Depressive Disorders

Depressive disorders include disruptive mood dysregulation disorder, major depressive disorder (including major depressive episode), persistent depressive disorder, premenstrual dysphoric disorder, substance/medication-induced depressive disorder, depressive disorder due to another medical condition, other specified depressive disorder, and unspecified depressive disorder. The common feature of all of these disorders is the presence of sad, empty, or irritable mood, accompanied by related changes that significantly affect the individual's capacity to function (e.g., somatic and cognitive changes in major depressive disorder and persistent depressive disorder). What differs among them are issues of duration, timing, or presumed etiology.

In order to address concerns in the United States and, increasingly, internationally about the potential for the overdiagnosis and treatment of bipolar disorder in children, a new diagnosis, disruptive mood dysregulation disorder, referring to the presentation of children with persistent irritability and frequent episodes of extreme behavioral dyscontrol, is added to the depressive disorders for children up to 12 years of age. Its placement in this chapter reflects the finding that children with this symptom pattern typically develop unipolar depressive disorders or anxiety disorders, rather than bipolar disorders, as they mature into adolescence and adulthood.

Major depressive disorder represents the classic condition in this group of disorders. It is characterized by discrete episodes of at least 2 weeks' duration (although most episodes last considerably longer) involving clear-cut changes in affect, cognition, and neurovegetative functions and interepisode remissions. A diagnosis based on a single episode is possible, although the disorder is a recurrent one in the majority of cases. Careful consideration should be given to the delineation of normal sadness and grief from a major depressive episode. Bereavement may induce great suffering, but it does not typically induce an episode of major depressive disorder. When they do occur together, the depressive symptoms and functional impairment tend to be more severe and the prognosis is worse compared with bereavement that is not accompanied by major depressive disorder. Bereavement-related major depressive episodes tend to occur in persons with other vulnerabilities to depressive disorders.

A more chronic form of depression, persistent depressive disorder, can be diagnosed when the mood disturbance continues for at least 2 years in adults or 1 year in children. This diagnosis, new in DSM-5, includes the DSM-IV diagnostic categories of chronic major depression and dysthymia.

After careful scientific review of the evidence, premenstrual dysphoric disorder has been moved from an appendix of DSM-IV ("Criteria Sets and Axes Provided for Further Study") to Section II of DSM-5. Almost 20 years of additional research on this condition has confirmed a specific and treatment-responsive form of depressive disorder that begins sometime following ovulation and remits within a few days of menses and has a marked impact on functioning.

A large number of substances of abuse, some prescribed medications, and several medical

conditions can be associated with depression-like phenomena. This fact is recognized in the diagnoses of substance/medication-induced depressive disorder and depressive disorder due to another medical condition.

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Disruptive Mood Dysregulation Disorder

Diagnostic Criteria F34.81

A. Severe recurrent temper outbursts manifested verbally (e.g., verbal rages) and/or behaviorally (e.g., physical aggression toward people or property) that are grossly out of proportion in intensity or duration to the situation or provocation.

B. The temper outbursts are inconsistent with developmental level.

C. The temper outbursts occur, on average, three or more times per week.

D. The mood between temper outbursts is persistently irritable or angry most of the day, nearly every day, and is observable by others (e.g., parents, teachers, peers).

E. Criteria A–D have been present for 12 or more months. Throughout that time, the individual has not had a period lasting 3 or more consecutive months without all of the symptoms in Criteria A–D.

F. Criteria A and D are present in at least two of three settings (i.e., at home, at school, with peers) and are severe in at least one of these.

G. The diagnosis should not be made for the first time before age 6 years or after age 18 years.

H. By history or observation, the age at onset of Criteria A–E is before 10 years.

I. There has never been a distinct period lasting more than 1 day during which the full symptom criteria, except duration, for a manic or hypomanic episode have been met.

   Note: Developmentally appropriate mood elevation, such as occurs in the context of a highly positive event or its anticipation, should not be considered as a symptom of mania or hypomania.

J. The behaviors do not occur exclusively during an episode of major depressive disorder and are not better explained by another mental disorder (e.g., autism spectrum disorder, posttraumatic stress disorder, separation anxiety disorder, persistent depressive disorder).

   Note: This diagnosis cannot coexist with oppositional defiant disorder, intermittent explosive disorder, or bipolar disorder, though it can coexist with others, including major depressive disorder, attention-deficit/hyperactivity disorder, conduct disorder, and substance use disorders. Individuals whose symptoms meet criteria for both disruptive mood dysregulation disorder and

oppositional defiant disorder should only be given the diagnosis of disruptive mood dysregulation disorder. If an individual has ever experienced a manic or hypomanic episode, the diagnosis of disruptive mood dysregulation disorder should not be assigned.

K. The symptoms are not attributable to the physiological effects of a substance or another medical or neurological condition.

Diagnostic Features

The core feature of disruptive mood dysregulation disorder is chronic severe, persistent irritability. This severe irritability has two prominent clinical manifestations, the first of which is frequent temper outbursts. These outbursts typically occur in response to frustration and can be verbal or behavioral (the latter in the form of aggression against property, self, or others). They must occur frequently (i.e., on average, three or more times per week) (Criterion C) over at least 1 year in at least two settings (Criteria E and F), such as in the home and at school, and they must be developmentally inappropriate (Criterion B). The second manifestation of severe irritability consists of chronic, persistently irritable or angry mood that is present between the severe temper outbursts. This irritable or angry mood must be characteristic of the child, being present most of the day, nearly every day, and noticeable by others in the child's environment (Criterion D).

The clinical presentation of disruptive mood dysregulation disorder must be carefully distinguished from presentations of other, related conditions, particularly pediatric bipolar disorder. In fact, disruptive mood dysregulation disorder was added to DSM-5 to address the considerable concern about the appropriate classification and treatment of children who present with chronic, persistent irritability relative to children who present with classic (i.e., episodic) bipolar disorder.

Some researchers view severe, nonepisodic irritability as characteristic of bipolar disorder in children, although both DSM-IV and DSM-5 require that both children and adults have distinct episodes of mania or hypomania to qualify for the diagnosis of bipolar I disorder. During the latter decades of the twentieth century, this contention by researchers that severe, nonepisodic irritability is a manifestation of pediatric mania coincided with an upsurge in the rates at which clinicians assigned the diagnosis of bipolar disorder to their pediatric patients. This sharp increase in rates appears to be attributable to clinicians combining at least two clinical presentations into a single category. That is, both classic, episodic presentations of mania and nonepisodic presentations of severe irritability have been labeled as bipolar disorder in children. In DSM-5, the term *bipolar disorder* is explicitly reserved for episodic presentations of bipolar symptoms. DSM-IV did not include a diagnosis designed to capture youths whose hallmark symptoms consisted of very severe, nonepisodic irritability, whereas DSM-5, with the inclusion of disruptive mood dysregulation disorder, provides a distinct category for such presentations.

Prevalence

Disruptive mood dysregulation disorder is common among children presenting to pediatric

mental health clinics. Prevalence estimates of the disorder in the community are unclear. In a population-based cohort study of Brazilian 11-year-olds that used a specific module for disruptive mood dysregulation disorder, the prevalence was 2.5%.

Consistent gender differences in prevalence have not been reported in population samples, although clinic samples report a male preponderance. For example, up to 80% of children presenting to clinics in Turkey with features of disruptive mood dysregulation disorder in a chart review were boys. Data suggest that the diagnosis may be more common in younger age groups (e.g., 8.2% in a community sample of 6-year-olds in the United States).

Development and Course

The onset of disruptive mood dysregulation disorder must be before age 10 years, and the diagnosis should not be applied to children with a developmental age of younger than 6 years. It is unknown whether the condition presents only in this age-delimited fashion. Because the symptoms of disruptive mood dysregulation disorder are likely to change as children mature, use of the diagnosis should be restricted to age groups similar to those in which validity has been established (6–18 years). Approximately half of children with disruptive mood dysregulation disorder living in a predominantly rural area in a large U.S. study continue to have symptoms that meet criteria for the condition 1 year later, although those children whose symptoms no longer meet the threshold for the diagnosis often have persistent, clinically impairing irritability. Rates of conversion from severe, nonepisodic irritability to bipolar disorder are very low. Instead, children with disruptive mood dysregulation disorder are at increased risk to develop unipolar depressive and/or anxiety disorders in adulthood.

Risk and Prognostic Factors

Temperamental. Children with chronic irritability typically exhibit complicated psychiatric histories. In such children, a relatively extensive history of chronic irritability is common, typically manifesting before full criteria for the syndrome are met. Such prediagnostic presentations may have qualified for a diagnosis of oppositional defiant

disorder. Many children with disruptive mood dysregulation disorder have symptoms that also meet criteria for attention-deficit/hyperactivity disorder (ADHD) and for an anxiety disorder, with such diagnoses often being present from a relatively early age. For some children, the criteria for major depressive disorder may also be met.

Environmental. Factors associated with disrupted family life, such as psychological abuse or neglect, parental psychiatric disorder, limited parental education, single-parent household, early trauma, death of a parent, parental grief, divorce, and malnutrition (e.g., vitamin deficiency), are associated with the core behaviors of disruptive mood dysregulation disorder.

Genetic and physiological. Data suggest that a family history of depression may be a risk factor for disruptive mood dysregulation disorder. Consistent with this, twin data suggest that the association between early irritability and later unipolar depression and anxiety may be, in part, genetically mediated.

Compared with children with pediatric bipolar disorder or other mental illnesses, those with

disruptive mood dysregulation disorder exhibit both commonalities and differences in information-processing deficits. For example, face-emotion labeling deficits, as well as perturbed decision-making and cognitive control, are present in children with bipolar disorder as well as those with disruptive mood dysregulation disorder. Importantly, however, the same behavioral deficit may be associated with different patterns of neural dysfunction. There is also evidence for disorder-specific dysfunction, such as during tasks assessing attention deployment in response to emotional stimuli, which has demonstrated unique signs of dysfunction in children with chronic irritability.

Culture-Related Diagnostic Issues

Culture-related data on disruptive mood dysregulation disorder are limited. However, sociocultural factors affect the presentation of core psychological features of the disorder, including impulsivity as well as emotion, reward, threat, and behavior dysregulation, especially in settings characterized by severe social disruption, such as postconflict zones or communities affected by long-standing racism and discrimination. It is important to distinguish disruptive mood dysregulation disorder from adaptive responses to adversity that are context-dependent and transitory.

Sex- and Gender-Related Diagnostic Issues

There is some evidence from twin studies that while irritability has a strong genetic component in both sexes, patterns differ for boys and girls. For boys, genetic factors appear to account for an increasing amount of the variance of the phenotype of irritability throughout childhood. While genetic factors account for a large proportion of the variance of the irritability phenotype in school-age girls, this decreases into adolescence and young adulthood, with environmental influences playing a greater role. How this genetic risk for irritability translates into risk and prognosis for disruptive mood dysregulation disorder, per se, is not yet known.

Functional Consequences of Disruptive Mood Dysregulation Disorder

Chronic, severe irritability, such as is seen in disruptive mood dysregulation disorder, is associated with marked disruption in a child’s family and peer relationships, as well as in school performance. Because of their extremely low frustration tolerance, such children generally have difficulty succeeding in school; they are often unable to participate in the activities typically enjoyed by healthy children; their family life is severely disrupted by their outbursts and irritability; and they have trouble initiating or sustaining friendships. Levels of dysfunction in children with bipolar disorder and disruptive mood

dysregulation disorder are generally comparable. Both conditions cause severe disruption in the lives of the affected individual and his or her family. In both disruptive mood dysregulation disorder and pediatric bipolar disorder, aggression and psychiatric hospitalization are common.

Differential Diagnosis

Because chronically irritable children and adolescents typically present with complex histories, the diagnosis of disruptive mood dysregulation disorder must be made while considering the presence or absence of multiple other conditions. Despite the need to consider many other syndromes, differentiation of disruptive mood dysregulation disorder from bipolar disorder and oppositional defiant disorder requires particularly careful assessment.

Bipolar disorders. The central feature differentiating disruptive mood dysregulation disorder and bipolar disorders in children involves the longitudinal course of the core symptoms. In children, as in adults, bipolar I disorder and bipolar II disorder manifest as an episodic illness with discrete episodes of mood perturbation that can be differentiated from the child's typical presentation. The mood perturbation that occurs during a manic episode is distinctly different from the child's usual mood. In addition, during a manic episode, the change in mood must be accompanied by the onset, or worsening, of associated cognitive, behavioral, and physical symptoms (e.g., distractibility, increased goal-directed activity), which are also present to a degree that is distinctly different from the child's usual baseline. Thus, in the case of a manic episode, parents (and, depending on developmental level, children) should be able to identify a distinct time period during which the child's mood and behavior were markedly different from usual. In contrast, the irritability of disruptive mood dysregulation disorder is persistent and is present over many months; while it may wax and wane to a certain degree, severe irritability is characteristic of the child with disruptive mood dysregulation disorder. Thus, while bipolar disorders are episodic conditions, disruptive mood dysregulation disorder is not. In fact, the diagnosis of disruptive mood dysregulation disorder cannot be assigned to a child who has ever experienced a full-duration hypomanic or manic episode (irritable or euphoric) or who has ever had a manic or hypomanic episode lasting more than 1 day. Another central differentiating feature between bipolar disorders and disruptive mood dysregulation disorder is the presence of elevated or expansive mood and grandiosity. These symptoms are common features of mania but are not characteristic of disruptive mood dysregulation disorder.

