate heritable component. Individuals with first-degree relatives, such as parents or siblings, who have been diagnosed with depression are at a significantly higher lifetime risk of developing the condition themselves. The interaction between genetic susceptibility and environmental stressors is believed to influence the onset and progression of depressive disorders.

Several biological mechanisms have been associated with the development of depression. One of the most widely studied factors is the imbalance of neurotransmitters, particularly serotonin, norepinephrine, and dopamine, which regulate mood and emotional responses.

Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis can lead to abnormal stress hormone production, contributing to depressive symptoms. In addition, chronic neuroinflammation, reduced neuroplasticity, and decreased production of brain-derived neurotrophic factor (BDNF) may impair the brain's ability to adapt and recover from stress. Structural and functional changes in brain regions such as the hippocampus, amygdala, and prefrontal cortex have also been observed in individuals with depression.

Psychological factors significantly influence both the onset and persistence of depression. Individuals who exhibit negative cognitive patterns, including persistent pessimism and self-critical thinking, are more likely to develop depressive symptoms. Low self-esteem, inadequate coping skills, and maladaptive responses to stress further increase vulnerability. Childhood trauma, including emotional, physical, or sexual abuse, has been strongly associated with an elevated risk of depression later in life. Additionally, certain personality traits, particularly neuroticism, predispose individuals to heightened emotional sensitivity and an increased likelihood of experiencing depressive episodes.

Environmental and social circumstances are major contributors to depression, particularly when stressful life events accumulate over time. Experiences such as bereavement, financial hardship, unemployment, domestic violence, social isolation, and chronic stress can trigger or worsen depressive symptoms. Limited social support and prolonged exposure to adverse living conditions may further compromise mental well-being. Research has consistently shown that adverse childhood experiences, including neglect, abuse, and household dysfunction, substantially increase the risk of developing depression during adolescence and adulthood.

Depression commonly coexists with a variety of chronic medical conditions, creating a bidirectional relationship in which each condition can worsen the other. Individuals with diabetes, cardiovascular disease, cancer, Parkinson's disease, stroke, and chronic pain disorders have a higher prevalence of depression compared to the general population. The psychological burden of managing long-term illnesses, combined with biological changes associated with these diseases, contributes to depressive symptoms. Furthermore, certain medications, alcohol misuse, and substance abuse may either precipitate or exacerbate depression, highlighting the importance of comprehensive medical evaluation when diagnosing and treating depressive disorders.

3. Diagnosis of Depression

Diagnosis of depression primarily relies on a comprehensive clinical assessment based on the criteria outlined in the *Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR)* or the *International Classification of Diseases (ICD-11)*. A thorough evaluation includes a detailed medical and psychiatric history, assessment of symptom severity and duration, evaluation of functional impairment, and identification of potential medical or psychiatric conditions that may contribute to depressive symptoms. The diagnostic process also involves ruling out alternative causes and assessing the individual's risk of self-harm or suicide.

According to the DSM-5-TR, the diagnosis of Major Depressive Disorder (MDD) requires the presence of five or more symptoms during the same two-week period, with at least one symptom being either a persistently depressed mood or a marked loss of interest or pleasure in most activities. Additional symptoms include significant changes in sleep patterns, appetite or body weight, persistent fatigue or loss of energy, impaired concentration or decision-making, feelings of worthlessness or excessive guilt, psychomotor agitation or retardation,

and recurrent thoughts of death or suicidal ideation. These symptoms must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning and should not be attributable to substance use or another medical condition. Several validated screening instruments are widely used to identify individuals at risk of depression and to assess symptom severity. The Patient Health Questionnaire-9 (PHQ-9) is one of the most commonly used self-report tools for evaluating depression severity, while the shorter PHQ-2 serves as an initial screening instrument in primary care settings. Other widely accepted assessment tools include the Beck Depression Inventory-II (BDI-II), which measures symptom severity from the patient's perspective, the Hamilton Depression Rating Scale (HAM-D), a clinician-administered instrument used to evaluate treatment response, and the Montgomery-Åsberg Depression Rating Scale (MADRS), which is particularly useful for monitoring changes in depressive symptoms during treatment. Although these instruments provide valuable clinical information, they are intended to support rather than replace a comprehensive clinical interview and professional judgment.

