dysphoria during childhood. Expressions of anatomic dysphoria are more common and salient in adolescents and adults once secondary sex characteristics have developed.

Adolescent and adult natal males with early-onset gender dysphoria are almost always sexually attracted to men (androphilic). Adolescents and adults with late-onset gender dysphoria frequently engage in transvestic behavior with sexual excitement. The majority of these individuals are gynephilic or sexually attracted to other posttransition natal males with late-onset gender dysphoria. A substantial percentage of adult males with late-onset gender dysphoria cohabit with or are married to natal females. After gender transition, many self-identify as lesbian. Among adult natal males with gender dysphoria, the early-onset group seeks out clinical care for hormone treatment and reassignment surgery at an earlier age than does the late-onset group. The late-onset group may have more fluctuations in the degree of gender dysphoria and be more ambivalent about and less likely satisfied after gender reassignment surgery.

In both adolescent and adult natal females, the most common course is the early-onset form of gender dysphoria. The late-onset form is much less common in natal females compared with natal males. As in natal males with gender dysphoria, there may have been a period in which the gender dysphoria desisted and these individuals self-identified as lesbian; however, with recurrence of gender dysphoria, clinical consultation is sought, often with the desire for hormone treatment and reassignment surgery. Parents of natal adolescent females with the late-onset form also report surprise, as no signs of childhood gender dysphoria were evident. Expressions of anatomic dysphoria are much more common and salient in adolescents and adults than in children.

Adolescent and adult natal females with early-onset gender dysphoria are almost always gynephilic. Adolescents and adults with the late-onset form of gender dysphoria are usually androphilic and after gender transition self-identify as gay men. Natal females with the late-onset form do not have co-occurring transvestic behavior with sexual excitement.

Gender dysphoria in association with a disorder of sex development. Most individuals with a disorder of sex development who develop gender dysphoria have already come to medical attention at an early age. For many, starting at birth, issues of gender assignment were raised by physicians and parents. Moreover, as infertility is quite common for this group, physicians are more willing to perform cross-sex hormone treatments and genital surgery before adulthood.

Disorders of sex development in general are frequently associated with gender-atypical behavior starting in early childhood. However, in the majority of cases, this does not lead to gender dysphoria. As individuals with a disorder of sex development become aware of their medical history and condition, many experience uncertainty about their gender, as opposed to developing a firm conviction that they are another gender. However, most do not progress to gender transition. Gender dysphoria and gender transition may vary considerably as a function of a disorder of sex development, its severity, and assigned gender.

Risk and Prognostic Factors

Temperamental. For individuals with gender dysphoria without a disorder of sex development, atypical gender behavior among individuals with early-onset gender dysphoria develops in early preschool age, and it is possible that a high degree of atypicality makes the development of gender dysphoria and its persistence into adolescence and adulthood more likely.

Environmental. Among individuals with gender dysphoria without a disorder of sex development, males with gender dysphoria (in both childhood and adolescence) more commonly have older brothers than do males without the condition. Additional predisposing

factors under consideration, especially in individuals with late-onset gender dysphoria (adolescence, adulthood), include habitual fetishistic transvestism developing into autogynephilia (i.e., sexual arousal associated with the thought or image of oneself as a woman) and other forms of more general social, psychological, or developmental problems.

Genetic and physiological. For individuals with gender dysphoria without a disorder of sex development, some genetic contribution is suggested by evidence for (weak) familiality of transsexualism among nontwin siblings, increased concordance for transsexualism in monozygotic compared with dizygotic same-sex twins, and some degree of heritability of gender dysphoria. As to endocrine findings, no endogenous systemic abnormalities in sex-hormone levels have been found in 46,XY individuals, whereas there appear to be increased androgen levels (in the range found in hirsute women but far below normal male levels) in 46,XX individuals. Overall, current evidence is insufficient to label gender dysphoria without a disorder of sex development as a form of intersexuality limited to the central nervous system.

In gender dysphoria associated with a disorder of sex development, the likelihood of later gender dysphoria is increased if prenatal production and utilization (via receptor sensitivity) of androgens are grossly atypical relative to what is usually seen in individuals with the same assigned gender. Examples include 46,XY individuals with a history of normal male prenatal hormone milieu but inborn nonhormonal genital defects (as in cloacal bladder exstrophy or penile agenesis) and who have been assigned to the female gender. The likelihood of gender dysphoria is further enhanced by additional, prolonged, highly gender-atypical postnatal androgen exposure with somatic virilization as may occur in female-raised and noncastrated 46,XY individuals with 5-alpha reductase-2 deficiency or 17-beta-hydroxysteroid dehydrogenase-3 deficiency or in female-raised 46,XX individuals with classical congenital adrenal hyperplasia with prolonged periods of non-adherence to glucocorticoid replacement therapy. However, the prenatal androgen milieu is more closely related to gendered behavior than to gender identity. Many individuals with disorders of sex development and markedly gender-atypical behavior do not develop gender dysphoria. Thus, gender-atypical behavior by itself should not be interpreted as an indicator of current or future gender dysphoria. There appears to be a higher rate of gender dysphoria and patient-initiated gender change from assigned female to male than from assigned male to female in 46,XY individuals with a disorder of sex development.

Culture-Related Diagnostic Issues

Individuals with gender dysphoria have been reported across many countries and cultures. The equivalent of gender dysphoria has also been reported in individuals living in cultures with institutionalized gender categories other than male or female. It is unclear whether with these individuals the diagnostic criteria for gender dysphoria would be met.

Diagnostic Markers

Individuals with a somatic disorder of sex development show some correlation of final gender identity outcome with the degree of prenatal androgen production and utilization. However, the correlation is not robust enough for the biological factor, where ascertainable, to replace a detailed and comprehensive diagnostic interview evaluation for gender dysphoria.

Functional Consequences of Gender Dysphoria

Preoccupation with cross-gender wishes may develop at all ages after the first 2–3 years of childhood and often interfere with daily activities. In older children, failure to develop age-typical same-sex peer relationships and skills may lead to isolation from peer groups and to distress. Some children may refuse to attend school because of teasing and harass-

ment or pressure to dress in attire associated with their assigned sex. Also in adolescents and adults, preoccupation with cross-gender wishes often interferes with daily activities. Relationship difficulties, including sexual relationship problems, are common, and functioning at school or at work may be impaired. Gender dysphoria, along with atypical gender expression, is associated with high levels of stigmatization, discrimination, and victimization, leading to negative self-concept, increased rates of mental disorder comorbidity, school dropout, and economic marginalization, including unemployment, with attendant social and mental health risks, especially in individuals from resource-poor family backgrounds. In addition, these individuals' access to health services and mental health services may be impeded by structural barriers, such as institutional discomfort or inexperience in working with this patient population.

Differential Diagnosis

Nonconformity to gender roles. Gender dysphoria should be distinguished from simple nonconformity to stereotypical gender role behavior by the strong desire to be of another gender than the assigned one and by the extent and pervasiveness of gender-variant activities and interests. The diagnosis is not meant to merely describe nonconformity to stereotypical gender role behavior (e.g., "tomboyism" in girls, "girly-boy" behavior in boys, occasional cross-dressing in adult men). Given the increased openness of atypical gender expressions by individuals across the entire range of the transgender spectrum, it is important that the clinical diagnosis be limited to those individuals whose distress and impairment meet the specified criteria.

Transvestic disorder. Transvestic disorder occurs in heterosexual (or bisexual) adolescent and adult males (rarely in females) for whom cross-dressing behavior generates sexual excitement and causes distress and/or impairment without drawing their primary gender into question. It is occasionally accompanied by gender dysphoria. An individual with transvestic disorder who also has clinically significant gender dysphoria can be given both diagnoses. In many cases of late-onset gender dysphoria in gynephilic natal males, transvestic behavior with sexual excitement is a precursor.

Body dysmorphic disorder. An individual with body dysmorphic disorder focuses on the alteration or removal of a specific body part because it is perceived as abnormally formed, not because it represents a repudiated assigned gender. When an individual's presentation meets criteria for both gender dysphoria and body dysmorphic disorder, both diagnoses can be given. Individuals wishing to have a healthy limb amputated (termed by some *body integrity identity disorder*) because it makes them feel more "complete" usually do not wish to change gender, but rather desire to live as an amputee or a disabled person.

Schizophrenia and other psychotic disorders. In schizophrenia, there may rarely be delusions of belonging to some other gender. In the absence of psychotic symptoms, insistence by an individual with gender dysphoria that he or she is of some other gender is not considered a delusion. Schizophrenia (or other psychotic disorders) and gender dysphoria may co-occur.

Other clinical presentations. Some individuals with an emasculinization desire who develop an alternative, nonmale/nonfemale gender identity do have a presentation that meets criteria for gender dysphoria. However, some males seek castration and/or penectomy for aesthetic reasons or to remove psychological effects of androgens without changing male identity; in these cases, the criteria for gender dysphoria are not met.

Comorbidity

Clinically referred children with gender dysphoria show elevated levels of emotional and behavioral problems—most commonly, anxiety, disruptive and impulse-control, and de-

pressive disorders. In prepubertal children, increasing age is associated with having more behavioral or emotional problems; this is related to the increasing non-acceptance of gender-variant behavior by others. In older children, gender-variant behavior often leads to peer ostracism, which may lead to more behavioral problems. The prevalence of mental health problems differs among cultures; these differences may also be related to differences in attitudes toward gender variance in children. However, also in some non-Western cultures, anxiety has been found to be relatively common in individuals with gender dysphoria, even in cultures with accepting attitudes toward gender-variant behavior. Autism spectrum disorder is more prevalent in clinically referred children with gender dysphoria than in the general population. Clinically referred adolescents with gender dysphoria appear to have comorbid mental disorders, with anxiety and depressive disorders being the most common. As in children, autism spectrum disorder is more prevalent in clinically referred adolescents with gender dysphoria than in the general population. Clinically referred adults with gender dysphoria may have coexisting mental health problems, most commonly anxiety and depressive disorders.

Other Specified Gender Dysphoria

302.6 (F64.8)

This category applies to presentations in which symptoms characteristic of gender dysphoria 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 gender dysphoria. The other specified gender dysphoria category is used in situations in which the clinician chooses to communicate the specific reason that the presentation does not meet the criteria for gender dysphoria. This is done by recording "other specified gender dysphoria" followed by the specific reason (e.g., "brief gender dysphoria").

An example of a presentation that can be specified using the "other specified" designation is the following:

The current disturbance meets symptom criteria for gender dysphoria, but the duration is less than 6 months.

Unspecified Gender Dysphoria

302.6 (F64.9)

This category applies to presentations in which symptoms characteristic of gender dysphoria 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 gender dysphoria. The unspecified gender dysphoria category is used in situations in which the clinician chooses *not* to specify the reason that the criteria are not met for gender dysphoria, and includes presentations in which there is insufficient information to make a more specific diagnosis.

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Disruptive, Impulse-Control, and Conduct Disorders

Disruptive, impulse-control, and conduct disorders include conditions involving problems in the self-control of emotions and behaviors. While other disorders in DSM-5 may also involve problems in emotional and/or behavioral regulation, the disorders in this chapter are unique in that these problems are manifested in behaviors that violate the rights of others (e.g., aggression, destruction of property) and/or that bring the individual into significant conflict with societal norms or authority figures. The underlying causes of the problems in the self-control of emotions and behaviors can vary greatly across the disorders in this chapter and among individuals within a given diagnostic category.

The chapter includes oppositional defiant disorder, intermittent explosive disorder, conduct disorder, antisocial personality disorder (which is described in the chapter "Personality Disorders"), pyromania, kleptomania, and other specified and unspecified disruptive, impulse-control, and conduct disorders. Although all the disorders in the chapter involve problems in both emotional and behavioral regulation, the source of variation among the disorders is the relative emphasis on problems in the two types of self-control. For example, the criteria for conduct disorder focus largely on poorly controlled behaviors that violate the rights of others or that violate major societal norms. Many of the behavioral symptoms (e.g., aggression) can be a result of poorly controlled emotions such as anger. At the other extreme, the criteria for intermittent explosive disorder focus largely on such poorly controlled emotion, outbursts of anger that are disproportionate to the interpersonal or other provocation or to other psychosocial stressors. Intermediate in impact to these two disorders is oppositional defiant disorder, in which the criteria are more evenly distributed between emotions (anger and irritation) and behaviors (argumentativeness and defiance). Pyromania and kleptomania are less commonly used diagnoses characterized by poor impulse control related to specific behaviors (fire setting or stealing) that relieve internal tension. Other specified disruptive, impulse-control, and conduct disorder is a category for conditions in which there are symptoms of conduct disorder, oppositional defiant disorder, or other disruptive, impulse-control, and conduct disorders, but the number of symptoms does not meet the diagnostic threshold for any of the disorders in this chapter, even though there is evidence of clinically significant impairment associated with the symptoms.

The disruptive, impulse-control, and conduct disorders all tend to be more common in males than in females, although the relative degree of male predominance may differ both across disorders and within a disorder at different ages. The disorders in this chapter tend to have first onset in childhood or adolescence. In fact, it is very rare for either conduct disorder or oppositional defiant disorder to first emerge in adulthood. There is a developmental relationship between oppositional defiant disorder and conduct disorder, in that most cases of conduct disorder previously would have met criteria for oppositional defiant disorder, at least in those cases in which conduct disorder emerges prior to adolescence. However, most children with oppositional defiant disorder do not eventually develop conduct disorder. Furthermore, children with oppositional defiant disorder are at risk for eventually developing other problems besides conduct disorder, including anxiety and depressive disorders.

Many of the symptoms that define the disruptive, impulse-control, and conduct disorders are behaviors that can occur to some degree in typically developing individuals. Thus, it is critical that the frequency, persistence, pervasiveness across situations, and im-

pairment associated with the behaviors indicative of the diagnosis be considered relative to what is normative for a person's age, gender, and culture when determining if they are symptomatic of a disorder.

The disruptive, impulse-control, and conduct disorders have been linked to a common externalizing spectrum associated with the personality dimensions labeled as *disinhibition* and (inversely) *constraint* and, to a lesser extent, negative emotionality. These shared personality dimensions could account for the high level of comorbidity among these disorders and their frequent comorbidity with substance use disorders and antisocial personality disorder. However, the specific nature of the shared diathesis that constitutes the externalizing spectrum remains unknown.

Oppositional Defiant Disorder

Diagnostic Criteria **313.81** (F91.3)

A. A pattern of angry/irritable mood, argumentative/defiant behavior, or vindictiveness lasting at least 6 months as evidenced by at least four symptoms from any of the following categories, and exhibited during interaction with at least one individual who is not a sibling.

Angry/Irritable Mood

1. Often loses temper.
2. Is often touchy or easily annoyed.
3. Is often angry and resentful.

Argumentative/Defiant Behavior

4. Often argues with authority figures or, for children and adolescents, with adults.
5. Often actively defies or refuses to comply with requests from authority figures or with rules.
6. Often deliberately annoys others.
7. Often blames others for his or her mistakes or misbehavior.

Vindictiveness

8. Has been spiteful or vindictive at least twice within the past 6 months.

Note: The persistence and frequency of these behaviors should be used to distinguish a behavior that is within normal limits from a behavior that is symptomatic. For children younger than 5 years, the behavior should occur on most days for a period of at least 6 months unless otherwise noted (Criterion A8). For individuals 5 years or older, the behavior should occur at least once per week for at least 6 months, unless otherwise noted (Criterion A8). While these frequency criteria provide guidance on a minimal level of frequency to define symptoms, other factors should also be considered, such as whether the frequency and intensity of the behaviors are outside a range that is normative for the individual's developmental level, gender, and culture.

B. The disturbance in behavior is associated with distress in the individual or others in his or her immediate social context (e.g., family, peer group, work colleagues), or it impacts negatively on social, educational, occupational, or other important areas of functioning.

C. The behaviors do not occur exclusively during the course of a psychotic, substance use, depressive, or bipolar disorder. Also, the criteria are not met for disruptive mood dysregulation disorder.

Specify current severity:

Mild: Symptoms are confined to only one setting (e.g., at home, at school, at work, with peers).

Moderate: Some symptoms are present in at least two settings.
Severe: Some symptoms are present in three or more settings.

Specifiers

It is not uncommon for individuals with oppositional defiant disorder to show symptoms only at home and only with family members. However, the pervasiveness of the symptoms is an indicator of the severity of the disorder.

Diagnostic Features

The essential feature of oppositional defiant disorder is a frequent and persistent pattern of angry/irritable mood, argumentative/defiant behavior, or vindictiveness (Criterion A). It is not unusual for individuals with oppositional defiant disorder to show the behavioral features of the disorder without problems of negative mood. However, individuals with the disorder who show the angry/irritable mood symptoms typically show the behavioral features as well.

The symptoms of oppositional defiant disorder may be confined to only one setting, and this is most frequently the home. Individuals who show enough symptoms to meet the diagnostic threshold, even if it is only at home, may be significantly impaired in their social functioning. However, in more severe cases, the symptoms of the disorder are present in multiple settings. Given that the pervasiveness of symptoms is an indicator of the severity of the disorder, it is critical that the individual's behavior be assessed across multiple settings and relationships. Because these behaviors are common among siblings, they must be observed during interactions with persons other than siblings. Also, because symptoms of the disorder are typically more evident in interactions with adults or peers whom the individual knows well, they may not be apparent during a clinical examination.

The symptoms of oppositional defiant disorder can occur to some degree in individuals without this disorder. There are several key considerations for determining if the behaviors are symptomatic of oppositional defiant disorder. First, the diagnostic threshold of four or more symptoms within the preceding 6 months must be met. Second, the persistence and frequency of the symptoms should exceed what is normative for an individual's age, gender, and culture. For example, it is not unusual for preschool children to show temper tantrums on a weekly basis. Temper outbursts for a preschool child would be considered a symptom of oppositional defiant disorder only if they occurred on most days for the preceding 6 months, if they occurred with at least three other symptoms of the disorder, and if the temper outbursts contributed to the significant impairment associated with the disorder (e.g., led to destruction of property during outbursts, resulted in the child being asked to leave a preschool).