Oppositional defiant disorder. While symptoms of oppositional defiant disorder typically do occur in children with disruptive mood dysregulation disorder, mood symptoms of disruptive mood dysregulation disorder are relatively rare in children with oppositional defiant disorder. The key features that warrant the diagnosis of disruptive mood dysregulation disorder in children whose symptoms also meet criteria for oppositional defiant disorder are the presence of severe and frequently recurrent outbursts and a persistent disruption in mood between outbursts. In addition, the diagnosis of disruptive mood dysregulation disorder requires severe impairment in at least one setting (i.e., home, school, or among peers) and mild to moderate impairment in a second setting. For this reason, while most children whose symptoms meet criteria for disruptive mood dysregulation disorder will also have a presentation that meets criteria for oppositional defiant disorder, the reverse is not the case. That is, in only approximately 15% of individuals with oppositional defiant disorder would criteria for disruptive mood dysregulation disorder be met. Moreover, even for children in whom criteria for both disorders are met, only the diagnosis of disruptive mood dysregulation disorder should be made. Finally, both the prominent mood symptoms in disruptive mood dysregulation disorder and the high risk for depressive and anxiety disorders in follow-up studies justify placement of disruptive mood dysregulation disorder among the depressive disorders in DSM-5. (Oppositional defiant disorder is included in the chapter "Disruptive, Impulse-Control, and Conduct

Disorders.") This reflects the more prominent mood component among individuals with disruptive mood dysregulation disorder, as compared with individuals with oppositional defiant disorder. Nevertheless, it also should be noted that disruptive mood dysregulation disorder appears to carry a high risk for behavioral problems as well as mood problems.

Attention-deficit/hyperactivity disorder, major depressive disorder, anxiety disorders, and autism spectrum disorder. Unlike children diagnosed with bipolar disorder or oppositional defiant disorder—for whom a diagnosis of disruptive mood dysregulation disorder cannot be given even if the symptoms meet diagnostic criteria for that disorder—children whose symptoms meet criteria for disruptive mood dysregulation disorder also can receive a comorbid diagnosis of ADHD, major depressive disorder, and/or anxiety disorder. However, children whose irritability is present only in the context of a major depressive episode or persistent depressive disorder should receive one of those diagnoses rather than disruptive mood dysregulation disorder. Children with disruptive mood dysregulation disorder may have symptoms that also meet criteria for an anxiety disorder and can receive both diagnoses, but children whose irritability is manifest only in the context of exacerbation of an anxiety disorder should receive the relevant anxiety disorder diagnosis rather than disruptive mood dysregulation disorder. In addition, children with autism spectrum disorders frequently present with temper outbursts when, for example, their routines are disturbed. In that instance, the temper outbursts would be considered secondary to the autism spectrum disorder, and the child should not receive the diagnosis of disruptive mood dysregulation disorder.

Intermittent explosive disorder. Children with symptoms suggestive of intermittent explosive disorder present with instances of severe temper outbursts, much like children with disruptive mood dysregulation disorder. However, unlike disruptive mood dysregulation disorder, intermittent explosive disorder does not require the individual's mood to be persistently irritable or angry between outbursts. In addition, a diagnosis of intermittent explosive disorder involving verbal aggression or physical aggression that does not result in damage to property or physical injury to animals or other individuals occurring at least twice weekly can be made after only 3 months of symptoms, in contrast to the 12-month requirement for disruptive mood dysregulation disorder. Thus, these two diagnoses should not be made in the same child. For children with outbursts and intercurrent, persistent irritability, only the diagnosis of disruptive mood dysregulation disorder should be made.

Comorbidity

Rates of comorbidity in disruptive mood dysregulation disorder are extremely high. It is rare to find individuals whose symptoms meet criteria for disruptive mood dysregulation disorder alone. Comorbidity between disruptive mood dysregulation disorder and other DSM-defined syndromes appears higher than for many other pediatric mental illnesses; the strongest overlap is with oppositional defiant disorder. Not only is the overall rate of comorbidity high in disruptive mood dysregulation disorder, but also the range of comorbid illnesses appears particularly diverse. These children typically present to the clinic with a wide range of disruptive behavior, mood, anxiety, and even autism spectrum symptoms and diagnoses. However, children with

disruptive mood dysregulation disorder should not have symptoms that meet criteria for bipolar disorder, as in that context, only the bipolar disorder diagnosis should be made. If children have symptoms that meet criteria for oppositional defiant disorder or intermittent explosive disorder *and* disruptive mood dysregulation disorder, only the diagnosis of disruptive mood dysregulation disorder should be assigned. Also, as noted earlier, the diagnosis of disruptive mood dysregulation disorder should not be assigned if the symptoms occur only in an anxiety-provoking context, when the routines of a child with autism spectrum disorder or obsessive-compulsive disorder are disturbed, or in the context of a major depressive episode.

Major Depressive Disorder

Diagnostic Criteria

A. Five (or more) 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.

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

   1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
   2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
   3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (**Note:** In children, consider failure to make expected weight gain.)
   4. Insomnia or hypersomnia nearly every day.
   5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
   6. Fatigue or loss of energy nearly every day.
   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. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
   9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation

without a specific plan, or a suicide attempt or a specific plan for committing suicide.

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

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

Note: Criteria A–C represent a major depressive episode.

Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the context of loss.[1]

D. At least one major depressive episode is not better explained by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic episode or a hypomanic episode.

Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

Coding and Recording Procedures

The diagnostic code for major depressive disorder is based on whether this is a single or recurrent episode, current severity, presence of psychotic features, and remission status. Current severity and psychotic features are only indicated if full criteria are currently met for a major depressive episode. Remission specifiers are only indicated if the full criteria are not currently met for a major depressive episode. Codes are as follows:

Severity/course specifier	Single episode	Recurrent episode*
Mild (p. 214)	F32.0	F33.0
Moderate (p. 214)	F32.1	F33.1
Severe (p. 214)	F32.2	F33.2
With psychotic features** (pp. 212–213)	F32.3	F33.3
In partial remission (p. 214)	F32.4	F33.41

In full remission (p. 214)	F32.5	F33.42
Unspecified	F32.9	F33.9

*For an episode to be considered recurrent, there must be an interval of at least 2 consecutive months between separate episodes in which criteria are not met for a major depressive episode. The definitions of specifiers are found on the indicated pages.

**If psychotic features are present, code the "with psychotic features" specifier irrespective of episode severity.

In recording the name of a diagnosis, terms should be listed in the following order: major depressive disorder, single or recurrent episode, severity/psychotic/remission specifiers, followed by as many of the following specifiers without codes that apply to the current episode (or the most recent episode if the major depressive disorder is in partial or full remission). **Note:** The specifier "with seasonal pattern" describes the pattern of recurrent major depressive episodes.

Specify if:

With anxious distress (pp. 210–211)

With mixed features (p. 211)

With melancholic features (pp. 211–212)

With atypical features (p. 212)

With mood-congruent psychotic features (p. 213)

With mood-incongruent psychotic features (p. 213)

With catatonia (p. 213). **Coding note:** Use additional code F06.1.

With peripartum onset (p. 213)

With seasonal pattern (applies to pattern of recurrent major depressive episodes) (p. 214)

Diagnostic Features

Major depressive disorder is defined by the presence of at least one major depressive episode occurring in the absence of a history of manic or hypomanic episodes. The essential feature of a major depressive episode is a period lasting at least 2 weeks during which there is either depressed mood or the loss of interest or pleasure in all or nearly all activities for most of the day nearly every day (Criterion A). The individual must also experience at least four additional symptoms during the same 2-week period, drawn from a list that includes changes in appetite or weight, sleep, and psychomotor activity; decreased energy; feelings of worthlessness or guilt; difficulty thinking, concentrating, or making decisions; or thoughts of death, suicidal ideation, a suicide attempt, or a specific plan for suicidal behavior. To count toward a diagnosis of a major depressive episode, a symptom must either be newly present or have clearly worsened compared with the individual's pre-episode status. Moreover, the symptoms must occur nearly every day, for at least 2 consecutive weeks, with the exception of thoughts of death and suicidal ideation, which must be recurrent, and attempting suicide or making a specific plan, which only needs to

occur once. The episode must be accompanied by clinically significant distress or impairment in social, occupational, or other important areas of functioning. For some individuals with milder episodes, functioning may appear to be normal but requires markedly increased effort. The presenting complaint is often insomnia or fatigue rather than depressed mood or loss of interest; thus, the failure to probe for accompanying depressive symptoms can result in underdiagnosis. Fatigue and sleep disturbance are present in a high proportion of cases; psychomotor disturbances are much less common but are indicative of greater overall severity, as is the presence of delusional or near-delusional guilt.

The mood in a major depressive episode is often described by the individual as depressed, sad, hopeless, discouraged, or “down in the dumps” (Criterion A1). In some cases, sadness may be denied at first but may subsequently be elicited by interview (e.g., by pointing out that the individual looks as if he or she is about to cry). In some individuals who complain of feeling “blah,” having no feelings, or feeling anxious, the presence of a depressed mood can be inferred from the individual’s facial expression and demeanor. Some individuals emphasize somatic complaints (e.g., bodily aches and pains) rather than reporting feelings of sadness. Many individuals report or exhibit increased irritability (e.g., persistent anger, a tendency to respond to events with angry outbursts or blaming others, an exaggerated sense of frustration over minor matters). In children and adolescents, an irritable or cranky mood may develop rather than a sad or dejected mood. This presentation should be differentiated from a pattern of irritability when frustrated.

Diminished interest or pleasure in usual activities is nearly always present, at least to some degree. Individuals may report feeling less interested in hobbies, “not caring anymore,” or not feeling any enjoyment in activities that were previously considered pleasurable (Criterion A2). Family members often notice social withdrawal or neglect of pleasurable avocations (e.g., a formerly avid golfer no longer plays, a child who used to enjoy soccer finds excuses not to practice). In some individuals, there is a significant reduction from previous levels of sexual interest or desire.

Appetite change may involve either a reduction or an increase. Some depressed individuals report that they have to force themselves to eat. Others may eat more and may crave specific foods (e.g., sweets or other carbohydrates). When appetite changes are severe (in either direction), there may be a significant loss or gain in weight, or, in children, a failure to make expected weight gains may be noted (Criterion A3).

Sleep disturbance may take the form of either difficulty sleeping or sleeping excessively (Criterion A4). When insomnia is present, it typically takes the form of middle insomnia (i.e., waking up during the night and then having difficulty returning to sleep) or terminal insomnia (i.e., waking too early and being unable to return to sleep). Initial insomnia (i.e., difficulty falling asleep) may also occur. Individuals who present with oversleeping (hypersomnia) may experience prolonged sleep episodes at night or increased daytime sleep. Sometimes the reason that the individual seeks treatment is for the disturbed sleep.

Psychomotor changes include agitation (e.g., the inability to sit still, pacing, hand-wringing; or pulling or rubbing of the skin, clothing, or other objects) or retardation (e.g., slowed speech, thinking, and body movements; increased pauses before answering; speech that is decreased in

volume, inflection, amount, or variety of content, or muteness) (Criterion A5). The psychomotor agitation or retardation must be severe enough to be observable by others and not represent merely subjective feelings. Individuals who display either psychomotor disturbance (i.e., psychomotor agitation or retardation) are likely to have histories of the other.

Decreased energy, tiredness, and fatigue are common (Criterion A6). An individual may report sustained fatigue without physical exertion. Even the smallest tasks seem to require substantial effort. The efficiency with which tasks are accomplished may be reduced. For example, an individual may complain that washing and dressing in the morning are exhausting and take twice as long as usual. This symptom accounts for much of the impairment resulting from major depressive disorder, both during acute episodes and when remission is incomplete.

The sense of worthlessness or guilt associated with a major depressive episode may include unrealistic negative evaluations of one's worth or guilty preoccupations or ruminations over minor past failings (Criterion A7). Such individuals often misinterpret neutral or trivial day-to-day events as evidence of personal defects and have an exaggerated sense of responsibility for untoward events. The sense of worthlessness or guilt may be of delusional proportions (e.g., an individual who is convinced that he or she is personally responsible for world poverty). Blaming oneself for being sick and for failing to meet occupational or interpersonal responsibilities as a result of the depression is very common and, unless delusional, is not considered sufficient to meet this criterion.

