DEPRESSION VS. DEMENTIA IN THE ELDERLY
PART I
9 CE hours

About the author
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Learning Objectives
► Define depression, dementia, delirium, and pseudo-dementia.
► Appreciate the epidemiology of dementia and depression present in the elderly population.
► Identify the current screening guidelines for dementia and depression.
► Describe the pathophysiology of major depression.
► List the non-modifiable risk factors for depression.
► List the modifiable risk factors for depression.
► Describe the pathophysiology of dementia.
► List the non-modifiable risk factors for dementia.
► List the modifiable risk factors for dementia.
► Describe the pathophysiology of pseudo-dementia.
► List the non-modifiable risk factors for pseudo-dementia.
► List the modifiable risk factors for pseudo-dementia.
► Describe the pathophysiology of delirium.
► Identify the problems associated in differentiating depression from dementia in the elderly.
► Categorize the different types of depression and dementia.
► Discuss the signs and symptoms of depression and dementia.
► Explain the importance of the correct diagnosis of dementia and depression.
► Discuss the diagnostic tools available to aid in the diagnosis of dementia and depression.
► Identify the diagnostic imaging used in the diagnosis of dementia and depression.
► Discuss the application of a full neuropsychological evaluation in the diagnosis of dementia and depression.
► Describe the treatment options for both dementia and depression.
Evaluate the effectiveness of each treatment option in the care of depression and dementia in the elderly.

Explain the side effects of the medical management of dementia and depression.

Identify the lifestyle factors that affect the development of dementia and depression in the elderly.

Discuss the role of mental exercise and activity in the prevention of depression and dementia.

Examine the options available to health care workers for the evaluation of disease progression of dementia and depression in the elderly.

Identify other factors, such as comorbidities, medications, and family members that play a role in the management, progression and prevention of dementia and depression in the elderly.

Evaluate the potential benefit of future preventive measures and treatment options for depression and dementia in the elderly.

Identify the role of the most current advancement in neuropsychological research.

Communicate the importance of disease education to patients and families who suffer from either dementia or depression.

Introduction
Dementia and depression are two separate mental health problems that are frequently encountered in medical practice and social interaction with the elderly population. Approximately 50% of patients who present with late-onset depression have some form of cognitive impairment. The extremely high crossover between the signs and symptoms of depression and dementia in the elderly make it a challenging task to both diagnose and manage the two diseases appropriately.

Moreover, current literature suggests that the prevalence of depression in patients with dementia has been reported to be between 10% and 70%. Depression has been identified to be both a risk factor and a premonitory symptom of dementia. This course is an in-depth academic review of the multifaceted relationship that exists between the two conditions. The course will cover definitions, epidemiology, related concepts, diagnostic tools and challenges, treatment, and emerging research. The operational issues and the instruments underlying their relationship are also emphasized.

The association between the two illnesses is far from decisive, but this course will help health care professionals review the most important factors of the respective diseases and offer guidance on the clinical challenges that are presented with them.

**Dementia** consists of several symptoms that manifest as an overall impairment in higher-level thought processes and cognitive abilities of an individual. Dementia can impair new memory formation and learning ability; affect recall, comprehension, and judgment; and impair other significant mental abilities. While dementia is usually seen in geriatric patients, it is not unusual for young adults to suffer from early-onset dementia as well [3].

**Delirium** is a rapid onset psychiatric condition where the patient presents as confused and disoriented (to place, time, or date). The severity of the condition varies from patient to patient. Some patients experience additional changes in cognitive or visual perception, as well as alterations to their sleeping patterns. Others may also have visual or auditory hallucinations.

**Depression** is a psychiatric disorder characterized by the presence of a low mood and a lack of willingness to participate in tasks or activities that affect an individual’s emotional, mental, and physical state [1].
Depressed individuals often experience several of the following: loneliness, hopelessness, irritability, anxiety, or suicidal thoughts. They may also become anhedonic, meaning they no longer derive pleasure from previously pleasurable activities such as exercising or going out and socializing with friends.

In the elderly, it has been found that depression is often an underdiagnosed and untreated condition. It is estimated that approximately 15% of the elderly population worldwide suffer from depression; at least 40% of geriatric patients in nursing homes have some form of depression. While the statistics suggest that the condition affects a large percentage of the elderly population, it is not part of the normal process of aging. In fact, it is one of the most treatable disorders in the elderly [2].

While the statistics seem to indicate that a large portion of the elderly is depressed, depression still seems to be more common among young adults [5]. Depression is an important public health issue that needs to be addressed because the rise in the risk of suicide, as well as the reduction in the overall physical and mental functioning of depressed individuals, can incur social and economic costs [4].

**Age of Onset of Depression**

Approximately half of depressed geriatric patients experienced their first depressive episode as young adults. This is known as early-onset depression, which can be managed, but can reoccur several times throughout a person’s lifetime. The other half has their first depressive episode later in life (typically at 55 to 65 years)—this is known as late-onset depression.

Individuals with early-onset depression are more likely to have relatives who are also depressed, which suggests that it may be influenced by genetics. It is also correlated with higher comorbid psychiatric or personality disorders [7].

Individuals who have late-onset depression have clinical presentations and specific risk factors that differ from patients who have had at least one depressive episode as young adults [6]. However, the current literature is inconclusive. Some studies have found a correlation between late-onset depression and stroke or cerebrovascular accident (CVA) and other related risk factors [8]. Other studies have found no significant correlation between these events [7]. Studies have also found that patients with late-onset depression may have a higher risk of developing dementia or other cognitive deficits [9].

**Epidemiology**

While prevalence rates vary from country to country, overall, depression is one of the leading causes of deaths worldwide [10]. For example, Americans are more likely to be depressed than the Japanese (prevalence rates of 17% and 3%, respectively). In general, 8% to 12% of individuals experience at least one depressive episode throughout their lifetimes, with most experiencing their first episode at 30 to 40 years of age [11-13]. Women are twice as likely to be depressed as men.

The risk of experiencing a depressive episode is also correlated with environmental factors and other comorbid diseases [14-17]. In particular, it has been found that people in urban areas are more likely to be depressed than people in rural areas. Lower socioeconomic status also appears to be a risk factor for depression [17]. Comorbid neurological and cardiovascular disorders such as multiple sclerosis, Parkinson’s disease, and myocardial infarction increase the risk of depression [14-16].

In the United States, approximately 1% of the total population experience some form of depression, with the prevalence rates significantly higher in women (1.4% for females, 0.4% for males) [18, 19]. While the highest prevalence rates of depression is found in 25- to 44-year-old patients, the number of clinically significant symptoms associated with the condition increase with older individuals. Five million
depressed individuals are elderly and 20% of these depressed elderly individuals are considered to have major depression [18]. In long-term care facilities, approximately 12% to 30% of residents are depressed [19]. In primary care settings, 17% to 37% of elderly patients are depressed; approximately 30% of these are diagnosed with major depression [2].

Geriatric patients diagnosed with depression are usually found to have specific comorbid diseases [20, 21]. Chronic health conditions correlated with high rates of depression include:

- Alzheimer’s disease (20% to 40%)
- Stroke (30% to 60%)
- Coronary heart disease (8% to 44%)
- Parkinson’s disease (40%)
- Cancer (1% to 40%)
- Dementia (17% to 31%)

In the elderly, depression has a prevalence rate of 1% to 5% worldwide, with clinically significant symptoms found in 15% of elderly living in the community [5, 22]. As in the general population, elderly women also have higher rates of depression than elderly men. Depression is seen in 5% to 10% of elderly medical outpatient cases; 10% to 12% of elderly medical inpatients; and 14% to 42% of residents of long-term care facilities [22, 24].

Race or ethnicity does not seem to have an effect in the prevalence rate of depression, but the symptoms appear to be more common in Hispanics than in non-Hispanic Caucasians [23].

**Clinical Presentation of Depression in the Elderly (vs. in Young Adults)**

Compared with young adults, elderly patients are less likely to feel dysphoric or worthless [25]. Geriatric patients also report loss of concentration, poor memory, changes in sleep cycle, sleep disturbances or insomnia, fatigue, hopelessness, or loss of interest in living more often than young adults [26].

Geriatric patients are often found to have impaired higher-level thought processes and slower cognitive functions or responses [27]. Elderly females are more prone to changes in appetite, while elderly males are more prone to experiencing increased agitation [28].

Diagnosing depression is harder when there is a comorbid medical condition with similar symptoms; for example, cancer patients often lose weight and experience fatigue—symptoms also present in depression. Thus, depression can be overdiagnosed or underdiagnosed depending on the health care provider.

Elderly patients with neurological disorders often exhibit different symptoms of depression (less anhedonia and dysphoria) compared with geriatric patients with no neurological damage. A depressive episode that manifests after a stroke, especially a stroke resulting in right hemisphere damage, is usually associated with vegetative symptoms and is less likely to include dysphoria [29]. Patients with Parkinson’s disease usually experience a milder form of depression [30].

Patients with Alzheimer’s disease are diagnosed with a comorbid depressive disorder when three of the nine criteria for depression are present—excluding lack of concentration, which can also be present in some Alzheimer’s patients without depressive disorder. (The diagnosis of major depressive disorder requires the presence of at least five symptoms.) Patients with Alzheimer’s and depression often experience less weight loss, fatigue, and muscle weakness than patients with vascular/multi-infarct dementia and depression [31].
Etiology
Biological and genetic factors play an important role in depressive disorder. Neurological degeneration and various diseases, especially cardiovascular diseases, can be risk factors for depression. A family history of depressive disorders is also a risk factor.

Stressful life events, such as death of family members or friends, can also trigger depression. The criteria for diagnosis have been revised in the DSM-5 to include bereavement as a possible cause of depression.

Genetic Risk
Studies have found several genes that may influence the development of depression. The interaction of genetic and environmental factors may also increase the risk of depression [32].

Depression can occur in an individual with no family history of the illness. However, twin studies suggest that individuals with clinically depressed first-degree relatives are three times more likely to have depression than the general population [37].

Some studies say that genes that produce serotonin may be involved in the development of depressive disorder. Most antidepressants affect the production or uptake of serotonin in the brain [38]. Genetics seems to play a less important role in the development of depression in the elderly (late-onset depression). However, some genetic markers have been found to be specific to depression in geriatric patients. Some of the genes affecting depression in the elderly seem to be gender-specific—the polymorphism of the 5-HTR2A gene promoter is associated with elderly men but not elderly women.

It is important to note that the involvement of the genes mentioned above is still theoretical. For example, research has established that ApoE is a risk factor for Alzheimer’s disease, but there are no studies yet that conclusively prove that ApoE is also involved in depression [8, 39, 40].

Biological Risk Factors
Aging comes with biological changes that affect the health of the elderly. Changes in the cardiovascular, endocrine, and immune systems of the elderly may predispose them to depression.

In geriatric patients, depression usually has a comorbid medical condition. Chronic cardiovascular diseases, degenerative neurological conditions, and cerebrovascular accidents have all been identified as major risk factors for depression. Immune suppression or infection, as well as cancer, have also been found to trigger depression. Several imbalances in the endocrine system such as hypo- or hyperthyroidism have also been correlated to the development of depressive disorder [41].

Various physiologic changes have also been observed in depressed patients. These include elevated levels of IGF-1 (insulin-like growth factor 1), increased adrenocortical activity, and inflammation [42]. Depression has also been correlated to osteoporosis, suggesting that elevated levels of inflammatory markers may also play a role in depression.

Depression may also occur as a side effect of various prescription drugs used to treat other conditions. These include antihypertensive drugs (such as beta-blockers and calcium channel blockers), neurological drugs, benzodiazepines, corticosteroids, digoxin, hormone replacements, interferon, and chemotherapy drugs [24, 42].

Medications That May Cause Depression
Depression in older people with concomitant medical disease usually has a poor prognosis, and usually leads to higher rates of morbidity and disability [43]. In some cases, depression in the elderly can make the management of other diseases more difficult. For example, loss of appetite secondary to depression is one of the leading causes of weight loss in older adults, and weight loss is generally associated with weakness and failure to thrive [4]. Loss of appetite may also lead to poor nutritional status and nutritional deficiencies, which also play a vital role in the genesis of depression. Low levels of vitamin B12 and the ratio of omega-6 to omega-3 fatty acids seems to be associated with depression in the elderly, even when other risk factors are well controlled [41].

It has also been observed that depression earlier in life also predisposes an individual to depression when older. Additionally, depression earlier in life may predispose an individual to vascular disease, which, in turn, can increase the risk of depression at later stages, particularly in the elderly. This close association between the two diseases suggests a common pathological process [41]. For instance, the serotonin transporter promoter polymorphism 5-HTTLPR is strongly associated with depression, as well as elevated platelet factor IV and beta-thromboglobulin levels, resulting in increased platelet activation [42, 4].

**Depression and Cardiovascular Disease**

Depression is especially prevalent in patients with cardiovascular disease. Depression increases the risk of coronary artery disease (CAD) approximately 1½ to 2 times that of otherwise healthy individuals [44]. Approximately 20% to 25% of cardiac disease patients experience major depression, and another 20% to 25% report symptoms of depression that do not meet criteria for major depressive disorder (MDD) [45]. Depression in heart disease patients may lead to increased rate of rehospitalization, disability, mortality, slower recovery, and increased health care costs [46].

Several mechanisms are thought to be responsible for a close relationship between cardiovascular disease and depression [46]. These include:

- Poor compliance to treatment and lifestyle recommendations.
- Shared genetic influences.
- Sympathetic impairments.
- Neuroendocrine and immune impairments.
- Autonomic dysfunction.
- Impaired inflammatory systems.
- Increased platelet activity.
- Cerebrovascular disease.