The symptoms of the disorder often are part of a pattern of problematic interactions with others. Furthermore, individuals with this disorder typically do not regard themselves as angry, oppositional, or defiant. Instead, they often justify their behavior as a response to unreasonable demands or circumstances. Thus, it can be difficult to disentangle the relative contribution of the individual with the disorder to the problematic interactions he or she experiences. For example, children with oppositional defiant disorder may have experienced a history of hostile parenting, and it is often impossible to determine if the child's behavior caused the parents to act in a more hostile manner toward the child, if the parents' hostility led to the child's problematic behavior, or if there was some combination of both. Whether or not the clinician can separate the relative contributions of potential causal factors should not influence whether or not the diagnosis is made. In the event that the child may be living in particularly poor conditions where neglect or mistreatment may occur (e.g., in institutional settings), clinical attention to reducing the contribution of the environment may be helpful.

Associated Features Supporting Diagnosis

In children and adolescents, oppositional defiant disorder is more prevalent in families in which child care is disrupted by a succession of different caregivers or in families in which harsh, inconsistent, or neglectful child-rearing practices are common. Two of the most common co-occurring conditions with oppositional defiant disorder are attention-deficit/hyperactivity disorder (ADHD) and conduct disorder (see the section "Comorbidity" for this disorder). Oppositional defiant disorder has been associated with increased risk for suicide attempts, even after comorbid disorders are controlled for.

Prevalence

The prevalence of oppositional defiant disorder ranges from 1% to 11%, with an average prevalence estimate of around 3.3%. The rate of oppositional defiant disorder may vary depending on the age and gender of the child. The disorder appears to be somewhat more prevalent in males than in females (1.4:1) prior to adolescence. This male predominance is not consistently found in samples of adolescents or adults.

Development and Course

The first symptoms of oppositional defiant disorder usually appear during the preschool years and rarely later than early adolescence. Oppositional defiant disorder often precedes the development of conduct disorder, especially for those with the childhood-onset type of conduct disorder. However, many children and adolescents with oppositional defiant disorder do not subsequently develop conduct disorder. Oppositional defiant disorder also conveys risk for the development of anxiety disorders and major depressive disorder, even in the absence of conduct disorder. The defiant, argumentative, and vindictive symptoms carry most of the risk for conduct disorder, whereas the angry-irritable mood symptoms carry most of the risk for emotional disorders.

Manifestations of the disorder across development appear consistent. Children and adolescents with oppositional defiant disorder are at increased risk for a number of problems in adjustment as adults, including antisocial behavior, impulse-control problems, substance abuse, anxiety, and depression.

Many of the behaviors associated with oppositional defiant disorder increase in frequency during the preschool period and in adolescence. Thus, it is especially critical during these development periods that the frequency and intensity of these behaviors be evaluated against normative levels before it is decided that they are symptoms of oppositional defiant disorder.

Risk and Prognostic Features

Temperamental. Temperamental factors related to problems in emotional regulation (e.g., high levels of emotional reactivity, poor frustration tolerance) have been predictive of the disorder.

Environmental. Harsh, inconsistent, or neglectful child-rearing practices are common in families of children and adolescents with oppositional defiant disorder, and these parenting practices play an important role in many causal theories of the disorder.

Genetic and physiological. A number of neurobiological markers (e.g., lower heart rate and skin conductance reactivity; reduced basal cortisol reactivity; abnormalities in the prefrontal cortex and amygdala) have been associated with oppositional defiant disorder. However, the vast majority of studies have not separated children with oppositional defiant disorder from those with conduct disorder. Thus, it is unclear whether there are markers specific to oppositional defiant disorder.

Culture-Related Diagnostic Issues

The prevalence of the disorder in children and adolescents is relatively consistent across countries that differ in race and ethnicity.

Functional Consequences of Oppositional Defiant Disorder

When oppositional defiant disorder is persistent throughout development, individuals with the disorder experience frequent conflicts with parents, teachers, supervisors, peers, and romantic partners. Such problems often result in significant impairments in the individual's emotional, social, academic, and occupational adjustment.

Differential Diagnosis

Conduct disorder. Conduct disorder and oppositional defiant disorder are both related to conduct problems that bring the individual in conflict with adults and other authority figures (e.g., teachers, work supervisors). The behaviors of oppositional defiant disorder are typically of a less severe nature than those of conduct disorder and do not include aggression toward people or animals, destruction of property, or a pattern of theft or deceit. Furthermore, oppositional defiant disorder includes problems of emotional dysregulation (i.e., angry and irritable mood) that are not included in the definition of conduct disorder.

Attention-deficit/hyperactivity disorder. ADHD is often comorbid with oppositional defiant disorder. To make the additional diagnosis of oppositional defiant disorder, it is important to determine that the individual's failure to conform to requests of others is not solely in situations that demand sustained effort and attention or demand that the individual sit still.

Depressive and bipolar disorders. Depressive and bipolar disorders often involve negative affect and irritability. As a result, a diagnosis of oppositional defiant disorder should not be made if the symptoms occur exclusively during the course of a mood disorder.

Disruptive mood dysregulation disorder. Oppositional defiant disorder shares with disruptive mood dysregulation disorder the symptoms of chronic negative mood and temper outbursts. However, the severity, frequency, and chronicity of temper outbursts are more severe in individuals with disruptive mood dysregulation disorder than in those with oppositional defiant disorder. Thus, only a minority of children and adolescents whose symptoms meet criteria for oppositional defiant disorder would also be diagnosed with disruptive mood dysregulation disorder. When the mood disturbance is severe enough to meet criteria for disruptive mood dysregulation disorder, a diagnosis of oppositional defiant disorder is not given, even if all criteria for oppositional defiant disorder are met.

Intermittent explosive disorder. Intermittent explosive disorder also involves high rates of anger. However, individuals with this disorder show serious aggression toward others that is not part of the definition of oppositional defiant disorder.

Intellectual disability (intellectual developmental disorder). In individuals with intellectual disability, a diagnosis of oppositional defiant disorder is given only if the oppositional behavior is markedly greater than is commonly observed among individuals of comparable mental age and with comparable severity of intellectual disability.

Language disorder. Oppositional defiant disorder must also be distinguished from a failure to follow directions that is the result of impaired language comprehension (e.g., hearing loss).

Social anxiety disorder (social phobia). Oppositional defiant disorder must also be distinguished from defiance due to fear of negative evaluation associated with social anxiety disorder.

Comorbidity

Rates of oppositional defiant disorder are much higher in samples of children, adolescents, and adults with ADHD, and this may be the result of shared temperamental risk factors. Also, oppositional defiant disorder often precedes conduct disorder, although this appears to be most common in children with the childhood-onset subtype. Individuals with oppositional defiant disorder are also at increased risk for anxiety disorders and major depressive disorder, and this seems largely attributable to the presence of the angry-irritable mood symptoms. Adolescents and adults with oppositional defiant disorder also show a higher rate of substance use disorders, although it is unclear if this association is independent of the comorbidity with conduct disorder.

Intermittent Explosive Disorder

Diagnostic Criteria **312.34 (F63.81)**

A. Recurrent behavioral outbursts representing a failure to control aggressive impulses as manifested by either of the following:
   1. Verbal aggression (e.g., temper tantrums, tirades, verbal arguments or fights) or physical aggression toward property, animals, or other individuals, occurring twice weekly, on average, for a period of 3 months. The physical aggression does not result in damage or destruction of property and does not result in physical injury to animals or other individuals.
   2. Three behavioral outbursts involving damage or destruction of property and/or physical assault involving physical injury against animals or other individuals occurring within a 12-month period.

B. The magnitude of aggressiveness expressed during the recurrent outbursts is grossly out of proportion to the provocation or to any precipitating psychosocial stressors.

C. The recurrent aggressive outbursts are not premeditated (i.e., they are impulsive and/or anger-based) and are not committed to achieve some tangible objective (e.g., money, power, intimidation).

D. The recurrent aggressive outbursts cause either marked distress in the individual or impairment in occupational or interpersonal functioning, or are associated with financial or legal consequences.

E. Chronological age is at least 6 years (or equivalent developmental level).

F. The recurrent aggressive outbursts are not better explained by another mental disorder (e.g., major depressive disorder, bipolar disorder, disruptive mood dysregulation disorder, a psychotic disorder, antisocial personality disorder, borderline personality disorder) and are not attributable to another medical condition (e.g., head trauma, Alzheimer's disease) or to the physiological effects of a substance (e.g., a drug of abuse, a medication). For children ages 6–18 years, aggressive behavior that occurs as part of an adjustment disorder should not be considered for this diagnosis.

Note: This diagnosis can be made in addition to the diagnosis of attention-deficit/hyperactivity disorder, conduct disorder, oppositional defiant disorder, or autism spectrum disorder when recurrent impulsive aggressive outbursts are in excess of those usually seen in these disorders and warrant independent clinical attention.

Diagnostic Features

The impulsive (or anger-based) aggressive outbursts in intermittent explosive disorder have a rapid onset and, typically, little or no prodromal period. Outbursts typically last for less

than 30 minutes and commonly occur in response to a minor provocation by a close intimate or associate. Individuals with intermittent explosive disorder often have less severe episodes of verbal and/or nondamaging, nondestructive, or noninjurious physical assault (Criterion A1) in between more severe destructive/assaultive episodes (Criterion A2). Criterion A1 defines frequent (i.e., twice weekly, on average, for a period of 3 months) aggressive outbursts characterized by temper tantrums, tirades, verbal arguments or fights, or assault without damage to objects or without injury to animals or other individuals. Criterion A2 defines infrequent (i.e., three in a 1-year period) impulsive aggressive outbursts characterized by damaging or destroying an object, regardless of its tangible value, or by assaulting/striking or otherwise causing physical injury to an animal or to another individual. Regardless of the nature of the impulsive aggressive outburst, the core feature of intermittent explosive disorder is failure to control impulsive aggressive behavior in response to subjectively experienced provocation (i.e., psychosocial stressor) that would not typically result in an aggressive outburst (Criterion B). The aggressive outbursts are generally impulsive and/or anger-based, rather than premeditated or instrumental (Criterion C) and are associated with significant distress or impairment in psychosocial function (Criterion D). A diagnosis of intermittent explosive disorder should not be given to individuals younger than 6 years, or the equivalent developmental level (Criterion E), or to individuals whose aggressive outbursts are better explained by another mental disorder (Criterion F). A diagnosis of intermittent explosive disorder should not be given to individuals with disruptive mood dysregulation disorder or to individuals whose impulsive aggressive outbursts are attributable to another medical condition or to the physiological effects of a substance (Criterion F). In addition, children ages 6–18 years should not receive this diagnosis when impulsive aggressive outbursts occur in the context of an adjustment disorder (Criterion F).

Associated Features Supporting Diagnosis

Mood disorders (unipolar), anxiety disorders, and substance use disorders are associated with intermittent explosive disorder, although onset of these disorders is typically later than that of intermittent explosive disorder.

Prevalence

One-year prevalence data for intermittent explosive disorder in the United States is about 2.7% (narrow definition). Intermittent explosive disorder is more prevalent among younger individuals (e.g., younger than 35–40 years), compared with older individuals (older than 50 years), and in individuals with a high school education or less.

Development and Course

The onset of recurrent, problematic, impulsive aggressive behavior is most common in late childhood or adolescence and rarely begins for the first time after age 40 years. The core features of intermittent explosive disorder, typically, are persistent and continue for many years.

The course of the disorder may be episodic, with recurrent periods of impulsive aggressive outbursts. Intermittent explosive disorder appears to follow a chronic and persistent course over many years. It also appears to be quite common regardless of the presence or absence of attention-deficit/hyperactivity disorder (ADHD) or disruptive, impulse-control, and conduct disorders (e.g., conduct disorder, oppositional defiant disorder).

Risk and Prognostic Factors

Environmental. Individuals with a history of physical and emotional trauma during the first two decades of life are at increased risk for intermittent explosive disorder.

Genetic and physiological. First-degree relatives of individuals with intermittent explosive disorder are at increased risk for intermittent explosive disorder, and twin studies have demonstrated a substantial genetic influence for impulsive aggression.

Research provides neurobiological support for the presence of serotonergic abnormalities, globally and in the brain, specifically in areas of the limbic system (anterior cingulate) and orbitofrontal cortex in individuals with intermittent explosive disorder. Amygdala responses to anger stimuli, during functional magnetic resonance imaging scanning, are greater in individuals with intermittent explosive disorder compared with healthy individuals.

Culture-Related Diagnostic Issues

The lower prevalence of intermittent explosive disorder in some regions (Asia, Middle East) or countries (Romania, Nigeria), compared with the United States, suggests that information about recurrent, problematic, impulsive aggressive behaviors either is not elicited on questioning or is less likely to be present, because of cultural factors.

Gender-Related Diagnostic Issues

In some studies the prevalence of intermittent explosive disorder is greater in males than in females (odds ratio = 1.4–2.3); other studies have found no gender difference.

Functional Consequences of Intermittent Explosive Disorder

Social (e.g., loss of friends, relatives, marital instability), occupational (e.g., demotion, loss of employment), financial (e.g., due to value of objects destroyed), and legal (e.g., civil suits as a result of aggressive behavior against person or property; criminal charges for assault) problems often develop as a result of intermittent explosive disorder.

Differential Diagnosis

A diagnosis of intermittent explosive disorder should not be made when Criteria A1 and/or A2 are only met during an episode of another mental disorder (e.g., major depressive disorder, bipolar disorder, psychotic disorder), or when impulsive aggressive outbursts are attributable to another medical condition or to the physiological effects of a substance or medication. This diagnosis also should not be made, particularly in children and adolescents ages 6–18 years, when the impulsive aggressive outbursts occur in the context of an adjustment disorder. Other examples in which recurrent, problematic, impulsive aggressive outbursts may, or may not, be diagnosed as intermittent explosive disorder include the following.

Disruptive mood dysregulation disorder. In contrast to intermittent explosive disorder, disruptive mood dysregulation disorder is characterized by a persistently negative mood state (i.e., irritability, anger) most of the day, nearly every day, between impulsive aggressive outbursts. A diagnosis of disruptive mood dysregulation disorder can only be given when the onset of recurrent, problematic, impulsive aggressive outbursts is before age 10 years. Finally, a diagnosis of disruptive mood dysregulation disorder should not be made for the first time after age 18 years. Otherwise, these diagnoses are mutually exclusive.

Antisocial personality disorder or borderline personality disorder. Individuals with antisocial personality disorder or borderline personality disorder often display recurrent, problematic impulsive aggressive outbursts. However, the level of impulsive aggression in individuals with antisocial personality disorder or borderline personality disorder is lower than that in individuals with intermittent explosive disorder.

Delirium, major neurocognitive disorder, and personality change due to another medical condition, aggressive type. A diagnosis of intermittent explosive disorder should not be made when aggressive outbursts are judged to result from the physiological effects of another diagnosable medical condition (e.g., brain injury associated with a change in personality characterized by aggressive outbursts; complex partial epilepsy). Nonspecific abnormalities on neurological examination (e.g., "soft signs") and nonspecific electroencephalographic changes are compatible with a diagnosis of intermittent explosive disorder unless there is a diagnosable medical condition that better explains the impulsive aggressive outbursts.

Substance intoxication or substance withdrawal. A diagnosis of intermittent explosive disorder should not be made when impulsive aggressive outbursts are nearly always associated with intoxication with or withdrawal from substances (e.g., alcohol, phencyclidine, cocaine and other stimulants, barbiturates, inhalants). However, when a sufficient number of impulsive aggressive outbursts also occur in the absence of substance intoxication or withdrawal, and these warrant independent clinical attention, a diagnosis of intermittent explosive disorder may be given.

Attention-deficit/hyperactivity disorder, conduct disorder, oppositional defiant disorder, or autism spectrum disorder. Individuals with any of these childhood-onset disorders may exhibit impulsive aggressive outbursts. Individuals with ADHD are typically impulsive and, as a result, may also exhibit impulsive aggressive outbursts. While individuals with conduct disorder can exhibit impulsive aggressive outbursts, the form of aggression characterized by the diagnostic criteria is proactive and predatory. Aggression in oppositional defiant disorder is typically characterized by temper tantrums and verbal arguments with authority figures, whereas impulsive aggressive outbursts in intermittent explosive disorder are in response to a broader array of provocation and include physical assault. The level of impulsive aggression in individuals with a history of one or more of these disorders has been reported as lower than that in comparable individuals whose symptoms also meet intermittent explosive disorder Criteria A through E. Accordingly, if Criteria A through E are also met, and the impulsive aggressive outbursts warrant independent clinical attention, a diagnosis of intermittent explosive disorder may be given.

Comorbidity

Depressive disorders, anxiety disorders, and substance use disorders are most commonly comorbid with intermittent explosive disorder. In addition, individuals with antisocial personality disorder or borderline personality disorder, and individuals with a history of disorders with disruptive behaviors (e.g., ADHD, conduct disorder, oppositional defiant disorder), are at greater risk for comorbid intermittent explosive disorder.

Conduct Disorder

Diagnostic Criteria

A. A repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated, as manifested by the presence of at least three of the following 15 criteria in the past 12 months from any of the categories below, with at least one criterion present in the past 6 months:

Aggression to People and Animals

1. Often bullies, threatens, or intimidates others.
2. Often initiates physical fights.
3. Has used a weapon that can cause serious physical harm to others (e.g., a bat, brick, broken bottle, knife, gun).

4. Has been physically cruel to people.
5. Has been physically cruel to animals.
6. Has stolen while confronting a victim (e.g., mugging, purse snatching, extortion, armed robbery).
7. Has forced someone into sexual activity.

Destruction of Property

8. Has deliberately engaged in fire setting with the intention of causing serious damage.
9. Has deliberately destroyed others' property (other than by fire setting).

Deceitfulness or Theft

10. Has broken into someone else's house, building, or car.
11. Often lies to obtain goods or favors or to avoid obligations (i.e., "cons" others).
12. Has stolen items of nontrivial value without confronting a victim (e.g., shoplifting, but without breaking and entering; forgery).