Many individuals report impaired ability to think, concentrate, or make even minor decisions (Criterion A8). They may appear easily distracted or complain of memory difficulties. Those engaged in cognitively demanding pursuits are often unable to function. In children, a precipitous drop in grades may reflect poor concentration. In elderly individuals, memory difficulties may be the chief complaint and may be mistaken for early signs of a dementia ("pseudodementia"). When the major depressive episode is successfully treated, the memory problems often fully abate. However, in some individuals, particularly elderly persons, a major depressive episode may sometimes be the initial presentation of an irreversible dementia.

Thoughts of death, suicidal ideation, or suicide attempts (Criterion A9) are common. They may range from a passive wish not to awaken in the morning or a belief that others would be better off if the individual were dead, to transient but recurrent thoughts of dying by suicide, to a specific suicide plan. More severely suicidal individuals may have put their affairs in order (e.g., updated wills, settled debts), acquired needed materials (e.g., a rope or a gun), and chosen a location and time to accomplish the suicide. Motivations for suicide may include a desire to give up in the face of perceived insurmountable obstacles,

an intense wish to end what is perceived as an unending and excruciatingly painful emotional state, an inability to foresee any enjoyment in life, or the wish to not be a burden to others. The resolution of such thinking may be a more meaningful measure of diminished suicide risk than denial of further plans for suicide.

The degree of impairment associated with a major depressive episode varies, but even in milder cases, there must be either clinically significant distress or some interference in social, occupational, or other important areas of functioning (Criterion B). If impairment is severe, the individual may lose the ability to function socially or occupationally. In extreme cases, the

individual may be unable to perform minimal self-care (e.g., feeding and clothing self) or to maintain minimal personal hygiene.

The individual's report of symptoms may be compromised by difficulties in concentrating, impaired memory, or a tendency to deny, discount, or explain away symptoms. Information from additional informants can be especially helpful in clarifying the course of current or prior major depressive episodes and in assessing whether there have been any manic or hypomanic episodes. Because major depressive episodes can begin gradually, a review of clinical information that focuses on the worst part of the current episode may be most likely to detect the presence of symptoms.

The evaluation of the symptoms of a major depressive episode is especially difficult when they occur in an individual who also has another medical condition (e.g., cancer, stroke, myocardial infarction, diabetes, pregnancy). Some of the criterion signs and symptoms of a major depressive episode are identical to those of another medical condition (e.g., weight loss with untreated diabetes; fatigue with cancer; hypersomnia early in pregnancy; insomnia later in pregnancy or the postpartum). Such symptoms count toward a major depressive diagnosis except when they are clearly and fully attributable to another medical condition. Nonvegetative symptoms of dysphoria, anhedonia, guilt or worthlessness, impaired concentration or indecision, and suicidal thoughts should be assessed with particular care in such cases. Definitions of major depressive episodes that have been modified to include only these nonvegetative symptoms appear to identify nearly the same individuals as do the full criteria.

Associated Features

Major depressive disorder is associated with high mortality, much of which is accounted for by suicide; however, it is not the only cause. For example, depressed individuals admitted to nursing homes have a markedly increased likelihood of death in the first year. Individuals frequently present with tearfulness, irritability, brooding, obsessive rumination, anxiety, phobias, excessive worry over physical health, and complaints of pain (e.g., headaches; joint, abdominal, or other pains). In children, separation anxiety may occur.

Although an extensive literature exists describing neuroanatomical, neuroendocrinological, and neurophysiological correlates of major depressive disorder, no laboratory test has yielded results of sufficient sensitivity and specificity to be used as a diagnostic tool for this disorder. Until recently, hypothalamic-pituitary-adrenal axis hyperactivity had been the most extensively investigated abnormality associated with major depressive episodes, and it appears to be associated with melancholia (a particularly severe type of depression), psychotic features, and risks for eventual suicide. Molecular studies have also implicated peripheral factors, including genetic variants in neurotrophic factors and pro-inflammatory cytokines. Additionally, volumetric and functional magnetic resonance imaging studies provide evidence for abnormalities in specific neural systems supporting emotion processing, reward seeking, and emotion regulation in adults with major depression.

Prevalence

Twelve-month prevalence of major depressive disorder in the United States is approximately 7%, with marked differences by age group such that the prevalence in 18- to 29-year-old

individuals is threefold higher than the prevalence in individuals age 60 years or older. The most reproducible finding in the epidemiology of major depressive disorder has been a higher prevalence in females, an effect that peaks in adolescence and then stabilizes. Women experience approximately twofold higher rates than men, especially between menarche and menopause. Women report more atypical symptoms of depression characterized by hypersomnia, increased appetite, and leaden paralysis compared with men.

Systematic reviews show that the 12-month and point prevalence of major depressive disorder vary eight- to ninefold across global geographic regions. In the United States, prevalence increased from 2005 to 2015, with steeper rates of increase for youth compared with older groups. After stratification by ethnoracial groups, non-Hispanic Whites showed a significant increase in prevalence after adjustment for demographic characteristics, whereas no significant change in rate of depression was observed among non-Hispanic Blacks or Hispanics.

Development and Course

Major depressive disorder may first appear at any age, but the likelihood of onset increases markedly with puberty. In the United States, incidence appears to peak in the 20s; however, first onset in late life is not uncommon.

The course of major depressive disorder is quite variable, such that some individuals rarely, if ever, experience remission (a period of 2 or more months with no symptoms, or only one or two symptoms to no more than a mild degree), while others experience many years with few or no symptoms between discrete episodes. The course of depression may reflect social-structural adversity associated with poverty, racism, and marginalization.

It is important to distinguish individuals who present for treatment during an exacerbation of a chronic depressive illness from those whose symptoms developed recently. Chronicity of depressive symptoms substantially increases the likelihood of underlying personality, anxiety, and substance use disorders and decreases the likelihood that treatment will be followed by full symptom resolution. It is therefore useful to ask individuals presenting with depressive symptoms to identify the last period of at least 2 months during which they were entirely free of depressive symptoms. Cases in which depressive symptoms are present for more days than not might warrant an additional diagnosis of persistent depressive disorder.

Recovery from a major depressive episode begins within 3 months of onset for 40% of individuals with major depression and within 1 year for 80% of individuals. Recency of onset is a strong determinant of the likelihood of near-term recovery, and many individuals who have been depressed for only several months can be expected to recover spontaneously. Features associated with lower recovery rates, other than current episode duration, include psychotic features, prominent anxiety, personality disorders, and symptom severity.

The risk of recurrence becomes progressively lower over time as the duration of remission increases. The risk is higher in individuals whose preceding episode was severe, in younger individuals, and in individuals who have already experienced multiple episodes. The persistence of even mild depressive symptoms during remission is a powerful predictor of recurrence.

Many bipolar illnesses begin with one or more depressive episodes, and a substantial proportion of individuals who initially appear to have major depressive disorder will prove, in

time, to instead have a bipolar disorder. This is more likely in individuals with onset of the illness in adolescence, those with psychotic features, and those with a family history of bipolar illness. The presence of a "with mixed features" specifier also increases the risk for future manic or hypomanic diagnosis. Major depressive disorder, particularly with psychotic features, may also transition into schizophrenia, a change that is much more frequent than the reverse.

There are no clear effects of current age on the course or treatment response of major depressive disorder. Some symptom differences exist, though, such that hypersomnia and hyperphagia are more likely in younger individuals, and melancholic symptoms, particularly psychomotor disturbances, are more common in older individuals. Depressions with earlier ages at onset are more familial and more likely to involve personality disturbances. The course of major depressive disorder within individuals does not generally change with aging. Mean times to recovery do not change over multiple episodes, and the likelihood of being in an episode does not generally increase or decrease with time.

Risk and Prognostic Factors

Temperamental. Negative affectivity (neuroticism) is a well-established risk factor for the onset of major depressive disorder, and high levels appear to render individuals more likely to develop depressive episodes in response to stressful life events.

Environmental. Adverse childhood experiences, particularly when they are multiple and of diverse types, constitute a set of potent risk factors for major depressive disorder. Women may be disproportionately at risk for adverse childhood experiences, including sexual abuse, that may contribute to the increased prevalence of depression in this group. Other social determinants of mental health, such as low income, limited formal education, racism, and other forms of discrimination, are associated with higher risk of major depressive disorder. Stressful life events are well recognized as precipitants of major depressive episodes, but the presence or absence of adverse life events near the onset of episodes does not appear to provide a useful guide to prognosis or treatment selection. Etiologically, women are disproportionately affected by major risk factors for depression across the life span, including interpersonal trauma.

Genetic and physiological. First-degree family members of individuals with major depressive disorder have a risk for major depressive disorder two- to fourfold higher than that of the general population. Relative risks appear to be higher for early-onset and recurrent forms. Heritability is approximately 40%, and the personality trait neuroticism accounts for a substantial portion of this genetic liability.

Women may also be at risk for depressive disorders in relation to specific reproductive life stages, including in the premenstrual period, postpartum, and in perimenopause.

Course modifiers. Essentially all major nonmood disorders (i.e., anxiety, substance use, trauma- and stressor-related, feeding and eating, and obsessive-compulsive and related disorders) increase the risk of an individual developing depression. Major depressive episodes that develop against the background of another disorder often follow a more refractory course. Substance use, anxiety, and borderline personality disorders are among the most common of these, and the presenting depressive symptoms may obscure and delay their recognition. However, sustained

clinical improvement in depressive symptoms may depend on the appropriate treatment of underlying illnesses. Chronic or disabling medical conditions also increase risks for major depressive episodes. Prevalent illnesses such as diabetes, morbid obesity, and cardiovascular disease are often complicated by depressive episodes, and these episodes are more likely to become chronic than are depressive episodes in medically healthy individuals.

Culture-Related Diagnostic Issues

Although there is substantial cross-cultural variation in the prevalence, course, and symptomatology of depression, a syndrome similar to major depressive disorder can be identified across diverse cultural contexts. Symptoms commonly associated with depression across cultural contexts, not listed in the DSM criteria, include social isolation or loneliness, anger, crying, and diffuse pain. A wide range of other somatic complaints are

common and vary by cultural context. Understanding the significance of these symptoms requires exploring their meaning in local social contexts.

Symptoms of major depressive disorder may be underdetected or underreported, potentially leading to misdiagnosis, including overdiagnosis of schizophrenia spectrum disorders in some ethnic and racialized groups facing discrimination. Cross-nationally, higher levels of income inequality in a society are associated with higher prevalence of major depressive disorder. In the United States, the chronicity of major depressive disorder appears to be higher among African Americans and Caribbean Blacks compared with non-Latinx Whites, possibly because of the impact of racism, discrimination, greater sociostructural adversity, and lack of access to quality mental health care.

Sex- and Gender-Related Diagnostic Issues

There are no clear differences between genders in treatment response or functional consequences. There is some evidence for sex and gender differences in phenomenology and course of illness. Women tend to experience more disturbances in appetite and sleep, including atypical features such as hyperphagia and hypersomnia, and are more likely to experience interpersonal sensitivity and gastrointestinal symptoms. Men with depression, however, may be more likely than depressed women to report greater frequencies and intensities of maladaptive self-coping and problem-solving strategies, including alcohol or other drug misuse, risk taking, and poor impulse control.

Association With Suicidal Thoughts or Behavior

Age-adjusted rates of suicide in the United States have increased from 10.5 to 14.0 per 100,000 over the past two decades. An earlier review of the literature indicated that individuals with depressive illness have a 17-fold increased risk for suicide over the age- and sex-adjusted general population rate. The likelihood of suicide attempts lessens in middle and late life, although the risk of death by suicide does not. The possibility of suicidal behavior exists at all times during major depressive episodes. The most consistently described risk factor is a past history of suicide attempts or threats, but it should be remembered that most deaths by suicide are not preceded by

nonfatal attempts. Anhedonia has a particularly strong association with suicidal ideation. Other features associated with an increased risk for death by suicide include being single, living alone, social disconnectedness, early life adversity, availability of lethal methods such as a firearm, sleep disturbance, cognitive and decision-making deficits, and having prominent feelings of hopelessness. Women attempt suicide at a higher rate than men, while men are more likely to complete suicide. The difference in suicide rate between men and women with depressive disorders is smaller than in the population as a whole, however. Comorbidities, including aggressive-impulsive traits, borderline personality disorder, substance use disorder, anxiety, other medical conditions, and functional impairment, increase risk for future suicidal behavior.

Functional Consequences of Major Depressive Disorder

Many of the functional consequences of major depressive disorder derive from individual symptoms. Impairment can be very mild, such that many of those who interact with the affected individual are unaware of depressive symptoms. Impairment may, however, range to complete incapacity such that the depressed individual is unable to attend to basic self-care needs or is mute or catatonic. For individuals seen in general medical settings, those with major depressive disorder have more pain and physical illness and greater decreases in physical, social, and role functioning. Depressed women report greater functional impairment in their relationships than men.