It is estimated that approximately 15% of patients with cardiovascular disease and approximately 20% of patients who had coronary artery bypass graft (CABG) surgery experience depression [47]. A number of research studies have observed that depression and mental stress have a negative impact on a person’s cardiac health, in particular:

- Long-term unmanaged stress and depression can lead to hypertension, arterial damage, arrhythmia, and an impaired immune system.
- Patients who experience depression tend to have increased platelet reactivity, decreased heart variability, and elevated proinflammatory markers, which makes the patient vulnerable to cardiovascular disease.
- Depression also increases the risk of myocardial ischemia or thrombosis, especially in individuals with cardiovascular disease.
One research study found that if depression persists after recovery from a cardiovascular event, the mortality rate increases to approximately 17% within 6 months after myocardial ischemia. It was also observed that mortality was only 3% in the absence of depression [48].

Depression also has an adverse impact on a patient’s recovery from cardiac surgery—it can worsen fatigue and intensify pain in these patients. It can also trigger withdrawal and, ultimately, social isolation of the patient.

Patients with cardiac failure and depression are susceptible to readmission to the hospital and have a greater mortality rate.

It is believed that genetic factors also play an important role in determining a patient’s propensity for depression, as well as the risk of recurrent adverse cardiac events after myocardial ischemia [49].

Patients with cardiac disease and depression have poor medical and exercise compliance compared with patients with cardiac disease who do not experience depression [50-52].

Depression is also linked to poor lifestyle habits, such as smoking, lack of exercise, increased alcohol intake, poor dietary and sleeping patterns, and inadequate social support. All these habits hinder optimum management of cardiac disease.

The American Heart Association (AHA) has recommended that all cardiac patients be screened for depression with the help of the Patient Health Questionnaire (PHQ-2) (See below.) [53].

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The Patient Health Questionnaire – PHQ-2

Over the past 2 weeks, how often have you been bothered by any of the following problems?

**Little interest or pleasure in doing things.**

0 = Not at all  
1 = Several days  
2 = More than half the days  
3 = Nearly every day

**Feeling down, depressed, or hopeless.**

0 = Not at all  
1 = Several days  
2 = More than half the days  
3 = Nearly every day

Total point score: __________

**Score interpretation:**

<table>
<thead>
<tr>
<th>Probability of major depressive</th>
<th>Probability of any depressive disorder</th>
</tr>
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<table>
<thead>
<tr>
<th>order</th>
<th>disorder (percent)</th>
<th>(percent)</th>
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<td>36.9</td>
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<tr>
<td>2</td>
<td>21.1</td>
<td>48.3</td>
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<tr>
<td>3</td>
<td>38.4</td>
<td>75.0</td>
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<td>45.5</td>
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<tr>
<td>5</td>
<td>56.4</td>
<td>84.6</td>
</tr>
<tr>
<td>6</td>
<td>78.6</td>
<td>92.9</td>
</tr>
</tbody>
</table>

Patient Health Questionnaire-2 (PHQ-2). This questionnaire is used as the initial screening test for major depressive episode.


**Depression and Diabetes**

Almost 15% of patients with type 2 diabetes experience major depression, and approximately 20% experience increased depressive symptoms [54]. In a systematic review, it was found depression is more prevalent among patients with type 2 diabetes (17.6%) compared with those without diabetes (9.8%) [55]. It was also observed that depression is more prevalent among female diabetic patients (23.8%) compared with male diabetic patients (12.8%).

A number of clinical studies have observed that diabetic patients have a greater likelihood of experiencing depression than non-diabetic patients. A review was conducted to study association between diabetes and depression [56]. It was found that depression increased the risk of type 2 diabetes by about 60%, and type 2 diabetes moderately increased the risk of depression (15%).

The exact relationship between diabetes and depression is still unclear. According to one hypothesis, depression increases the risk of developing diabetes. It is hypothesized that depression causes increased counter-regulatory hormone release, altered glucose transport function, and enhanced immunoinflammatory activation [57]. All of these factors enhance insulin resistance and islet beta-cell dysfunction, leading to increased susceptibility to diabetes.

According to another hypothesis, depression in diabetic patients results from chronic stressors emanating from a chronic medical condition such as diabetes [58]. There is strong evidence that depression among diabetics is associated with poor diabetes outcomes, such as poor glycemic control [59]. Another longitudinal study observed that depression was associated with persistently elevated HbA1c levels [60].
Some researchers have proposed that the presence of depressive symptoms indicates poor compliance in self-care, especially with medications and diet and exercise regimens [61]. A systematic review of treatment compliance among patients with diabetes and depression indicated a strong relationship between depression and non-compliance with treatment [62].

Recent studies have found that depression in diabetic patients increases the risk of mortality [63-65]. Recent guidelines indicate that because individuals with diabetes are more susceptible to depression, it is essential to periodically assess and monitor these patients for it [66]. Recent studies have indicated that risk of diabetes mellitus is greater in patients who experience depression and appears to be independent of health behaviors and other risk factors [67, 68]. Recent studies have strongly suggested that depression is a risk factor for diabetes, and not the other way around.

**Depression and Dementia**

Depression and dementia are seen commonly in the elderly. Depression in elderly adults with and without dementia usually goes undetected and untreated [69, 70]. Prevalence of depression in elderly persons with dementia varies significantly [71] because of variations in sampling and assessment of diagnostic criteria [71, 72].

Still controversial is whether depression before dementia represents a risk factor for dementia or a prodromal feature of dementia [73, 74]. It is suspected that depression can be a risk factor for dementia and also an early sign of dementia, with both conditions arising from similar neuropathological changes. Dementia may be a risk factor for depression because of a psychological reaction to the cognitive and behavioral changes associated with dementia. It is important to treat depression in individuals with dementia because it adds an additional burden to quality of life.

**Differentiating Dementia and Depression**
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Dementia</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Insidious, indeterminate</td>
<td>Relatively rapid, associated with mood changes</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>Usually long</td>
<td>Usually short</td>
</tr>
<tr>
<td>Orientation, mood, behavior, affect</td>
<td>Impaired, inconsistent, fluctuating depressed/anxious, complaints worse than on testing</td>
<td>Intact, diurnal variation</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>Consistent; stable or worsening</td>
<td>Inconsistent, fluctuating</td>
</tr>
<tr>
<td>Neurologic defects</td>
<td>Often present (e.g., agnosia, dysphasia, apraxia)</td>
<td>Absent</td>
</tr>
<tr>
<td>Disabilities</td>
<td>Concealed by patient</td>
<td>Highlighted by patient</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Memory impairment</td>
<td>Does not remember recent events, often unaware of memory loss. Onset of memory loss occurs before mood change.</td>
<td>Concentration poor, patient complains of memory loss of recent and remote events, follows onset of depressed mood</td>
</tr>
<tr>
<td>Psychiatric history</td>
<td>None</td>
<td>Often, history of depression</td>
</tr>
<tr>
<td>Answers to questions</td>
<td>Near answers</td>
<td>“Don’t know” answers</td>
</tr>
<tr>
<td>Performance</td>
<td>Tries hard, but is unconcerned about losses</td>
<td>Does not try hard but is more distressed by losses</td>
</tr>
<tr>
<td>Associations</td>
<td>Unsociability, uncooperative, hostility, emotional instability, reduced alertness, confusion, disorientation</td>
<td>Appetite and sleep disturbances, suicidal thoughts</td>
</tr>
</tbody>
</table>

**Other Neurological Disorders**

Prevalence of major depression is greatest among stroke patients (20% to 25%) [75]; intermediate among those with Parkinson’s disease (15% to 20%) [76]; and lower in those with Alzheimer’s disease (10% to
Comorbid depression is linked to functional impairment [77]. For instance, in Parkinson’s disease, depressive symptoms may lead to increased motor disturbance [78]. It is also observed that depression usually develops in the course of neurological illness, and depression is a risk factor for development of stroke [79] and Parkinson’s disease [80]. Neuroanatomical, as well as chemical, changes in the central nervous system (CNS) are important risk factors for depression in the elderly and usually carry poor prognosis.

It is believed that basal ganglia, subcortical, and frontal white matter lesions are associated with depression-executive dysfunction syndrome [42, 46]. Structural abnormalities in different areas of the brain are seen in elderly patients experiencing depression [4, 42]. Depression in elderly persons is associated with reduction in glial cells and neuronal abnormalities.

Vascular, inflammatory, and neuroanatomic risk factors are associated with depression in the elderly. In a recent study, the following observations were noted [81]:
- Neuroanatomic risk factors were linked to lack of concentration and psychomotor change.
- Vascular risk factors were linked to sleep impairments, psychomotor change, and loss of energy.
- Inflammatory risk factors were linked to appetite and sleep changes, loss of energy, concentration impairments, and thoughts of death.

It was also observed that minor depression is more closely associated with inflammatory risk factors than other factors (vascular or degenerative).

**Depression and Anxiety Disorder**
Anxiety typically precedes depression [82], suggesting that anxiety may be a risk factor for depression in the elderly [83]. Anxiety disorders seen in the elderly with depression can be as high as 50% [84, 85], and some studies estimate the prevalence rate of anxiety disorders from 25% to more than 80% in elderly patients with depression [84, 86]. Depression in the presence of anxiety is more severe, persistent, and difficult to treat, especially in the elderly [86, 87]. Elderly persons who experience anxiety and depression have higher rates of suicide, disability, and somatic symptoms compared with those who experience depression alone [86, 88]. Anxiety also leads to greater risk of cognitive impairment among the elderly with treated depression [89].

**Sleep**
Sleep disturbance is a risk factor for depression in the elderly. Approximately 90% of patients with depression complain of poor sleep quality and insomnia affects 25% of elderly males and 40% of elderly females [90].

A number of studies have observed that insomnia usually precedes depression [91]. Insomnia is a risk factor for development of both new-onset and persistence of depression in the elderly. Residual symptoms of insomnia usually linger, even after remission of a depressive episode, and indicate earlier relapse. New research studies have indicated that depression is better managed if insomnia is treated concurrently [92].

**Psychological Risk Factors**
Many psychological factors that might increase the probability of depression in the elderly are related to earlier episodes of depression [93]. Neuroticism has a strong relationship with depression in the elderly and is both a genetic, as well as a psychological, risk for depression [94]. Depression in the elderly is linked to a ruminative coping style, which is one where the patient internalizes their problems and worries too much [95].
Social Risk Factors

Stressful Life Events
Prominent stressful events in old age include:

- Financial problems.
- Bereavement.
- A new disease or disability in self or family member.
- Major changes in living situation.
- Interpersonal conflict.

Retirement is typically not associated with depression in the elderly; however, depression is seen more frequently in men who retire prematurely [96]. Research studies examining recent events have observed that major impacts occur within the first few months (6 months), and the majority of people are fairly resilient.

It has been noted that long-past events also may contribute to risk. Long-standing susceptibilities or vulnerabilities may modify the consequences of stressful events on depression in elderly. For instance, there is an increased risk of depression in elderly persons following hip fractures [97]. Cognitive style may also affect an individual’s response to stressful life events. The response seems to depend on the interaction between cognitive style and the kind of stressful event.

Depression in elderly persons with higher sociotropy scores is closely associated with stressful life events that bring interpersonal natural loss or disruption, whereas depression in the elderly with higher autonomy scores is closely associated with negative events linked to achievement [98]. It is observed that depressed individuals behave in certain ways that increase the risk of stressful events in the future [99]. Rumination, (a compulsive, focused attention on negative feelings and experiences from the past), which has been associated with decreased social support, may play an important role in depression.

A stressful event, such as loss of loved ones that occurs frequently as one becomes older, is known as bereavement. Depressive symptoms are a natural emotional reaction to loss, but symptoms that persist for more than 2 months may indicate depression. Some researchers believe that depression associated with bereavement is actually complicated grief, which manifests as symptoms of traumatic distress and separation distress [100]. However, some argue that complicated grief and major depression have a lot in common, with few differences [101]. A recent study on depression in the elderly observed that bereavement greatly increased (tripled) the risk of depression [102]. However, the risk of depression because of bereavement is less for the elderly than for those who are middle-aged. It seems older persons are better equipped to handle the loss of loved ones than younger adults because of better adaptation capabilities [103]. Compared with females, males are more susceptible to depression after loss of a spouse. Men also remain in depression for a longer period of time. For females, financial stress is the major mediator of depression or depressive symptoms, whereas for males, the major mediator is household chores or management [104].

Providing adequate care for a loved one can also trigger stress, which becomes more common with age. However, recent studies found no significant differences in depression between caregivers and non-caregivers [105]. It has been found that the risk of depression is higher among individuals caring for a person with dementia than among those caring for a person with a physical disability [106]. Furthermore, the rate of depression increases significantly in the caregiver if the care recipient has severe distress-behavior problems [106]. Some researchers believe that the rate of depression increases in these caregivers because of their restricted normal activities [107].
**Problems with Social Support**
Troubled relationships, including marital conflict, depression in the spouse, and perceived family criticism, may play a role in development of depression in elderly persons [108]. Loneliness is associated with depression in elderly people, although they are less lonely than their younger counterparts.

Social support that is perceived as unhelpful or excessive can also be a risk factor for depression. Several studies have observed that it is the quality, not quantity, of social support that matters in the development of depression in the elderly. It has been found that, even with good social support, depression is more common among elderly people with physical limitations who value independence [109].