Serious Violations of Rules

13. Often stays out at night despite parental prohibitions, beginning before age 13 years.
14. Has run away from home overnight at least twice while living in the parental or parental surrogate home, or once without returning for a lengthy period.
15. Is often truant from school, beginning before age 13 years.

B. The disturbance in behavior causes clinically significant impairment in social, academic, or occupational functioning.

C. If the individual is age 18 years or older, criteria are not met for antisocial personality disorder.

Specify whether:

312.81 (F91.1) Childhood-onset type: Individuals show at least one symptom characteristic of conduct disorder prior to age 10 years.

312.82 (F91.2) Adolescent-onset type: Individuals show no symptom characteristic of conduct disorder prior to age 10 years.

312.89 (F91.9) Unspecified onset: Criteria for a diagnosis of conduct disorder are met, but there is not enough information available to determine whether the onset of the first symptom was before or after age 10 years.

Specify if:

With limited prosocial emotions: To qualify for this specifier, an individual must have displayed at least two of the following characteristics persistently over at least 12 months and in multiple relationships and settings. These characteristics reflect the individual's typical pattern of interpersonal and emotional functioning over this period and not just occasional occurrences in some situations. Thus, to assess the criteria for the specifier, multiple information sources are necessary. In addition to the individual's self-report, it is necessary to consider reports by others who have known the individual for extended periods of time (e.g., parents, teachers, co-workers, extended family members, peers).

Lack of remorse or guilt: Does not feel bad or guilty when he or she does something wrong (exclude remorse when expressed only when caught and/or facing punishment). The individual shows a general lack of concern about the negative consequences of his or her actions. For example, the individual is not remorseful after hurting someone or does not care about the consequences of breaking rules.

Callous—lack of empathy: Disregards and is unconcerned about the feelings of others. The individual is described as cold and uncaring. The person appears more concerned about the effects of his or her actions on himself or herself, rather than their effects on others, even when they result in substantial harm to others.

Unconcerned about performance: Does not show concern about poor/problematic performance at school, at work, or in other important activities. The individual does not put forth the effort necessary to perform well, even when expectations are clear, and typically blames others for his or her poor performance.

Shallow or deficient affect: Does not express feelings or show emotions to others, except in ways that seem shallow, insincere, or superficial (e.g., actions contradict the emotion displayed; can turn emotions "on" or "off" quickly) or when emotional expressions are used for gain (e.g., emotions displayed to manipulate or intimidate others).

Specify current severity:

Mild: Few if any conduct problems in excess of those required to make the diagnosis are present, and conduct problems cause relatively minor harm to others (e.g., lying, truancy, staying out after dark without permission, other rule breaking).

Moderate: The number of conduct problems and the effect on others are intermediate between those specified in "mild" and those in "severe" (e.g., stealing without confronting a victim, vandalism).

Severe: Many conduct problems in excess of those required to make the diagnosis are present, or conduct problems cause considerable harm to others (e.g., forced sex, physical cruelty, use of a weapon, stealing while confronting a victim, breaking and entering).

Subtypes

Three subtypes of conduct disorder are provided based on the age at onset of the disorder. Onset is most accurately estimated with information from both the youth and the caregiver; estimates are often 2 years later than actual onset. Both subtypes can occur in a mild, moderate, or severe form. An unspecified-onset subtype is designated when there is insufficient information to determine age at onset.

In childhood-onset conduct disorder, individuals are usually male, frequently display physical aggression toward others, have disturbed peer relationships, may have had oppositional defiant disorder during early childhood, and usually have symptoms that meet full criteria for conduct disorder prior to puberty. Many children with this subtype also have concurrent attention-deficit/hyperactivity disorder (ADHD) or other neurodevelopmental difficulties. Individuals with childhood-onset type are more likely to have persistent conduct disorder into adulthood than are those with adolescent-onset type. As compared with individuals with childhood-onset type, individuals with adolescent-onset conduct disorder are less likely to display aggressive behaviors and tend to have more normative peer relationships (although they often display conduct problems in the company of others). These individuals are less likely to have conduct disorder that persists into adulthood. The ratio of males to females with conduct disorder is more balanced for the adolescent-onset type than for the childhood-onset type.

Specifiers

A minority of individuals with conduct disorder exhibit characteristics that qualify for the "with limited prosocial emotions" specifier. The indicators of this specifier are those that have often been labeled as callous and unemotional traits in research. Other personality features, such as thrill seeking, fearlessness, and insensitivity to punishment, may also distinguish those with characteristics described in the specifier. Individuals with characteristics described in this specifier may be more likely than other individuals with conduct disorder to engage in aggression that is planned for instrumental gain. Individuals with conduct disorder of any subtype or any level of severity can have characteristics that qualify for the specifier "with limited prosocial emotions," although individuals with the specifier are more likely to have childhood-onset type and a severity specifier rating of severe.

Although the validity of self-report to assess the presence of the specifier has been supported in some research contexts, individuals with conduct disorder with this specifier may not readily admit to the traits in a clinical interview. Thus, to assess the criteria for the specifier, multiple information sources are necessary. Also, because the indicators of the specifier are characteristics that reflect the individual's typical pattern of interpersonal and emotional functioning, it is important to consider reports by others who have known the individual for extended periods of time and across relationships and settings (e.g., parents, teachers, co-workers, extended family members, peers).

Diagnostic Features

The essential feature of conduct disorder is a repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated (Criterion A). These behaviors fall into four main groupings: aggressive conduct that causes or threatens physical harm to other people or animals (Criteria A1–A7); nonaggressive conduct that causes property loss or damage (Criteria A8–A9); deceitfulness or theft (Criteria A10–A12); and serious violations of rules (Criteria A13–A15). Three or more characteristic behaviors must have been present during the past 12 months, with at least one behavior present in the past 6 months. The disturbance in behavior causes clinically significant impairment in social, academic, or occupational functioning (Criterion B). The behavior pattern is usually present in a variety of settings, such as home, at school, or in the community. Because individuals with conduct disorder are likely to minimize their conduct problems, the clinician often must rely on additional informants. However, informants' knowledge of the individual's conduct problems may be limited if they have inadequately supervised the individual or the individual has concealed symptom behaviors.

Individuals with conduct disorder often initiate aggressive behavior and react aggressively to others. They may display bullying, threatening, or intimidating behavior (including bullying via messaging on Web-based social media) (Criterion A1); initiate frequent physical fights (Criterion A2); use a weapon that can cause serious physical harm (e.g., a bat, brick, broken bottle, knife, gun) (Criterion A3); be physically cruel to people (Criterion A4) or animals (Criterion A5); steal while confronting a victim (e.g., mugging, purse snatching, extortion, armed robbery) (Criterion A6); or force someone into sexual activity (Criterion A7). Physical violence may take the form of rape, assault, or, in rare cases, homicide. Deliberate destruction of others' property may include deliberate fire setting with the intention of causing serious damage (Criterion A8) or deliberate destroying of other people's property in other ways (e.g., smashing car windows, vandalizing school property) (Criterion A9). Acts of deceitfulness or theft may include breaking into someone else's house, building, or car (Criterion A10); frequently lying or breaking promises to obtain goods or favors or to avoid debts or obligations (e.g., "conning" other individuals) (Criterion A11); or stealing items of nontrivial value without confronting the victim (e.g., shoplifting, forgery, fraud) (Criterion A12).

Individuals with conduct disorder may also frequently commit serious violations of rules (e.g., school, parental, workplace). Children with conduct disorder often have a pattern, beginning before age 13 years, of staying out late at night despite parental prohibitions (Criterion A13). Children may also show a pattern of running away from home overnight (Criterion A14). To be considered a symptom of conduct disorder, the running away must have occurred at least twice (or only once if the individual did not return for a lengthy period). Runaway episodes that occur as a direct consequence of physical or sexual abuse do not typically qualify for this criterion. Children with conduct disorder may often be truant from school, beginning prior to age 13 years (Criterion A15).

Associated Features Supporting Diagnosis

Especially in ambiguous situations, aggressive individuals with conduct disorder frequently misperceive the intentions of others as more hostile and threatening than is the

case and respond with aggression that they then feel is reasonable and justified. Personality features of trait negative emotionality and poor self-control, including poor frustration tolerance, irritability, temper outbursts, suspiciousness, insensitivity to punishment, thrill seeking, and recklessness, frequently co-occur with conduct disorder. Substance misuse is often an associated feature, particularly in adolescent females. Suicidal ideation, suicide attempts, and completed suicide occur at a higher-than-expected rate in individuals with conduct disorder.

Prevalence

One-year population prevalence estimates range from 2% to more than 10%, with a median of 4%. The prevalence of conduct disorder appears to be fairly consistent across various countries that differ in race and ethnicity. Prevalence rates rise from childhood to adolescence and are higher among males than among females. Few children with impairing conduct disorder receive treatment.

Development and Course

The onset of conduct disorder may occur as early as the preschool years, but the first significant symptoms usually emerge during the period from middle childhood through middle adolescence. Oppositional defiant disorder is a common precursor to the childhood-onset type of conduct disorder. Conduct disorder may be diagnosed in adults, however, symptoms of conduct disorder usually emerge in childhood or adolescence, and onset is rare after age 16 years. The course of conduct disorder after onset is variable. In a majority of individuals, the disorder remits by adulthood. Many individuals with conduct disorder—particularly those with adolescent-onset type and those with few and milder symptoms—achieve adequate social and occupational adjustment as adults. However, the early-onset type predicts a worse prognosis and an increased risk of criminal behavior, conduct disorder, and substance-related disorders in adulthood. Individuals with conduct disorder are at risk for later mood disorders, anxiety disorders, posttraumatic stress disorder, impulse-control disorders, psychotic disorders, somatic symptom disorders, and substance-related disorders as adults.

Symptoms of the disorder vary with age as the individual develops increased physical strength, cognitive abilities, and sexual maturity. Symptom behaviors that emerge first tend to be less serious (e.g., lying, shoplifting), whereas conduct problems that emerge last tend to be more severe (e.g., rape, theft while confronting a victim). However, there are wide differences among individuals, with some engaging in the more damaging behaviors at an early age (which is predictive of a worse prognosis). When individuals with conduct disorder reach adulthood, symptoms of aggression, property destruction, deceitfulness, and rule violation, including violence against co-workers, partners, and children, may be exhibited in the workplace and the home, such that antisocial personality disorder may be considered.

Risk and Prognostic Factors

Temperamental. Temperamental risk factors include a difficult undercontrolled infant temperament and lower-than-average intelligence, particularly with regard to verbal IQ.

Environmental. Family-level risk factors include parental rejection and neglect, inconsistent child-rearing practices, harsh discipline, physical or sexual abuse, lack of supervision, early institutional living, frequent changes of caregivers, large family size, parental criminality, and certain kinds of familial psychopathology (e.g., substance-related disorders). Community-level risk factors include peer rejection, association with a delinquent peer group, and neighborhood exposure to violence. Both types of risk factors tend to be more common and severe among individuals with the childhood-onset subtype of conduct disorder.

Genetic and physiological. Conduct disorder is influenced by both genetic and environmental factors. The risk is increased in children with a biological or adoptive parent or a sibling with conduct disorder. The disorder also appears to be more common in children of biological parents with severe alcohol use disorder, depressive and bipolar disorders, or schizophrenia or biological parents who have a history of ADHD or conduct disorder. Family history particularly characterizes individuals with the childhood-onset subtype of conduct disorder. Slower resting heart rate has been reliably noted in individuals with conduct disorder compared with those without the disorder, and this marker is not characteristic of any other mental disorder. Reduced autonomic fear conditioning, particularly low skin conductance, is also well documented. However, these psychophysiological findings are not diagnostic of the disorder. Structural and functional differences in brain areas associated with affect regulation and affect processing, particularly frontotemporal-limbic connections involving the brain's ventral prefrontal cortex and amygdala, have been consistently noted in individuals with conduct disorder compared with those without the disorder. However, neuroimaging findings are not diagnostic of the disorder.

Course modifiers. Persistence is more likely for individuals with behaviors that meet criteria for the childhood-onset subtype and qualify for the specifier "with limited prosocial emotions". The risk that conduct disorder will persist is also increased by co-occurring ADHD and by substance abuse.

Culture-Related Diagnostic Issues

Conduct disorder diagnosis may at times be potentially misapplied to individuals in settings where patterns of disruptive behavior are viewed as near-normative (e.g., in very threatening, high-crime areas or war zones). Therefore, the context in which the undesirable behaviors have occurred should be considered.

Gender-Related Diagnostic Issues

Males with a diagnosis of conduct disorder frequently exhibit fighting, stealing, vandalism, and school discipline problems. Females with a diagnosis of conduct disorder are more likely to exhibit lying, truancy, running away, substance use, and prostitution. Whereas males tend to exhibit both physical aggression and relational aggression (behavior that harms social relationships of others), females tend to exhibit relatively more relational aggression.

Functional Consequences of Conduct Disorder

Conduct disorder behaviors may lead to school suspension or expulsion, problems in work adjustment, legal difficulties, sexually transmitted diseases, unplanned pregnancy, and physical injury from accidents or fights. These problems may preclude attendance in ordinary schools or living in a parental or foster home. Conduct disorder is often associated with an early onset of sexual behavior, alcohol use, tobacco smoking, use of illegal substances, and reckless and risk-taking acts. Accident rates appear to be higher among individuals with conduct disorder compared with those without the disorder. These functional consequences of conduct disorder may predict health difficulties when individuals reach midlife. It is not uncommon for individuals with conduct disorder to come into contact with the criminal justice system for engaging in illegal behavior. Conduct disorder is a common reason for treatment referral and is frequently diagnosed in mental health facilities for children, especially in forensic practice. It is associated with impairment that is more severe and chronic than that experienced by other clinic-referred children.

Differential Diagnosis

Oppositional defiant disorder. Conduct disorder and oppositional defiant disorder are both related to symptoms that bring the individual in conflict with adults and other au-

thority figures (e.g., parents, teachers, work supervisors). The behaviors of oppositional defiant disorder are typically of a less severe nature than those of individuals with conduct disorder and do not include aggression toward individuals or animals, destruction of property, or a pattern of theft or deceit. Furthermore, oppositional defiant disorder includes problems of emotional dysregulation (i.e., angry and irritable mood) that are not included in the definition of conduct disorder. When criteria are met for both oppositional defiant disorder and conduct disorder, both diagnoses can be given.

Attention-deficit/hyperactivity disorder. Although children with ADHD often exhibit hyperactive and impulsive behavior that may be disruptive, this behavior does not by itself violate societal norms or the rights of others and therefore does not usually meet criteria for conduct disorder. When criteria are met for both ADHD and conduct disorder, both diagnoses should be given.

Depressive and bipolar disorders. Irritability, aggression, and conduct problems can occur in children or adolescents with a major depressive disorder, a bipolar disorder, or disruptive mood dysregulation disorder. The behaviorial problems associated with these mood disorders can usually be distinguished from the pattern of conduct problems seen in conduct disorder based on their course. Specifically, persons with conduct disorder will display substantial levels of aggressive or non-aggressive conduct problems during periods in which there is no mood disturbance, either historically (i.e., a history of conduct problems predating the onset of the mood disturbance) or concurrently (i.e., display of some conduct problems that are premeditated and do not occur during periods of intense emotional arousal). In those cases in which criteria for conduct disorder and a mood disorder are met, both diagnoses can be given.

Intermittent explosive disorder. Both conduct disorder and intermittent explosive disorder involve high rates of aggression. However, the aggression in individuals with intermittent explosive disorder is limited to impulsive aggression and is not premeditated, and it is not committed in order to achieve some tangible objective (e.g., money, power, intimidation). Also, the definition of intermittent explosive disorder does not include the nonaggressive symptoms of conduct disorder. If criteria for both disorders are met, the diagnosis of intermittent explosive disorder should be given only when the recurrent impulsive aggressive outbursts warrant independent clinical attention.

Adjustment disorders. The diagnosis of an adjustment disorder (with disturbance of conduct or with mixed disturbance of emotions and conduct) should be considered if clinically significant conduct problems that do not meet the criteria for another specific disorder develop in clear association with the onset of a psychosocial stressor and do not resolve within 6 months of the termination of the stressor (or its consequences). Conduct disorder is diagnosed only when the conduct problems represent a repetitive and persistent pattern that is associated with impairment in social, academic, or occupational functioning.

Comorbidity

ADHD and oppositional defiant disorder are both common in individuals with conduct disorder, and this comorbid presentation predicts worse outcomes. Individuals who show the personality features associated with antisocial personality disorder often violate the basic rights of others or violate major age-appropriate societal norms, and as a result their pattern of behavior often meets criteria for conduct disorder. Conduct disorder may also co-occur with one or more of the following mental disorders: specific learning disorder, anxiety disorders, depressive or bipolar disorders, and substance-related disorders. Academic achievement, particularly in reading and other verbal skills, is often below the level expected on the basis of age and intelligence and may justify the additional diagnosis of specific learning disorder or a communication disorder.

Antisocial Personality Disorder

Criteria and text for antisocial personality disorder can be found in the chapter "Personality Disorders." Because this disorder is closely connected to the spectrum of "externalizing" conduct disorders in this chapter, as well as to the disorders in the adjoining chapter "Substance-Related and Addictive Disorders," it is dual coded here as well as in the chapter "Personality Disorders."

Pyromania

Diagnostic Criteria **312.33 (F63.1)**

A. Deliberate and purposeful fire setting on more than one occasion.
B. Tension or affective arousal before the act.
C. Fascination with, interest in, curiosity about, or attraction to fire and its situational contexts (e.g., paraphernalia, uses, consequences).
D. Pleasure, gratification, or relief when setting fires or when witnessing or participating in their aftermath.
E. The fire setting is not done for monetary gain, as an expression of sociopolitical ideology, to conceal criminal activity, to express anger or vengeance, to improve one's living circumstances, in response to a delusion or hallucination, or as a result of impaired judgment (e.g., in major neurocognitive disorder, intellectual disability [intellectual developmental disorder], substance intoxication).
F. The fire setting is not better explained by conduct disorder, a manic episode, or antisocial personality disorder.