Differential Diagnosis

Manic episodes with irritable mood or with mixed features. Major depressive episodes with prominent irritable mood may be difficult to distinguish from manic episodes with irritable mood or with mixed features. This distinction requires a careful clinical evaluation of the presence of sufficient manic symptoms to meet threshold criteria (i.e., three if mood is manic, four if mood is irritable but not manic).

Bipolar I disorder, bipolar II disorder, or other specified bipolar and related disorder. Major depressive episodes along with a history of a manic or hypomanic episode preclude the diagnosis of major depressive disorder. Major depressive episodes with a history of hypomanic episodes and without a history of manic episodes indicate a diagnosis of bipolar II disorder, whereas major depressive episodes with a history of manic episodes (with or without hypomanic episodes) indicate a diagnosis of bipolar I disorder. On the other hand, presentations of major depressive episodes with a history of periods of hypomania that do not meet criteria for a hypomanic episode may be diagnosed as either other specified bipolar and related disorder or major depressive disorder depending on where the clinician judges the presentation to best fall. For example, the presentation may be best considered other specified bipolar and related disorder because of the clinical significance of the subthreshold hypomanic symptoms, or the presentation may be best considered a case of major depressive disorder with some subthreshold hypomanic symptoms in between episodes.

Depressive disorder due to another medical condition. A diagnosis of depressive disorder due to another medical condition requires the presence of an etiological medical condition. Major

depressive disorder is not diagnosed if the major depressive–like episodes are all attributable to the direct pathophysiological consequence of a specific medical condition (e.g., multiple sclerosis, stroke, hypothyroidism).

Substance/medication-induced depressive disorder. This disorder is distinguished from major depressive disorder by the fact that a substance (e.g., a drug of abuse, a medication, a toxin) appears to be etiologically related to the mood disturbance. For example, depressed mood that occurs only in the context of withdrawal from cocaine would be diagnosed as cocaine-induced depressive disorder.

Persistent depressive disorder. Persistent depressive disorder is characterized by depressed mood, more days than not, for at least 2 years. If criteria are met for both major depressive disorder and persistent depressive disorder, both can be diagnosed.

Premenstrual dysphoric disorder. Premenstrual dysphoric disorder is characterized by dysphoric mood that is present in the final week before the onset of menses, that starts to improve within a few days after the onset of menses, and that becomes minimal or absent in the week postmenses. By contrast, the episodes of major depressive disorder are not temporally connected to the menstrual cycle.

Disruptive mood dysregulation disorder. Disruptive mood dysregulation disorder is characterized by severe, recurrent temper outbursts manifested verbally and/or behaviorally, accompanied by persistent or labile mood, most of the day, nearly every day, in between the outbursts. In contrast, in major depressive disorder, irritability is confined to the major depressive episodes.

Major depressive episodes superimposed on schizophrenia, delusional disorder, schizophreniform disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder.

Depressive symptoms may be present during schizophrenia, delusional disorder, schizophreniform disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder. Most commonly, such depressive symptoms can be considered associated features of these disorders and do not merit a

separate diagnosis. However, when the depressive symptoms meet full criteria for a major depressive episode, a diagnosis of other specified depressive disorder may be made in addition to the diagnosis of the psychotic disorder.

Schizoaffective disorder. Schizoaffective disorder differs from major depressive disorder, with psychotic features, by the requirement that in schizoaffective disorder, delusions or hallucinations are present for at least 2 weeks in the absence of a major depressive episode.

Attention-deficit/hyperactivity disorder. Distractibility and low frustration tolerance can occur in both attention-deficit/hyperactivity disorder (ADHD) and a major depressive episode; if the criteria are met for both, ADHD may be diagnosed in addition to the mood disorder. However, the clinician must be cautious not to overdiagnose a major depressive episode in children with ADHD whose disturbance in mood is characterized by irritability rather than by sadness or loss of interest.

Adjustment disorder with depressed mood. A major depressive episode that occurs in response to a psychosocial stressor is distinguished from adjustment disorder, with depressed mood, by the

fact that the full criteria for a major depressive episode are not met in adjustment disorder.

Bereavement. Bereavement is the experience of losing a loved one to death. It generally triggers a grief response that may be intense and may involve many features that overlap with symptoms characteristic of a major depressive episode, such as sadness, difficulty sleeping, and poor concentration. Features that help differentiate a bereavement-related grief response from a major depressive episode include the following: the predominant affects in grief are feelings of emptiness and loss, whereas in a major depressive episode they are persistent depressed mood and a diminished ability to experience pleasure. Moreover, the dysphoric mood of grief is likely to decrease in intensity over days to weeks and occurs in waves that tend to be associated with thoughts or reminders of the deceased, whereas the depressed mood in a major depressive episode is more persistent and not tied to specific thoughts or preoccupations. It is important to note that in a vulnerable individual (e.g., someone with a past history of major depressive disorder), bereavement may trigger not only a grief response but also the development of an episode of depression or the worsening of an existing episode.

Sadness. Finally, periods of sadness are inherent aspects of the human experience. These periods should not be diagnosed as a major depressive episode unless criteria are met for severity (i.e., five out of nine symptoms), duration (i.e., most of the day, nearly every day for at least 2 weeks), and clinically significant distress or impairment. The diagnosis other specified depressive disorder may be appropriate for presentations of depressed mood with clinically significant impairment that do not meet criteria for duration or severity.

Comorbidity

Other disorders with which major depressive disorder frequently co-occurs are substance-related disorders, panic disorder, generalized anxiety disorder, posttraumatic stress disorder, obsessive-compulsive disorder, anorexia nervosa, bulimia nervosa, and borderline personality disorder.

While women are more likely than men to report comorbid anxiety disorders, bulimia nervosa, and somatoform disorder (somatic symptom and related disorders), men are more likely to report comorbid alcohol and substance abuse.

Persistent Depressive Disorder

Diagnostic Criteria F34.1

This disorder represents a consolidation of DSM-IV-defined chronic major depressive disorder and dysthymic disorder.

A. Depressed mood for most of the day, for more days than not, as indicated by either subjective account or observation by others, for at least 2 years.

   Note: In children and adolescents, mood can be irritable and duration must be at least 1 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 2-year period (1 year for children or adolescents) of the disturbance, the individual has never been without the symptoms in Criteria A and B for more than 2 months at a time.

D. Criteria for a major depressive disorder may be continuously present for 2 years.

E. There has never been a manic episode or a hypomanic episode.

F. The disturbance is not better explained by a persistent schizoaffective disorder, schizophrenia, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder.

G. The symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hypothyroidism).

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

Note: If criteria are sufficient for a diagnosis of a major depressive episode at any time during the 2-year period of depressed mood, then a separate diagnosis of major depression should be made in addition to the diagnosis of persistent depressive disorder along with the relevant specifier (e.g., with intermittent major depressive episodes, with current episode).

Specify if:

With anxious distress (pp. 210–211)

With atypical features (p. 212)

Specify if:

In partial remission (p. 214)

In full remission (p. 214)

Specify if:

Early onset: If onset is before age 21 years.

Late onset: If onset is at age 21 years or older.

Specify if (for most recent 2 years of persistent depressive disorder):

With pure dysthymic syndrome: Full criteria for a major depressive episode have not been met in at least the preceding 2 years.

With persistent major depressive episode: Full criteria for a major depressive episode have been met throughout the preceding 2-year period.

With intermittent major depressive episodes, with current episode: Full criteria for a major depressive episode are currently met, but there have been periods of at least 8 weeks in at least the preceding 2 years with symptoms below the threshold for a full major depressive episode.

With intermittent major depressive episodes, without current episode: Full criteria for a major depressive episode are not currently met, but there has been one or more major depressive episodes in at least the preceding 2 years.

Specify current severity:

Mild (p. 214)

Moderate (p. 214)

Severe (p. 214)

Diagnostic Features

The essential feature of persistent depressive disorder is a depressed mood that occurs for most of the day, for more days than not, for at least 2 years, or at least 1 year for children and adolescents (Criterion A). This disorder represents a consolidation of DSM-IV-defined chronic major depressive disorder and dysthymic disorder. Major depression may precede persistent depressive disorder, and major depressive episodes may occur during persistent depressive disorder. Individuals whose symptoms meet major depressive disorder criteria for 2 years should be given a diagnosis of persistent depressive disorder as well as major depressive disorder.

Individuals with persistent depressive disorder describe their mood as sad or "down in the dumps." During periods of depressed mood, at least two of the six symptoms from Criterion B are present. Because these symptoms have become a part of the individual's day-to-day experience, particularly in the case of early onset (e.g., "I've always been this way"), they may not be reported unless the individual is directly prompted. During the 2-year period (1 year for children or adolescents), any symptom-free intervals that have occurred have lasted no longer than 2 months (Criterion C).

Prevalence

Persistent depressive disorder is effectively an amalgam of DSM-IV dysthymic disorder and chronic major depressive episode. The 12-month prevalence in the United States is approximately 0.5% for dysthymic disorder and 1.5% for chronic major depressive disorder, with prevalence among women approximately 1.5 and 2 times higher than prevalence among men for each of these diagnoses, respectively. Based on studies using comparable ascertainment procedures, the lifetime and 12-month estimates of DSM-IV dysthymia may be higher in high-income than in low- and middle-income countries. However, the disorder is associated with elevated risk of suicidal outcomes and comparable levels of disability wherever it occurs.

Development and Course

Persistent depressive disorder often has an early and insidious onset (i.e., in childhood, adolescence, or early adult life) and, by definition, a chronic course. Borderline personality disorder is a particularly robust risk factor for persistent depressive disorder. When persistent

depressive disorder and borderline personality disorder coexist, the covariance of the corresponding features over time suggests the operation of a common mechanism. Early onset (i.e., before age 21 years) is associated with a higher likelihood of comorbid personality disorders and substance use disorders.

When symptoms rise to the level of a major depressive episode, they are likely to subsequently revert to a lower level. However, depressive symptoms are much less likely to resolve fully in a given period of time in the context of persistent depressive disorder than they are in a nonchronic major depressive episode.

Risk and Prognostic Factors

Temperamental. Factors predictive of poorer long-term outcome include higher levels of negative affectivity (neuroticism), greater symptom severity, poorer global functioning, and presence of anxiety disorders or conduct disorder.

Environmental. Childhood risk factors include parental loss or separation and childhood adversity.

Genetic and physiological. There are no clear differences in illness development, course, or family history between DSM-IV dysthymic disorder and chronic major depressive disorder. Earlier findings pertaining to either disorder are therefore likely to apply to persistent depressive disorder. It is thus likely that individuals with persistent depressive disorder will have a higher proportion of first-degree relatives with persistent depressive disorder than do individuals with nonchronic major depressive disorder, and more depressive disorders in general.

A number of brain regions (e.g., prefrontal cortex, anterior cingulate, amygdala, hippocampus) have been implicated in persistent depressive disorder. Possible polysomnographic abnormalities exist as well.

Culture-Related Diagnostic Issues

The perceived abnormality or tolerance of chronic depressive symptoms may vary across cultures, affecting symptom detection and treatment acceptability. For example, some social groups or age cohorts may consider long-standing depressive symptoms to be normal reactions to adversity.

Association With Suicidal Thoughts or Behavior

Persistent depressive disorder is associated with elevated risk of suicidal outcomes and comparable levels of disability, whether the disorder occurs in high-, middle-, or low-income countries.

Functional Consequences of Persistent Depressive Disorder

The degree to which persistent depressive disorder impacts social and occupational functioning is likely to vary widely, but effects can be as great as or greater than those of major depressive disorder.

Differential Diagnosis

Major depressive disorder. If there is a depressed mood for more days than not plus two or more persistent depressive disorder Criterion B symptoms for 2 years or more, then the diagnosis of persistent depressive disorder is made. If the symptom criteria are sufficient for a diagnosis of a major depressive episode at any time during this period, then the additional diagnosis of major depression should be made. The comorbid presence of major depressive episodes during this period should also be noted by assigning the appropriate course specifier to the persistent depressive disorder diagnosis as follows: If the individual's symptoms currently meet full criteria for a major depressive episode, and there have been periods of at least 8 weeks in at least the preceding 2 years with symptoms below the threshold for a full major depressive episode, then the specifier "with intermittent major depressive episodes, with current episode" would be assigned. If full criteria for a major depressive episode are not currently met but there has been one or more major depressive episodes in at least the preceding 2 years, then the specifier "with intermittent major depressive episodes, without current episode" is assigned. If a major depressive episode

has persisted for at least a 2-year duration and remains present, then the specifier "with persistent major depressive episode" is used. If the individual has not experienced an episode of major depression in the last 2 years, then the specifier "with pure dysthymic syndrome" is used.