**Socioeconomic Factors**
Poor financial health is considered to be a frequent stressful life event by most of the elderly [99]. It has been observed that economically disadvantaged elderly persons have a greater risk of depression [110]. Furthermore, weak socioeconomic status early in life also increases propensity for depression throughout life because of malnutrition, reduced opportunities for health care and education, or other mechanisms. The negative impact of poor socioeconomic status may become significant in elderly people when there is a greater risk of worsening of economic and health status.
**Depression: Risk and Protective Factors factors in the Elderly**

### General risk factors that increase risk throughout life

#### Biological risks
- Hereditary (runs in families)
- Being a woman rather than a man
- Low serotonin or high cortisol (brain chemicals)
- Low testosterone (a hormone, mainly a “male” hormone, but women have it, too)
- High blood pressure or hypertension
- Stroke
- Medical illness and overall poor function (e.g., problems walking)
- Alcohol abuse and dependence

#### Psychological risks
- Personality disorder
- Neuroticism (neurosis = means poor ability to adapt, inability to change one’s life patterns, and the inability to develop a richer, more complex, more satisfying personality)
- Learned helplessness
- Cognitive distortions (overreaction to life events; misinterpretation of life events; exaggerate exaggeration of their adverse outcomes; catastrophizing too much)
- Lack of emotional control and self-efficacy (low skills to control emotions and low belief in one’s capacity to succeed at tasks)

#### Social risks
- Stressful life events and daily hassles
- Bereavement (grief experienced by loss of a loved one due to death)
- Socio-economic disadvantage (being poor or having a low income)
- Impaired social support (lack of friends and family for fellowship and support)

### Risk and protective factors especially important in late life

#### Biological risks
- Genetics (runs in families)
- Low DHEA (a hormone)
- Poor blood flow in the brain (also called “ischemia”)
- Alzheimer’s Disease

#### Protective factors
- Socio-emotional selectivity (focus on the positive for the remainder of life)
- Wisdom (applying life’s lessons in a positive way to deal with today’s challenges)

---

**Protective Factors**

The majority of elderly people go through financial and physical disabilities, bereavement, grief, or other stressful life events. Furthermore, they also undergo degenerative changes in immune, neurological, and other biological aspects. However, the majority of these individuals also do not experience depression.
Extensive research was conducted to study factors that protect against depression from biological risks and stressful life events. The important themes that emerged from this review and other studies were:

- The importance of resources related to health, cognitive function, and socioeconomic status.
- The life experiences of elderly people have taught them psychological strategies and ways to use social support to manage their health-related stresses.
- The role of meaningful engagement, whether in terms of social and religion activities or volunteer work.

Elderly people also regulate their emotions better in stressful conditions compared with young adults. As individuals age, they experience fewer negative effects [111]. Compared with younger adults, elderly people are less reactive to stressors, especially those involving interpersonal relationships [112]. Also, elderly people usually show less reactivity to daily stressors and show less affective reactivity in response to cognitive challenges [113]. The elderly are more likely to put things into perspective, a cognitive strategy that helps reduce depressive symptoms or depression [95]. They tend to focus more on positive and emotionally meaningful experiences, indicating better emotion regulation [114].

Other psychological factors that prevent depressive disorders include a sense of mastery or self-efficacy and a positive self-concept. Several studies have reported a close association of disability with lower self-efficacy and mastery resulting in higher depressive symptom scores. Disability may result in a reduction of an individual’s appraised ability to attain goals; however, some individuals reduce their activities because of disability, and the lack of engagement in activities results in poor skills and lack of self-efficacy.

It has been found that activity restriction leads to increased levels of depression among the elderly with functional impairment [107]; however, satisfactory replacement of lost activities may result in normalization of depression or depressive symptoms [115]. Religious activities may also play an important role in reducing the risk of depression in the elderly [116]. Effective health engagement control strategies are linked with reduction in depressive symptoms, as well as reduced secretion of the stress hormone cortisol [117].

Researchers are also studying factors that may reduce the effects of biological susceptibility to depression in the elderly. The impact of physical exercise, coping strategies, stress reduction strategies, and hormone replacement therapy on depression and depressive symptoms is also being investigated.

**Depression and Suicide**

Depression is one of the most common conditions associated with suicide in the elderly [118]. The risk of depression greatly increases with comorbid conditions and degree of disability. Approximately 4% of those with an inpatient admission for depression commit suicide [119]. Furthermore, suicide among the elderly is more likely to be associated with depression than suicide in other age groups [120]. Globally, suicide rates are three to four times greater among men than women at all ages, but the differential further increases in elderly people [121].

Suicide rates show wide variations by ethnicity. In the United States, suicide rates are highest for Caucasians and Native Americans, while rates are comparatively low for African-Americans and lowest for Latinos. However, suicide rates among the elderly have declined for the past few years. Suicidal behavior in elderly persons differs in many ways from that seen earlier in the lifespan. Compared with any other age group, suicidal behavior by elderly persons is more likely to be deadly. Suicides committed by elderly persons reflect a greater intensity and planning compared with any other age group [122].
Elderly persons usually do not verbalize suicidal thoughts compared with others; however, they have higher rates of death ideation. Studies show that the majority of elderly persons who commit suicide—approximately 75%—had visited a doctor within a month before death [123]. Physical illnesses have also been associated with higher suicide rates among the elderly [124]. Some researchers have suggested that a rigid personality style also increases propensity for suicide. Excessive alcohol consumption also increases risk for suicide among elderly.

<table>
<thead>
<tr>
<th>Suicide and Major Depression: The Rule of Seven</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ One out of seven people with recurrent depressive illness commit suicide.</td>
</tr>
<tr>
<td>■ Seventy percent of suicides have depressive illness.</td>
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<tr>
<td>■ Seventy percent of suicides see their primary-care practitioner within 4 weeks of suicide.</td>
</tr>
<tr>
<td>■ Suicide is the seventh leading cause of death in the United States.</td>
</tr>
</tbody>
</table>

**Signs and symptoms of depression in the elderly**

Prominent signs and syndrome of depression in elderly include:

- Persistent sadness
- Fatigue and decreased energy
- Abandoning or losing interest in hobbies or other pleasurable pastimes
- Social withdrawal and isolation (reluctance to be with friends, engage in activities, or leave home)
- Weight loss or loss of appetite
- Sleep disturbances (difficulty falling asleep or staying asleep, oversleeping, or daytime sleepiness)
- Loss of self-worth (worries about being a burden, feelings of guilt, worthlessness, self-loathing)
- Increased use of alcohol or other drugs
- Fixation on death; suicidal thoughts or attempts

**Depression in the Elderly Without Sadness**

Depression and sadness seem to go hand-in-hand; however, elderly people with depression often do not feel sad at all. They may complain of lack of motivation, a lack of energy, or physical problems. In fact, a lot of elderly persons report physical complaints such as pain due to arthritis or worsening headaches as the predominant symptoms of depression. Elderly persons who do not feel sad or depressed may still have major depression.
Unexplained or aggravated aches and pains
Feelings of hopelessness or helplessness
Anxiety and worries
Memory problems
Lack of motivation and energy
Slowed movement and speech
Irritability
Loss of interest in socializing and hobbies
Neglecting personal care (skipping meals, forgetting meds, neglecting personal hygiene)

### Symptoms of Depression

<table>
<thead>
<tr>
<th>Most important</th>
<th>Important</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressed mood most of the day, almost every day (by either subjective report [feels sad or empty], or observation made by others [appears tearful]). Diminished interest or pleasure in most activities most of the time.</td>
<td>Difficulty making decisions.</td>
</tr>
<tr>
<td></td>
<td>Feelings of helplessness.</td>
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<tr>
<td></td>
<td>Feelings of worthlessness or hopelessness.</td>
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<tr>
<td></td>
<td>Inappropriate feelings of guilt.</td>
</tr>
<tr>
<td></td>
<td>Psychomotor agitation or retardation not attributable to other causes.</td>
</tr>
<tr>
<td></td>
<td>Social withdrawal, avoidance of social interactions or going out.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sometimes helpful</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>(In general, these symptoms tend to be more common among the elderly.)</td>
<td>Appetite changes.</td>
</tr>
<tr>
<td></td>
<td>Morning sluggishness and lack of energy that improves markedly later in the day.</td>
</tr>
<tr>
<td></td>
<td>Change in ability to think or concentrate.</td>
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<tr>
<td></td>
<td>Change in activities of daily living (ADLs).</td>
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<tr>
<td></td>
<td>Family history of mood disorders.</td>
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<td></td>
<td>Fatigue or loss of energy, worse than baseline.</td>
</tr>
<tr>
<td></td>
<td>Insomnia or hypersomnia nearly every day.</td>
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<tr>
<td></td>
<td>Increased complaints of pain.</td>
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<tr>
<td></td>
<td>Preoccupation with poor health or physical limitations.</td>
</tr>
<tr>
<td></td>
<td>Weight loss or gain.</td>
</tr>
</tbody>
</table>

Adapted from Alexopoulos, et al.

### Major Depressive Episode

According to the American Psychiatric Association DSM-IV-TR criteria, at least one of the two main depressive symptoms, depressed mood and anhedonia, should be present to make a diagnosis of a major depressive episode (MDE) [126]. According to DSM-IV-TR, major depressive disorder is categorized as a mood disorder [127] (See below). The diagnosis depends upon the presence of a single or recurrent
MDE(s). Further qualifiers are needed for classification of both the episode itself and to determine the course of the disorder.

The category “Depressive Disorder Not Otherwise Specified” is diagnosed if the depressive episode’s clinical picture does not meet the criteria for a MDE.

**American Psychiatric Association DSM-IV-TR Criteria**

Five or more of the following symptoms must present for a minimum of 2 weeks to diagnose a depressive disorder:

- Depressed mood.
- Loss of interest or pleasure in activities.
- Changes in weight or appetite.
- Insomnia or hypersomnia.
- Psychomotor agitation or retardation.
- Low energy.
- Feelings of worthlessness.
- Poor concentration.
- Recurrent suicidal ideation or suicide attempt.

**Atypical presentation of depressed older adult**

- Denies sadness or depressed mood.
- May exhibit other symptoms of depression.
- Unexplained somatic complaints.
- Hopelessness.
- Helplessness.
- Anxiety and worries.
- Memory complaints (may or may not have objective signs of cognitive impairment).
- Anhedonia.
- Slowed movement.
- Irritability.
- General lack of interest in personal care.

The most important and essential feature of a MDE is a minimum period of 2 weeks during which a patient experiences a depressed mood [128] or anhedonia (loss of interest or pleasure in almost all activities). In addition to these core symptoms, the individual should also have a minimum of four additional symptoms that includes changes in appetite or weight, sleep (insomnia), and psychomotor activity; decreased energy (fatigue); feelings of guilt or worthlessness; difficulty thinking, making decisions or lack of concentration; or recurrent thoughts of death or suicidal ideation, or attempts.

The symptoms should have been experienced for the first time (newly present) or should have deteriorated compared with the individual’s pre-episode status. The symptoms are present for most of the day, almost daily, for a minimum period of 2 consecutive weeks.

The episode is accompanied by marked distress or impairment in almost all the spheres, including occupational, social, or other core areas of functioning. Some individuals may appear to have normal functioning but require significantly greater effort. The mood is usually described as depressed, hopeless, down or sad, or discouraged. Some individuals may complain about somatic symptoms, such as body pains, and many experience increased irritability. Social withdrawal is frequently observed by the individual’s family members.
Psychomotor changes are frequently seen in a MDE and include agitation or retardation and changes in speech with respect to volume, amount and inflection, or variety of content, or muteness. These symptoms should be significant enough to be noticed by others and not restricted to only subjective feelings.

A person may complain about sustained fatigue almost every day. Even menial tasks such as washing and dressing require a significant effort. Almost every day, the individual experiences extreme fatigue [128]. The patient may report a sense of worthlessness or guilt that may include impractical negative evaluations regarding self-worth or guilt with delusional proportions.

Many individuals experience a poor ability to think, make decisions, or concentrate. Memory impairments may be the principal complaint of the elderly and can easily be misinterpreted as pseudodementia. Memory problems usually resolve after successful treatment of a MDE; however, in the elderly, this episode sometimes can be the initial clinical presentation of an irreversible dementia. Some individuals may have suicidal ideation or thoughts of death with varying intensity, frequency, and lethality.

An individual cannot be diagnosed with an episode of MDE if the symptoms meet criteria for a mixed episode. A mixed episode is characterized by the symptoms of both a manic episode and a MDE almost daily for at least 1 week [129]. The degree or extent of impairment linked with a MDE may vary, but there must be either the presence of clinically significant distress or some interference in social, occupational, or other crucial areas of functioning.

In a case of severe impairment, the individual may be unable to function occupationally or socially. In extreme cases, the individual may not be able to maintain minimal personal hygiene or perform minimal self-care. A thorough interview is necessary to elicit symptoms associated with a MDE. Additional information from family members and friends may help in determining the course of current or prior MDEs and in ascertaining a past history of manic or hypomanic episodes.

It is difficult to evaluate symptoms of a MDE when they are present in an individual with a general medical condition, such as stroke, diabetes, cancer, or myocardial infarction. Symptoms such as weight loss in untreated diabetes and fatigue experienced in cancer point toward a MDE, except when they are clearly known to be caused by a general medical condition. Similarly, if the signs and symptoms are caused by hallucinations or mood-incongruent delusions, they do not support the diagnosis of a MDE. A MDE is not caused by the direct physiological effects of a substance abuse or a general medical condition.

### Diagnosis of Depression depression – DSM-IV-TR Criteria

<table>
<thead>
<tr>
<th>Major depressive episode criterion:</th>
</tr>
</thead>
</table>

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19
A. **At least five of the following symptoms** have been present during the same 2-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:

1. 1. **Depressed mood** most of the day, nearly every day, as indicated either by subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful).
2. 2. Markedly **diminished interest or pleasure in all, or almost all, activities** most of the day, nearly every day (as indicated either by subjective account or observation made by others).
3. 3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5 percent of body weight in a month), or decrease or increase in appetite nearly every day.
4. 4. **Insomnia** or **hypersomnia** nearly every day.
5. 5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. 6. **Fatigue** or loss of energy nearly every day.
7. 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. 9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or specific plan for committing suicide
10.