Diagnostic Features

The essential feature of pyromania is the presence of multiple episodes of deliberate and purposeful fire setting (Criterion A). Individuals with this disorder experience tension or affective arousal before setting a fire (Criterion B). There is a fascination with, interest in, curiosity about, or attraction to fire and its situational contexts (e.g., paraphernalia, uses, consequences) (Criterion C). Individuals with this disorder are often regular "watchers" at fires in their neighborhoods, may set off false alarms, and derive pleasure from institutions, equipment, and personnel associated with fire. They may spend time at the local fire department, set fires to be affiliated with the fire department, or even become firefighters. Individuals with this disorder experience pleasure, gratification, or relief when setting the fire, witnessing its effects, or participating in its aftermath (Criterion D). The fire setting is not done for monetary gain, as an expression of sociopolitical ideology, to conceal criminal activity, to express anger or vengeance, to improve one's living circumstances, or in response to a delusion or a hallucination (Criterion E). The fire setting does not result from impaired judgment (e.g., in major neurocognitive disorder or intellectual disability [intellectual developmental disorder]). The diagnosis is not made if the fire setting is better explained by conduct disorder, a manic episode, or antisocial personality disorder (Criterion F).

Associated Features Supporting Diagnosis

Individuals with pyromania may make considerable advance preparation for starting a fire. They may be indifferent to the consequences to life or property caused by the fire, or

they may derive satisfaction from the resulting property destruction. The behaviors may lead to property damage, legal consequences, or injury or loss of life to the fire setter or to others. Individuals who impulsively set fires (who may or may not have pyromania) often have a current or past history of alcohol use disorder.

Prevalence

The population prevalence of pyromania is not known. The lifetime prevalence of fire setting, which is just one component of pyromania and not sufficient for a diagnosis by itself, was reported as 1.13% in a population sample, but the most common comorbidities were antisocial personality disorder, substance use disorder, bipolar disorder, and pathological gambling (gambling disorder). In contrast, pyromania as a primary diagnosis appears to be very rare. Among a sample of persons reaching the criminal system with repeated fire setting, only 3.3% had symptoms that met full criteria for pyromania.

Development and Course

There are insufficient data to establish a typical age at onset of pyromania. The relationship between fire setting in childhood and pyromania in adulthood has not been documented. In individuals with pyromania, fire-setting incidents are episodic and may wax and wane in frequency. Longitudinal course is unknown. Although fire setting is a major problem in children and adolescents (over 40% of those arrested for arson offenses in the United States are younger than 18 years), pyromania in childhood appears to be rare. Juvenile fire setting is usually associated with conduct disorder, attention-deficit/hyperactivity disorder, or an adjustment disorder.

Gender-Related Diagnostic Issues

Pyromania occurs much more often in males, especially those with poorer social skills and learning difficulties.

Differential Diagnosis

Other causes of intentional fire setting. It is important to rule out other causes of fire setting before giving the diagnosis of pyromania. Intentional fire setting may occur for profit, sabotage, or revenge; to conceal a crime; to make a political statement (e.g., an act of terrorism or protest); or to attract attention or recognition (e.g., setting a fire in order to discover it and save the day). Fire setting may also occur as part of developmental experimentation in childhood (e.g., playing with matches, lighters, or fire).

Other mental disorders. A separate diagnosis of pyromania is not given when fire setting occurs as part of conduct disorder, a manic episode, or antisocial personality disorder, or if it occurs in response to a delusion or a hallucination (e.g., in schizophrenia) or is attributable to the physiological effects of another medical condition (e.g., epilepsy). The diagnosis of pyromania should also not be given when fire setting results from impaired judgment associated with major neurocognitive disorder, intellectual disability, or substance intoxication.

Comorbidity

There appears to be a high co-occurrence of substance use disorders, gambling disorder, depressive and bipolar disorders, and other disruptive, impulse-control, and conduct disorders with pyromania.

Kleptomania

Diagnostic Criteria **312.32 (F63.2)**

A. Recurrent failure to resist impulses to steal objects that are not needed for personal use or for their monetary value.
B. Increasing sense of tension immediately before committing the theft.
C. Pleasure, gratification, or relief at the time of committing the theft.
D. The stealing is not committed to express anger or vengeance and is not in response to a delusion or a hallucination.
E. The stealing is not better explained by conduct disorder, a manic episode, or antisocial personality disorder.

Diagnostic Features

The essential feature of kleptomania is the recurrent failure to resist impulses to steal items even though the items are not needed for personal use or for their monetary value (Criterion A). The individual experiences a rising subjective sense of tension before the theft (Criterion B) and feels pleasure, gratification, or relief when committing the theft (Criterion C). The stealing is not committed to express anger or vengeance, is not done in response to a delusion or hallucination (Criterion D), and is not better explained by conduct disorder, a manic episode, or antisocial personality disorder (Criterion E). The objects are stolen despite the fact that they are typically of little value to the individual, who could have afforded to pay for them and often gives them away or discards them. Occasionally the individual may hoard the stolen objects or surreptitiously return them. Although individuals with this disorder will generally avoid stealing when immediate arrest is probable (e.g., in full view of a police officer), they usually do not preplan the thefts or fully take into account the chances of apprehension. The stealing is done without assistance from, or collaboration with, others.

Associated Features Supporting Diagnosis

Individuals with kleptomania typically attempt to resist the impulse to steal, and they are aware that the act is wrong and senseless. The individual frequently fears being apprehended and often feels depressed or guilty about the thefts. Neurotransmitter pathways associated with behavioral addictions, including those associated with the serotonin, dopamine, and opioid systems, appear to play a role in kleptomania as well.

Prevalence

Kleptomania occurs in about 4%–24% of individuals arrested for shoplifting. Its prevalence in the general population is very rare, at approximately 0.3%–0.6%. Females outnumber males at a ratio of 3:1.

Development and Course

Age at onset of kleptomania is variable, but the disorder often begins in adolescence. However, the disorder may begin in childhood, adolescence, or adulthood, and in rare cases in late adulthood. There is little systematic information on the course of kleptomania, but three typical courses have been described: sporadic with brief episodes and long periods of remission; episodic with protracted periods of stealing and periods of remission; and chronic with some degree of fluctuation. The disorder may continue for years, despite multiple convictions for shoplifting.

Risk and Prognostic Factors

Genetic and physiological. There are no controlled family history studies of kleptomania. However, first-degree relatives of individuals with kleptomania may have higher rates of obsessive-compulsive disorder than the general population. There also appears to be a higher rate of substance use disorders, including alcohol use disorder, in relatives of individuals with kleptomania than in the general population.

Functional Consequences of Kleptomania

The disorder may cause legal, family, career, and personal difficulties.

Differential Diagnosis

Ordinary theft. Kleptomania should be distinguished from ordinary acts of theft or shoplifting. Ordinary theft (whether planned or impulsive) is deliberate and is motivated by the usefulness of the object or its monetary worth. Some individuals, especially adolescents, may also steal on a dare, as an act of rebellion, or as a rite of passage. The diagnosis is not made unless other characteristic features of kleptomania are also present. Kleptomania is exceedingly rare, whereas shoplifting is relatively common.

Malingering. In malingering, individuals may simulate the symptoms of kleptomania to avoid criminal prosecution.

Antisocial personality disorder and conduct disorder. Antisocial personality disorder and conduct disorder are distinguished from kleptomania by a general pattern of antisocial behavior.

Manic episodes, psychotic episodes, and major neurocognitive disorder. Kleptomania should be distinguished from intentional or inadvertent stealing that may occur during a manic episode, in response to delusions or hallucinations (as in, e.g., schizophrenia), or as a result of a major neurocognitive disorder.

Comorbidity

Kleptomania may be associated with compulsive buying as well as with depressive and bipolar disorders (especially major depressive disorder), anxiety disorders, eating disorders (particularly bulimia nervosa), personality disorders, substance use disorders (especially alcohol use disorder), and other disruptive, impulse-control, and conduct disorders.

Other Specified Disruptive, Impulse-Control, and Conduct Disorder

312.89 (F91.8)

This category applies to presentations in which symptoms characteristic of a disruptive, impulse-control, and conduct 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 disruptive, impulse-control, and conduct disorders diagnostic class. The other specified disruptive, impulse-control, and conduct 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 disruptive, impulse-control, and conduct disorder. This is done by recording "other specified disruptive, impulse-control, and conduct disorder" followed by the specific reason (e.g., "recurrent behavioral outbursts of insufficient frequency").

Unspecified Disruptive, Impulse-Control, and Conduct Disorder

312.9 (F91.9)

This category applies to presentations in which symptoms characteristic of a disruptive, impulse-control, and conduct 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 disruptive, impulse-control, and conduct disorders diagnostic class. The unspecified disruptive, impulse-control, and conduct 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 disruptive, impulse-control, and conduct disorder, and includes presentations in which there is insufficient information to make a more specific diagnosis (e.g., in emergency room settings).

Substance-Related and Addictive Disorders

The substance-related disorders encompass 10 separate classes of drugs: alcohol; caffeine; cannabis; hallucinogens (with separate categories for phencyclidine [or similarly acting arylcyclohexylamines] and other hallucinogens); inhalants; opioids; sedatives, hypnotics, and anxiolytics; stimulants (amphetamine-type substances, cocaine, and other stimulants); tobacco; and other (or unknown) substances. These 10 classes are not fully distinct. All drugs that are taken in excess have in common direct activation of the brain reward system, which is involved in the reinforcement of behaviors and the production of memories. They produce such an intense activation of the reward system that normal activities may be neglected. Instead of achieving reward system activation through adaptive behaviors, drugs of abuse directly activate the reward pathways. The pharmacological mechanisms by which each class of drugs produces reward are different, but the drugs typically activate the system and produce feelings of pleasure, often referred to as a "high." Furthermore, individuals with lower levels of self-control, which may reflect impairments of brain inhibitory mechanisms, may be particularly predisposed to develop substance use disorders, suggesting that the roots of substance use disorders for some persons can be seen in behaviors long before the onset of actual substance use itself.

In addition to the substance-related disorders, this chapter also includes gambling disorder, reflecting evidence that gambling behaviors activate reward systems similar to those activated by drugs of abuse and produce some behavioral symptoms that appear comparable to those produced by the substance use disorders. Other excessive behavioral patterns, such as Internet gaming, have also been described, but the research on these and other behavioral syndromes is less clear. Thus, groups of repetitive behaviors, which some term *behavioral addictions,* with such subcategories as "sex addiction," "exercise addiction," or "shopping addiction," are not included because at this time there is insufficient peer-reviewed evidence to establish the diagnostic criteria and course descriptions needed to identify these behaviors as mental disorders.

The substance-related disorders are divided into two groups: substance use disorders and substance-induced disorders. The following conditions may be classified as substance-induced: intoxication, withdrawal, and other substance/medication-induced mental disorders (psychotic disorders, bipolar and related disorders, depressive disorders, anxiety disorders, obsessive-compulsive and related disorders, sleep disorders, sexual dysfunctions, delirium, and neurocognitive disorders).

The current section begins with a general discussion of criteria sets for a substance use disorder, substance intoxication and withdrawal, and other substance/medication-induced mental disorders, at least some of which are applicable across classes of substances. Reflecting some unique aspects of the 10 substance classes relevant to this chapter, the remainder of the chapter is organized by the class of substance and describes their unique aspects. To facilitate differential diagnosis, the text and criteria for the remaining substance/medication-induced mental disorders are included with disorders with which they share phenomenology (e.g., substance/medication-induced depressive disorder is in the chapter "Depressive Disorders"). The broad diagnostic categories associated with each specific group of substances are shown in Table 1.

TABLE 1 Diagnoses associated with substance class

	Psychotic disorders	Bipolar disorders	Depressive disorders	Anxiety disorders	Obsessive-compulsive and related disorders	Sleep disorders	Sexual dysfunctions	Delirium	Neurocognitive disorders	Substance use disorders	Substance intoxication	Substance withdrawal
Alcohol	I/W	I/W	I/W	I/W		I/W	I/W	I/W	I/W/P	X	X	X
Caffeine				I		I/W					X	X
Cannabis	I			I		I/W		I		X	X	X
Hallucinogens												
Phencyclidine	I	I	I	I				I		X	X	
Other hallucinogens	I*	I	I	I				I		X	X	
Inhalants	I		I	I				I	I/P	X	X	
Opioids			I/W	W		I/W	I/W	I/W		X	X	X
Sedatives, hypnotics, or anxiolytics	I/W	I/W	I/W	W		I/W	I/W	I/W	I/W/P	X	X	X
Stimulants**	I	I/W	I/W	I/W	I/W	I/W	I	I		X	X	X
Tobacco						W				X		X
Other (or unknown)	I/W	I/W	I/W	I/W	I/W	I/W	I/W	I/W	I/W/P	X	X	X

Note. X = The category is recognized in DSM-5.
I = The specifier "with onset during intoxication" may be noted for the category.
W = The specifier "with onset during withdrawal" may be noted for the category.
I/W = Either "with onset during intoxication" or "with onset during withdrawal" may be noted for the category.
P = The disorder is persisting.
*Also hallucinogen persisting perception disorder (flashbacks).
**Includes amphetamine-type substances, cocaine, and other or unspecified stimulants.

Substance-Related Disorders

Substance Use Disorders

Features

The essential feature of a substance use disorder is a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems. As seen in Table 1, the diagnosis of a substance use disorder can be applied to all 10 classes included in this chapter except caffeine. For certain classes some symptoms are less salient, and in a few instances not all symptoms apply (e.g., withdrawal symptoms are not specified for phencyclidine use disorder, other hallucinogen use disorder, or inhalant use disorder).

An important characteristic of substance use disorders is an underlying change in brain circuits that may persist beyond detoxification, particularly in individuals with severe disorders. The behavioral effects of these brain changes may be exhibited in the repeated relapses and intense drug craving when the individuals are exposed to drug-related stimuli. These persistent drug effects may benefit from long-term approaches to treatment.

Overall, the diagnosis of a substance use disorder is based on a pathological pattern of behaviors related to use of the substance. To assist with organization, Criterion A criteria can be considered to fit within overall groupings of *impaired control, social impairment, risky use,* and *pharmacological criteria.* Impaired control over substance use is the first criteria grouping (Criteria 1–4). The individual may take the substance in larger amounts or over a longer period than was originally intended (Criterion 1). The individual may express a persistent desire to cut down or regulate substance use and may report multiple unsuccessful efforts to decrease or discontinue use (Criterion 2). The individual may spend a great deal of time obtaining the substance, using the substance, or recovering from its effects (Criterion 3). In some instances of more severe substance use disorders, virtually all of the individual's daily activities revolve around the substance. Craving (Criterion 4) is manifested by an intense desire or urge for the drug that may occur at any time but is more likely when in an environment where the drug previously was obtained or used. Craving has also been shown to involve classical conditioning and is associated with activation of specific reward structures in the brain. Craving is queried by asking if there has ever been a time when they had such strong urges to take the drug that they could not think of anything else. Current craving is often used as a treatment outcome measure because it may be a signal of impending relapse.

Social impairment is the second grouping of criteria (Criteria 5–7). Recurrent substance use may result in a failure to fulfill major role obligations at work, school, or home (Criterion 5). The individual may continue substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (Criterion 6). Important social, occupational, or recreational activities may be given up or reduced because of substance use (Criterion 7). The individual may withdraw from family activities and hobbies in order to use the substance.

Risky use of the substance is the third grouping of criteria (Criteria 8–9). This may take the form of recurrent substance use in situations in which it is physically hazardous (Criterion 8). The individual may continue substance use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (Criterion 9). The key issue in evaluating this criterion is not the existence of the problem, but rather the individual's failure to abstain from using the substance despite the difficulty it is causing.

Pharmacological criteria are the final grouping (Criteria 10 and 11). Tolerance (Criterion 10) is signaled by requiring a markedly increased dose of the substance to achieve the desired effect or a markedly reduced effect when the usual dose is consumed. The degree to which tolerance develops varies greatly across different individuals as well as across substances and may involve a variety of central nervous system effects. For example, tolerance to respiratory depression and tolerance to sedating and motor coordination may develop at different rates, depending on the substance. Tolerance may be difficult to determine by history alone, and laboratory tests may be helpful (e.g., high blood levels of the substance coupled with little evidence of intoxication suggest that tolerance is likely). Tolerance must also be distinguished from individual variability in the initial sensitivity to the effects of particular substances. For example, some first-time alcohol drinkers show very little evidence of intoxication with three or four drinks, whereas others of similar weight and drinking histories have slurred speech and incoordination.

Withdrawal (Criterion 11) is a syndrome that occurs when blood or tissue concentrations of a substance decline in an individual who had maintained prolonged heavy use of the substance. After developing withdrawal symptoms, the individual is likely to consume the substance to relieve the symptoms. Withdrawal symptoms vary greatly across the classes of substances, and separate criteria sets for withdrawal are provided for the drug classes. Marked and generally easily measured physiological signs of withdrawal are common with alcohol, opioids, and sedatives, hypnotics, and anxiolytics. Withdrawal signs and symptoms with stimulants (amphetamines and cocaine), as well as tobacco and cannabis, are often present but may be less apparent. Significant withdrawal has *not* been documented in humans after repeated use of phencyclidine, other hallucinogens, and inhalants; therefore, this criterion is not included for these substances. Neither tolerance nor withdrawal is necessary for a diagnosis of a substance use disorder. However, for most classes of substances, a past history of withdrawal is associated with a more severe clinical course (i.e., an earlier onset of a substance use disorder, higher levels of substance intake, and a greater number of substance-related problems).

Symptoms of tolerance and withdrawal occurring during appropriate medical treatment with prescribed medications (e.g., opioid analgesics, sedatives, stimulants) are specifically *not* counted when diagnosing a substance use disorder. The appearance of normal, expected pharmacological tolerance and withdrawal during the course of medical treatment has been known to lead to an erroneous diagnosis of "addiction" even when these were the only symptoms present. Individuals whose *only* symptoms are those that occur as a result of medical treatment (i.e., tolerance and withdrawal as part of medical care when the medications are taken as prescribed) should not receive a diagnosis solely on the basis of these symptoms. However, prescription medications can be used inappropriately, and a substance use disorder can be correctly diagnosed when there are other symptoms of compulsive, drug-seeking behavior.