Other specified depressive disorder. Because the criteria for a major depressive episode include symptoms (i.e., markedly diminished interest or pleasure in activities; psychomotor agitation or retardation; recurrent thoughts of death, suicidal ideation, suicide attempt or plan) that are absent from the symptom list for persistent depressive disorder (i.e., depressed mood and two out of six Criterion B symptoms), a very limited number of individuals will have depressive symptoms that have persisted longer than 2 years but that do not meet criteria for persistent depressive disorder. If full criteria for a major depressive episode have been met at some point during the current episode of illness, a diagnosis of major depressive disorder would apply. Otherwise, a diagnosis of other specified depressive disorder or unspecified depressive disorder should be given.

Bipolar I and bipolar II disorders. A history of a manic or hypomanic episode precludes the diagnosis of persistent depressive disorder. A history of manic episodes (with or without hypomanic episodes) indicates a diagnosis of bipolar I disorder. A history of hypomanic episodes (without any history of manic episodes in individuals with persistent depressive presentations during which criteria have been met for a major depressive episode) warrants a diagnosis of bipolar II disorder. Other specified bipolar disorder applies to individuals whose presentations include a history of hypomanic episodes along with persistent depressive presentation that has never met full criteria for a major depressive episode.

Cyclothymic disorder. A diagnosis of cyclothymic disorder precludes the diagnosis of persistent depressive disorder. Thus, if during the period lasting at least 2 years of depressed mood for most of the day, for more days than not, 1) there are numerous periods with hypomanic symptoms that do not meet criteria for a hypomanic episode, 2) there have not been any symptom-free periods of more than 2 months at a time, and 3) criteria have never been met for a major depressive, manic, or hypomanic episode, then the diag-nosis would be cyclothymic disorder instead of

persistent depressive disorder.

Psychotic disorders. Depressive symptoms are a common associated feature of chronic psychotic disorders (e.g., schizoaffective disorder, schizophrenia, delusional disorder). A separate diagnosis of persistent depressive disorder is not made if the symptoms occur only during the course of the psychotic disorder (including residual phases).

Depressive or bipolar and related disorder due to another medical condition. Persistent depressive disorder must be distinguished from a depressive or bipolar and related disorder due to another medical condition. The diagnosis is depressive or bipolar and related disorder due to another medical condition if the mood disturbance is judged, based on history, physical examination, or laboratory findings, to be attributable to the direct pathophysiological effects of a specific, usually chronic, medical condition (e.g., multiple sclerosis). If it is judged that the depressive symptoms are not attributable to the physiological effects of another medical condition, then the primary mental disorder (e.g., persistent depressive disorder) is recorded, and the medical condition is noted as a concomitant medical condition (e.g., diabetes mellitus).

Substance/medication-induced depressive or bipolar and related disorder. A substance/medication-induced depressive or bipolar and related disorder is distinguished from persistent depressive disorder when a substance (e.g., a drug of abuse, a medication, a toxin) is judged to be etiologically related to the mood disturbance.

Personality disorders. A personality disorder is characterized by an enduring pattern of inner experience and behavior that deviates markedly from the expectations of the

individual's culture, with onset by adolescence or early adulthood. Personality disorders commonly co-occur with persistent depressive disorder. If criteria are met for persistent depressive disorder and a personality disorder, both may be diagnosed.

Comorbidity

In comparison to individuals with major depressive disorder, those with persistent depressive disorder are at higher risk for psychiatric comorbidity in general, and for anxiety disorders, substance use disorders, and personality disorders in particular. Early-onset persistent depressive disorder is strongly associated with DSM-5 Cluster B and C personality disorders.

Premenstrual Dysphoric Disorder

Diagnostic Criteria F32.81

A. In the majority of menstrual cycles, at least five symptoms must be present in the final week before the onset of menses, start to *improve* within a few days after the onset of menses, and become *minimal* or absent in the week postmenses.

B. One (or more) of the following symptoms must be present:

1. Marked affective lability (e.g., mood swings; feeling suddenly sad or tearful, or increased sensitivity to rejection).
2. Marked irritability or anger or increased interpersonal conflicts.
3. Marked depressed mood, feelings of hopelessness, or self-deprecating thoughts.
4. Marked anxiety, tension, and/or feelings of being keyed up or on edge.

C. One (or more) of the following symptoms must additionally be present, to reach a total of *five* symptoms when combined with symptoms from Criterion B above.

1. Decreased interest in usual activities (e.g., work, school, friends, hobbies).
2. Subjective difficulty in concentration.
3. Lethargy, easy fatigability, or marked lack of energy.
4. Marked change in appetite; overeating; or specific food cravings.
5. Hypersomnia or insomnia.
6. A sense of being overwhelmed or out of control.
7. Physical symptoms such as breast tenderness or swelling, joint or muscle pain, a sensation of "bloating," or weight gain.

Note: The symptoms in Criteria A–C must have been met for most menstrual cycles that occurred in the preceding year.

D. The symptoms cause clinically significant distress or interference with work, school, usual social activities, or relationships with others (e.g., avoidance of social activities; decreased productivity and efficiency at work, school, or home).

E. The disturbance is not merely an exacerbation of the symptoms of another disorder, such as major depressive disorder, panic disorder, persistent depressive disorder, or a personality disorder (although it may co-occur with any of these disorders).

F. Criterion A should be confirmed by prospective daily ratings during at least two symptomatic cycles. (**Note:** The diagnosis may be made provisionally prior to this confirmation.)

G. The symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, other treatment) or another medical condition (e.g., hyperthyroidism).

Recording Procedures

If symptoms have not been confirmed by prospective daily ratings of at least two symptomatic cycles, "provisional" should be noted after the name of the diagnosis (i.e., "premenstrual dysphoric disorder, provisional").

Diagnostic Features

The essential features of premenstrual dysphoric disorder are the expression of mood lability, irritability, dysphoria, and anxiety symptoms that occur repeatedly during the premenstrual phase of the cycle and remit around the onset of menses or shortly thereafter. These symptoms may be accompanied by behavioral and physical symptoms. Symptoms must have occurred in most of the menstrual cycles during the past year and must have an adverse effect on work or social functioning. The intensity and/or expressivity of the accompanying symptoms may be closely related to social and cultural background characteristics as well as religious beliefs, social tolerance, attitude toward the female reproductive cycle, and female gender role issues more generally.

Typically, symptoms peak around the time of the onset of menses. Although it is not uncommon for symptoms to linger into the first few days of menses, the individual must have a symptom-free period in the follicular phase after the menstrual period begins. While the core symptoms include mood and anxiety symptoms, behavioral and somatic symptoms commonly also occur. However, the presence of somatic and/or behavioral symptoms in the absence of mood and/or anxious symptoms is not sufficient for a diagnosis. Symptoms are of comparable severity (but not duration) to those of other mental disorders, such as a major depressive episode or generalized anxiety disorder. In order to confirm a provisional diagnosis, daily prospective symptom ratings are required for at least two symptomatic cycles.

Symptoms must cause clinically significant distress and/or an obvious and marked impairment in the ability to function socially or occupationally in the week prior to menses.

Associated Features

Delusions and hallucinations have been described in the late luteal phase of the menstrual cycle but are rare.

Prevalence

The 12-month prevalence of premenstrual dysphoric disorder in the community has been estimated at 5.8% based on a large study from Germany. Another study that looked at prevalence over two menstrual cycles found 1.3% of menstruating women with the disorder in the United States. Estimates based on retrospective reports are often higher than those based on prospective daily ratings. Yet, estimates based on a daily record of symptoms for 1–2 months may not be fully representative, because those with the most severe symptoms may be unable to sustain the rating process. The most rigorous estimate of premenstrual dysphoric disorder prevalence in the United States using prospective ratings of two consecutive menstrual cycles was 1.3% for women whose symptoms met diagnostic criteria, who experienced functional impairment, and had no co-occurring mental disorder. The prevalence of premenstrual dysphoric disorder symptoms in adolescent girls may be higher than that observed in adult women.

Development and Course

Onset of premenstrual dysphoric disorder can occur at any point after menarche. Incidence of new cases over a 40-month follow-up period in Germany is 2.5% (95% confidence interval = 1.7–3.7). Symptoms cease after menopause, although cyclical hormone replacement can trigger the re-expression of symptoms.

Risk and Prognostic Factors

Environmental. Environmental factors associated with the expression of premenstrual dysphoric disorder include stress, history of interpersonal trauma, seasonal changes, and sociocultural aspects of female sexual behavior in general, and female gender roles in particular.

Genetic and physiological. No studies have examined heritability in premenstrual dysphoric disorder specifically. Estimates for heritability of premenstrual dysphoric symptoms range between 30% and 80%, although it remains unclear whether the symptoms themselves are heritable or whether they are simply associated with other heritable factors or traits.

Culture-Related Diagnostic Issues

Premenstrual dysphoric disorder has been observed in individuals in the United States, Europe, India, Nigeria, Brazil, and Asia, with a broad prevalence range. Nevertheless, as with most mental disorders, frequency, intensity, and expressivity of symptoms; perceived consequences; help-seeking patterns; and management may be significantly influenced by social and cultural factors, such as a history of sexual abuse or domestic violence, limited social support, and cultural variations in attitudes toward menstruation.

Diagnostic Markers

As indicated earlier, the diagnosis of premenstrual dysphoric disorder is appropriately confirmed by 2 months of prospective symptom ratings. A number of scales, including the Daily Rating of Severity of Problems and the Visual Analogue Scales for Premenstrual Mood Symptoms, have undergone validation and are commonly used in clinical trials for premenstrual dysphoric disorder. The Premenstrual Tension Syndrome Rating Scale has a self-report and an observer version, both of which have been validated and used widely to measure illness severity in women who have premenstrual dysphoric disorder.

Association With Suicidal Thoughts or Behavior

The premenstrual phase has been considered by some to be a risk period for suicide.

Functional Consequences of Premenstrual Dysphoric Disorder

Impairment in social functioning may be manifested by discord in the intimate partner relationship and problems with children, other family members, or friends that occur only in association with the premenstrual dysphoric disorder (i.e., as opposed to chronic interpersonal problems). Impairments in work and health-related quality of life are also prominent. There is evidence that premenstrual dysphoric disorder can be associated with impairments in function and health-related quality of life that are on par with those observed in major depressive disorder and persistent depressive disorder.

Differential Diagnosis

Premenstrual syndrome. Premenstrual syndrome differs from premenstrual dysphoric disorder in

that premenstrual syndrome does not require a minimum of five symptoms nor mood-related symptomatology, and it is generally considered to be less severe than premenstrual dysphoric disorder. Premenstrual syndrome may be more common than premenstrual dysphoric disorder; its estimated prevalence varies with numbers that hover at about 20%. While premenstrual syndrome shares the feature of symptom expression during the premenstrual phase of the menstrual cycle, the presence of somatic or

behavioral symptoms, without the required affective symptoms, likely meets criteria for premenstrual syndrome and not for premenstrual dysphoric disorder.

Dysmenorrhea. Dysmenorrhea is a syndrome of painful menses, but this is distinct from a syndrome characterized by affective changes. Moreover, symptoms of dysmenorrhea begin with the onset of menses, whereas symptoms of premenstrual dysphoric disorder, by definition, begin before the onset of menses, even if they linger into the first few days of menses.

Bipolar disorder, major depressive disorder, and persistent depressive disorder. Many women with (either naturally occurring or substance/medication-induced) bipolar or major depressive disorder or persistent depressive disorder believe that they have premenstrual dysphoric disorder. However, when they chart symptoms, they realize that the symptoms do not follow a premenstrual pattern. Because the onset of menses constitutes a memorable event, they may report that symptoms occur only during the premenstruum or that symptoms worsen premenstrually. This is one of the rationales for the requirement that symptoms be confirmed by daily prospective ratings. The process of differential diagnosis, particularly if the clinician relies on retrospective symptoms only, is made more difficult because of the overlap between symptoms of premenstrual dysphoric disorder and some other diagnoses. The overlap of symptoms is particularly salient for differentiating premenstrual dysphoric disorder from major depressive episodes, persistent depressive disorder, bipolar disorders, and borderline personality disorder.

Use of hormonal treatments. Some women who present with moderate to severe premenstrual symptoms may be using hormonal treatments, including hormonal contraceptives. If such symptoms occur after initiation of exogenous hormone use, the symptoms may be attributable to the use of hormones rather than to the underlying condition of premenstrual dysphoric disorder. If the woman stops hormones and the symptoms disappear, then this is consistent with substance/medication-induced depressive disorder.

Other medical conditions. Women with chronic medical conditions may experience symptoms of premenstrual dysphoria. As with any depressive disorder, medical conditions that could better account for the symptoms should be ruled out, such as thyroid deficiency and anemia.