Also:
B. The symptoms do not meet criteria for a mixed episode.

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to the direct physiological effects of a substance (e.g. a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

E. The symptoms are not better accounted for by bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

**Major depressive disorder, single episode criterion:**

A. Presence of a single major depressive episode
B. The major depressive episode is not better accounted for by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.
C. There has never been a manic episode, a mixed episode, or a hypomanic episode.

If the full criteria are currently met for a Major major Depressive depressive Episode, specify its current clinical status and/or features:
- Mild, moderate, severe without psychotic feature/s/ severe with psychotic features.
- Chronic.
- With Catatonic catatonic Features features.
- With Melancholic melancholic Features features.
- With Atypical atypical Features features.
- With Postpartum postpartum Onset onset.

If the full criteria are not currently met for a Major major Depressive depressive Episode episode, specify the current clinical status of the Major major Depressive depressive Disorder disorder or features of the most recent episode:
- In Partial partial Remission remission, In in Full full Remission remission.
- Chronic.
- With Catatonic catatonic Features features.
- With Melancholic melancholic Features features.
- With Atypical atypical Features features.
- With Postpartum postpartum Onset onset.

**Major depressive disorder, recurrent criterion:**

A. A. Presence of two or more major depressive episodes (each separated by at least 2 months in which criteria are not met for a major depressive episode.)
B. B. The major depressive episodes are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.
C. C. There has never been a manic episode, a mixed episode, or a hypomanic episode.

If the full criteria are currently met for a Major major Depressive depressive Episode episode, specify its current clinical status and/or features:
- Mild, moderate, severe without psychotic feature s/severe with psychotic Features features.
- Chronic.
- With Catatonic catatonic Features features.
- With Melancholic melancholic Features features.
- With Atypical atypical Features features.
- With Postpartum postpartum Onset onset.

If the full criteria are not currently met for a Major major Depressive depressive Episode episode, specify the current clinical status of the Major major Depressive depressive Disorder disorder or features of the most recent episode:
- In partial remission, in full remission.
- Chronic.
- With Catatonic catatonic Features features.
- With Melancholic melancholic Features features.
- With Atypical atypical Features features.
- With Postpartum postpartum Onset onset.

Specify:
- Longitudinal Course course Specifiers specifiers (with and without interepisode recovery).
- With Seasonal seasonal Pattern pattern.
Adapted from: Practice Guideline for the Treatment of Patients With Major Depressive Disorder (MDD), Third Edition, American Psychiatric Association, 2010

**Associated Features and Disorders**

Individuals with a MDE may present with the following symptoms:
- Irritability.
- Tearfulness.
- Brooding.
- Obsessive rumination.
- Anxiety.
- Phobias.
- Somatic symptoms.
- Complaints of pain.

Some people have problematic intimate relationships, comparatively less satisfying social lives or interactions, or impaired sexual function. Psychosocial stressors such as the death of a spouse or loved one, or divorce/marital separation often precede a MDE. The most serious consequence of a MDE is suicide, either attempted or completed. The suicide rate is particularly higher for people with psychotic features, a history of attempted suicides, concurrent alcohol or drug abuse, or a family history of completed suicides.

**Laboratory Findings**

There are no diagnostic laboratory findings for a MDE; however, a number of findings are found to be abnormal in individuals with a MDE compared with normal healthy people. Laboratory findings are usually abnormal in episodes with psychotic or melancholic features and in severely depressed individuals.

Sleep EEG abnormalities are present in approximately 40% to 60% of outpatients and up to 90% of inpatients with MDE. It has been observed that these sleep abnormalities can be present even after clinical remission or precede the MDE onset among high-risk individuals for a mood disorder.

**Course**

Symptoms of MDEs usually develop over days to weeks. Before the onset of a full MDE, a prodromal period that may include symptoms of anxiety and mild depression may persist for a few weeks to several months. The duration of a MDE is also variable. An untreated episode usually persists for 4 months, irrespective of age at onset.

In approximately 20% to 30% of cases, some depressive symptoms are inadequate to meet full criteria for a MDE and may continue for a few months to years and may be linked with some disability or distress. Partial remission after a MDE seems to be predictive of an identical pattern after subsequent episodes. In approximately 10% of the cases, the full criteria for a MDE continue to be met for 2 or more years.

**Differential Diagnosis**

MDEs should be distinguished from a mood disorder caused by a general medical condition. When the mood disturbance develops because of a particular general medical condition such as stroke, it is designated as a mood disorder due to a general medical condition. The diagnosis is made on the basis of a patient’s history, physical examination, or laboratory findings. A substance-induced mood disorder develops because of a particular substance, such as a drug, medication, or toxin that is associated with mood disturbance.
In the elderly, it becomes more difficult to ascertain the etiology of the cognitive symptoms caused by dementia or by a MDE. A complete medical examination and evaluation of the onset of the disturbance, course of illness, temporal sequencing of symptoms association with cognition and depression, and response to the treatment help determine the exact cause.

The premorbid state of the person can help differentiate a MDE from dementia. People with dementia generally tend to have a premorbid history of worsening cognitive function, whereas people with a MDE tend to have a relatively normal premorbid state and abrupt cognitive decline.

A MDE with a prominent irritable mood can be tricky to differentiate from manic episodes or from mixed episodes. A thorough clinical evaluation of the presence of manic symptoms is necessary in such cases. A patient is diagnosed with a mixed episode if criteria are met for both a manic episode and a MDE (except for the 2-week duration) and almost daily for a minimum period of 1 week.

**Major Depressive Disorder (MDD)**

Major depressive disorder (MDD) is a clinical course that is always characterized by one or more MDE(s) without a history of manic, mixed, or hypomanic episodes. However, if symptoms of mania or hypomania develop as a consequence of antidepressants, toxins, or drug abuse, the diagnosis of MDD remains unchanged and appropriate and an additional diagnosis should be noted according to the features presented.

**Associated Features and Disorders**

People with MDD have a high mortality rate, and approximately 15% of individuals with severe MDD commit suicide. Mortality increases with age and is almost fourfold in individuals over 55 years of age. There is a significant increase in mortality rate in people with MDD who are admitted to nursing homes, especially in the first year of admission.

In general medical settings, individuals with MDD experience more pain and physical illness and decreased social, physical, and role functioning. MDD may be preceded by dysthymia. About 10% of individuals with dysthymia alone will go on to have a first MDE. Other mental disorders, such as panic disorder and substance abuse disorders, frequently develop concurrently.

**Laboratory Findings**

The laboratory findings of MDD are similar to those found in a MDE. There are no diagnostic findings for MDD; however, elevated glucocorticoid levels and EEG sleep alterations are observed in some individuals with psychotic features and those with more severe episodes or with melancholic features. The majority of laboratory abnormalities are present only with depressive symptoms; however, recent studies have shown some sleep EEG abnormalities persist even during clinical remission or may precede the onset of the MDE.

People with chronic or severe general medical conditions are more prone to develop MDD. Approximately 20% to 25% of individuals with certain general medical conditions, such as diabetes, myocardial infarction, or stroke, will develop MDD. In the presence of MDD, the treatment and overall management of such conditions is more difficult and complex with poor prognosis. Prognosis of MDD is poor in the presence of concomitant chronic general medical conditions.

**Prevalence**

The lifetime risk for MDD varies from 10% to 25% for women and from 5% to 12% for men. There is a relationship between the prevalence rates for MDD and education, ethnicity, income, or marital status.
The average age of MDD onset is mid-20s, although it may begin at any age. Recent epidemiological data indicate that age at onset is decreasing for those more recently born.

**Course**

The course of recurrent MDD is variable. Some people experience isolated episodes that may occur at long intervals of time (i.e., several years) without any depressive symptoms, whereas some experience strings of episodes, and still other individuals experience increasingly frequent episodes as they age.

Some studies have observed that the periods of remission usually last longer early in the course of MDD. The number of prior episodes is associated with a greater likelihood of developing a subsequent MDE. Approximately 60% of individuals with MDD, single episode have a greater likelihood of having a second episode—this trend increases with the increase in number of episodes.

**Subtypes**

In addition to noting the severity, length, and presence of psychotic features, there are five more subtypes of MDD, known as specifiers. If the full criteria are met for a MDE, specifiers can be used to appropriately diagnose the current clinical status of the episode and to appropriately describe features of the current episode.

**Melancholic Depression**

This is characterized by at least one of these symptoms: anhedonia or lack of mood reactivity in response to pleasurable stimuli. It is also characterized by at least three of the signs and symptoms: depression that is distinct from grief or loss, severe weight loss, significant anorexia (but not anorexia nervosa) or loss of appetite, early morning awakening, psychomotor agitation or retardation, excessive guilt, and worse or bad mood in the morning [130].

<table>
<thead>
<tr>
<th>DSM-IV-TR Specifier Criteria for Melancholic Features</th>
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<tbody>
<tr>
<td>Specify if:</td>
</tr>
<tr>
<td>With melancholic features (can be applied to the current or most recent Major Depressive Episode in Major Depressive Disorder and to a Major Depressive Episode in Bipolar I or Bipolar II Disorder only if it is the most recent type of mood episode).</td>
</tr>
<tr>
<td>• Either of the following, occurring during the most severe period of the current episode:</td>
</tr>
<tr>
<td>• Loss of pleasure in all, or almost all, activities.</td>
</tr>
<tr>
<td>• Lack of reactivity to usually pleasurable stimuli (does not feel much better, even temporarily, when something good happens).</td>
</tr>
<tr>
<td>• Three (or more) of the following:</td>
</tr>
<tr>
<td>• Distinct quality of depressed mood (i.e., the depressed mood is experienced as distinctly different from the kind of feeling experienced after the death of a loved one).</td>
</tr>
<tr>
<td>• Depression regularly worse in the morning.</td>
</tr>
<tr>
<td>• Early morning awakening (at least two hours before usual time of awakening).</td>
</tr>
<tr>
<td>• Marked psychomotor retardation or agitation.</td>
</tr>
<tr>
<td>• Significant anorexia or weight loss.</td>
</tr>
<tr>
<td>• Excessive or inappropriate guilt.</td>
</tr>
</tbody>
</table>
A. Either of the following, occurring during the most severe period of the current episode:
   (1) loss of pleasure in all, or almost all, activities
   (2) lack of reactivity to usually pleasurable stimuli (does not feel much better, even temporarily, when something good happens)
B. Three (or more) of the following:
   (1) distinct quality of depressed mood (i.e., the depressed mood is experienced as distinctly different from the kind of feeling experienced after the death of a loved one)
   (2) depression regularly worse in the morning
   (3) early morning awakening (at least 2 hours before usual time of awakening)
   (4) marked psychomotor retardation or agitation
   (5) significant anorexia or weight loss
   (6) excessive or inappropriate guilt

Atypical Depression
Atypical depression is characterized by mood reactivity (paradoxical anhedonia) and positivity, substantial weight gain or increased appetite, hypersomnia, leaden paralysis (a sensation of heaviness in limbs), and marked social impairment because of hypersensitivity to perceived interpersonal rejection.

**DSM-IV Specifier Criteria for Atypical Features**

Specify if:

With Atypical atypical Features features (can be applied when these features predominate during the most recent 2 weeks of a current Major Depressive Episode in Major Depressive Disorder or in Bipolar I or Bipolar II Disorder when a current Major Depressive Episode is the most recent type of mood episode, or when these features predominate during the most recent 2 years of Dysthymic Disorder; if the Major Depressive Episode is not current, it applies if the feature predominates during any 2-week period)

| A. Mood reactivity (i.e., mood brightens in response to actual or potential positive events). |
| B. Two (or more) of the following features: |
| 1. Significant weight gain or increase in appetite. |
| 2. Hypersomnia. |
| 3. Leaden paralysis (i.e., heavy, leaden feelings in arms or legs). |
| 4. Long-standing pattern of interpersonal rejection sensitivity (not limited to episodes of mood disturbance) that results in significant social or occupational impairment. |

Criteria are not met for With Melancholic Features or With Catatonic Features during the same episode. A. Mood reactivity (i.e., mood brightens in response to actual or potential positive events)

| C. events |
| D. B. Two (or more) of the following features: |
| E. (1) significant weight gain or increase in appetite |
F. (2) hypersomnia
G. (3) leaden paralysis (i.e., heavy, leaden feelings in arms or legs)
H. (4) long-standing pattern of interpersonal rejection sensitivity (not limited to episodes of mood disturbance) that results in significant social or occupational impairment
I. C. Criteria are not met for With Melancholic Features or With Catatonic Features during the same episode.
J.

Catatonic depression
This is a severe and rare form of major depression involving motor immobility, motor hyperactivity, extreme negativism, peculiarities of voluntary movement, mutism, echolalia, or echopraxia. Catatonic symptoms are observed in schizophrenia or in manic episodes, or neuroleptic malignant syndrome.

It is not recognized as a distinct disorder, but is closely associated with certain psychiatric conditions, including:

- Schizophrenia (catatonic type).
- Post-traumatic stress disorder.
- Bipolar disorder.
- Depression.
- Substance abuse or overdose.
- Encephalitis.
- autoimmune Autoimmune disorders.
- Stroke.
- Benzodiazepine withdrawal [132-134].

DSM-IV-TR Criteria for Catatonic Features Specifier
Specify if:
With Catatonic Features (can be applied to the current or most recent Major Depressive Episode, Manic Episode, or Mixed Episode in Major Depressive Disorder, Bipolar I Disorder, or Bipolar II Disorder).