Severity and Specifiers

Substance use disorders occur in a broad range of severity, from mild to severe, with severity based on the number of symptom criteria endorsed. As a general estimate of severity, a *mild* substance use disorder is suggested by the presence of two to three symptoms, *moderate* by four to five symptoms, and *severe* by six or more symptoms. Changing severity across time is also reflected by reductions or increases in the frequency and/or dose of substance use, as assessed by the individual's own report, report of knowledgeable others, clinician's observations, and biological testing. The following course specifiers and descriptive features specifiers are also available for substance use disorders: "in early remission," "in sustained remission," "on maintenance therapy," and "in a controlled environment." Definitions of each are provided within respective criteria sets.

Recording Procedures for Substance Use Disorders

The clinician should use the code that applies to the class of substances but record the name of the *specific substance.* For example, the clinician should record 304.10 (F13.20) moderate alprazolam use disorder (rather than moderate sedative, hypnotic, or anxiolytic use disorder) or 305.70 (F15.10) mild methamphetamine use disorder (rather than mild stimulant use disorder). For substances that do not fit into any of the classes (e.g., anabolic steroids), the appropriate code for "other substance use disorder" should be used and the specific substance indicated (e.g., 305.90 [F19.10] mild anabolic steroid use disorder). If the substance taken by the individual is unknown, the code for the class "other (or unknown)" should be used (e.g., 304.90 [F19.20] severe unknown substance use disorder). If criteria are met for more than one substance use disorder, all should be diagnosed (e.g., 304.00 [F11.20] severe heroin use disorder; 304.20 [F14.20] moderate cocaine use disorder).

The appropriate ICD-10-CM code for a substance use disorder depends on whether there is a comorbid substance-induced disorder (including intoxication and withdrawal). In the above example, the diagnostic code for moderate alprazolam use disorder, F13.20, reflects the absence of a comorbid alprazolam-induced mental disorder. Because ICD-10-CM codes for substance-induced disorders indicate both the presence (or absence) and severity of the substance use disorder, ICD-10-CM codes for substance use disorders can be used only in the absence of a substance-induced disorder. See the individual substance-specific sections for additional coding information.

Note that the word *addiction* is not applied as a diagnostic term in this classification, although it is in common usage in many countries to describe severe problems related to compulsive and habitual use of substances. The more neutral term *substance use disorder* is used to describe the wide range of the disorder, from a mild form to a severe state of chronically relapsing, compulsive drug taking. Some clinicians will choose to use the word *addiction* to describe more extreme presentations, but the word is omitted from the official DSM-5 substance use disorder diagnostic terminology because of its uncertain definition and its potentially negative connotation.

Substance-Induced Disorders

The overall category of substance-induced disorders includes intoxication, withdrawal, and other substance/medication-induced mental disorders (e.g., substance-induced psychotic disorder, substance-induced depressive disorder).

Substance Intoxication and Withdrawal

Criteria for substance intoxication are included within the substance-specific sections of this chapter. The essential feature is the development of a reversible substance-specific syndrome due to the recent ingestion of a substance (Criterion A). The clinically significant problematic behavioral or psychological changes associated with intoxication (e.g., belligerence, mood lability, impaired judgment) are attributable to the physiological effects of the substance on the central nervous system and develop during or shortly after use of the substance (Criterion B). The symptoms are not attributable to another medical condition and are not better explained by another mental disorder (Criterion D). Substance intoxication is common among those with a substance use disorder but also occurs frequently in individuals without a substance use disorder. This category does *not* apply to tobacco.

The most common changes in intoxication involve disturbances of perception, wakefulness, attention, thinking, judgment, psychomotor behavior, and interpersonal behavior. Short-term, or "acute," intoxications may have different signs and symptoms than

sustained, or "chronic," intoxications. For example, moderate cocaine doses may initially produce gregariousness, but social withdrawal may develop if such doses are frequently repeated over days or weeks.

When used in the physiological sense, the term *intoxication* is broader than substance intoxication as defined here. Many substances may produce physiological or psychological changes that are not necessarily problematic. For example, an individual with tachycardia from substance use has a physiological effect, but if this is the only symptom in the absence of problematic behavior, the diagnosis of intoxication would not apply. Intoxication may sometimes persist beyond the time when the substance is detectable in the body. This may be due to enduring central nervous system effects, the recovery of which takes longer than the time for elimination of the substance. These longer-term effects of intoxication must be distinguished from withdrawal (i.e., symptoms initiated by a decline in blood or tissue concentrations of a substance).

Criteria for substance withdrawal are included within the substance-specific sections of this chapter. The essential feature is the development of a substance-specific problematic behavioral change, with physiological and cognitive concomitants, that is due to the cessation of, or reduction in, heavy and prolonged substance use (Criterion A). The substance-specific syndrome causes clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion C). The symptoms are not due to another medical condition and are not better explained by another mental disorder (Criterion D). Withdrawal is usually, but not always, associated with a substance use disorder. Most individuals with withdrawal have an urge to re-administer the substance to reduce the symptoms.

Route of Administration and Speed of Substance Effects

Routes of administration that produce more rapid and efficient absorption into the bloodstream (e.g., intravenous, smoking, intranasal "snorting") tend to result in a more intense intoxication and an increased likelihood of an escalating pattern of substance use leading to withdrawal. Similarly, rapidly acting substances are more likely than slower-acting substances to produce immediate intoxication.

Duration of Effects

Within the same drug category, relatively short-acting substances tend to have a higher potential for the development of withdrawal than do those with a longer duration of action. However, longer-acting substances tend to have longer withdrawal duration. The half-life of the substance parallels aspects of withdrawal: the longer the duration of action, the longer the time between cessation and the onset of withdrawal symptoms and the longer the withdrawal duration. In general, the longer the acute withdrawal period, the less intense the syndrome tends to be.

Use of Multiple Substances

Substance intoxication and withdrawal often involve several substances used simultaneously or sequentially. In these cases, each diagnosis should be recorded separately.

Associated Laboratory Findings

Laboratory analyses of blood and urine samples can help determine recent use and the specific substances involved. However, a positive laboratory test result does not by itself indicate that the individual has a pattern of substance use that meets criteria for a substance-induced or substance use disorder, and a negative test result does not by itself rule out a diagnosis.

Laboratory tests can be useful in identifying withdrawal. If the individual presents with withdrawal from an unknown substance, laboratory tests may help identify the substance and may also be helpful in differentiating withdrawal from other mental disorders.

In addition, normal functioning in the presence of high blood levels of a substance suggests considerable tolerance.

Development and Course

Individuals ages 18–24 years have relatively high prevalence rates for the use of virtually every substance. Intoxication is usually the initial substance-related disorder and often begins in the teens. Withdrawal can occur at any age as long as the relevant drug has been taken in sufficient doses over an extended period of time.

Recording Procedures for Intoxication and Withdrawal

The clinician should use the code that applies to the class of substances but record the name of the *specific substance*. For example, the clinician should record 292.0 (F13.239) secobarbital withdrawal (rather than sedative, hypnotic, or anxiolytic withdrawal) or 292.89 (F15.129) methamphetamine intoxication (rather than stimulant intoxication). Note that the appropriate ICD-10-CM diagnostic code for intoxication depends on whether there is a comorbid substance use disorder. In this case, the F15.129 code for methamphetamine indicates the presence of a comorbid mild methamphetamine use disorder. If there had been no comorbid methamphetamine use disorder, the diagnostic code would have been F15.929. ICD-10-CM coding rules require that all withdrawal codes imply a comorbid moderate to severe substance use disorder for that substance. In the above case, the code for secobarbital withdrawal (F13.239) indicates the comorbid presence of a moderate to severe secobarbital use disorder. See the coding note for the substance-specific intoxication and withdrawal syndromes for the actual coding options.

For substances that do not fit into any of the classes (e.g., anabolic steroids), the appropriate code for "other substance intoxication" should be used and the specific substance indicated (e.g., 292.89 [F19.929] anabolic steroid intoxication). If the substance taken by the individual is unknown, the code for the class "other (or unknown)" should be used (e.g., 292.89 [F19.929] unknown substance intoxication). If there are symptoms or problems associated with a particular substance but criteria are not met for any of the substance-specific disorders, the unspecified category can be used (e.g., 292.9 [F12.99] unspecified cannabis-related disorder).

As noted above, the substance-related codes in ICD-10-CM combine the substance use disorder aspect of the clinical picture and the substance-induced aspect into a single combined code. Thus, if both heroin withdrawal and moderate heroin use disorder are present, the single code F11.23 is given to cover both presentations. In ICD-9-CM, separate diagnostic codes (292.0 and 304.00) are given to indicate withdrawal and a moderate heroin use disorder, respectively. See the individual substance-specific sections for additional coding information.

Substance/Medication-Induced Mental Disorders

The substance/medication-induced mental disorders are potentially severe, usually temporary, but sometimes persisting central nervous system (CNS) syndromes that develop in the context of the effects of substances of abuse, medications, or several toxins. They are distinguished from the substance use disorders, in which a cluster of cognitive, behavioral, and physiological symptoms contribute to the continued use of a substance despite significant substance-related problems. The substance/medication-induced mental disorders may be induced by the 10 classes of substances that produce substance use disorders, or by a great variety of other medications used in medical treatment. Each substance-induced mental disorder is described in the relevant chapter (e.g., "Depressive Disorders," "Neurocognitive Disorders"), and therefore, only a brief description is offered here. All substance/medication-induced disorders share common characteristics. It is important to recognize these common features to aid in the detection of these disorders. These features are described as follows:

A. The disorder represents a clinically significant symptomatic presentation of a relevant mental disorder.
B. There is evidence from the history, physical examination, or laboratory findings of both of the following:
   1. The disorder developed during or within 1 month of a substance intoxication or withdrawal or taking a medication; and
   2. The involved substance/medication is capable of producing the mental disorder.
C. The disorder is not better explained by an independent mental disorder (i.e., one that is not substance- or medication-induced). Such evidence of an independent mental disorder could include the following:
   1. The disorder preceded the onset of severe intoxication or withdrawal or exposure to the medication; or
   2. The full mental disorder persisted for a substantial period of time (e.g., at least 1 month) after the cessation of acute withdrawal or severe intoxication or taking the medication. This criterion does not apply to substance-induced neurocognitive disorders or hallucinogen persisting perception disorder, which persist beyond the cessation of acute intoxication or withdrawal.
D. The disorder does not occur exclusively during the course of a delirium.
E. The disorder causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Features

Some generalizations can be made regarding the categories of substances capable of producing clinically relevant substance-induced mental disorders. In general, the more sedating drugs (sedative, hypnotics, or anxiolytics, and alcohol) can produce prominent and clinically significant depressive disorders during intoxication, while anxiety conditions are likely to be observed during withdrawal syndromes from these substances. Also, during intoxication, the more stimulating substances (e.g., amphetamines and cocaine) are likely to be associated with substance-induced psychotic disorders and substance-induced anxiety disorders, with substance-induced major depressive episodes observed during withdrawal. Both the more sedating and more stimulating drugs are likely to produce significant but temporary sleep and sexual disturbances. An overview of the relationship between specific categories of substances and specific psychiatric syndromes is presented in Table 1.

The medication-induced conditions include what are often idiosyncratic CNS reactions or relatively extreme examples of side effects for a wide range of medications taken for a variety of medical concerns. These include neurocognitive complications of anesthetics, antihistamines, antihypertensives, and a variety of other medications and toxins (e.g., organophosphates, insecticides, carbon monoxide), as described in the chapter on neurocognitive disorders. Psychotic syndromes may be temporarily experienced in the context of anticholinergic, cardiovascular, and steroid drugs, as well as during use of stimulant-like and depressant-like prescription or over-the-counter drugs. Temporary but severe mood disturbances can be observed with a wide range of medications, including steroids, antihypertensives, disulfiram, and any prescription or over-the-counter depressant or stimulant-like substances. A similar range of medications can be associated with temporary anxiety syndromes, sexual dysfunctions, and conditions of disturbed sleep.

In general, to be considered a substance/medication-induced mental disorder, there must be evidence that the disorder being observed is not likely to be better explained by an independent mental condition. The latter are most likely to be seen if the mental disorder was present before the severe intoxication or withdrawal or medication administration, or, with the exception of several substance-induced persisting disorders listed in Table 1, continued more than 1 month after cessation of acute withdrawal, severe intoxication, or use

of the medications. When symptoms are only observed during a delirium (e.g., alcohol withdrawal delirium), the mental disorder should be diagnosed as a delirium, and the psychiatric syndrome occurring during the delirium should not also be diagnosed separately, as many symptoms (including disturbances in mood, anxiety, and reality testing) are commonly seen during agitated, confused states. The features associated with each relevant major mental disorder are similar whether observed with independent or substance/medication-induced mental disorders. However, individuals with substance/medication-induced mental disorders are likely to also demonstrate the associated features seen with the specific category of substance or medication, as listed in other subsections of this chapter.

Development and Course

Substance-induced mental disorders develop in the context of intoxication or withdrawal from substances of abuse, and medication-induced mental disorders are seen with prescribed or over-the-counter medications that are taken at the suggested doses. Both conditions are usually temporary and likely to disappear within 1 month or so of cessation of acute withdrawal, severe intoxication, or use of the medication. Exceptions to these generalizations occur for certain long-duration substance-induced disorders: substance-associated neurocognitive disorders that relate to conditions such as alcohol-induced neurocognitive disorder, inhalant-induced neurocognitive disorder, and sedative-, hypnotic-, or anxiolytic-induced neurocognitive disorder; and hallucinogen persisting perception disorder ("flashbacks"; see the section "Hallucinogen-Related Disorders" later in this chapter). However, most other substance/medication-induced mental disorders, regardless of the severity of the symptoms, are likely to improve relatively quickly with abstinence and unlikely to remain clinically relevant for more than 1 month after complete cessation of use.

As is true of many consequences of heavy substance use, some individuals are more and others less prone toward specific substance-induced disorders. Similar types of predispositions may make some individuals more likely to develop psychiatric side effects of some types of medications, but not others. However, it is unclear whether individuals with family histories or personal prior histories with independent psychiatric syndromes are more likely to develop the induced syndrome once the consideration is made as to whether the quantity and frequency of the substance was sufficient to lead to the development of a substance-induced syndrome.

There are indications that the intake of substances of abuse or some medications with psychiatric side effects in the context of a preexisting mental disorder is likely to result in an intensification of the preexisting independent syndrome. The risk for substance/medication-induced mental disorders is likely to increase with both the quantity and the frequency of consumption of the relevant substance.

The symptom profiles for the substance/medication-induced mental disorders resemble independent mental disorders. While the symptoms of substance/medication-induced mental disorders can be identical to those of independent mental disorders (e.g., delusions, hallucinations, psychoses, major depressive episodes, anxiety syndromes), and although they can have the same severe consequences (e.g., suicide), most induced mental disorders are likely to improve in a matter of days to weeks of abstinence.

The substance/medication-induced mental disorders are an important part of the differential diagnoses for the independent psychiatric conditions. The importance of recognizing an induced mental disorder is similar to the relevance of identifying the possible role of some medical conditions and medication reactions before diagnosing an independent mental disorder. Symptoms of substance- and medication-induced mental disorders may be identical cross-sectionally to those of independent mental disorders but have different treatments and prognoses from the independent condition.

Functional Consequences of Substance/Medication-Induced Mental Disorders

The same consequences related to the relevant independent mental disorder (e.g., suicide attempts) are likely to apply to the substance/medication-induced mental disorders, but these are likely to disappear within 1 month after abstinence. Similarly, the same functional consequences associated with the relevant substance use disorder are likely to be seen for the substance-induced mental disorders.

Recording Procedures for Substance/Medication-Induced Mental Disorders

Coding notes and separate recording procedures for ICD-9-CM and ICD-10-CM codes for other specific substance/medication-induced mental disorders are provided in other chapters of the manual with disorders with which they share phenomenology (see the substance/medication-induced mental disorders in these chapters: "Schizophrenia Spectrum and Other Psychotic Disorders," "Bipolar and Related Disorders," "Depressive Disorders," "Anxiety Disorders," "Obsessive-Compulsive and Related Disorders," "Sleep-Wake Disorders," "Sexual Dysfunctions," and "Neurocognitive Disorders"). Generally, for ICD-9-CM, if a mental disorder is induced by a substance use disorder, a separate diagnostic code is given for the specific substance use disorder, in addition to the code for the substance/medication-induced mental disorder. For ICD-10-CM, a single code combines the substance-induced mental disorder with the substance use disorder. A separate diagnosis of the comorbid substance use disorder is not given, although the name and severity of the specific substance use disorder (when present) are used when recording the substance/medication-induced mental disorder. ICD-10-CM codes are also provided for situations in which the substance/medication-induced mental disorder is not induced by a substance use disorder (e.g., when a disorder is induced by one-time use of a substance or medication). Additional information needed to record the diagnostic name of the substance/medication-induced mental disorder is provided in the section "Recording Procedures" for each substance/medication-induced mental disorder in its respective chapter.

Alcohol-Related Disorders

Alcohol Use Disorder
Alcohol Intoxication
Alcohol Withdrawal
Other Alcohol-Induced Disorders
Unspecified Alcohol-Related Disorder

Alcohol Use Disorder

Diagnostic Criteria

A. A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Alcohol is often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.

3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.
4. Craving, or a strong desire or urge to use alcohol.
5. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
8. Recurrent alcohol use in situations in which it is physically hazardous.
9. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of alcohol.
11. Withdrawal, as manifested by either of the following:
    a. The characteristic withdrawal syndrome for alcohol (refer to Criteria A and B of the criteria set for alcohol withdrawal, pp. 499–500).
    b. Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms.

Specify if:

In early remission: After full criteria for alcohol use disorder were previously met, none of the criteria for alcohol use disorder have been met for at least 3 months but for less than 12 months (with the exception that Criterion A4, "Craving, or a strong desire or urge to use alcohol," may be met).

In sustained remission: After full criteria for alcohol use disorder were previously met, none of the criteria for alcohol use disorder have been met at any time during a period of 12 months or longer (with the exception that Criterion A4, "Craving, or a strong desire or urge to use alcohol," may be met).