Comorbidity

A major depressive episode is the most frequently reported previous disorder in individuals presenting with premenstrual dysphoric disorder. A wide range of medical conditions (e.g., migraine, asthma, allergies, seizure disorders) or other mental disorders (e.g., depressive and bipolar disorders, anxiety disorders, bulimia nervosa, substance use disorders) may worsen in the

premenstrual phase; however, the absence of a symptom-free period during the postmenstrual interval obviates a diagnosis of premenstrual dysphoric disorder. These conditions are better considered premenstrual exacerbation of a current mental disorder or medical condition. Although the diagnosis of premenstrual dysphoric disorder should not be assigned in situations in which an individual experiences only a premenstrual exacerbation of another mental or physical disorder, it can be considered in addition to the diagnosis of another mental disorder or medical condition if the individual experiences symptoms and changes in level of functioning that are characteristic of premenstrual dysphoric disorder and markedly different from the symptoms experienced as part of the ongoing disorder.

Substance/Medication-Induced Depressive Disorder

Diagnostic Criteria

A. A prominent and persistent disturbance in mood that predominates in the clinical picture and is characterized by depressed mood or markedly diminished interest or pleasure in all, or almost all, activities.

B. There is evidence from the history, physical examination, or laboratory findings of both (1) and (2):

   1. The symptoms in Criterion A developed during or soon after substance intoxication or withdrawal or after exposure to or withdrawal from a medication.
   2. The involved substance/medication is capable of producing the symptoms in Criterion A.

C. The disturbance is not better explained by a depressive disorder that is not substance/medication-induced. Such evidence of an independent depressive disorder could include the following:

   The symptoms preceded the onset of the substance/medication use; the symptoms persist for a substantial period of time (e.g., about 1 month) after the cessation of acute withdrawal or severe intoxication; or there is other evidence suggesting the existence of an independent non-substance/medication-induced depressive disorder (e.g., a history of recurrent non-substance/medication-related episodes).

D. The disturbance does not occur exclusively during the course of a delirium.

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Note: This diagnosis should be made instead of a diagnosis of substance intoxication or substance withdrawal only when the symptoms in Criterion A predominate in the clinical picture and when they are sufficiently severe to warrant

clinical attention.

Coding note: The ICD-10-CM codes for the [specific substance/medication]-induced depressive disorders are indicated in the table below. Note that the ICD-10-CM code depends on whether or not there is a comorbid substance use disorder present for the same class of substance. In any case, an additional separate diagnosis of a substance use disorder is not given. If a mild substance use disorder is comorbid with the substance-induced depressive disorder, the 4th position character is "1," and the clinician should record "mild [substance] use disorder" before the substance-induced depressive disorder (e.g., "mild cocaine use disorder with cocaine-induced depressive disorder"). If a moderate or severe substance use disorder is comorbid with the substance-induced depressive disorder, the 4th position character is "2," and the clinician should record "moderate [substance] use disorder" or "severe [substance] use disorder," depending on the severity of the comorbid substance use disorder. If there is no comorbid substance use disorder (e.g., after a one-time heavy use of the substance), then the 4th position character is "9," and the clinician should record only the substance-induced depressive disorder.

	ICD-10-CM		
	With mild use disorder	**With moderate or severe use disorder**	**Without use disorder**
Alcohol	F10.14	F10.24	F10.94
Phencyclidine	F16.14	F16.24	F16.94
Other hallucinogen	F16.14	F16.24	F16.94
Inhalant	F18.14	F18.24	F18.94
Opioid	F11.14	F11.24	F11.94
Sedative, hypnotic, or anxiolytic	F13.14	F13.24	F13.94
Amphetamine-type substance (or other stimulant)	F15.14	F15.24	F15.94
Cocaine	F14.14	F14.24	F14.94
Other (or unknown) substance	F19.14	F19.24	F19.94

Specify (see Table 1 in the chapter "Substance-Related and Addictive Disorders," which indicates whether "with onset during intoxication" and/or "with onset during withdrawal" applies to a given substance class; or *specify* "with onset after medication use"):

With onset during intoxication: If criteria are met for intoxication with the substance and the symptoms develop during intoxication.

With onset during withdrawal: If criteria are met for withdrawal from the substance and the symptoms develop during, or shortly after, withdrawal.

With onset after medication use: If symptoms developed at initiation of medication, with a change in use of medication, or during withdrawal of

medication.

Recording Procedures

The name of the substance/medication-induced depressive disorder begins with the specific substance (e.g., cocaine, dexamethasone) that is presumed to be causing the depressive symptoms. The diagnostic code is selected from the table included in the criteria set, which is based on the drug class and presence or absence of a comorbid substance use disorder. For substances that do not fit into any of the classes (e.g., dexamethasone), the code for "other (or unknown) substance" should be used; and in cases in which a substance is judged to be an etiological factor but the specific class of substance is unknown, the same code should also be used.

When recording the name of the disorder, the comorbid substance use disorder (if any) is listed first, followed by the word "with," followed by the name of the substance-induced depressive disorder, followed by the specification of onset (i.e., onset during intoxication, onset during withdrawal). For example, in the case of depressive symptoms occurring during withdrawal in a man with a severe cocaine use disorder, the diagnosis is F14.24 severe cocaine use disorder with cocaine-induced depressive disorder, with onset during withdrawal. A separate diagnosis of the comorbid severe cocaine use disorder is not given. If the substance-induced depressive disorder occurs without a comorbid substance use disorder (e.g., after a one-time heavy use of the substance), no accompanying substance use disorder is noted (e.g., F16.94 phencyclidine-induced depressive disorder, with onset during intoxication). When more than one substance is judged to play a significant role in the development of depressive

mood symptoms, each should be listed separately (e.g., F15.24 severe methylphenidate use disorder with methylphenidate-induced depressive disorder, with onset during withdrawal; F19.94 dexamethasone-induced depressive disorder, with onset during intoxication).

Diagnostic Features

The essential feature of substance/medication-induced depressive disorder is a prominent and persistent disturbance in mood that predominates in the clinical picture and is characterized by depressed mood or markedly diminished interest or pleasure in all, or almost all, activities (Criterion A) that is due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or a toxin exposure) (Criterion B). In order to meet criteria for the diagnosis, the depressive symptoms must have developed during or soon after substance intoxication or withdrawal or after exposure to or withdrawal from a medication, as evidenced by clinical history, physical examination, or laboratory findings (Criterion B1), and the involved substance/medication must be capable of producing the depressive symptoms (Criterion B2). In addition, the depressed symptoms are not better explained by a non-substance/medication-induced depressive disorder.

Evidence of an independent depressive disorder includes the observation that the depressive symptoms preceded the onset of substance/medication use, the depressive symptoms persist beyond a substantial period of time after the cessation of acute withdrawal or severe intoxication,

or there is other evidence that suggests the existence of an independent non-substance/medication-induced depressive disorder (Criterion C), such as a history of recurrent non-substance-induced depressive episodes. This diagnosis should not be made when symptoms occur exclusively during the course of a delirium (Criterion D). Finally, the diagnosis requires that the substance/medication-induced depressive symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion E). The substance-induced depressive disorder diagnosis should be made instead of a diagnosis of substance intoxication or substance withdrawal only when the symptoms in Criterion A predominate in the clinical picture and are sufficiently severe to warrant independent clinical attention.

The two categories of drugs of abuse most likely to cause a substance/medication-induced depressive disorder are depressants (e.g., intoxication with alcohol, benzodiazepines and other sedative, hypnotic, or anxiolytic drugs) and stimulants (e.g., withdrawal from amphetamine-type substances and cocaine). Some medications (e.g., steroids; antihypertensive medications such as clonidine, guanethidine, methyldopoa, and reserpine; interferon; L-dopa) are especially likely to cause substance/medication-induced depressive syndromes. Substances implicated in medication-induced depressive disorder, with varying degrees of evidence, include antibiotics, antiviral agents (efavirenz), cardiovascular agents (beta-blockers and calcium channel blockers, retinoic acid derivatives (isotretinoin), antidepressants, anticonvulsants, antimigraine agents (triptans), antipsychotics, hormonal agents (corticosteroids, oral contraceptives, gonadotropin-releasing hormone agonists, tamoxifen), chemotherapeutic drugs, and smoking cessation agents (varenicline). This list is likely to grow as new compounds are synthesized.

Clear clinical histories and careful judgment are essential in determining whether the substance of abuse or medication is truly associated with induced depressive symptoms or whether the symptoms are better understood as constituting an independent depressive disorder. A diagnosis of a substance/medication-induced depressive disorder is most likely if the individual was taking high doses of a relevant drug of abuse or medication and there is no past history of independent depressive episodes. For example, a depressive episode that developed in the context of heavy use of a relevant substance of abuse or within the first several weeks of beginning alpha-methyldopa (an antihypertensive agent) in an individual with no history of major depressive disorder would qualify for the diagnosis of a substance- or medication-induced depressive disorder. In some cases, a previously established condition (e.g., major depressive disorder, recurrent) can recur while the individual is

coincidentally taking a drug or medication that has the capacity to cause depressive symptoms (e.g., alcohol and/or stimulants in context of heavy use, L-dopa, oral contraceptives). In all of these cases, the clinician must make a judgment as to whether the medication is causative in this particular situation.

A substance/medication-induced depressive disorder is distinguished from an independent depressive disorder by the onset or course, or by other factors associated with the substance or medication use. There must be evidence from the history, physical examination, or laboratory findings of use of a drug of abuse or a medication that is capable of producing depressive symptoms after exposure to, withdrawal from, or intoxication with that substance prior to the

onset of the depressive disorder. The neurochemical changes associated with intoxication and withdrawal states for some substances can be relatively protracted, and thus intense depressive symptoms can last for a longer period after the cessation of substance use and still be consistent with a diagnosis of a substance/medication-induced depressive disorder.

Prevalence

The lifetime rate of alcohol- and stimulant-induced depressive episodes has been reported to be 40% or higher among individuals with relevant substance use disorders. However, in a nationally representative U.S. adult population, the lifetime prevalence of substance/medication-induced depressive disorder in the absence of a lifetime history of non-substance-induced depressive disorder was only 0.26%. These data indicate that special care must be taken to search for and address substance-induced conditions in individuals with alcohol and stimulant use disorders.

Development and Course

A depressive disorder associated with the use of substances (e.g., alcohol, amphetamine-type substances and/or cocaine, or a prescribed treatment for medical conditions) must have its onset while the individual is using the substance or during withdrawal, if there is a withdrawal syndrome associated with the substance. Most often, the depressive disorder has its onset within the first few weeks or 1 month of heavy use of the substance. Once the substance is discontinued, the depressive symptoms usually remit within days to several weeks, depending on the half-life of the substance/medication and the presence of a withdrawal syndrome. If symptoms persist 4 weeks beyond the expected time course of withdrawal of a particular substance/medication, other causes for the depressive mood symptoms should be considered.

There are several prospective controlled trials examining the association of depressive symptoms with use of a prescribed medication, but most reports on this topic involve retrospective series of individuals entering treatment, or participants in large cross-sectional studies. More studies exist regarding the clinical course of alcohol- and illicit drug–induced depressions, and most support the contention that the substance-induced conditions are very likely to fade away within a relatively short time after abstinence. Equally important are indications that individuals with significant residual depressive symptoms following treatment for substance use disorders have a greater likelihood of relapse into their substance use.

Risk and Prognostic Factors

Risk factors for substance-induced depressive disorder include a history of antisocial personality disorder, schizophrenia, and bipolar disorder; a history of stressful life events in the past 12 months; a history of prior drug-induced depressions; and a family history of substance use disorders. In addition, neurochemical changes associated with alcohol and other drugs of abuse often contribute to depressive and anxiety symptoms during withdrawal that subsequently influence ongoing substance use and reduce the likelihood of remission of substance use disorders. The course of substance-induced depressive disorder may be worsened by social-structural adversity associated with poverty, racism, and marginalization.

Sex- and Gender-Related Diagnostic Issues

Among individuals with a substance use disorder, the risk for developing a substance-induced depressive disorder appears to be similar in men and women.

Diagnostic Markers

Laboratory assays of the suspected substance in the blood or urine are of limited value in identifying substance-induced depressive disorder because blood and urine levels are often negative when an individual comes for evaluation, reflecting the fact that substance-induced depressions can last for up to 4 weeks after use of the drug of abuse or medication has ceased. Therefore, a positive test value only means that an individual has had recent experience with a substance but by itself does not establish a time course or other characteristics that are likely to be associated with substance-induced depressive disorder. However, as is true of most mental disorders, the most important data in diagnosing these conditions come from a detailed clinical history and the mental status examination.

Association With Suicidal Thoughts or Behavior

The risk of suicide attempts is higher among individuals with possible alcohol use disorder experiencing depressive episodes, whether substance induced or independent of substances, as compared with control subjects.