The clinical picture is dominated by at least two of the following:
1. Motoric immobility as evidenced by catalepsy (including W3)(IJ flexibility) or stupor.
2. Excessive motor activity (that is apparently purposeless and not influenced by external stimuli).
3. Extreme negativism (an apparently motiveless resistance to all instructions or maintenance of a rigid posture against attempts to be moved) or mutism.
4. Peculiarities of voluntary movement as evidenced by posturing (inappropriate or bizarre postures), stereotyped movements, prominent mannerisms, or prominent grimacing.
5. Echolalia or echopraxia.

Seasonal Affective Disorder
Seasonal affective disorder (SAD) is a form of depression in which depressive episodes occur in particular seasons (autumn or winter), and resolve in particular season (summer or spring). The diagnosis is established when a minimum of two episodes have developed in colder months, with none at other times, during a 2-year period or longer. The prevalence of winter-type seasonal depression varies with age, latitude, and sex. Prevalence of SAD is greater in people living at higher latitudes and in young adults, especially women. Elderly men are less prone to this disorder.

DSM-IV-TR Specifier Criteria for Seasonal Patterns

Specify if:
With Seasonal Pattern (can be applied to the pattern of Major Depressive Episodes in Bipolar I Disorder, Bipolar II Disorder, or Major Depressive Disorder, Recurrent)

There has been a regular temporal relationship between the onset of Major Depressive Episodes in Bipolar I or Bipolar II Disorder or Major Depressive Disorder, Recurrent, and a particular time of the year (e.g., regular appearance of the Major Depressive Episode in the fall or winter).

Note: Do not include cases in which there is an obvious effect of seasonal-related psychosocial stressors (e.g., regularly being unemployed every winter).

Full remissions (or a change from depression to mania or hypomania) also occur at a characteristic time of the year (e.g., depression disappears in the spring).

In the last 2 years, two Major Depressive Episodes have occurred that demonstrate the temporal seasonal relationships defined in Criteria A and B, and no Non-seasonal Major Depressive
Episodes have occurred during that same period.
Seasonal Major Depressive Episodes (as described above) substantially outnumber the non-seasonal Major Depressive Episodes that may have occurred over the individual’s lifetime.

A. There has been a regular temporal relationship between the onset of Major Depressive Episodes in Bipolar I or Bipolar II Disorder or Major Depressive Disorder, Recurrent, and a particular time of the year (e.g., regular appearance of the Major Depressive Episode in the fall or winter).

Note: Do not include cases in which there is an obvious effect of seasonal related psychosocial stressors (e.g., regularly being unemployed every winter).

B. Full remissions (or a change from depression to mania or hypomania) also occur at a characteristic time of the year (e.g., depression disappears in the spring).

C. In the last 2 years, two Major Depressive Episodes have occurred that demonstrate the temporal seasonal relationships defined in Criteria A and B, and no Non-seasonal Major Depressive Episodes have occurred during that same period.

D. Seasonal Major Depressive Episodes (as described above) substantially outnumber the non-seasonal Major Depressive Episodes that may have occurred over the individual’s lifetime.
Geriatric Depression Scale – Short Form

Think over the past week and answer the questions below as “yes” or “no.”

<table>
<thead>
<tr>
<th>Question</th>
<th>* answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Are you basically satisfied with your life?</td>
<td>Yes – *NO</td>
</tr>
<tr>
<td>2) Have you dropped many of your activities and interests?</td>
<td>*YES – No</td>
</tr>
<tr>
<td>3) Do you feel that your life is empty?</td>
<td>*YES – No</td>
</tr>
<tr>
<td>4) Do you often get bored?</td>
<td>*YES – No</td>
</tr>
<tr>
<td>5) Are you in good spirits most of the time?</td>
<td>Yes Yes – *NO</td>
</tr>
<tr>
<td>6) Are you afraid that something bad is going to happen to you?</td>
<td>*YES – No</td>
</tr>
<tr>
<td>7) Do you feel happy most of the time?</td>
<td>Yes – *NO</td>
</tr>
<tr>
<td>8) Do you often feel helpless?</td>
<td>*YES – No</td>
</tr>
<tr>
<td>9) Do you prefer to stay at home, rather than going out and doing new things?</td>
<td>*YES – No</td>
</tr>
<tr>
<td>10) Do you feel you have more problems with memory than most people?</td>
<td>*YES – No</td>
</tr>
<tr>
<td>11) Do you think it is wonderful to be alive now?</td>
<td>Yes *NO</td>
</tr>
<tr>
<td>12) Do you feel pretty worthless the way you are now?</td>
<td>*YES – No</td>
</tr>
<tr>
<td>13) Do you feel full of energy?</td>
<td>Yes – *NO</td>
</tr>
<tr>
<td>14) Do you feel that your situation is hopeless?</td>
<td>*YES – No</td>
</tr>
<tr>
<td>15) Do you think that most people are better off than you are?</td>
<td>*YES – No</td>
</tr>
</tbody>
</table>

TOTAL * SCORE =

If the answer marked with an asterisk (*) score is 10 or greater, or if numbers 1, 5, 7, 11, and 13 are answered with the a * answer, then the individual may be depressed and should consult with their his or her own doctor or other qualified health professional. Health professionals should proceed with a referral and/or treatment plans as necessary.

Dysthymia (Dysthymic Disorder)

Dysthymic disorder (dysthymia) is characterized by a chronically depressed mood that is experienced for most of the day, more days than not, for at least 2 years. Compared with MDD, dysthymia encompasses symptoms of chronic depression that are less severe but longer-lasting [136]. People experiencing dysthymic disorder describe their mood as sad or “down in the dumps.”
During periods of depressed mood, people experience at least one of the following additional symptoms:
- Poor appetite or overeating.
- Insomnia or hypersomnia.
- Low energy or fatigue.
- Low self-esteem.
- Lack of concentration or impaired decision-making.
- Feelings of hopelessness.

In more severe forms of dysthymic disorder, an individual may even withdraw from activities of daily living [137]. Dysthymia often develops concurrently with other psychological disorders, making its detection even more difficult and complex, which adds a level of complexity in determining the its presence, especially when the symptoms of other psychological disorders overlap with the its symptoms [138].

People with dysthymia also have a greater incidence of comorbid disease. It is also extremely important to look for signs of other mood disorders, such as major depression, generalized anxiety disorder, drug or alcohol abuse, and personality disorder.

With elderly people who experience dysthymia, the psychological symptoms are generally linked to medical diseases and conditions and stressful life events and losses. Diagnosis of dysthymia is considered only if the initial 2-year period of dysthymic symptoms is free of MDEs. If the chronic depressive symptoms include MDEs during the initial 2 years and all the criteria of MDEs are met, then the diagnosis is considered to be MDD.

**Specifiers**

Specifiers indicating age at onset and the characteristic pattern of symptoms may be used:
- **Early onset.** Symptoms are observed before 21 years of age. Individuals have a greater likelihood of developing subsequent MDEs.
- **Late onset.** Symptoms occur at 21 years of age or older.
- **With atypical features.** The pattern of symptoms during the most recent 2 years of the disorder meets the criteria for “with atypical features.”

**Associated Features and Disorders**

The associated features of dysthymia are identical to those for MDEs.

The most frequent symptoms observed in dysthymia are:
- Feelings of inadequacy.
- Feelings of guilt or brooding.
- Subjective feelings of irritability or excessive anger.
- Anhedonia (loss of interest or pleasure).
- Social withdrawal.
- Decreased activity or productivity.

Compared with individuals with MDEs, vegetative symptoms, such as psychomotor symptoms or changes in sleep and appetite, are observed less commonly in dysthymic disorder. It has been observed that the presence of dysthymia without a prior MDE greatly increases the risk for developing MDD.

**Specific Age and Gender Features**

- Compared with men, women have a greater likelihood (almost threefold) of developing dysthymia. The lifetime prevalence of dysthymia is approximately 6%.
### DSM-IV-TR Diagnostic criteria for Dysthymic Disorder

| A. | Depressed mood for most of the day, for more days than not, as indicated either by subjective account or observation by others, for at least 2 two years. Note: In children and adolescents, mood can be irritable and duration must be at least 1 one year. |
| B. | Presence, while depressed, of two (or more) of the following: |
| 1. | Poor appetite or overeating. |
| 2. | Insomnia or hypersomnia. |
| 3. | Low energy or fatigue. |
| 4. | Low self-esteem. |
| 5. | Poor concentration or difficulty making decisions. |
| 6. | Feelings of hopelessness. |
| C. | During the 22-year period (1 1 year for children or adolescents) of the disturbance, the person has never been without the symptoms in Criteria A and 8 for more than 2 months at a time. |
| D. | No Major Depressive Episode has been present during the first 2 years of the disturbance (1 year for children and adolescents); i.e., the disturbance is not better accounted for by chronic Major Depressive Disorder, or Major Depressive Disorder, In Partial Remission. Note: There may have been a previous Major Depressive Episode provided there was a full remission (no significant signs or symptoms for 2 months) before development of the Dysthymic Disorder. In addition, after the initial 2 years (1 year in children or adolescents) of Dysthymic Disorder, there may be superimposed episodes of Major Depressive Disorder, in which case both diagnoses may be given when the criteria are met for a Major Depressive Episode. |
| E. | There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode, and criteria have never been met for Cyclothymic Disorder. |
| F. | The disturbance does not occur exclusively during the course of a chronic Psychotic Disorder, such as Schizophrenia or Delusional Disorder. |
| G. | The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism). |
| H. | The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. |
| I. | Depressive disorder not otherwise specified |

**Depressive disorder not otherwise specified**

The “depressive disorder not otherwise specified” category encompass various types of disorders with depressive features that do not meet the criteria for major depressive disorder, dysthymia, adjustment disorder with depressed mood, or adjustment disorder with mixed anxiety and depressed mood.
Examples of depressive disorder otherwise specified include:

1. **Premenstrual dysphoric disorder (PMDD):** This is a severe form of premenstrual syndrome, [139] that is observed in 3-8 percent of women [140]. It is a diagnosis associated predominantly with the luteal phase of the menstrual cycle. Up to one-third of women in such cases report residual symptoms even in the first 2-3 days of the follicular phase [141]. It follows a predictable, cyclic pattern where the symptoms begin in the late luteal phase and end shortly after menstruation begins [142]. Most frequent symptoms associated with PMDD include:

   - Feeling of sadness or markedly depressed mood.
   - Intense tension or marked anxiety.
   - Marked affective lability.
   - Chronic fatigue.
   - Decreased interest in activities.

   These symptoms are so intense and severe that they interfere with daily activities at home, office, school, etc. Individual An individual may be absent for at least 1 week postmenses.

2. **Minor depressive disorder:** This condition is a mood disorder that encompasses episodes of at least 2 weeks of depressive symptoms, but with less than five items required for the diagnosis of MDD [143].

**Bipolar Disorder**

Bipolar disorder is a psychiatric diagnosis for a mood disorder. People with bipolar disorder experience alternative episodes of mania or hypomania with episodes of depression. The key feature of Bipolar I Disorder disorder is a clinical course that is characterized by the occurrence of one or more manic episodes or mixed episodes. Often individuals also experience one or more MDE (Major major Depressive depressive episodes). Young people initially tend to have more depressive episodes [144].

Because diagnosis of a bipolar disorder requires a hypomanic or manic episode, many patients are initially diagnosed with major depression [145].

Bipolar disorder is less prevalent in the elderly, but the number of psychiatric admissions remains unchanged compared to other age groups. It has been observed that elderly persons experience
symptoms at a later age. The later onset of mania is associated with more neurologic difficulties and impairment.

There seems to be more variation in presentation and course of bipolar disorder in elderly. Some clinical studies have observed that among the elderly with bipolar disorder, mania is less intense, and mixed episodes are more frequent with relatively poor response to treatment.

Overall, bipolar disorder in the elderly has more similarities than differences from younger adults [146, 147]. In the elderly, detection and management of bipolar disorder may get complicated because of concomitant dementia or the adverse effects of drugs being taken for other disease and conditions [148].

Associated features of Bipolar bipolar I Disorder

Approximately 10-15 percent of individuals with Bipolar bipolar I Disorder disorder commit completed suicide. Suicidal attempts and ideation are more likely to occur when the individual is in a depressive or mixed state. Violent behavior may be observed during severe manic episodes or during those with psychotic features.

Other problems encountered by individuals with bipolar I disorder are occupational failure, school failure and truancy, marital problems, and other episodic antisocial behavior. Individuals with earlier onset of bipolar I disorder have a greater likelihood of having a history of current alcohol or drug abuse. Individuals with Bipolar I disorder tend to have worse course of illness if they are concomitantly using alcohol or other substances.

Laboratory findings

There are no laboratory findings that are diagnostic for Bipolar bipolar I Disorder disorder. Imaging studies of individuals with Bipolar bipolar I Disorder disorder tend to show increased rates of lesions in the right hemisphere, or bilateral subcortical or periventricular lesions.

Hypothyroidism (current or past) or laboratory evidence of mild thyroid hypofunction may be linked with rapid cycling. Hyperthyroidism may trigger or worsen manic symptoms in individuals with a preexisting mood disorder.

Recent studies in the United States have reported that Bipolar bipolar I Disorder disorder is equally distributed among men and women. The first episode in males is usually a manic episode, whereas in females it tends to be MDE or major depressive episode. In men, manic Episodes episodes equals or
exceeds the number of MDE, whereas in women, MDE predominates. Rapid cycling is more frequently observed in women than in men.

Some studies have indicated that women may be more prone to depressive or mixed mood symptoms.