Specify if:

In a controlled environment: This additional specifier is used if the individual is in an environment where access to alcohol is restricted.

Code based on current severity: Note for ICD-10-CM codes: If an alcohol intoxication, alcohol withdrawal, or another alcohol-induced mental disorder is also present, do not use the codes below for alcohol use disorder. Instead, the comorbid alcohol use disorder is indicated in the 4th character of the alcohol-induced disorder code (see the coding note for alcohol intoxication, alcohol withdrawal, or a specific alcohol-induced mental disorder). For example, if there is comorbid alcohol intoxication and alcohol use disorder, only the alcohol intoxication code is given, with the 4th character indicating whether the comorbid alcohol use disorder is mild, moderate, or severe: F10.129 for mild alcohol use disorder with alcohol intoxication or F10.229 for a moderate or severe alcohol use disorder with alcohol intoxication.

Specify current severity:

305.00 (F10.10) Mild: Presence of 2–3 symptoms.

303.90 (F10.20) Moderate: Presence of 4–5 symptoms.

303.90 (F10.20) Severe: Presence of 6 or more symptoms.

Specifiers

"In a controlled environment" applies as a further specifier of remission if the individual is both in remission and in a controlled environment (i.e., in early remission in a controlled environment or in sustained remission in a controlled environment). Examples of these environments are closely supervised and substance-free jails, therapeutic communities, and locked hospital units.

Severity of the disorder is based on the number of diagnostic criteria endorsed. For a given individual, changes in severity of alcohol use disorder across time are also reflected by reductions in the frequency (e.g., days of use per month) and/or dose (e.g., number of standard drinks consumed per day) of alcohol used, as assessed by the individual's self-report, report of knowledgeable others, clinician observations, and, when practical, biological testing (e.g., elevations in blood tests as described in the section "Diagnostic Markers" for this disorder).

Diagnostic Features

Alcohol use disorder is defined by a cluster of behavioral and physical symptoms, which can include withdrawal, tolerance, and craving. Alcohol withdrawal is characterized by withdrawal symptoms that develop approximately 4–12 hours after the reduction of intake following prolonged, heavy alcohol ingestion. Because withdrawal from alcohol can be unpleasant and intense, individuals may continue to consume alcohol despite adverse consequences, often to avoid or to relieve withdrawal symptoms. Some withdrawal symptoms (e.g., sleep problems) can persist at lower intensities for months and can contribute to relapse. Once a pattern of repetitive and intense use develops, individuals with alcohol use disorder may devote substantial periods of time to obtaining and consuming alcoholic beverages.

Craving for alcohol is indicated by a strong desire to drink that makes it difficult to think of anything else and that often results in the onset of drinking. School and job performance may also suffer either from the aftereffects of drinking or from actual intoxication at school or on the job; child care or household responsibilities may be neglected; and alcohol-related absences may occur from school or work. The individual may use alcohol in physically hazardous circumstances (e.g., driving an automobile, swimming, operating machinery while intoxicated). Finally, individuals with an alcohol use disorder may continue to consume alcohol despite the knowledge that continued consumption poses significant physical (e.g., blackouts, liver disease), psychological (e.g., depression), social, or interpersonal problems (e.g., violent arguments with spouse while intoxicated, child abuse).

Associated Features Supporting Diagnosis

Alcohol use disorder is often associated with problems similar to those associated with other substances (e.g., cannabis; cocaine; heroin; amphetamines; sedatives, hypnotics, or anxiolytics). Alcohol may be used to alleviate the unwanted effects of these other substances or to substitute for them when they are not available. Symptoms of conduct problems, depression, anxiety, and insomnia frequently accompany heavy drinking and sometimes precede it.

Repeated intake of high doses of alcohol can affect nearly every organ system, especially the gastrointestinal tract, cardiovascular system, and the central and peripheral nervous systems. Gastrointestinal effects include gastritis, stomach or duodenal ulcers, and, in about 15% of individuals who use alcohol heavily, liver cirrhosis and/or pancreatitis. There is also an increased rate of cancer of the esophagus, stomach, and other parts of the gastrointestinal tract. One of the most commonly associated conditions is low-grade hypertension. Cardiomyopathy and other myopathies are less common but occur at an in-

creased rate among those who drink very heavily. These factors, along with marked increases in levels of triglycerides and low-density lipoprotein cholesterol, contribute to an elevated risk of heart disease. Peripheral neuropathy may be evidenced by muscular weakness, paresthesias, and decreased peripheral sensation. More persistent central nervous system effects include cognitive deficits, severe memory impairment, and degenerative changes in the cerebellum. These effects are related to the direct effects of alcohol or of trauma and to vitamin deficiencies (particularly of the B vitamins, including thiamine). One devastating central nervous system effect is the relatively rare alcohol-induced persisting amnestic disorder, or Wernicke-Korsakoff syndrome, in which the ability to encode new memory is severely impaired. This condition would now be described within the chapter "Neurocognitive Disorders" and would be termed a *substance/medication-induced neurocognitive disorder*.

Alcohol use disorder is an important contributor to suicide risk during severe intoxication and in the context of a temporary alcohol-induced depressive and bipolar disorder. There is an increased rate of suicidal behavior as well as of completed suicide among individuals with the disorder.

Prevalence

Alcohol use disorder is a common disorder. In the United States, the 12-month prevalence of alcohol use disorder is estimated to be 4.6% among 12- to 17-year-olds and 8.5% among adults age 18 years and older in the United States. Rates of the disorder are greater among adult men (12.4%) than among adult women (4.9%). Twelve-month prevalence of alcohol use disorder among adults decreases in middle age, being greatest among individuals 18- to 29-years-old (16.2%) and lowest among individuals age 65 years and older (1.5%).

Twelve-month prevalence varies markedly across race/ethnic subgroups of the U.S. population. For 12- to 17-year-olds, rates are greatest among Hispanics (6.0%) and Native Americans and Alaska Natives (5.7%) relative to whites (5.0%), African Americans (1.8%), and Asian Americans and Pacific Islanders (1.6%). In contrast, among adults, the 12-month prevalence of alcohol use disorder is clearly greater among Native Americans and Alaska Natives (12.1%) than among whites (8.9%), Hispanics (7.9%), African Americans (6.9%), and Asian Americans and Pacific Islanders (4.5%).

Development and Course

The first episode of alcohol intoxication is likely to occur during the mid-teens. Alcohol-related problems that do not meet full criteria for a use disorder or isolated problems may occur prior to age 20 years, but the age at onset of an alcohol use disorder with two or more of the criteria clustered together peaks in the late teens or early to mid 20s. The large majority of individuals who develop alcohol-related disorders do so by their late 30s. The first evidence of withdrawal is not likely to appear until after many other aspects of an alcohol use disorder have developed. An earlier onset of alcohol use disorder is observed in adolescents with preexisting conduct problems and those with an earlier onset of intoxication.

Alcohol use disorder has a variable course that is characterized by periods of remission and relapse. A decision to stop drinking, often in response to a crisis, is likely to be followed by a period of weeks or more of abstinence, which is often followed by limited periods of controlled or nonproblematic drinking. However, once alcohol intake resumes, it is highly likely that consumption will rapidly escalate and that severe problems will once again develop.

Alcohol use disorder is often erroneously perceived as an intractable condition, perhaps based on the fact that individuals who present for treatment typically have a history of many years of severe alcohol-related problems. However, these most severe cases represent only a small proportion of individuals with this disorder, and the typical individual with the disorder has a much more promising prognosis.

Among adolescents, conduct disorder and repeated antisocial behavior often co-occur with alcohol- and with other substance-related disorders. While most individuals with alcohol use disorder develop the condition before age 40 years, perhaps 10% have later onset. Age-related physical changes in older individuals result in increased brain susceptibility to the depressant effects of alcohol; decreased rates of liver metabolism of a variety of substances, including alcohol; and decreased percentages of body water. These changes can cause older people to develop more severe intoxication and subsequent problems at lower levels of consumption. Alcohol-related problems in older people are also especially likely to be associated with other medical complications.

Risk and Prognostic Factors

Environmental. Environmental risk and prognostic factors may include cultural attitudes toward drinking and intoxication, the availability of alcohol (including price), acquired personal experiences with alcohol, and stress levels. Additional potential mediators of how alcohol problems develop in predisposed individuals include heavier peer substance use, exaggerated positive expectations of the effects of alcohol, and suboptimal ways of coping with stress.

Genetic and physiological. Alcohol use disorder runs in families, with 40%–60% of the variance of risk explained by genetic influences. The rate of this condition is three to four times higher in close relatives of individuals with alcohol use disorder, with values highest for individuals with a greater number of affected relatives, closer genetic relationships to the affected person, and higher severity of the alcohol-related problems in those relatives. A significantly higher rate of alcohol use disorders exists in the monozygotic twin than in the dizygotic twin of an individual with the condition. A three- to fourfold increase in risk has been observed in children of individuals with alcohol use disorder, even when these children were given up for adoption at birth and raised by adoptive parents who did not have the disorder.

Recent advances in our understanding of genes that operate through intermediate characteristics (or phenotypes) to affect the risk of alcohol use disorder can help to identify individuals who might be at particularly low or high risk for alcohol use disorder. Among the low-risk phenotypes are the acute alcohol-related skin flush (seen most prominently in Asians). High vulnerability is associated with preexisting schizophrenia or bipolar disorder, as well as impulsivity (producing enhanced rates of all substance use disorders and gambling disorder), and a high risk specifically for alcohol use disorder is associated with a low level of response (low sensitivity) to alcohol. A number of gene variations may account for low response to alcohol or modulate the dopamine reward systems; it is important to note, however, that any one gene variation is likely to explain only 1%–2% of the risk for these disorders.

Course modifiers. In general, high levels of impulsivity are associated with an earlier onset and more severe alcohol use disorder.

Culture-Related Diagnostic Issues

In most cultures, alcohol is the most frequently used intoxicating substance and contributes to considerable morbidity and mortality. An estimated 3.8% of all global deaths and 4.6% of global disability-adjusted life-years are attributable to alcohol. In the United States, 80% of adults (age 18 years and older) have consumed alcohol at some time in their lives, and 65% are current drinkers (last 12 months). An estimated 3.6% of the world population (15–64 years old) has a current (12-month) alcohol use disorder, with a lower prevalence (1.1%) found in the African region, a higher rate (5.2%) found in the American region (North, South, and Central America and the Caribbean), and the highest rate (10.9%) found in the Eastern Europe region.

Polymorphisms of genes for the alcohol-metabolizing enzymes alcohol dehydrogenase and aldehyde dehydrogenase are most often seen in Asians and affect the response to alcohol. When consuming alcohol, individuals with these gene variations can experience a flushed face and palpitations, reactions that can be so severe as to limit or preclude future alcohol consumption and diminish the risk for alcohol use disorder. These gene variations are seen in as many as 40% of Japanese, Chinese, Korean, and related groups worldwide and are related to lower risks for the disorder.

Despite small variations regarding individual criterion items, the diagnostic criteria perform equally well across most race/ethnicity groups.

Gender-Related Diagnostic Issues

Males have higher rates of drinking and related disorders than females. However, because females generally weigh less than males, have more fat and less water in their bodies, and metabolize less alcohol in their esophagus and stomach, they are likely to develop higher blood alcohol levels per drink than males. Females who drink heavily may also be more vulnerable than males to some of the physical consequences associated with alcohol, including liver disease.

Diagnostic Markers

Individuals whose heavier drinking places them at elevated risk for alcohol use disorder can be identified both through standardized questionnaires and by elevations in blood test results likely to be seen with regular heavier drinking. These measures do not establish a diagnosis of an alcohol-related disorder but can be useful in highlighting individuals for whom more information should be gathered. The most direct test available to measure alcohol consumption cross-sectionally is *blood alcohol concentration,* which can also be used to judge tolerance to alcohol. For example, an individual with a concentration of 150 mg of ethanol per deciliter (dL) of blood who does not show signs of intoxication can be presumed to have acquired at least some degree of tolerance to alcohol. At 200 mg/dL, most nontolerant individuals demonstrate severe intoxication.

Regarding laboratory tests, one sensitive laboratory indicator of heavy drinking is a modest elevation or high-normal levels (>35 units) of gamma-glutamyltransferase (GGT). This may be the only laboratory finding. At least 70% of individuals with a high GGT level are persistent heavy drinkers (i.e., consuming eight or more drinks daily on a regular basis). A second test with comparable or even higher levels of sensitivity and specificity is carbohydrate-deficient transferrin (CDT), with levels of 20 units or higher useful in identifying individuals who regularly consume eight or more drinks daily. Since both GGT and CDT levels return toward normal within days to weeks of stopping drinking, both state markers may be useful in monitoring abstinence, especially when the clinician observes increases, rather than decreases, in these values over time—a finding indicating that the person is likely to have returned to heavy drinking. The combination of tests for CDT and GGT may have even higher levels of sensitivity and specificity than either test used alone. Additional useful tests include the mean corpuscular volume (MCV), which may be elevated to high-normal values in individuals who drink heavily—a change that is due to the direct toxic effects of alcohol on erythropoiesis. Although the MCV can be used to help identify those who drink heavily, it is a poor method of monitoring abstinence because of the long half-life of red blood cells. Liver function tests (e.g., alanine aminotransferase [ALT] and alkaline phosphatase) can reveal liver injury that is a consequence of heavy drinking. Other potential markers of heavy drinking that are more nonspecific for alcohol but can help the clinician think of the possible effects of alcohol include elevations in blood levels or lipids (e.g., triglycerides and high-density lipoprotein cholesterol) and high-normal levels of uric acid.

Additional diagnostic markers relate to signs and symptoms that reflect the consequences often associated with persistent heavy drinking. For example, dyspepsia, nausea, and bloat-

ing can accompany gastritis, and hepatomegaly, esophageal varices, and hemorrhoids may reflect alcohol-induced changes in the liver. Other physical signs of heavy drinking include tremor, unsteady gait, insomnia, and erectile dysfunction. Males with chronic alcohol use disorder may exhibit decreased testicular size and feminizing effects associated with reduced testosterone levels. Repeated heavy drinking in females is associated with menstrual irregularities and, during pregnancy, spontaneous abortion and fetal alcohol syndrome. Individuals with preexisting histories of epilepsy or severe head trauma are more likely to develop alcohol-related seizures. Alcohol withdrawal may be associated with nausea, vomiting, gastritis, hematemesis, dry mouth, puffy blotchy complexion, and mild peripheral edema.

Functional Consequences of Alcohol Use Disorder

The diagnostic features of alcohol use disorder highlight major areas of life functioning likely to be impaired. These include driving and operating machinery, school and work, interpersonal relationships and communication, and health. Alcohol-related disorders contribute to absenteeism from work, job-related accidents, and low employee productivity. Rates are elevated in homeless individuals, perhaps reflecting a downward spiral in social and occupational functioning, although most individuals with alcohol use disorder continue to live with their families and function within their jobs.

Alcohol use disorder is associated with a significant increase in the risk of accidents, violence, and suicide. It is estimated that one in five intensive care unit admissions in some urban hospitals is related to alcohol and that 40% of individuals in the United States experience an alcohol-related adverse event at some time in their lives, with alcohol accounting for up to 55% of fatal driving events. Severe alcohol use disorder, especially in individuals with antisocial personality disorder, is associated with the commission of criminal acts, including homicide. Severe problematic alcohol use also contributes to disinhibition and feelings of sadness and irritability, which contribute to suicide attempts and completed suicides.

Unanticipated alcohol withdrawal in hospitalized individuals for whom a diagnosis of alcohol use disorder has been overlooked can add to the risks and costs of hospitalization and to time spent in the hospital.

Differential Diagnosis

Nonpathological use of alcohol. The key element of alcohol use disorder is the use of heavy doses of alcohol with resulting repeated and significant distress or impaired functioning. While most drinkers sometimes consume enough alcohol to feel intoxicated, only a minority (less than 20%) ever develop alcohol use disorder. Therefore, drinking, even daily, in low doses and occasional intoxication do not by themselves make this diagnosis.

Sedative, hypnotic, or anxiolytic use disorder. The signs and symptoms of alcohol use disorder are similar to those seen in sedative, hypnotic, or anxiolytic use disorder. The two must be distinguished, however, because the course may be different, especially in relation to medical problems.

Conduct disorder in childhood and adult antisocial personality disorder. Alcohol use disorder, along with other substance use disorders, is seen in the majority of individuals with antisocial personality and preexisting conduct disorder. Because these diagnoses are associated with an early onset of alcohol use disorder as well as a worse prognosis, it is important to establish both conditions.

Comorbidity

Bipolar disorders, schizophrenia, and antisocial personality disorder are associated with a markedly increased rate of alcohol use disorder, and several anxiety and depressive disorders

may relate to alcohol use disorder as well. At least a part of the reported association between depression and moderate to severe alcohol use disorder may be attributable to temporary, alcohol-induced comorbid depressive symptoms resulting from the acute effects of intoxication or withdrawal. Severe, repeated alcohol intoxication may also suppress immune mechanisms and predispose individuals to infections and increase the risk for cancers.

Alcohol Intoxication

Diagnostic Criteria

A. Recent ingestion of alcohol.
B. Clinically significant problematic behavioral or psychological changes (e.g., inappropriate sexual or aggressive behavior, mood lability, impaired judgment) that developed during, or shortly after, alcohol ingestion.
C. One (or more) of the following signs or symptoms developing during, or shortly after, alcohol use:
    1. Slurred speech.
    2. Incoordination.
    3. Unsteady gait.
    4. Nystagmus.
    5. Impairment in attention or memory.
    6. Stupor or coma.
D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance.