Differential Diagnosis

Substance intoxication and withdrawal. Depressive symptoms occur commonly in substance intoxication and substance withdrawal. A diagnosis of substance-induced depressive disorder should be made instead of a diagnosis of substance intoxication or substance withdrawal when the mood symptoms are sufficiently severe to warrant independent clinical attention. For example, dysphoric mood is a characteristic feature of cocaine withdrawal. Substance-induced depressive disorder with onset during withdrawal should be diagnosed instead of cocaine withdrawal only if the mood disturbance in Criterion A predominates in the clinical picture and is sufficiently severe to be a separate focus of attention and treatment.

Independent depressive disorder. A substance/medication-induced depressive disorder is distinguished from an independent depressive disorder by the fact that even though a substance is taken in high enough amounts to be possibly etiologically related to the symptoms, if the depressive syndrome is observed at times other than when the substance or medication is being used, it should be diagnosed as an independent depressive disorder.

Depressive disorder due to another medical condition. Because individuals with medical conditions often take medications for those conditions, the clinician must consider the possibility that the mood symptoms are caused by the physiological consequences of the medical condition rather than the medication, in which case depressive disorder due to another medical condition is diagnosed. The history often provides the primary basis for such a judgment. At times, a change in the treatment for the medical condition (e.g., medication substitution or discontinuation) may be needed to determine empirically whether the medication is the causative agent. If the clinician has ascertained that the disturbance is a function of both another medical condition and substance use or withdrawal, then both diagnoses (i.e., depressive disorder due to another medical

condition and substance/medication-induced depressive disorder) may be given. When there is insufficient evidence to determine whether the depressive symptoms are associated with substance (including a medication) ingestion or withdrawal or with another medical condition or are independent (i.e., not a function of either a substance or another medical condition), a diagnosis of other specified depressive disorder or unspecified depressive disorder is indicated.

Comorbidity

In one study using DSM-IV, comparing individuals with independent major depressive disorder and no comorbid substance use disorder and individuals with substance/medication-induced depressive disorder, those with substance/medication-induced depressive disorder had higher rates of comorbidity with any DSM-IV mental disorder; were more likely to have specific disorders of tobacco use disorder, gambling disorder, and antisocial personality disorder; and were less likely to have persistent depressive disorder. Compared with individuals with major depressive disorder and a comorbid substance use disorder, individuals with substance/medication-induced depressive disorder are more likely to have alcohol or other substance use disorder; however, they are less likely to have persistent depressive disorder.

Depressive Disorder Due to Another Medical Condition

Diagnostic Criteria

A. A prominent and persistent disturbance in mood that predominates in the clinical picture and is characterized by depressed mood or markedly diminished interest or pleasure in all, or almost all, activities.

B. There is evidence from the history, physical examination, or laboratory findings that the disturbance is the direct pathophysiological consequence of another medical condition.

C. The disturbance is not better explained by another mental disorder (e.g., adjustment disorder, with depressed mood, in which the stressor is a serious medical condition).

D. The disturbance does not occur exclusively during the course of a delirium.

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Coding note: The ICD-10-CM code depends on the specifier (see below).

Specify if:

F06.31 With depressive features: Full criteria are not met for a major depressive episode.

F06.32 With major depressive–like episode: Full criteria are met (except Criterion C) for a major depressive episode.

F06.34 With mixed features: Symptoms of mania or hypomania are also present but do not predominate in the clinical picture.

Coding note: Include the name of the other medical condition in the name of the mental disorder (e.g., F06.31 depressive disorder due to hypothyroidism, with depressive features). The other medical condition should also be coded and listed separately immediately before the depressive disorder due to the medical condition (e.g., E03.9 hypothyroidism; F06.31 depressive disorder due to hypothyroidism, with depressive features).

Diagnostic Features

The essential feature of depressive disorder due to another medical condition is a prominent and persistent period of depressed mood or markedly diminished interest or pleasure in all, or almost all, activities that predominates in the clinical picture (Criterion A) and that is thought to be due to the physiological effects of another medical condition (Criterion B). In determining whether the mood disturbance is due to another medical condition, the clinician must first establish the presence of another medical condition. Further, the clinician must establish that the mood disturbance is etiologically related to another medical condition through a physiological

mechanism. A careful and comprehensive assessment of multiple factors is necessary to make this judgment. Although there are no infallible guidelines for determining whether the relationship between the mood disturbance and another medical condition is etiological, several considerations provide some guidance in this area. One consideration is the presence of a temporal association between the onset, exacerbation, or remission of another medical condition and that of the mood disturbance. A second consideration is the presence of features that are atypical of independent depressive disorders (e.g., atypical age at onset or course or absence of family history). Evidence from the literature that suggests that there can be a direct association between another medical condition in question and the development of mood symptoms can provide a useful context in the assessment of a particular situation.

Associated Features

Etiology (i.e., a causal relationship to another medical condition based on best clinical evidence) is the key variable in depressive disorder due to another medical condition. The listing of the medical conditions that are said to be able to induce major depression is never complete, and the clinician's best judgment is the essence of this diagnosis.

There are clear associations, as well as some neuroanatomical correlates, of depression with cerebrovascular accident (CVA), Huntington's disease, Parkinson's disease, and traumatic brain injury (TBI). Among the neuroendocrine conditions most closely associated with depression are Cushing's syndrome and hypothyroidism. Autoimmune disorders, such systemic lupus erythematosus, and deficiencies of certain vitamins, such as vitamin B_{12}, have also been linked to depression. There are numerous other conditions thought to be associated with depression, such as multiple sclerosis. However, the literature's support for a causal association is greater

with some conditions than with others. Currently, there is support for a direct pathophysiological mechanism for depressive symptoms in focal lesions (CVA, TBI, neoplasm) affecting certain brain regions, Parkinson's disease, Huntington's disease, hypothyroidism, Cushing's syndrome, and pancreatic cancer.

Prevalence

Sex differences in prevalence depend somewhat on the sex difference associated with the medical condition (e.g., systemic lupus erythematosus is more common in women; stroke is somewhat more common in middle-age men compared with women).

Development and Course

Following stroke, the onset of depression appears to be acute, occurring within a few days of the CVA in the largest case series. However, in some cases, onset of the depression is weeks to months following the CVA. In the largest series, the duration of the major depressive episode following stroke was 9–11 months on average. With Parkinson's disease and Huntington's disease, depression often precedes the major motor impairments and cognitive impairments associated with each condition. This is more prominently the case for Huntington's disease, in which depression is considered to be the first neuropsychiatric symptom. There is some observational evidence that depression is less common as the neurocognitive disorder due to Huntington's disease progresses. In some individuals with static brain injuries and other central nervous system diseases, mood symptoms may be episodic (i.e., recurring) over the course of the disorder. In Cushing's syndrome and hypothyroidism, depression can be an early manifestation of the disease. In pancreatic cancer, depression often precedes other features.

Risk and Prognostic Factors

The risk of acute onset of a major depressive disorder following a CVA (within 1 day to a week of the event) appears to be strongly correlated with lesion location, with greatest risk associated with left frontal strokes and least risk apparently associated with right frontal lesions

in those individuals who present within days of the stroke. The association with frontal regions and laterality is not observed in depressive states that occur in the 2–6 months following stroke, perhaps indicative of later depressive symptoms representing major depressive disorder, adjustment disorder, or demoralization. In individuals with Parkinson's disease, early age at onset, greater burden of motor symptoms, and longer duration of the disease have been associated with depression. Risk of depression after TBI has been associated with female gender, prior depressive disorder, early psychiatric symptoms following injury, lower brain volume, and unemployment.

Sex- and Gender-Related Diagnostic Issues

Women may be at differentially higher risk for developing depression in the setting of cardiovascular disease, particularly poststroke.

Diagnostic Markers

Diagnostic markers pertain to those associated with the medical condition (e.g., steroid levels in blood or urine to help corroborate the diagnosis of Cushing's disease, which can be associated with manic or depressive syndromes).

Association With Suicidal Thoughts or Behavior

There are no epidemiological studies that provide evidence to differentiate the risk of suicide from a major depressive episode due to another medical condition compared with the risk from a major depressive episode in general. There are case reports of suicides in association with major depressive episodes associated with another medical condition. There is a clear association between serious medical illnesses and suicide, particularly shortly after onset or diagnosis of the illness. Thus, it would be prudent to assume that the risk of suicide for major depressive episodes associated with medical conditions is not less than that for other forms of major depressive episode, and might even be greater.

Differential Diagnosis

Depressive disorders not due to another medical condition. Determination of whether a medical condition accompanying a depressive disorder is causing the disorder depends on a) the absence of an episode(s) of depressive episodes prior to the onset of the medical condition, b) the probability that the associated medical condition has a potential to promote or cause a depressive disorder, and c) a course of the depressive symptoms shortly after the onset or worsening of the medical condition, especially if the depressive symptoms remit near the time that the medical disorder is effectively treated or remits.

Medication-induced depressive disorder. An important caveat is that some medical conditions are treated with medications (e.g., steroids or alpha-interferon) that can induce depressive or manic symptoms. In these cases, clinical judgment, based on all the evidence in hand, is the best way to try to separate the most likely and/or the most important of two etiological factors (i.e., association with the medical condition vs. a substance-induced syndrome).

Delirium and major or mild neurocognitive disorder. A separate diagnosis of depressive disorder due to another medical condition is not given if the depressive disturbance occurs exclusively during the course of a delirium. However, a diagnosis of depressive disorder due to another medical condition may be given in addition to a diagnosis of major or mild neurocognitive disorder if the depressive disturbance is judged to be a physiological consequence of the pathological process causing the neurocognitive disorder and if symptoms of depression are a prominent part of the clinical presentation.

Adjustment disorders. It is important to differentiate a depressive episode from an adjustment disorder, as the onset of the medical condition is in itself a life stressor that could

bring on either an adjustment disorder or an episode of major depression. The major differentiating elements are the pervasiveness of the depressive picture and the number and quality of the depressive symptoms that the individual reports or demonstrates on the mental

status examination. The differential diagnosis of the associated medical conditions is relevant but largely beyond the scope of the present manual.

Demoralization. Demoralization is a common reaction to chronic medical illness. It is marked by a sense of subjective incompetence, helplessness, and hopelessness, and a desire to give up. It is often accompanied by depressive symptoms such as low mood and fatigue. Demoralization typically lacks the anhedonia associated with depressive disorder due to another medical condition, and individuals will generally find pleasure in previously meaningful activities and be able to experience moments of happiness.

Comorbidity

Conditions comorbid with depressive disorder due to another medical condition are those associated with the medical conditions of etiological relevance. It has been noted that delirium can occur before or along with depressive symptoms in individuals with a variety of medical conditions, such as Cushing's disease. The association of anxiety symptoms, usually generalized symptoms, is common in depressive disorders, regardless of cause.

Other Specified Depressive Disorder

F32.89

This category applies to presentations in which symptoms characteristic of a depressive disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for any of the disorders in the depressive disorders diagnostic class and do not meet criteria for adjustment disorder with depressed mood or adjustment disorder with mixed anxiety and depressed mood. The other specified depressive disorder category is used in situations in which the clinician chooses to communicate the specific reason that the presentation does not meet the criteria for any specific depressive disorder. This is done by recording "other specified depressive disorder" followed by the specific reason (e.g., "short-duration depressive episode").

Examples of presentations that can be specified using the "other specified" designation include the following:

1. **Recurrent brief depression:** Concurrent presence of depressed mood and at least four other symptoms of depression for 2–13 days at least once per month (not associated with the menstrual cycle) for at least 12 consecutive months in an individual whose presentation has never met criteria for any other depressive or bipolar disorder and does not currently meet active or residual criteria for any psychotic disorder.
2. **Short-duration depressive episode (4–13 days):** Depressed affect and at least four of the other eight symptoms of a major depressive episode associated with clinically significant distress or impairment that persists for more than 4 days, but less than 14 days, in an individual whose presentation has never met criteria for any other depressive or bipolar disorder, does not currently meet active or

residual criteria for any psychotic disorder, and does not meet criteria for recurrent brief depression.

3. **Depressive episode with insufficient symptoms:** Depressed affect and at least one of the other eight symptoms of a major depressive episode associated with clinically significant distress or impairment that persist for at least 2 weeks in an individual whose presentation has never met criteria for any other depressive or bipolar disorder, does not currently meet active or residual criteria for any psychotic disorder, and does not meet criteria for mixed anxiety and depressive disorder symptoms.

4. **Major depressive episode superimposed** on schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorder. **Note:** Major depressive episodes that are part of schizoaffective disorder do not merit an additional diagnosis of other specified depressive disorder.