The lifetime prevalence of Bipolar I Disorder disorder varies from 0.4-1.6 percent. Average age at onset is around about 20 years. The majority of individuals (more than 90 percent) who experience a single manic episode subsequently experience more episodes.

### DSM-IV-TR Diagnostic criteria for Bipolar I Disorder, Single Manic Episode

<table>
<thead>
<tr>
<th>Presence of only one Manic Episode and no past Major Depressive Episodes. Note: Recurrence is defined as either a change in polarity from depression or an interval of at least 2 months without manic symptoms.</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Manic Episode is not better accounted for by Schizoaffective Disorder and is not superimposed on Schizophrenia, Schizophreniform Disorder. Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.</td>
</tr>
</tbody>
</table>

#### A. Presence of only one Manic Episode and no past Major Depressive Episodes.

Note: Recurrence is defined as either a change in polarity from depression or an interval of at least 2 months without manic symptoms.

#### B. The Manic Episode is not better accounted for by Schizoaffective Disorder and is no superimposed on Schizophrenia, Schizophreniform Disorder. Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

*Specify if:*

**Mixed:** if symptoms meet criteria for a Mixed Episode

If the full criteria are currently met for a Manic, Mixed, or Major Depressive Episode *specify its current clinical status* and/or features:

**Mild, Moderate, Severe Without Psychotic Features/Severe With Psychotic**
Features.

With Catatonic Features.

With Postpartum Onset.

If the full criteria are not currently met for a Manic, Mixed, or Major Depressive Episode, specify the current clinical status of the Bipolar I Disorder or features of the most recent episode:

In Partial Remission, In Full Remission.

With Catatonic Features Features.

With Postpartum Onset.
### DSM IV-TR Diagnostic criteria for Bipolar I Disorder, Most Recent Episode Hypomanic

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Currently (or most recently) in a Hypomanic Episode.</td>
</tr>
<tr>
<td>B. There has previously been at least one Manic Episode or Mixed Episode.</td>
</tr>
<tr>
<td>C. The mood symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.</td>
</tr>
<tr>
<td>D. The mood episodes in Criteria A and B are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.</td>
</tr>
</tbody>
</table>

**Specify:**

- Longitudinal Longitudinal Course Specifiers (With and Without Interepisode Recovery):
  - With Seasonal Pattern (applies only to the pattern of Major Depressive Episodes).
  - With Rapid Cycling.

### DSM IV-TR Diagnostic criteria for Bipolar I Disorder, Most Recent Episode Manic

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Currently (or most recently) in a Hypomanic Episode.</td>
</tr>
<tr>
<td>B. There has previously been at least one Manic Episode or Mixed Episode.</td>
</tr>
<tr>
<td>C. The mood symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.</td>
</tr>
<tr>
<td>D. The mood episodes in Criteria A and B are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.</td>
</tr>
</tbody>
</table>

**Specify:**

- Longitudinal Longitudinal Course Specifiers (With and Without Interepisode Recovery):
  - With Seasonal Pattern (applies only to the pattern of Major Depressive Episodes).
  - With Rapid Cycling.
A. Currently (or most recently) in a Manic Episode.

B. There has previously been at least one Major Depressive Episode, Manic Episode, or Mixed Episode.

C. The mood episodes in Criteria A and B are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

If the full criteria are currently met for a Manic Episode, specify its current clinical status and/or features:

- Mild, Moderate, Severe Without Psychotic Features
- Severe With Psychotic Features.
- With Catatonic Features.
- With Postpartum Onset.

If the full criteria are not currently met for a Manic Episode, specify the current clinical status of the Bipolar I Disorder and/or features of the most recent Manic Episode:

- In Partial Remission, In Full Remission.
- With Catatonic Features.
- With Postpartum Onset.

Specify:

- Longitudinal Course Specifiers (With and Without Interepisode Recovery):
  - With Seasonal Pattern (applies only to the pattern of Major Depressive Episodes).
  - With Rapid Cycling.
DSM-IV-TR Diagnostic criteria for Bipolar I Disorder, Most Recent Episode Mixed

A. Currently (or most recently) in a Mixed Episode.

B. There has previously been at least one Major Depressive Episode, Manic Episode, or Mixed Episode.

C. The mood episodes in Criteria A and B are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

If the full criteria are currently met for a Mixed Episode, specify its current clinical status and/or features:

- Mild, Moderate, Severe Without Psychotic Features/Severe With Psychotic Features.
- With Catatonic Features.
- With Postpartum Onset.

If the full criteria are not currently met for a Mixed Episode, specify the current clinical status of the Bipolar I Disorder and/or features of the most recent Mixed Episode:

- In Partial Remission, In Full Remission.
- With Catatonic Features.
- With Postpartum Onset – Specify:
  - Longitudinal Course Specifiers (With and Without Interepisode Recovery)
  - With Seasonal Pattern (applies only to the pattern of Major Depressive Episodes).
  - With Rapid Cycling Cycling.

Cyclothymic Disorder
Cyclothymic disorder or cyclothymia is a chronic, fluctuating mood disturbance characterized by alternating periods of hypomanic symptoms and depression, mild or moderate. Cyclothymic disorder is characterized by relatively short cycles of depression and hypomania that do not meet the diagnostic criterion for major affective syndromes [156].

Some of the prominent symptoms of the depressive episodes are:
- Lack of concentration and difficulty making decisions.
- Poor memory recall.
- Guilt and self-criticism.
- Low self-esteem.
- Pessimism.
- Self-destructive thinking.
- Constant sadness.
- Apathy.
- Hopelessness, helplessness, and irritability.

Other common symptoms include:
- Quick temper.
- Poor judgment.
- Lack of motivation.
- Lack of sexual desire.
- Social withdrawal, appetite change.
- Fatigue.
- Self-neglect.
- Insomnia.

Some of the prominent symptoms of the hypomanic episodes include:
- Euphoria—unusually good mood or cheerfulness.
- Extreme optimism.
- Inflated self-esteem.
- Rapid speech.
- Racing thoughts.
- Aggressive or hostile behavior.
- Lack of consideration for others.
- Agitation.
- Massively increased physical activity.
- Risky behavior.
- Spending sprees.
- Increased drive to achieve goals or perform well.
- Increased sexual drive.
- Decreased need for sleep.
- Tendency to be easily distracted.
- Inability to concentrate.

Cyclothymic disorder usually begins early in life with an insidious onset and a chronic course. Lifetime prevalence of cyclothymia is approximately 0.4% to 1%. Onset of cyclothymia late in adult life may indicate a mood disorder caused by a general medical condition.

<table>
<thead>
<tr>
<th>DSM-IV-TR Diagnostic criteria for Cyclothymic Disorder</th>
</tr>
</thead>
</table>

41
A. For at least 2 years, the presence of several periods with hypomanic symptoms and numerous periods with depressive symptoms that do not meet criteria for a Major Depressive Episode. Note: In children and adolescents, the duration must be at least 1 year.

B. During the above 2-year period (1 year in children and adolescents), the person has not been without the symptoms in Criterion A for more than 2 months at a time.

C. No Major Depressive Episode, Manic Episode, or Mixed Episode has been present during the first 2 years of the disturbance. Note: After the initial 2 years (1 year in children and adolescents) of Cyclothymic Disorder, there may be superimposed Manic or Mixed Episodes (in which case both Bipolar I Disorder and Cyclothymic Disorder may be diagnosed) or Major Depressive Episodes (in which case both Bipolar II Disorder and Cyclothymic Disorder may be diagnosed).

D. The symptoms in Criterion A are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism).

F. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

A. For at least 2 years, the presence of several periods with hypomanic symptoms and numerous periods with depressive symptoms that do not meet criteria for a Major Depressive Episode.

Note: In children and adolescents, the duration must be at least 1 year.

B. During the above 2-year period (1 year in children and adolescents), the person has not been without the symptoms in Criterion A for more than 2 months at a time.

C. No Major Depressive Episode, Manic Episode, or Mixed Episode has been present during the first 2 years of the disturbance.

Note: After the initial 2 years (1 year in children and adolescents) of Cyclothymic Disorder, there may be superimposed Manic or Mixed Episodes (in which case both Bipolar I Disorder and Cyclothymic Disorder may be diagnosed) or Major Depressive Episodes (in which case both Bipolar II Disorder and Cyclothymic Disorder may be diagnosed).

D. The symptoms in Criterion A are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism).

F. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

Neuroimaging

Clinical trial studies in the last few decades have shown that depression in the elderly is associated with structural changes in the brain, including ventricular enlargement.

Depression in the elderly is difficult to detect and diagnose, especially in non-mental health settings. Studies of the impact of the negative outcomes of depression on elderly people and the effect of psychiatric comorbidities have shown that depression in the elderly is a serious medical condition that not only adversely affects mood, but also negatively impacts cognitive and functional abilities. Advances in neuroimaging have shown structural and functional changes in the brains of elderly patients.
A great deal of research is being conducted with advanced neuroimaging techniques to study degenerative structural and functional changes in the elderly with depression. A study was conducted using magnetization transfer ratio (MTR) imaging to observe changes in the myelin integrity and white matter abnormalities in frontostriatal and limbic regions in the elderly with depression [160]. It was found that a number of elderly persons had lower MTR in several left hemisphere frontostriatal and limbic regions.

Several research studies are now using functional MRI (fMRI) to study brain function in late-life depression, especially the relationship between cognition and mood.

Vascular depression is closely associated with cerebrovascular disease and development of depression. A recent MRI study with diffusion tensor imaging (DTI) was conducted to determine the integrity of white matter tracks in elderly people with depression [163]. It was observed that among the depressed elderly, there were widespread abnormalities in DTI parameters, especially in prefrontal region. In elderly people with cognitive impairment, it is difficult to differentiate a depression from neurodegenerative disorder.

**Major Depressive Disorder**

Currently, the diagnosis of depression is predominantly based on behavioral symptoms and course of the illness, as the treatment guidelines are mainly based on clinical empirical evidence and expert consensus. In recent years, a lot of interest has been shown in neurobiological markers of depression. Several studies have shown that a combination of fMRI and pattern recognition techniques can differentiate between depressed and healthy individuals [169, 170, 171] and can also be beneficial in predicting response to the treatment [172, 173]. A recent study has observed that integration of predictions based on brain activity associated with affective and emotional processing significantly increased the accuracy to differentiate a heterogeneous group of patients with depression [170].

Neuroimaging technology has helped researchers understand the anatomical and functional changes occurring in the brain in patients with depression. The knowledge gained from imaging studies is catalyzing a paradigm shift in which depression is conceptualized as a condition that involves abnormalities of brain function and structure.

Diagnosis of depression necessitates a thorough medical history and complete medical and neurologic evaluations. The evaluation encompasses recent life changes, medical or neurologic symptoms, and social factors. A complete screening also includes:

- Electrolyte panel.
- Fasting serum glucose level.
- Complete blood cell count.
- Serum glutamic-oxaloacetic transaminase.
- Serum creatinine level.
- Sensitive thyroid-stimulating hormone.
- Chest radiography.
- Electrocardiography.
- Urinalysis.

A detailed neurologic examination is helpful in determining the need for further neuropsychological testing and neuroimaging. Neuropsychological testing is helpful in differentiating depressive disorders from central nervous system (CNS) disorders.

The principal aims of neuropsychological evaluation are to:

- Establish cognitive status.
- Distinguish depression from dementia or age-appropriate cognitive decline.
- Make psychological management recommendations on the basis of findings in the absence of symptoms of comorbid CNS disease. Structural neuroimaging may not add much to the evaluation.
CT or MRI is recommended if a patient has neurologic signs and symptoms. CT is an easy and cheap way to determine CNS pathology. MRI is a better imaging technique, especially for demyelinating or vascular conditions. CT is particularly useful in differentiating depression from dementia by establishing the presence of abnormalities in temporal and frontal areas.

**Components of a Neuropsychological Assessment History**

- Reason for evaluation; presenting symptoms.
- Medical, surgical, and behavioral health history.
- Medication history.
- Previous neuropsychological assessments.
- Educational and occupational background.
- Family medical and mental health history.
- Laboratory tests.
- Neuroimaging results.
- Patient examination.
  - In-depth interview (typically 1 to 2 hours).
  - In addition to the history mentioned above, interviews typically include birth and early development, abuse or neglect, childhood experiences, travel history, course of cognitive or neurologic symptoms, current work or academic performance, substance use, emotional functioning, personality characteristics, family dynamics, interpersonal relationships, legal circumstances, patient perspectives on illness and treatment, motivation, and observations of nonverbal neurobehavioral signs.
- Collateral information from multiple sources (e.g., spouse, friends, work supervisor).
- Standardized neuropsychological assessment instruments:
  - Domains typically assessed include intellectual abilities (IQ), academic skills (e.g., reading, spelling, arithmetic), attention (i.e., short-term, selective, and sustained), response inhibition, mental flexibility, reasoning, problem-solving, language comprehension, receptive and expressive vocabulary, verbal fluency, confrontation naming, visual and verbal memory (including learning, recall, and facilitated cued and recognition formats), visuospatial abilities, visuomotor speed and integration, cognitive processing speed, motor skills (i.e., strength, speed, and dexterity), and emotional status.

There is a significant detection rate of depression in the general population; depression in patients with medical illnesses is relatively common. Cognitive problems are a common feature of depression in the elderly. Significant cognitive dysfunction associated with depression may be an indication of dementia. Neuropsychological assessment may play a key role in determining the role of depression in elderly people, and therefore, has the potential benefit of medical intervention and psychotherapy [174, 175].

The table below outlines distinguishing features between depression and Alzheimer’s disease [176].