An important aspect of diagnosis is differentiating depression from other psychiatric and medical conditions that may present with similar symptoms. Bipolar disorder must be carefully excluded because treatment strategies differ substantially, and antidepressant therapy alone may precipitate manic episodes. Anxiety disorders, persistent depressive disorder (dysthymia), and substance-induced mood disorders can also resemble major depression and require careful evaluation. A detailed history of substance use, medication intake, and previous mood episodes is therefore essential for accurate diagnosis.

Medical conditions can also mimic or contribute to depressive symptoms and should be considered during the diagnostic process. Endocrine disorders such as hypothyroidism, nutritional deficiencies including vitamin B12 deficiency, neurological disorders such as dementia, and chronic systemic illnesses may present with symptoms similar to depression. Appropriate laboratory investigations and physical examinations are often necessary to identify these underlying conditions. Accurate differential diagnosis ensures that patients receive appropriate treatment while avoiding unnecessary or potentially ineffective interventions.

4. Current Treatment Approaches

Treatment of depression should be individualized based on the severity of symptoms, patient preferences, previous treatment response, coexisting medical or psychiatric conditions, and the presence of suicide risk. Clinical practice guidelines recommend a multidisciplinary approach that combines psychological, pharmacological, and lifestyle interventions to achieve optimal outcomes. For individuals with mild depression, psychotherapy alone may be sufficient, whereas moderate to severe depression often requires a combination of psychotherapy and antidepressant medication. Continuous monitoring and follow-up are essential to evaluate treatment response, medication adherence, and the emergence of adverse effects.

Psychotherapy is considered one of the most effective first-line treatments for depression, particularly in individuals with mild to moderate illness. Cognitive Behavioral Therapy (CBT) is the most extensively researched psychological intervention and focuses on identifying and modifying negative thought patterns and maladaptive behaviors. Other evidence-based therapies include Interpersonal Therapy (IPT), which addresses relationship difficulties contributing to depressive symptoms; Behavioral Activation, which encourages engagement in meaningful activities; Mindfulness-Based Cognitive Therapy (MBCT), which

combines cognitive therapy with mindfulness techniques to reduce relapse; and Problem-Solving Therapy, which helps patients develop practical coping strategies for life challenges. These therapeutic approaches improve emotional regulation, reduce symptom severity, and enhance long-term psychological well-being.

Pharmacotherapy plays a central role in the management of moderate to severe depression. Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) are generally recommended as first-line antidepressants because of their favorable safety profiles and effectiveness. Other antidepressant medications include bupropion, mirtazapine, tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOIs), which may be prescribed depending on the patient's clinical characteristics and previous response to treatment. Medication selection should carefully consider potential adverse effects, drug interactions, patient age, comorbid conditions, pregnancy status, and the risk of overdose. Regular follow-up is essential to monitor treatment effectiveness, medication adherence, and the occurrence of side effects.

Lifestyle modifications have emerged as valuable adjuncts to conventional depression treatment and contribute significantly to overall mental health. Regular physical activity has consistently been shown to reduce depressive symptoms by improving mood, promoting neuroplasticity, and reducing inflammation. Maintaining a balanced and nutritious diet, practicing good sleep hygiene, engaging in stress-reduction techniques such as meditation or yoga, strengthening social support networks, quitting smoking, and reducing alcohol misuse further enhance treatment outcomes. Although lifestyle interventions alone may not be sufficient for individuals with severe depression, they improve overall health, reduce relapse risk, and complement psychotherapy and pharmacotherapy.

For individuals with treatment-resistant depression or severe depressive episodes, advanced therapeutic options may be required. Brain stimulation therapies such as Electroconvulsive Therapy (ECT), Repetitive Transcranial Magnetic Stimulation (rTMS), and Vagus Nerve Stimulation (VNS) have demonstrated effectiveness in patients who do not respond adequately to conventional treatments. Among these, ECT remains one of the most effective interventions for severe depression, particularly when accompanied by psychotic features, catatonia, or imminent suicide risk. More recently, intravenous ketamine and intranasal esketamine have emerged as promising treatments for treatment-resistant depression. These agents produce rapid antidepressant effects, often within hours to days, and have shown particular benefit in reducing suicidal ideation. However, because of their potential adverse effects and limited long-term safety data, their use requires careful patient selection, administration under medical supervision, and ongoing monitoring.