Unspecified Depressive Disorder

F32.A

This category applies to presentations in which symptoms characteristic of a depressive disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for any of the disorders in the depressive disorders diagnostic class and do not meet criteria for adjustment disorder with depressed mood or adjustment disorder with mixed anxiety and depressed mood. The unspecified depressive disorder category is used in situations in which the clinician chooses *not* to specify the reason that the criteria are not met for a specific depressive disorder, and includes presentations for which there is insufficient information to make a more specific diagnosis (e.g., in emergency room settings).

Unspecified Mood Disorder

F39

This category applies to presentations in which symptoms characteristic of a mood disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not at the time of the evaluation meet the full criteria for any of the disorders in either the bipolar or the depressive disorders diagnostic classes and in which it is difficult to

choose between unspecified bipolar and related disorder and unspecified depressive disorder (e.g., acute agitation).

Specifiers for Depressive Disorders

Specify if:

With anxious distress: Anxious distress is defined as the presence of at least two of the following symptoms during the majority of days of the current major depressive episode (or the most recent major depressive episode if major depressive disorder is currently in partial or full remission) or current persistent depressive disorder:

1. Feeling keyed up or tense.
2. Feeling unusually restless.
3. Difficulty concentrating because of worry.
4. Fear that something awful may happen.
5. Feeling that the individual might lose control of himself or herself.

Specify current severity:

Mild: Two symptoms.

Moderate: Three symptoms.

Moderate-severe: Four or five symptoms.

Severe: Four or five symptoms and with motor agitation.

Note: Anxious distress has been noted as a prominent feature of both bipolar and major depressive disorder in both primary care and specialty mental health

settings. High levels of anxiety have been associated with higher suicide risk, longer duration of illness, and greater likelihood of treatment nonresponse. As a result, it is clinically useful to specify accurately the presence and severity levels of anxious distress for treatment planning and monitoring of response to treatment.

With mixed features:

A. At least three of the following manic/hypomanic symptoms are present during the majority of days of the current major depressive episode (or the most recent major depressive episode if major depressive disorder is currently in partial or full remission):

   1. Elevated, expansive mood.
   2. Inflated self-esteem or grandiosity.
   3. More talkative than usual or pressure to keep talking.

4. Flight of ideas or subjective experience that thoughts are racing.
5. Increase in energy or goal-directed activity (either socially, at work or school, or sexually).
6. Increased or excessive involvement in activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).
7. Decreased need for sleep (feeling rested despite sleeping less than usual; to be contrasted with insomnia).

B. Mixed symptoms are observable by others and represent a change from the person's usual behavior.

C. For individuals whose symptoms meet full criteria for either mania or hypomania, the diagnosis should be bipolar I or bipolar II disorder.

D. The mixed symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication or other treatment).

Note: Mixed features associated with a major depressive episode have been found to be a significant risk factor for the development of bipolar I or bipolar II disorder. As a result, it is clinically useful to note the presence of this specifier for treatment planning and monitoring of response to treatment.

With melancholic features:

A. One of the following is present during the most severe period of the current major depressive episode (or the most recent major depressive episode if major depressive disorder is currently in partial or full remission):
   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. A distinct quality of depressed mood characterized by profound despondency, despair, and/or moroseness or by so-called empty mood.
   2. Depression that is regularly worse in the morning.
   3. Early-morning awakening (i.e., at least 2 hours before usual awakening).
   4. Marked psychomotor agitation or retardation.
   5. Significant anorexia or weight loss.
   6. Excessive or inappropriate guilt.

Note: The specifier "with melancholic features" is applied if these features are present at the most severe stage of the episode. There is a near-complete absence of the

capacity for pleasure, not merely a diminution. A guideline for evaluating the lack

of reactivity of mood is that even highly desired events are not associated with marked brightening of mood. Either mood does not brighten at all, or it brightens only partially (e.g., up to 20%–40% of normal for only minutes at a time). The "distinct quality" of mood that is characteristic of the "with melancholic features" specifier is experienced as qualitatively different from that during a nonmelancholic depressive episode. A depressed mood that is described as merely more severe, longer lasting, or present without a reason is not considered distinct in quality. Psychomotor changes are nearly always present and are observable by others.

Melancholic features exhibit only a modest tendency to repeat across episodes in the same individual. They are more frequent in inpatients, as opposed to outpatients; are less likely to occur in milder than in more severe major depressive episodes; and are more likely to occur in individuals with psychotic features.

With atypical features: This specifier is applied when these features predominate during the majority of days of the current major depressive episode (or the most recent major depressive episode if major depressive disorder is currently in partial or full remission) or current persistent depressive disorder.

A. Mood reactivity (i.e., mood brightens in response to actual or potential positive events).

B. Two (or more) of the following:

   1. Significant weight gain or increase in appetite.
   2. Hypersomnia.
   3. Leaden paralysis (i.e., heavy, leaden feelings in arms or legs).
   4. A long-standing pattern of interpersonal rejection sensitivity (not limited to episodes of mood disturbance) that results in significant social or occupational impairment.

C. Criteria are not met for "with melancholic features" or "with catatonia" during the same episode.

Note: "Atypical depression" has historical significance (i.e., atypical in contradistinction to the more classical agitated, "endogenous" presentations of depression that were the norm when depression was rarely diagnosed in outpatients and almost never in adolescents or younger adults) and today does not connote an uncommon or unusual clinical presentation as the term might imply.

Mood reactivity is the capacity to be cheered up when presented with positive events (e.g., a visit from children, compliments from others). Mood may become euthymic (not sad) even for extended periods of time if the external circumstances remain favorable. Increased appetite may be manifested by an obvious increase in food intake or by weight gain. Hypersomnia may include either an extended period of nighttime sleep or daytime napping that totals at least 10 hours of sleep per day (or at least 2 hours more than when not

depressed). Leaden paralysis is defined as feeling heavy, leaden, or weighted down, usually in the arms or legs. This sensation is generally present for at least an hour a day but often lasts for many hours at a time. Unlike the other atypical features, pathological sensitivity to perceived interpersonal rejection is a trait that has an early onset and persists throughout most of adult life. Rejection sensitivity occurs when the person is and is not depressed, though it may be exacerbated during depressive periods.

With psychotic features: Delusions and/or hallucinations are present at any time in the current major depressive episode (or the most recent major depressive episode if major depressive disorder is currently in partial or full remission). If psychotic features are present, *specify* if mood-congruent or mood-incongruent:

With mood-congruent psychotic features: The content of all delusions and hallucinations is consistent with the typical depressive themes of personal inadequacy, guilt, disease, death, nihilism, or deserved punishment.

With mood-incongruent psychotic features: The content of the delusions or hallucinations does not involve typical depressive themes of personal inadequacy, guilt, disease, death, nihilism, or deserved punishment, or the content is a mixture of mood-incongruent and mood-congruent themes.

With catatonia: This specifier is applied to the current major depressive episode (or the most recent major depressive episode if major depressive disorder is currently in partial or full remission) if catatonic features are present during most of the episode. See criteria for catatonia associated with a mental disorder in the chapter “Schizophrenia Spectrum and Other Psychotic Disorders.”

With peripartum onset: This specifier is applied to the current major depressive episode (or the most recent major depressive episode if major depressive disorder is currently in partial or full remission) if onset of mood symptoms occurs during pregnancy or in the 4 weeks following delivery.

Note: Mood episodes can have their onset either during pregnancy or postpartum. About 50% of postpartum major depressive episodes begin prior to delivery. Thus, these episodes are referred to collectively as *peripartum* episodes.

Between conception and birth, about 9% of women will experience a major depressive episode. The best estimate for prevalence of a major depressive episode between birth and 12 months postpartum is just below 7%.

Peripartum-onset mood episodes can present either with or without psychotic features. Infanticide (a rare occurrence) is most often associated with postpartum psychotic episodes that are characterized by command hallucinations to kill the infant or delusions that the infant is possessed, but psychotic symptoms can also occur in severe postpartum mood episodes

without such specific delusions or hallucinations.

Postpartum mood (major depressive or manic) episodes with psychotic features appear to occur in from 1 in 500 to 1 in 1,000 deliveries and may be more common in primiparous women. The risk of postpartum episodes with psychotic features is particularly increased for women with prior postpartum psychotic mood episodes but is also elevated for those with a prior history of a depressive or bipolar disorder (especially bipolar I disorder) and those with a family history of bipolar disorders.

Once a woman has had a postpartum episode with psychotic features, the risk of recurrence with each subsequent delivery is between 30% and 50%. Postpartum episodes must be differentiated from delirium occurring in the postpartum period, which is distinguished by a fluctuating level of awareness or attention.

Peripartum-onset depressive disorders must be distinguished from the much more common “maternity blues,” or what is known in lay terms as “baby blues.” Maternity blues is not considered to be a mental disorder and is characterized by sudden changes in mood (e.g., the sudden onset of tearfulness in the absence of depression) that do not cause functional impairment and that are likely caused by physiological changes occurring after delivery. It is temporary and self-limited, typically improving quickly (within a week) without the need for treatment. Other symptoms of maternity blues include sleep disturbance and even confusion that can occur shortly after delivery.

Perinatal women may be at higher risk for depressive disorders due to thyroid abnormalities as well as other medical conditions that can cause depressive symptoms. If the depressive symptoms are judged to be due to another medical condition related to the perinatal period, depressive disorder due to another medical condition should be diagnosed instead of a major depressive episode, with peripartum onset.

With seasonal pattern: This specifier applies to recurrent major depressive disorder.

A. There has been a regular temporal relationship between the onset of major depressive episodes in major depressive disorder and a particular time of the year (e.g., in the fall or winter).

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

B. Full remissions 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 above and no nonseasonal major depressive episodes have occurred during that same period.

D. Seasonal major depressive episodes (as described above) substantially outnumber the nonseasonal major depressive episodes that may have occurred over the individual's lifetime.

Note: The specifier "with seasonal pattern" can apply to the pattern of major depressive episodes in major depressive disorder, recurrent. The essential feature is the onset and remission of major depressive episodes at characteristic times of the year. In most cases, the episodes begin in fall or winter and remit in spring. Less commonly, there may be recurrent summer depressive episodes. This pattern of onset and remission of episodes must have occurred during at least a 2-year period, without any nonseasonal episodes occurring during this period. In addition, the seasonal depressive episodes must substantially outnumber any nonseasonal depressive episodes over the individual's lifetime.

This specifier does not apply to those situations in which the pattern is better explained by seasonally linked psychosocial stressors (e.g., seasonal unemployment or school schedule). Major depressive episodes that occur in a seasonal pattern are often characterized by loss of energy, hypersomnia, overeating, weight gain, and a craving for carbohydrates.

The prevalence of winter-type seasonal pattern appears to vary with latitude, age, and sex. Prevalence increases with higher latitudes. Age is also a strong predictor of seasonality, with younger persons at higher risk for winter depressive episodes.

Specify if:

In partial remission: Symptoms of the immediately previous major depressive episode are present but full criteria are not met, or there is a period lasting less than 2 months without any significant symptoms of a major depressive episode following the end of such an episode.

In full remission: During the past 2 months, no significant signs or symptoms of the disturbance were present.

Specify current severity:

Severity is based on the number of criterion symptoms, the severity of those symptoms, and the degree of functional disability.

Mild: Few, if any, symptoms in excess of those required to make the diagnosis are present, the intensity of the symptoms is distressing but manageable, and the symptoms result in minor impairment in social or occupational functioning.

Moderate: The number of symptoms, intensity of symptoms, and/or functional impairment are between those specified for "mild" and "severe."

Severe: The number of symptoms is substantially in excess of that required to make the diagnosis, the intensity of the symptoms is seriously distressing and unmanageable, and the symptoms markedly interfere with social and

occupational functioning.

[1]In distinguishing grief from a major depressive episode (MDE), it is useful to consider that in grief the predominant affect is feelings of emptiness and loss, while in an MDE it is persistent depressed mood and the inability to anticipate happiness or pleasure. The dysphoria in grief is likely to decrease in intensity over days to weeks and occurs in waves, the so-called pangs of grief. These waves tend to be associated with thoughts or reminders of the deceased. The depressed mood of an MDE is more persistent and not tied to specific thoughts or preoccupations. The pain of grief may be accompanied by positive emotions and humor that are uncharacteristic of the pervasive unhappiness and misery characteristic of an MDE. The thought content associated with grief generally features a preoccupation with thoughts and memories of the deceased, rather than the self-critical or pessimistic ruminations seen in an MDE. In grief, self-esteem is generally preserved, whereas in an MDE feelings of worthlessness and self-loathing are common. If self-derogatory ideation is present in grief, it typically involves perceived failings vis-à-vis the deceased (e.g., not visiting frequently enough, not telling the deceased how much he or she was loved). If a bereaved individual thinks about death and dying, such thoughts are generally focused on the deceased and possibly about "joining" the deceased, whereas in an MDE such thoughts are focused on ending one's own life because of feeling worthless, undeserving of life, or unable to cope with the pain of depression.