<table>
<thead>
<tr>
<th>Measure</th>
<th>Alzheimer’s disease</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavior congruent with deficits</td>
<td>Usual</td>
<td>Unusual</td>
</tr>
<tr>
<td>Delusions</td>
<td>Mood independent</td>
<td>Mood congruent</td>
</tr>
<tr>
<td>Emotional reaction</td>
<td>Variable</td>
<td>Marked distress</td>
</tr>
<tr>
<td>Mood disorder</td>
<td>Environmentally responsive</td>
<td>Persistent</td>
</tr>
</tbody>
</table>
Clinical features useful in differentiating Alzheimer’s disease from depression

<table>
<thead>
<tr>
<th>Measure</th>
<th>Alzheimer’s disease</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient report of deficits</td>
<td>Variable</td>
<td>Abundant</td>
</tr>
<tr>
<td>Psychiatric history</td>
<td>Unusual</td>
<td>Usual</td>
</tr>
<tr>
<td>Symptom duration</td>
<td>Long</td>
<td>Short</td>
</tr>
<tr>
<td>Symptom progression</td>
<td>Slow</td>
<td>Rapid</td>
</tr>
<tr>
<td>Valuation of accomplishments</td>
<td>Variable</td>
<td>Minimized</td>
</tr>
</tbody>
</table>


Neuropsychological evaluation is a useful method of acquiring data on a patient’s cognitive, behavioral, motor, linguistic, and executive functioning. Neuropsychological evaluation is helpful in providing insight into the psychological aspect of an individual, which is difficult to assess with current imaging techniques.

Treatment
Depression is a treatable condition. Early detection, coupled with early and successful treatment of depression, leads to a shorter duration, reduction in symptoms, and relapse reduction. But, despite making rapid strides in detection and successful treatment of depression, many people are still reluctant to either accept the diagnosis or pursue the required treatment.

The treatment of depression may encompass the following therapies:
- Psychotherapy or counseling.
- Drug therapy.
- Combination of these therapies.

Psychiatric Management
Psychotherapy or counseling involves the interaction of a person with a health care professional about their problems, feelings, and relationships. Psychotherapy is the treatment of choice for individuals under the age of 18 [177]. There are several types of psychotherapies that are beneficial for the treatment of depression.

The goal of psychotherapy is usually to help the patient to better cope with symptoms of depression, enhance social skills, and gain self-confidence. Psychotherapy sessions are usually held once per week for approximately 30 to 60 minutes, but may be reduced with the progression of the treatment to once every other week. Psychiatric management encompasses a number of interventions and activities that psychiatrists provide to the patients with depression throughout the treatment, including:

- Establish and maintain a therapeutic alliance. It is important to involve the patient in decision-making and to address the patient’s concerns as well as preferences for treatment.
- Complete psychiatric assessment. A thorough diagnostic assessment should be done for establishing correct diagnosis, identifying other general medical conditions or psychiatric conditions that may need proper attention, and developing a comprehensive treatment plan for depression. A complete psychiatric evaluation encompasses:
  - History of the present illness and current symptoms.
  - Psychiatric history, including identification and history of past symptoms of mania, hypomania, or mixed episodes and respective treatment responses.
  - General medical history.
Personal history including information about psychological development and responses to life transitions and major life events.
Social, occupational, and family history (including mood disorders and suicide).
Review of the patient’s prescribed and over-the-counter medications.
Review of systems.
Mental status examination.
Physical examination.
Appropriate diagnostic tests as indicated to rule out possible general medical causes of depressive symptoms.
Additionally, patients should be evaluated for past and current drugs and other substance abuse that may cause precipitation and or exacerbation of depressive symptoms.

- Evaluate the safety of the patient. A continuous and careful evaluation for assessing suicide risk is essential for every patient with depression. A patient should be asked about suicidal ideation, thoughts, plans, intent, and behaviors. Specific psychiatric symptoms, such as severe anxiety and psychosis, as well as general medical conditions should be identified because these factors may trigger suicide in patients with depression. Past and recent suicide behavior should also be assessed thoroughly.

  Current stressors as well as protective factors should be delineated. Patient should also be asked about any family history of mental illness or suicide. Assessments of patients’ nutrition status, level of self-care, and hydration is also important, as they can be impaired because of severe symptoms of depression. Patients should also be evaluated to determine the overall effect of the depression on the individual’s abilities to care for dependents.

- Establish the appropriate setting for treatment. The treating clinician or psychiatrist should determine the least restrictive setting for optimum treatment of depression that aims for the patient’s safety and encourages improvement in the patient’s overall condition. The following factors should be included to determine the optimal setting:

  The patient’s symptom severity.
  Concomitant general medical or psychiatric conditions.
  Available support system.
  Level of functioning.
  The patient’s ability to self-care.
  The patient’s ability in accepting corrective feedback.
  Medical compliance.

  The appropriate treatment setting and the resulting benefit should be assessed regularly during the entire course of treatment.

- Evaluate functional impairment and quality of life. Depression can impair and adversely impact professional, social, and family relationships. It can also have an adverse effect on health, hygiene, and leisure activities. Patients’ activities in each of these spheres should also be evaluated. The aim of the treatment plan and interventions should be to maximize the patient’s level of functioning and to help the patient set goals based on his or her symptom severity and related impairments.
• Coordinate the patient’s care with other clinicians. Appropriate and constant coordination between treating clinicians, psychiatrist, and patient is essential for optimal care, treatment decisions, management, and harmonization of treatments. A thorough general medical evaluation should be conducted to rule out general medical causes of depression or its symptoms.

• Monitor the patient’s psychiatric status. It is necessary to monitor the patient’s response to treatment and concomitant medical or psychiatric condition. This helps to draft, develop, and fine-tune the treatment provided to the patient.

• Integration of measurements into psychiatric management. The treatment plan should match the requirements of the patient with the help of careful and systematic assessment of the psychiatric symptoms (type, frequency, and magnitude). The patient should be assessed regularly and periodically to assess benefits and side effects of treatment.

• Increase treatment adherence. The treating psychiatrist or clinician should be aware of the potential barriers to medical compliance to treatment adherence in patients with depression, especially those who are elderly. Patients with depression lack motivation and often become pessimistic. Additionally, adverse effects of antidepressants, problems in the therapeutic relationship, and economical or cultural barriers to treatment make adherence a difficult task. It is therefore essential for the treating psychiatrist or clinician to work closely and in collaboration with the patient and patient’s family. In addition, the treating psychiatrist or clinician should encourage patients to freely express their concerns or fears about the treatment or its side effects. Patients should be informed about treatment response and the importance of treatment adherence.

• Provide education to the patient and the family. Adequate education about the signs, symptoms, and treatment of depression should be given to the patient. If the patient is agreeable, his or her family members and other care providers should also be educated about depression, its effects, and the required treatment. Patient education also includes:
  - Ways to promote healthy behaviors, such as exercise, good sleep, and hygiene.
  - Good nutrition.
  - Decreased alcohol, tobacco, and substance abuse.

A combination of antidepressants and psychotherapy is considered to be the most effective treatment for chronic depression [178, 179]. The treatment of depression is divided into three phases:

9. Acute phase—involved treatment directed at the current depressive episode.
10. Continuation phase—aimed at preventing a relapse into the current episode.
11. Maintenance or prophylactic phase—aimed at the prevention of future episodes.

**Acute Phase**

The typical duration of an acute phase treatment of a MDE is approximately 6 to 12 weeks and is directed at inducing remission of the current depressive episode and attaining a patient’s baseline functioning...
level. Acute phase treatment may encompass pharmacotherapy, psychotherapy (depression-focused), combination therapy (medications and psychotherapy), or other somatic therapies such as electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), or light therapy.

Choice of an initial treatment modality depends upon clinical features (symptoms severity, presence of concomitant illness, or psychosocial stressors) and other determinants that include prior treatment experiences and patient preference.

**Pharmacotherapy**

The initial choice of treatment for patients with MDEs (unless ECT is planned) is an antidepressant medication. Several different classes of antidepressants are effective against depression [180]. The choice of an antidepressant is based on its perceived side effects, safety, pharmacodynamics, patient preference, and response of the medication in previous episodes of MDEs.

To find the most effective antidepressant, the dosages should be adjusted, different combinations should be tried, or if needed, should be changed. The average response rate to the initial antidepressant is generally about 50% [181]. Therapeutic effects are usually seen 3 to 8 weeks after the initiation of medication. Patients are usually warned not to stop antidepressants abruptly and to continue them for a minimum of 4 months to prevent recurrence of depression.

Factors to consider in selecting an antidepressant medication include:
- Patient preference.
- Nature of prior response to medication.
- Relative efficacy and effectiveness.
- Safety, tolerability, and potential side effects.
- Co-occurring psychiatric or general medical conditions.
- Potential drug interactions.
- Half-life of the drug.
- Cost of the drug.

Selective serotonin reuptake inhibitors (SSRIs) are the drugs of choice for the treatment of depression because of their relatively few and mild side effects and more potent effect in controlling symptoms of depression. Individuals who do not respond adequately to the first SSRI are usually switched to another, with improvement in approximately 50% of patients [182]. Selective serotonin reuptake inhibitors (SSRIs) Serotonin and norepinephrine reuptake inhibitors (SNRIs) Another popular and possibly more effective [183, 184] option is to change the medication to an atypical antidepressant such as bupropion or to add this medication to the existing pharmacotherapy [185].

After initiation of an antidepressant, the drug should be titrated to full dose, depending upon:
- Patient’s age.
- Treatment setting.
- Presence of concomitant disorder or illnesses.
- Concomitant drug treatment.
- Side effects of the drug.

The patient should be carefully, regularly, and systematically monitored to assess:
- Response to pharmacotherapy.
- Identify the side effects.
- Assess patient safety.
In case of severe or frequent side effects, the dose of the antidepressant should be lowered or the drug should be changed to another antidepressant with fewer side effects.

**Complementary and Alternative Treatments**

Complementary and alternative treatments are increasingly being used for the treatment of depression; however, evidence for their antidepressant effect is absent or limited at best.

**St. John’s wort**

St. John’s wort is a plant and herbal medicine widely used for treating depression. There is some scientific evidence that St. John’s wort is beneficial in milder forms of depression [210]. A clinical study has shown that St. John’s wort prescribed to patients with mild to moderate symptoms of a MDE in doses of 300 mg/day and 1,800 mg/day had superior efficacy to placebo [211].

However, St. John’s wort is not FDA-regulated as a drug and lacks proper standardization. Therefore, it is not FDA-approved and is not recommended for general use in the treatment of depression. St. John’s wort has a great potential for drug-drug interactions [212-214]. The combined use of an antidepressant such as MAOIs with St. John’s wort is contraindicated because of life-threatening drug interactions.

**S-adenosyl methionine**

S-adenosyl methionine (SAMe) is a naturally occurring molecule that is predominantly present in the liver and the brain [215]. SAMe is available as a prescription antidepressant in Europe for both parenteral and oral administration [218]. In the United States, it may be bought over-the-counter, but is not approved by the FDA.

Some studies have shown the safety and efficacy of SAMe in patients with MDD. It is considered to be more effective in the treatment of major depression than a placebo [219]. Compared with Tricyclic antidepressants, SAMe was found to be more effective and tolerable [220].

**Omega-3 fatty acids**

Omega-3 fatty acids are generally recommended as an adjunctive therapy for depression and mood disorders [221, 222]. There is no conclusive evidence to prove beneficial effects of omega-3 fatty acids in the acute treatment of MDD. Anecdotal evidence includes that it has been observed that people of Iceland have lower rates of depression, which may be because of large fish consumption [223] and fish is rich in omega-3 fatty acids.

**Folate**

Folate level is used to determine antidepressant response as well as an adjunctive treatment. Low folate blood levels are generally associated with poor treatment response to fluoxetine for MDD [224, 225], and higher folate levels are linked with better response to antidepressants [226]. Folate can be recommended as an adjunctive treatment for patients with MDD.

**Light therapy**

Several clinical trials have shown a beneficial effect from bright light therapy for SAD and nonseasonal MDD [227-231]. It is a low-risk and low-cost modality of treatment. The exact mechanism of action for light therapy is still unclear, but it seems to affect the serotonergic neurotransmitter system [232, 233]. It is believed that light therapy may increase the treatment response with antidepressants [234]. Greater intensity of light also seems to improve treatment efficacy [235]. Light therapy seems to increase the antidepressant benefits of partial sleep deprivation [236, 237].

**Yoga and exercise**
The efficacy of yoga in the treatment of depression is encouraging, but weak [239]. Exercise seems to provide a modest short-term beneficial effect; however, the evidence for any long-term improvement in major depression is poor [240].

**Psychotherapy**

Depression-focused psychotherapy alone is the initial treatment of choice for patients with mild to moderate MDEs. It is also the initial treatment of choice in patients with severe symptoms of depression. The choice of a particular type of psychotherapy depends on the treatment goals, patient preference, previous response to a particular psychotherapy, and the availability of providers in the specific psychotherapy. Patients receiving psychotherapy are carefully, regularly, and systematically monitored to determine treatment response and patient safety.

The frequency of psychotherapy sessions depends upon several factors, including:

- Treatment goals.
- Type of psychotherapy.
- Severity of symptoms, including suicidal ideation.
- Co-occurring disorders.
- Social supports.
- Treatment compliance.
- The need to monitor and treat depressive symptoms as well as a suicide risk.

Recent clinical studies have observed that cognitive behavioral therapy (CBT) is as effective as antidepressants for the treatment of moderate to severe depression [241]. Some research studies have shown that behavior therapy, also known as behavioral activation, [242] is superior to CBT [243]. Behavioral activation requires less time and results in comparatively longer-lasting changes in the depressive patients [244]. Interpersonal psychotherapy that focuses on the social and interpersonal relationships is an effective treatment for depression. This therapy is effective in developing or enhancing interpersonal skills in depressive patients, which allows better and effective communication and reduces stress [245].