Coding note: The ICD-9-CM code is **303.00.** The ICD-10-CM code depends on whether there is a comorbid alcohol use disorder. If a mild alcohol use disorder is comorbid, the ICD-10-CM code is **F10.129,** and if a moderate or severe alcohol use disorder is comorbid, the ICD-10-CM code is **F10.229.** If there is no comorbid alcohol use disorder, then the ICD-10-CM code is **F10.929.**

Diagnostic Features

The essential feature of alcohol intoxication is the presence of clinically significant problematic behavioral or psychological changes (e.g., inappropriate sexual or aggressive behavior, mood lability, impaired judgment, impaired social or occupational functioning) that develop during, or shortly after, alcohol ingestion (Criterion B). These changes are accompanied by evidence of impaired functioning and judgment and, if intoxication is intense, can result in a life-threatening coma. The symptoms must not be attributable to another medical condition (e.g., diabetic ketoacidosis), are not a reflection of conditions such as delirium, and are not related to intoxication with other depressant drugs (e.g., benzodiazepines) (Criterion D). The levels of incoordination can interfere with driving abilities and performance of usual activities to the point of causing accidents. Evidence of alcohol use can be obtained by smelling alcohol on the individual's breath, eliciting a history from the individual or another observer, and, when needed, having the individual provide breath, blood, or urine samples for toxicology analyses.

Associated Features Supporting Diagnosis

Alcohol intoxication is sometimes associated with amnesia for the events that occurred during the course of the intoxication ("blackouts"). This phenomenon may be related to the presence of a high blood alcohol level and, perhaps, to the rapidity with which this level is reached. During even mild alcohol intoxication, different symptoms are likely to be

observed at different time points. Evidence of mild intoxication with alcohol can be seen in most individuals after approximately two drinks (each standard drink is approximately 10–12 grams of ethanol and raises the blood alcohol concentration approximately 20 mg/dL). Early in the drinking period, when blood alcohol levels are rising, symptoms often include talkativeness, a sensation of well-being, and a bright, expansive mood. Later, especially when blood alcohol levels are falling, the individual is likely to become progressively more depressed, withdrawn, and cognitively impaired. At very high blood alcohol levels (e.g., 200–300 mg/dL), an individual who has not developed tolerance for alcohol is likely to fall asleep and enter a first stage of anesthesia. Higher blood alcohol levels (e.g., in excess of 300–400 mg/dL) can cause inhibition of respiration and pulse and even death in nontolerant individuals. The duration of intoxication depends on how much alcohol was consumed over what period of time. In general, the body is able to metabolize approximately one drink per hour, so that the blood alcohol level generally decreases at a rate of 15–20 mg/dL per hour. Signs and symptoms of intoxication are likely to be more intense when the blood alcohol level is rising than when it is falling.

Alcohol intoxication is an important contributor to suicidal behavior. There appears to be an increased rate of suicidal behavior, as well as of completed suicide, among persons intoxicated by alcohol.

Prevalence

The large majority of alcohol consumers are likely to have been intoxicated to some degree at some point in their lives. For example, in 2010, 44% of 12th-grade students admitted to having been "drunk in the past year," with more than 70% of college students reporting the same.

Development and Course

Intoxication usually occurs as an episode usually developing over minutes to hours and typically lasting several hours. In the United States, the average age at first intoxication is approximately 15 years, with the highest prevalence at approximately 18–25 years. Frequency and intensity usually decrease with further advancing age. The earlier the onset of regular intoxication, the greater the likelihood the individual will go on to develop alcohol use disorder.

Risk and Prognostic Factors

Temperamental. Episodes of alcohol intoxication increase with personality characteristics of sensation seeking and impulsivity.

Environmental. Episodes of alcohol intoxication increase with a heavy drinking environment.

Culture-Related Diagnostic Issues

The major issues parallel the cultural differences regarding the use of alcohol overall. Thus, college fraternities and sororities may encourage alcohol intoxication. This condition is also frequent on certain dates of cultural significance (e.g., New Year's Eve) and, for some subgroups, during specific events (e.g., wakes following funerals). Other subgroups encourage drinking at religious celebrations (e.g., Jewish and Catholic holidays), while still others strongly discourage all drinking or intoxication (e.g., some religious groups, such as Mormons, fundamentalist Christians, and Muslims).

Gender-Related Diagnostic Issues

Historically, in many Western societies, acceptance of drinking and drunkenness is more tolerated for males, but such gender differences may be much less prominent in recent years, especially during adolescence and young adulthood.

Diagnostic Markers

Intoxication is usually established by observing an individual's behavior and smelling alcohol on the breath. The degree of intoxication increases with an individual's blood or breath alcohol level and with the ingestion of other substances, especially those with sedating effects.

Functional Consequences of Alcohol Intoxication

Alcohol intoxication contributes to the more than 30,000 alcohol-related drinking deaths in the United States each year. In addition, intoxication with this drug contributes to huge costs associated with drunk driving, lost time from school or work, as well as interpersonal arguments and physical fights.

Differential Diagnosis

Other medical conditions. Several medical (e.g., diabetic acidosis) and neurological conditions (e.g., cerebellar ataxia, multiple sclerosis) can temporarily resemble alcohol intoxication.

Sedative, hypnotic, or anxiolytic intoxication. Intoxication with sedative, hypnotic, or anxiolytic drugs or with other sedating substances (e.g., antihistamines, anticholinergic drugs) can be mistaken for alcohol intoxication. The differential requires observing alcohol on the breath, measuring blood or breath alcohol levels, ordering a medical workup, and gathering a good history. The signs and symptoms of sedative-hypnotic intoxication are very similar to those observed with alcohol and include similar problematic behavioral or psychological changes. These changes are accompanied by evidence of impaired functioning and judgment—which, if intense, can result in a life-threatening coma—and levels of incoordination that can interfere with driving abilities and with performing usual activities. However, there is no smell as there is with alcohol, but there is likely to be evidence of misuse of the depressant drug in the blood or urine toxicology analyses.

Comorbidity

Alcohol intoxication may occur comorbidly with other substance intoxication, especially in individuals with conduct disorder or antisocial personality disorder.

Alcohol Withdrawal

Diagnostic Criteria

A. Cessation of (or reduction in) alcohol use that has been heavy and prolonged.
B. Two (or more) of the following, developing within several hours to a few days after the cessation of (or reduction in) alcohol use described in Criterion A:
   1. Autonomic hyperactivity (e.g., sweating or pulse rate greater than 100 bpm).
   2. Increased hand tremor.
   3. Insomnia.
   4. Nausea or vomiting.
   5. Transient visual, tactile, or auditory hallucinations or illusions.
   6. Psychomotor agitation.
   7. Anxiety.
   8. Generalized tonic-clonic seizures.
C. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

Specify if:

With perceptual disturbances: This specifier applies in the rare instance when hallucinations (usually visual or tactile) occur with intact reality testing, or auditory, visual, or tactile illusions occur in the absence of a delirium.

Coding note: The ICD-9-CM code is **291.81.** The ICD-10-CM code for alcohol withdrawal without perceptual disturbances is **F10.239,** and the ICD-10-CM code for alcohol withdrawal with perceptual disturbances is **F10.232.** Note that the ICD-10-CM code indicates the comorbid presence of a moderate or severe alcohol use disorder, reflecting the fact that alcohol withdrawal can only occur in the presence of a moderate or severe alcohol use disorder. It is not permissible to code a comorbid mild alcohol use disorder with alcohol withdrawal.

Specifiers

When hallucinations occur in the absence of delirium (i.e., in a clear sensorium), a diagnosis of substance/medication-induced psychotic disorder should be considered.

Diagnostic Features

The essential feature of alcohol withdrawal is the presence of a characteristic withdrawal syndrome that develops within several hours to a few days after the cessation of (or reduction in) heavy and prolonged alcohol use (Criteria A and B). The withdrawal syndrome includes two or more of the symptoms reflecting autonomic hyperactivity and anxiety listed in Criterion B, along with gastrointestinal symptoms.

Withdrawal symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion C). The symptoms must not be attributable to another medical condition and are not better explained by another mental disorder (e.g., generalized anxiety disorder), including intoxication or withdrawal from another substance (e.g., sedative, hypnotic, or anxiolytic withdrawal) (Criterion D).

Symptoms can be relieved by administering alcohol or benzodiazepines (e.g., diazepam). The withdrawal symptoms typically begin when blood concentrations of alcohol decline sharply (i.e., within 4–12 hours) after alcohol use has been stopped or reduced. Reflecting the relatively fast metabolism of alcohol, symptoms of alcohol withdrawal usually peak in intensity during the second day of abstinence and are likely to improve markedly by the fourth or fifth day. Following acute withdrawal, however, symptoms of anxiety, insomnia, and autonomic dysfunction may persist for up to 3–6 months at lower levels of intensity.

Fewer than 10% of individuals who develop alcohol withdrawal will ever develop dramatic symptoms (e.g., severe autonomic hyperactivity, tremors, alcohol withdrawal delirium). Tonic-clonic seizures occur in fewer than 3% of individuals.

Associated Features Supporting Diagnosis

Although confusion and changes in consciousness are not core criteria for alcohol withdrawal, alcohol withdrawal delirium (see "Delirium" in the chapter "Neurocognitive Disorders") may occur in the context of withdrawal. As is true for any agitated, confused state, regardless of the cause, in addition to a disturbance of consciousness and cognition, withdrawal delirium can include visual, tactile, or (rarely) auditory hallucinations (delirium tremens). When alcohol withdrawal delirium develops, it is likely that a clinically relevant medical condition may be present (e.g., liver failure, pneumonia, gastrointestinal bleeding, sequelae of head trauma, hypoglycemia, an electrolyte imbalance, postoperative status).

Prevalence

It is estimated that approximately 50% of middle-class, highly functional individuals with alcohol use disorder have ever experienced a full alcohol withdrawal syndrome. Among individuals with alcohol use disorder who are hospitalized or homeless, the rate of alcohol withdrawal may be greater than 80%. Less than 10% of individuals in withdrawal ever demonstrate alcohol withdrawal delirium or withdrawal seizures.

Development and Course

Acute alcohol withdrawal occurs as an episode usually lasting 4–5 days and only after extended periods of heavy drinking. Withdrawal is relatively rare in individuals younger than 30 years, and the risk and severity increase with increasing age.

Risk and Prognostic Factors

Environmental. The probability of developing alcohol withdrawal increases with the quantity and frequency of alcohol consumption. Most individuals with this condition are drinking daily, consuming large amounts (approximately more than eight drinks per day) for multiple days. However, there are large inter-individual differences, with enhanced risks for individuals with concurrent medical conditions, those with family histories of alcohol withdrawal (i.e., a genetic component), those with prior withdrawals, and individuals who consume sedative, hypnotic, or anxiolytic drugs.

Diagnostic Markers

Autonomic hyperactivity in the context of moderately high but falling blood alcohol levels and a history of prolonged heavy drinking indicate a likelihood of alcohol withdrawal.

Functional Consequences of Alcohol Withdrawal

Symptoms of withdrawal may serve to perpetuate drinking behaviors and contribute to relapse, resulting in persistently impaired social and occupational functioning. Symptoms requiring medically supervised detoxification result in hospital utilization and loss of work productivity. Overall, the presence of withdrawal is associated with greater functional impairment and poor prognosis.

Differential Diagnosis

Other medical conditions. The symptoms of alcohol withdrawal can also be mimicked by some medical conditions (e.g., hypoglycemia and diabetic ketoacidosis). Essential tremor, a disorder that frequently runs in families, may erroneously suggest the tremulousness associated with alcohol withdrawal.

Sedative, hypnotic, or anxiolytic withdrawal. Sedative, hypnotic, or anxiolytic withdrawal produces a syndrome very similar to that of alcohol withdrawal.

Comorbidity

Withdrawal is more likely to occur with heavier alcohol intake, and that might be most often observed in individuals with conduct disorder and antisocial personality disorder. Withdrawal states are also more severe in older individuals, individuals who are also dependent on other depressant drugs (sedative-hypnotics), and individuals who have had more alcohol withdrawal experiences in the past.

Other Alcohol-Induced Disorders

The following alcohol-induced disorders are described in other chapters of the manual with disorders with which they share phenomenology (see the substance/medication-induced mental disorders in these chapters): alcohol-induced psychotic disorder ("Schizophrenia Spectrum and Other Psychotic Disorders"); alcohol-induced bipolar disorder ("Bipolar and Related Disorders"); alcohol-induced depressive disorder ("Depressive Disorders"); alcohol-induced anxiety disorder ("Anxiety Disorders"); alcohol-induced sleep disorder ("Sleep-Wake Disorders"); alcohol-induced sexual dysfunction ("Sexual Dysfunctions"); and alcohol-induced major or mild neurocognitive disorder ("Neurocognitive Disorders"). For alcohol intoxication delirium and alcohol withdrawal delirium, see the criteria and discussion of delirium in the chapter "Neurocognitive Disorders." These alcohol-induced disorders are diagnosed instead of alcohol intoxication or alcohol withdrawal only when the symptoms are sufficiently severe to warrant independent clinical attention.

Features

The symptom profiles for an alcohol-induced condition resemble independent mental disorders as described elsewhere in DSM-5. However, the alcohol-induced disorder is temporary and observed after severe intoxication with and/or withdrawal from alcohol. While the symptoms can be identical to those of independent mental disorders (e.g., psychoses, major depressive disorder), and while they can have the same severe consequences (e.g., suicide attempts), alcohol-induced conditions are likely to improve without formal treatment in a matter of days to weeks after cessation of severe intoxication and/or withdrawal.

Each alcohol-induced mental disorder is listed in the relevant diagnostic section and therefore only a brief description is offered here. Alcohol-induced disorders must have developed in the context of severe intoxication and/or withdrawal from the substance capable of producing the mental disorder. In addition, there must be evidence that the disorder being observed is not likely to be better explained by another non-alcohol-induced mental disorder. The latter is likely to occur if the mental disorder was present before the severe intoxication or withdrawal, or continued more than 1 month after the cessation of severe intoxication and/or withdrawal. When symptoms are observed only during a delirium, they should be considered part of the delirium and not diagnosed separately, as many symptoms (including disturbances in mood, anxiety, and reality testing) are commonly seen during agitated, confused states. The alcohol-induced disorder must be clinically relevant, causing significant levels of distress or significant functional impairment. Finally, there are indications that the intake of substances of abuse in the context of a preexisting mental disorder are likely to result in an intensification of the preexisting independent syndrome.

The features associated with each relevant major mental disorder (e.g., psychotic episodes, major depressive disorder) are similar whether observed with an independent or an alcohol-induced condition. However, individuals with alcohol-induced disorders are likely to also demonstrate the associated features seen with an alcohol use disorder, as listed in the subsections of this chapter.

Rates of alcohol-induced disorders vary somewhat by diagnostic category. For example, the lifetime risk for major depressive episodes in individuals with alcohol use disorder is approximately 40%, but only about one-third to one-half of these represent independent major depressive syndromes observed outside the context of intoxication. Similar rates of alcohol-induced sleep and anxiety conditions are likely, but alcohol-induced psychotic episodes are fairly rare.

Development and Course

Once present, the symptoms of an alcohol-induced condition are likely to remain clinically relevant as long as the individual continues to experience severe intoxication and/or with-

drawal. While the symptoms are identical to those of independent mental disorders (e.g., psychoses, major depressive disorder), and while they can have the same severe consequences (e.g., suicide attempts), all alcohol-induced syndromes other than alcohol-induced neurocognitive disorder, amnestic confabulatory type (alcohol-induced persisting amnestic disorder), regardless of the severity of the symptoms, are likely to improve relatively quickly and unlikely to remain clinically relevant for more than 1 month after cessation of severe intoxication and/or withdrawal.

The alcohol-induced disorders are an important part of the differential diagnoses for the independent mental conditions. Independent schizophrenia, major depressive disorder, bipolar disorder, and anxiety disorders, such as panic disorder, are likely to be associated with much longer-lasting periods of symptoms and often require longer-term medications to optimize the probability of improvement or recovery. The alcohol-induced conditions, on the other hand, are likely to be much shorter in duration and disappear within several days to 1 month after cessation of severe intoxication and/or withdrawal, even without psychotropic medications.

The importance of recognizing an alcohol-induced disorder is similar to the relevance of identifying the possible role of some endocrine conditions and medication reactions before diagnosing an independent mental disorder. In light of the high prevalence of alcohol use disorders worldwide, it is important that these alcohol-induced diagnoses be considered before independent mental disorders are diagnosed.

Unspecified Alcohol-Related Disorder

291.9 (F10.99)

This category applies to presentations in which symptoms characteristic of an alcohol-related 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 specific alcohol-related disorder or any of the disorders in the substance-related and addictive disorders diagnostic class.

Caffeine-Related Disorders

Caffeine Intoxication
Caffeine Withdrawal
Other Caffeine-Induced Disorders
Unspecified Caffeine-Related Disorder

Caffeine Intoxication

Diagnostic Criteria **305.90 (F15.929)**

A. Recent consumption of caffeine (typically a high dose well in excess of 250 mg).
B. Five (or more) of the following signs or symptoms developing during, or shortly after, caffeine use:
   1. Restlessness.
   2. Nervousness.

3. Excitement.
4. Insomnia.
5. Flushed face.
6. Diuresis.
7. Gastrointestinal disturbance.
8. Muscle twitching.
9. Rambling flow of thought and speech.
10. Tachycardia or cardiac arrhythmia.
11. Periods of inexhaustibility.
12. Psychomotor agitation.

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

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance.

Diagnostic Features

Caffeine can be consumed from a number of different sources, including coffee, tea, caffeinated soda, "energy" drinks, over-the-counter analgesics and cold remedies, energy aids (e.g., drinks), weight-loss aids, and chocolate. Caffeine is also increasingly being used as an additive to vitamins and to food products. More than 85% of children and adults consume caffeine regularly. Some caffeine users display symptoms consistent with problematic use, including tolerance and withdrawal (see "Caffeine Withdrawal" later in this chapter); the data are not available at this time to determine the clinical significance of a caffeine use disorder and its prevalence. In contrast, there is evidence that caffeine withdrawal and caffeine intoxication are clinically significant and sufficiently prevalent.