5. Discussion

Current evidence indicates that depression is a complex and multifactorial mental health disorder resulting from the interaction of biological, psychological, social, and environmental factors rather than a single identifiable cause. Genetic predisposition, neurotransmitter imbalances, neuroendocrine dysfunction, inflammatory processes, adverse childhood experiences, chronic stress, and maladaptive cognitive patterns all contribute to the development and progression of depressive disorders. These interacting mechanisms explain the considerable variation in symptom presentation, disease severity, treatment response, and prognosis among individuals. Consequently, depression should be understood as a heterogeneous disorder that requires a comprehensive and individualized approach to diagnosis and management.

No single treatment is universally effective for all patients with depression because the disorder varies widely in its underlying causes and clinical manifestations. Current international clinical guidelines, including those from the American Psychiatric Association (APA), the National Institute for Health and Care Excellence (NICE), and the World Health Organization (WHO), consistently recommend that treatment decisions should be tailored to the individual's symptom severity, personal preferences, previous treatment response, coexisting medical or psychiatric conditions, functional impairment, and suicide risk. Early identification, timely intervention, and regular follow-up are essential for improving treatment outcomes and preventing relapse. A collaborative approach involving healthcare professionals, patients, and family members can further enhance adherence to treatment and long-term recovery.

For individuals with moderate-to-severe depression, combination therapy involving evidence-based psychotherapy and antidepressant medication has consistently demonstrated superior outcomes compared with either treatment alone. Psychological interventions such as Cognitive Behavioral Therapy (CBT), Interpersonal Therapy (IPT), and Mindfulness-Based Cognitive Therapy (MBCT) help patients develop healthier coping strategies, challenge negative thought patterns, and improve emotional regulation. Simultaneously, antidepressant medications restore neurotransmitter balance and alleviate core depressive symptoms. In addition to these conventional approaches, lifestyle modifications—including regular physical exercise, healthy nutrition, adequate sleep, stress management, smoking cessation, and reduced alcohol consumption—play an increasingly recognized role in supporting recovery and reducing the likelihood of recurrence. Integrating these interventions provides a holistic treatment strategy that addresses both the biological and psychosocial dimensions of depression.

Recent advances in psychiatric research have significantly expanded treatment options for individuals with treatment-resistant depression. Novel pharmacological therapies, particularly intravenous ketamine and intranasal esketamine, have demonstrated rapid antidepressant effects, especially among patients experiencing severe depressive symptoms or suicidal ideation. Likewise, neuromodulation techniques such as Electroconvulsive Therapy (ECT), Repetitive Transcranial Magnetic Stimulation (rTMS), and Vagus Nerve Stimulation (VNS) have shown considerable effectiveness in patients who fail to respond adequately to conventional treatments. These innovations provide new hope for individuals with chronic or refractory depression; however, careful patient selection, specialized clinical supervision, and long-term monitoring remain essential to ensure safety and optimize therapeutic outcomes.

Looking ahead, the future of depression research is increasingly focused on precision psychiatry, which aims to provide personalized treatment based on an individual's biological, genetic, psychological, and environmental characteristics. Advances in biomarker discovery, genomics, neuroimaging, and pharmacogenomics may enable clinicians to predict treatment response more accurately and select the most effective interventions for each patient. In addition, digital mental health technologies—including smartphone applications, wearable devices, telepsychiatry, and internet-based cognitive behavioral therapy—are improving access to mental healthcare, particularly in underserved populations. Artificial intelligence (AI) and machine learning are also emerging as valuable tools for early diagnosis, symptom monitoring, risk prediction, and personalized treatment planning. Although these technologies show considerable promise, further large-scale clinical studies are required to establish their long-term effectiveness, ethical implications, and integration into routine clinical practice. Continued research and innovation are expected to enhance the

understanding, prevention, diagnosis, and treatment of depression, ultimately improving patient outcomes and quality of life worldwide.

6. Conclusion

Depression remains a major public health challenge worldwide. Understanding its multifactorial risk factors facilitates early identification and prevention. Accurate diagnosis requires comprehensive assessment supported by validated screening instruments. Current treatment approaches combine psychotherapy, medication, lifestyle interventions, and advanced therapies for treatment-resistant cases. Continued research is expected to improve personalized treatment strategies and long-term outcomes.

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