Psychoanalysis, which aims for the resolution of unconscious mental conflicts [246], is also considered to be effective in patients with depression [247]. Psychodynamic psychotherapy, another popular technique, is based on psychoanalysis with social and interpersonal focus [248] and is as potent as antidepressants in patients with mild to moderate depression [249].

**Psychotherapy plus antidepressants**

Combination therapy may be indicated in patients with severe depression or with a history of recurrent depression. Individuals with mild or moderate depression are usually well managed with either antidepressants or psychotherapy. Combination therapy may be indicated in milder forms of interpersonal or psychosocial problems, intrapsychic conflict, or coexisting Axis II disorder. It is still not clear which therapy is a better option for a particular individual.

**Continuation Phase**

Continuation phase drug or pharmacotherapy is indicated following successful management with acute phase treatment with antidepressants. Duration of continuation therapy should be about 4 to 9 months. The primary goal of continuation treatment is to prevent relapse following remission [250-252]. The signs and symptoms of relapse should be carefully and systematically monitored during this phase as the relapse rate is highest during this period [263].
It has been observed that during the first 6 months following recovery from a MDE, the relapse rate may be about 20% in mixed samples [254-257] and about 85% in severely depressed in patients receiving electroconvulsive therapy [258, 259]. The relapse rate increases if pharmacotherapy (including ECT) is reduced in dose or intensity or altogether discontinued after initial recovery [259, 260]. The dose, intensity, and frequency of treatment should remain identical to what was prescribed in the acute phase.

Several clinical studies have found that patients who have shown good treatment response for the first episode of an uncomplicated MDE should continue to receive a full therapeutic dose of that drug for at a minimum period of 449 months after achieving full remission [261].

In case relapse is not achieved during the continuation phase, the drug dose is usually increased. Frequency of sessions or a shift in the psychotherapeutic focus is often required for patients undergoing psychotherapy.

**Maintenance Phase**

Maintenance phase of treatment starts after the patient completes the continuation phase treatment for chronic or recurrent MDEs without relapse. The primary goal of the maintenance phase is to prevent subsequent depression recurrence in susceptible patients. Patients who have encountered a minimum of three prior MDEs should receive maintenance treatment.

Approximately 20% of patients experience a MDE recurrence within the first 6 months after recovery [254]. Approximately 50% to 85% of patients will experience a minimum of one lifetime recurrence, often within 2 or 3 years [264].

Patients with prior MDEs are more prone to have subsequent affective episodes other than another MDE, such as a hypomanic, manic, or dysthymic episode [265].

Some clinical studies have shown that the risk of MDE recurrence increases by 16% with each successive episode [254]. Maintenance therapy may also be indicated for patients with additional risk factors for recurrence.

**Risk factors for recurrence of MDD:**

- Persistence of subthreshold depressive symptoms.
- Severity of initial and any subsequent episodes.
- Previous history of multiple episodes of MDD.
- Earlier age at onset.
- Presence of an additional non-affective psychiatric diagnosis.
- Presence of a chronic general medical disorder.
- Family history of psychiatric illness, especially mood disorder.
- Current psychosocial stressors or impairment.
- Negative cognitive style.
- Persistent sleep disturbances.

Additional factors that may play an important role in the need for maintenance therapy include:

- Patient preference.
- Presence of side effects during continuation therapy.
- Severity of prior MDEs, including factors such as suicide risk or psychosis.
The patient should be monitored periodically and systematically during this phase because of recurrence risk and to detect its symptoms. Usually, the therapy that was effective in the acute and continuation phases is good for the maintenance phase, too.

Antidepressants that are used for maintenance treatment have been studied extensively during the last few years. The outcomes of these clinical studies have shown that antidepressants are quite effective in preventing relapse during the maintenance phase [266-268]. A recent clinical study has shown that full-dose drug treatment is better than low-dose treatment during the maintenance phase [269].

But in spite of optimal maintenance treatment, drug therapy fails in 25% of cases, resulting in relapse [270, 271]. Clinical studies have also found that relapses are also associated with inadequate prophylactic effects of antidepressants [272].

In case of a relapse, treating clinicians usually use the same therapeutic approach used to treat incomplete responses to treatment, which includes:
- Increasing the dose of antidepressant.
- Changing to a different drug.
- Addition of another drug.
- Depression focused psychotherapy [271, 273].

Several studies have shown that psychotherapy is beneficial for MDEs. It has been found that once-monthly maintenance interpersonal psychotherapy is effective in preventing relapse in patients with a high risk for relapse [274]. Another study has demonstrated the efficacy of maintenance cognitive therapy given for more than 2 years for recurrent MDEs [275].

Some research studies have shown that the combination of antidepressants and psychotherapy may be more effective in preventing relapse than treatment with single modalities [276, 277]. The duration of the maintenance phase is variable and depends on the patient’s preferences, the frequency and severity of prior MDEs, and the tolerability of treatments.

Discontinuation of Treatment
In some cases, if maintenance-phase treatment is not indicated, discontinuation of treatment may be considered in stable patients subsequent to the continuation phase.

The discontinuation of treatment depends on the following factors:
- Persistence of subthreshold depressive symptoms.
- Severity of initial and any subsequent episodes.
- Prior history of multiple episodes of MDD.
- Earlier age at onset.
- Presence of an additional non-affective psychiatric diagnosis.
- Presence of a chronic general medical disorder.
- Family history of psychiatric illness, especially mood disorder.
- Current psychosocial stressors or impairment.
- Negative cognitive style.
- Persistent sleep disturbances.

Usually, the treatment effects of psychotherapy last longer and have a lower risk of relapse after discontinuation than pharmacotherapy. Patients should be carefully and systematically monitored during, and immediately after, the treatment is discontinued to ensure that remission is stable. The greatest relapse risk is observed in the initial 2 months after discontinuation of treatment; therefore, it is essential for patients to have a follow-up visit during this initial period.
If the patient is undergoing discontinuation of pharmacotherapy (drug treatment), it is best to taper the drug over several weeks. Discontinuation of psychotherapy depends on the type of therapy. Every patient should be made aware of the potential for a depressive relapse before the treatment discontinuation. Patients and their family members should be educated about early signs of MDEs, and a proper plan should be made in case the symptoms reoccur.

It is highly recommended to systematically assess the following factors:

- Symptoms of MDEs.
- Side effects of the treatment.
- Adherence.
- Functional status.

Treatment should be immediately started in case a patient experiences a recurrence. Usually, the patient is started on the same treatment to which he or she responded in the earlier treatment phases (i.e., the acute and continuation phases) [278].

Patients who have a recurrence following discontinuation of antidepressant therapy should be considered to have experienced another MDD episode and should receive adequate acute-phase treatment followed by continuation-phase treatment, and possibly maintenance-phase treatment.

CONCLUSION

Depression is a mental disorder that manifests as a state of low mood and aversion to activity that may negatively impact an individual’s thought processes, behavior, feelings, world view, and physical well-being. Depression in elderly people is common and widespread globally. It is generally undiagnosed and often untreated.

Individuals with depression may experience a wide variety of symptoms, including sadness, anhedonia, emptiness, hopelessness, anxiousness, and irritability. Depression in the elderly is an important public health problem because of its severe implications. It is closely associated with increased risk of suicide and morbidity, as well as reduced physical, social, and cognitive functioning, and increased inclination towards self-neglect.

Globally, depression is one of the leading causes of morbidity. Lifetime prevalence of depression varies from country to country, ranging from as little as 3% in Japan to as high as 17% in the United States. The risk of depression increases with neurological conditions, such as stroke, multiple sclerosis, Parkinson’s disease, or cardiovascular disease.

However, contrary to common belief, major depression seems to be less common among the elderly compared with young adults. Depression in elderly people may have distinctive signs and symptoms compared with younger adults. The elderly are less likely to endorse cognitive-affective symptoms of depression, such as worthlessness or dysphoria. They also complain more frequently about sleep disturbances, insomnia, fatigue, loss of interest in living, and hopelessness. They also complain about poor memory and loss of concentration.

Common clinical findings include slower cognitive function and executive dysfunction. It has also been found that depressed elderly women experience more appetite disturbances than men, and that elderly men experience more agitation.

Depression is difficult to diagnose when symptoms arise because of a medical condition. Depression is usually either overdiagnosed or underdiagnosed in the presence of another disease, such as cancer, that may cause weight loss and fatigue.
Biological factors become major determinants in the elderly. With aging or certain diseases, the human body undergoes cardiovascular and neurological changes that make the elderly susceptible to depression. However, it is important to note that age-related changes are ubiquitous, and physical disease is not rare, yet only a few elderly persons become the victim of depression. Genetic factors, age-related neurobiological changes, stressful events, and cognitive diathesis play an important role in triggering depression.

Depression is especially prevalent in patients with cardiovascular disease. Depression increases the risk of coronary artery disease (CAD) by approximately twice in otherwise healthy individuals. Depression is more prevalent among patients with type 2 diabetes compared with those without diabetes.

Depression and dementia often are seen together in the elderly. The prevalence of major depression is greatest among stroke patients. Vascular, inflammatory, and neuroanatomic risk factors are closely associated with depression in the elderly.

Depression is one of the most common conditions associated with suicide in the elderly. Depression and sadness seem to go hand-in-hand; however, elderly persons with depression do not always feel sad. These patients may complain of lack of motivation, a lack of energy, or physical problems.

Major depression is the most severe form of depression. According to the DSM-IV-TR, at least one of the two main depressive symptoms, depressed mood and anhedonia, should be present to make a diagnosis of a major depressive episode (MDE). Major depressive disorder (MDD) is a clinical course that is always characterized by one or more MDEs without a history of manic, mixed, or hypomanic episodes. The average age of MDD onset is the mid-20s, although it may begin at any age.

Seasonal affective disorder (SAD) is a form of depression in which depressive episodes occur in particular seasons (autumn or winter), and resolve in particular seasons (summer or spring). Elderly men are less prone to this disorder.

Dysthymic disorder, or dysthymia, is characterized by a chronically depressed mood that is experienced for most of the day, more days than not, for at least 2 years.

The “depressive disorder not otherwise specified” category encompasses various types of disorders with depressive features that do not meet the criteria for MDD, dysthymia, adjustment disorder with depressed mood, or adjustment disorder with mixed anxiety and depressed mood.

Cyclothymic disorder, or cyclothymia, is a chronic, fluctuating mood disturbance characterized by alternating periods of hypomanic symptoms and depression, mild or moderate. Cyclothymic disorder usually begins early in life with an insidious onset and a chronic course. Onset of cyclothymia in the elderly may indicate a mood disorder due to a general medical condition.

Neuroimaging is creating new waves in diagnosing dementia, although there currently is no imaging study that is diagnostic for depression. Various imaging studies, including CT, MRI, PET, SPECT studies, in the last few decades have shown that depression in the elderly is associated with structural changes in the brain, including ventricular enlargement.

Depression is a treatable condition. Early detection, coupled with early and successful treatment of depression, leads to a shorter duration, reduction in symptoms, and relapse reduction.

The treatment of depression may encompass psychotherapy, pharmacotherapy, or a combination of both. The initial choice of treatment for patients with a mild to moderate mild depressive episode is an antidepressant medication. Several different classes of antidepressants are effective against depression. Selective serotonin reuptake inhibitors (SSRIs) are drug of choice for the treatment of depression because of their relatively few and mild side effects and more potent effect in controlling symptoms of depression.
In elderly patients and others with malnutrition, autonomic disorders, or hypotension, tricyclic antidepressants can cause syncope or falls.

Depression-focused psychotherapy alone is the initial treatment of choice for patients with a mild to moderate major depressive episode. Combination therapy may be indicated in milder forms of interpersonal or psychosocial problems, intrapsychic conflict, or coexisting Axis II disorder.

All patients with depression or history of depression should be educated about depression and its treatment. If possible and feasible, a patient’s family members should also be educated about depression.

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DEPRESSION VS. DEMENTIA IN THE ELDERLY
PART I
Self Evaluation Exercises

Select the best answer for each question and check your answers at the bottom of the page.

You do not need to submit this self-evaluation exercise with your participant sheet.

1. Dementia is associated with a high rate of depression.
   TRUE   FALSE

2. Approximately half of depressed geriatric patients experienced their first depressive episode as young adults.
   TRUE   FALSE

3. Rates of depression among the elderly are highest in medical inpatients.
   TRUE   FALSE

4. Compared with young adults, elderly patients with neurological disorders tend to experience less dysphoria.
   TRUE   FALSE

5. The interaction of genetic and environmental factors may also increase the risk of depression.
   TRUE   FALSE

6. Depression in older people with concomitant medical disease has a good prognosis.
   TRUE   FALSE

7. Depression increases the risk of type 2 diabetes.
   TRUE   FALSE

8. Compared with dementia, depression has a shorter duration of symptoms.
   TRUE   FALSE

9. Weight loss is a prominent sign of depression in the elderly.
   TRUE   FALSE

10. Loss of interest or pleasure in almost all activities is a core symptom of depression in the elderly.
    TRUE   FALSE

11. Major depressive disorder (MDD) is a clinical course that is always characterized by one or more MDE(s) without a history of manic, mixed, or hypomanic episodes.
    TRUE   FALSE
12. People with MDD have a low mortality rate, and approximately 15% of individuals with severe MDD commit suicide.
   
   TRUE     FALSE

13. There are no diagnostic laboratory findings for major depressive episode.
   
   TRUE     FALSE

14. Mood reactivity is an essential component for the diagnosis of atypical depression.
   
   TRUE     FALSE