The essential feature of caffeine intoxication is recent consumption of caffeine and five or more signs or symptoms that develop during or shortly after caffeine use (Criteria A and B). Symptoms include restlessness, nervousness, excitement, insomnia, flushed face, diuresis, and gastrointestinal complaints, which can occur with low doses (e.g., 200 mg) in vulnerable individuals such as children, the elderly, or individuals who have not been exposed to caffeine previously. Symptoms that generally appear at levels of more than 1 g/day include muscle twitching, rambling flow of thought and speech, tachycardia or cardiac arrhythmia, periods of inexhaustibility, and psychomotor agitation. Caffeine intoxication may not occur despite high caffeine intake because of the development of tolerance. The signs or symptoms must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion C). The signs or symptoms must not be attributable to another medical condition and are not better explained by another mental disorder (e.g., an anxiety disorder) or intoxication with another substance (Criterion D).

Associated Features Supporting Diagnosis

Mild sensory disturbances (e.g., ringing in the ears and flashes of light) may occur with high doses of caffeine. Although large doses of caffeine can increase heart rate, smaller doses can slow heart rate. Whether excess caffeine intake can cause headaches is unclear. On physical examination, agitation, restlessness, sweating, tachycardia, flushed face, and increased bowel motility may be seen. Caffeine blood levels may provide important information for diagnosis, particularly when the individual is a poor historian, although these levels are not diagnostic by themselves in view of the individual variation in response to caffeine.

Prevalence

The prevalence of caffeine intoxication in the general population is unclear. In the United States, approximately 7% of individuals in the population may experience five or more symptoms along with functional impairment consistent with a diagnosis of caffeine intoxication.

Development and Course

Consistent with a half-life of caffeine of approximately 4–6 hours, caffeine intoxication symptoms usually remit within the first day or so and do not have any known long-lasting consequences. However, individuals who consume very high doses of caffeine (i.e., 5–10 g) may require immediate medical attention, as such doses can be lethal.

With advancing age, individuals are likely to demonstrate increasingly intense reactions to caffeine, with greater complaints of interference with sleep or feelings of hyperarousal. Caffeine intoxication among young individuals after consumption of highly caffeinated products, including energy drinks, has been observed. Children and adolescents may be at increased risk for caffeine intoxication because of low body weight, lack of tolerance, and lack of knowledge about the pharmacological effects of caffeine.

Risk and Prognostic Factors

Environmental. Caffeine intoxication is often seen among individuals who use caffeine less frequently or in those who have recently increased their caffeine intake by a substantial amount. Furthermore, oral contraceptives significantly decrease the elimination of caffeine and consequently may increase the risk of intoxication.

Genetic and physiological. Genetic factors may affect risk of caffeine intoxication.

Functional Consequences of Caffeine Intoxication

Impairment from caffeine intoxication may have serious consequences, including dysfunction at work or school, social indiscretions, or failure to fulfill role obligations. Moreover, extremely high doses of caffeine can be fatal. In some cases, caffeine intoxication may precipitate a caffeine-induced disorder.

Differential Diagnosis

Other mental disorders. Caffeine intoxication may be characterized by symptoms (e.g., panic attacks) that resemble primary mental disorders. To meet criteria for caffeine intoxication, the symptoms must not be associated with another medical condition or another mental disorder, such as an anxiety disorder, that could better explain them. Manic episodes; panic disorder; generalized anxiety disorder; amphetamine intoxication; sedative, hypnotic, or anxiolytic withdrawal or tobacco withdrawal; sleep disorders; and medication-induced side effects (e.g., akathisia) can cause a clinical picture that is similar to that of caffeine intoxication.

Other caffeine-induced disorders. The temporal relationship of the symptoms to increased caffeine use or to abstinence from caffeine helps to establish the diagnosis. Caffeine intoxication is differentiated from caffeine-induced anxiety disorder, with onset during intoxication (see "Substance/Medication-Induced Anxiety Disorder" in the chapter "Anxiety Disorders"), and caffeine-induced sleep disorder, with onset during intoxication (see "Substance/Medication-Induced Sleep Disorder" in the chapter "Sleep-Wake Disorders"), by the fact that the symptoms in these latter disorders are in excess of those usually associated with caffeine intoxication and are severe enough to warrant independent clinical attention.

Comorbidity

Typical dietary doses of caffeine have not been consistently associated with medical problems. However, heavy use (e.g., >400 mg) can cause or exacerbate anxiety and somatic symptoms and gastrointestinal distress. With acute, extremely high doses of caffeine, grand mal seizures and respiratory failure may result in death. Excessive caffeine use is associated with depressive disorders, bipolar disorders, eating disorders, psychotic disorders, sleep disorders, and substance-related disorders, whereas individuals with anxiety disorders are more likely to avoid caffeine.

Caffeine Withdrawal

Diagnostic Criteria **292.0 (F15.93)**

A. Prolonged daily use of caffeine.

B. Abrupt cessation of or reduction in caffeine use, followed within 24 hours by three (or more) of the following signs or symptoms:

   1. Headache.
   2. Marked fatigue or drowsiness.
   3. Dysphoric mood, depressed mood, or irritability.
   4. Difficulty concentrating.
   5. Flu-like symptoms (nausea, vomiting, or muscle pain/stiffness).

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

D. The signs or symptoms are not associated with the physiological effects of another medical condition (e.g., migraine, viral illness) and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

Diagnostic Features

The essential feature of caffeine withdrawal is the presence of a characteristic withdrawal syndrome that develops after the abrupt cessation of (or substantial reduction in) prolonged daily caffeine ingestion (Criterion B). The caffeine withdrawal syndrome is indicated by three or more of the following (Criterion B): headache; marked fatigue or drowsiness; dysphoric mood, depressed mood, or irritability; difficulty concentrating; and flu-like symptoms (nausea, vomiting, or muscle pain/stiffness). The withdrawal syndrome causes clinical significant distress or impairment in social, occupational, or other important areas of functioning (Criterion C). The symptoms must not be associated with the physiological effects of another medical condition and are not better explained by another mental disorder (Criterion D).

Headache is the hallmark feature of caffeine withdrawal and may be diffuse, gradual in development, throbbing, severe, and sensitive to movement. However, other symptoms of caffeine withdrawal can occur in the absence of headache. Caffeine is the most widely used behaviorally active drug in the world and is present in many different types of beverages (e.g., coffee, tea, maté, soft drinks, energy drinks), foods, energy aids, medications, and dietary supplements. Because caffeine ingestion is often integrated into social customs and daily rituals (e.g., coffee break, tea time), some caffeine consumers may be unaware of their physical dependence on caffeine. Thus, caffeine withdrawal symptoms could be unexpected and misattributed to other causes (e.g., the flu, migraine). Furthermore, caffeine withdrawal symptoms may occur when individuals are required to abstain from foods and beverages prior to medical procedures or when a usual caffeine dose is missed because of a change in routine (e.g., during travel, weekends).

The probability and severity of caffeine withdrawal generally increase as a function of usual daily caffeine dose. However, there is large variability among individuals and within individuals across different episodes in the incidence, severity, and time course of withdrawal symptoms. Caffeine withdrawal symptoms may occur after abrupt cessation of relatively low chronic daily doses of caffeine (i.e., 100 mg).

Associated Features Supporting Diagnosis

Caffeine abstinence has been shown to be associated with impaired behavioral and cognitive performance (e.g., sustained attention). Electroencephalographic studies have shown that caffeine withdrawal symptoms are significantly associated with increases in theta power and decreases in beta-2 power. Decreased motivation to work and decreased sociability have also been reported during caffeine withdrawal. Increased analgesic use during caffeine withdrawal has been documented.

Prevalence

More than 85% of adults and children in the United States regularly consume caffeine, with adult caffeine consumers ingesting about 280 mg/day on average. The incidence and prevalence of the caffeine withdrawal syndrome in the general population are unclear. In the United States, headache may occur in approximately 50% of cases of caffeine abstinence. In attempts to permanently stop caffeine use, more than 70% of individuals may experience at least one caffeine withdrawal symptom (47% may experience headache), and 24% may experience headache plus one or more other symptoms as well as functional impairment due to withdrawal. Among individuals who abstain from caffeine for at least 24 hours but are not trying to permanently stop caffeine use, 11% may experience headache plus one or more other symptoms as well as functional impairment. Caffeine consumers can decrease the incidence of caffeine withdrawal by using caffeine daily or only infrequently (e.g., no more than 2 consecutive days). Gradual reduction in caffeine over a period of days or weeks may decrease the incidence and severity of caffeine withdrawal.

Development and Course

Symptoms usually begin 12–24 hours after the last caffeine dose and peak after 1–2 days of abstinence. Caffeine withdrawal symptoms last for 2–9 days, with the possibility of withdrawal headaches occurring for up to 21 days. Symptoms usually remit rapidly (within 30–60 minutes) after re-ingestion of caffeine.

Caffeine is unique in that it is a behaviorally active drug that is consumed by individuals of nearly all ages. Rates of caffeine consumption and overall level of caffeine consumption increase with age until the early to mid-30s and then level off. Although caffeine withdrawal among children and adolescents has been documented, relatively little is known about risk factors for caffeine withdrawal among this age group. The use of highly caffeinated energy drinks is increasing with in young individuals, which could increase the risk for caffeine withdrawal.

Risk and Prognostic Factors

Temperamental. Heavy caffeine use has been observed among individuals with mental disorders, including eating disorders; smokers; prisoners; and drug and alcohol abusers. Thus, these individuals could be at higher risk for caffeine withdrawal upon acute caffeine abstinence.

Environmental. The unavailability of caffeine is an environmental risk factor for incipient withdrawal symptoms. While caffeine is legal and usually widely available, there are conditions in which caffeine use may be restricted, such as during medical procedures, pregnancy, hospitalizations, religious observances, wartime, travel, and research partici-

pation. These external environmental circumstances may precipitate a withdrawal syndrome in vulnerable individuals.

Genetic and physiological factors. Genetic factors appear to increase vulnerability to caffeine withdrawal, but no specific genes have been identified.

Course modifiers. Caffeine withdrawal symptoms usually remit within 30–60 minutes of reexposure to caffeine. Doses of caffeine significantly less than one's usual daily dose may be sufficient to prevent or attenuate caffeine withdrawal symptoms (e.g., consumption of 25 mg by an individual who typically consumes 300 mg).

Culture-Related Diagnostic Issues

Habitual caffeine consumers who fast for religious reasons may be at increased risk for caffeine withdrawal.

Functional Consequences of Caffeine Withdrawal Disorder

Caffeine withdrawal symptoms can vary from mild to extreme, at times causing functional impairment in normal daily activities. Rates of functional impairment range from 10% to 55% (median 13%), with rates as high as 73% found among individuals who also show other problematic features of caffeine use. Examples of functional impairment include being unable to work, exercise, or care for children; staying in bed all day; missing religious services; ending a vacation early; and cancelling a social gathering. Caffeine withdrawal headaches may be described by individuals as "the worst headaches" ever experienced. Decrements in cognitive and motor performance have also been observed.

Differential Diagnosis

Other medical disorders and medical side effects. Several disorders should be considered in the differential diagnosis of caffeine withdrawal. Caffeine withdrawal can mimic migraine and other headache disorders, viral illnesses, sinus conditions, tension, other drug withdrawal states (e.g., from amphetamines, cocaine), and medication side effects. The final determination of caffeine withdrawal should rest on a determination of the pattern and amount consumed, the time interval between caffeine abstinence and onset of symptoms, and the particular clinical features presented by the individual. A challenge dose of caffeine followed by symptom remission may be used to confirm the diagnosis.

Comorbidity

Caffeine withdrawal may be associated with major depressive disorder, generalized anxiety disorder, panic disorder, antisocial personality disorder in adults, moderate to severe alcohol use disorder, and cannabis and cocaine use.

Other Caffeine-Induced Disorders

The following caffeine-induced disorders are described in other chapters of the manual with disorders with which they share phenomenology (see the substance/medication-induced mental disorders in these chapters): caffeine-induced anxiety disorder ("Anxiety Disorders") and caffeine-induced sleep disorder ("Sleep-Wake Disorders"). These caffeine-induced disorders are diagnosed instead of caffeine intoxication or caffeine withdrawal only when the symptoms are sufficiently severe to warrant independent clinical attention.

Unspecified Caffeine-Related Disorder

292.9 (F15.99)

This category applies to presentations in which symptoms characteristic of a caffeine-related 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 specific caffeine-related disorder or any of the disorders in the substance-related and addictive disorders diagnostic class.

Cannabis-Related Disorders

Cannabis Use Disorder
Cannabis Intoxication
Cannabis Withdrawal
Other Cannabis-Induced Disorders
Unspecified Cannabis-Related Disorder

Cannabis Use Disorder

Diagnostic Criteria

A. A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:
   1. Cannabis is often taken in larger amounts or over a longer period than was intended.
   2. There is a persistent desire or unsuccessful efforts to cut down or control cannabis use.
   3. A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.
   4. Craving, or a strong desire or urge to use cannabis.
   5. Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school, or home.
   6. Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.
   7. Important social, occupational, or recreational activities are given up or reduced because of cannabis use.
   8. Recurrent cannabis use in situations in which it is physically hazardous.
   9. Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis.
   10. Tolerance, as defined by either of the following:
      a. A need for markedly increased amounts of cannabis to achieve intoxication or desired effect.
      b. Markedly diminished effect with continued use of the same amount of cannabis.
   11. Withdrawal, as manifested by either of the following:
      a. The characteristic withdrawal syndrome for cannabis (refer to Criteria A and B of the criteria set for cannabis withdrawal, pp. 517–518).

b. Cannabis (or a closely related substance) is taken to relieve or avoid withdrawal symptoms.

Specify if:

In early remission: After full criteria for cannabis use disorder were previously met, none of the criteria for cannabis use disorder have been met for at least 3 months but for less than 12 months (with the exception that Criterion A4, "Craving, or a strong desire or urge to use cannabis," may be met).

In sustained remission: After full criteria for cannabis use disorder were previously met, none of the criteria for cannabis use disorder have been met at any time during a period of 12 months or longer (with the exception that Criterion A4, "Craving, or a strong desire or urge to use cannabis," may be present).

Specify if:

In a controlled environment: This additional specifier is used if the individual is in an environment where access to cannabis is restricted.

Code based on current severity: Note for ICD-10-CM codes: If a cannabis intoxication, cannabis withdrawal, or another cannabis-induced mental disorder is also present, do not use the codes below for cannabis use disorder. Instead, the comorbid cannabis use disorder is indicated in the 4th character of the cannabis-induced disorder code (see the coding note for cannabis intoxication, cannabis withdrawal, or a specific cannabis-induced mental disorder). For example, if there is comorbid cannabis-induced anxiety disorder and cannabis use disorder, only the cannabis-induced anxiety disorder code is given, with the 4th character indicating whether the comorbid cannabis use disorder is mild, moderate, or severe: F12.180 for mild cannabis use disorder with cannabis-induced anxiety disorder or F12.280 for a moderate or severe cannabis use disorder with cannabis-induced anxiety disorder.

Specify current severity:

305.20 (F12.10) Mild: Presence of 2–3 symptoms.

304.30 (F12.20) Moderate: Presence of 4–5 symptoms.

304.30 (F12.20) Severe: Presence of 6 or more symptoms.

Specifiers

"In a controlled environment" applies as a further specifier of remission if the individual is both in remission and in a controlled environment (i.e., in early remission in a controlled environment or in sustained remission in a controlled environment). Examples of these environments are closely supervised and substance-free jails, therapeutic communities, and locked hospital units.

Changing severity across time in an individual may also be reflected by changes in the frequency (e.g., days of use per month or times used per day) and/or dose (e.g., amount used per episode) of cannabis, as assessed by individual self-report, report of knowledgeable others, clinician's observations, and biological testing.

Diagnostic Features

Cannabis use disorder and the other cannabis-related disorders include problems that are associated with substances derived from the cannabis plant and chemically similar synthetic compounds. Over time, this plant material has accumulated many names (e.g., weed, pot, herb, grass, reefer, mary jane, dagga, dope, bhang, skunk, boom, gangster, kif, and ganja). A concentrated extraction of the cannabis plant that is also commonly used is hashish. *Cannabis* is the generic and perhaps the most appropriate scientific term for the psychoactive substance(s) derived from the plant, and as such it is used in this manual to refer to all forms of cannabis-like substances, including synthetic cannabinoid compounds.

Synthetic oral formulations (pill/capsules) of delta-9-tetrahydrocannabinol (delta-9-THC) are available by prescription for a number of approved medical indications (e.g., for nausea and vomiting caused by chemotherapy; for anorexia and weight loss in individuals with AIDS). Other synthetic cannabinoid compounds have been manufactured and distributed for nonmedical use in the form of plant material that has been sprayed with a cannabinoid formulation (e.g., K2, Spice, JWH-018, JWH-073).

The cannabinoids have diverse effects in the brain, prominent among which are actions on CB1 and CB2 cannabinoid receptors that are found throughout the central nervous system. Endogenous ligands for these receptors behave essentially like neurotransmitters. The potency of cannabis (delta-9-THC concentration) that is generally available varies greatly, ranging from 1% to approximately 15% in typical cannabis plant material and 10%–20% in hashish. During the past two decades, a steady increase in the potency of seized cannabis has been observed.

Cannabis is most commonly smoked via a variety of methods: pipes, water pipes (bongs or hookahs), cigarettes (joints or reefers), or, most recently, in the paper from hollowed out cigars (blunts). Cannabis is also sometimes ingested orally, typically by mixing it into food. More recently, devices have been developed in which cannabis is "vaporized." Vaporization involves heating the plant material to release psychoactive cannabinoids for inhalation. As with other psychoactive substances, smoking (and vaporization) typically produces more rapid onset and more intense experiences of the desired effects.

Individuals who regularly use cannabis can develop all the general diagnostic features of a substance use disorder. Cannabis use disorder is commonly observed as the only substance use disorder experienced by the individual; however, it also frequently occurs concurrently with other types of substance use disorders (i.e., alcohol, cocaine, opioid). In cases for which multiple types of substances are used, many times the individual may minimize the symptoms related to cannabis, as the symptoms may be less severe or cause less harm than those directly related to the use of the other substances. Pharmacological and behavioral tolerance to most of the effects of cannabis has been reported in individuals who use cannabis persistently. Generally, tolerance is lost when cannabis use is discontinued for a significant period of time (i.e., for at least several months).

New to DSM-5 is the recognition that abrupt cessation of daily or near-daily cannabis use often results in the onset of a cannabis withdrawal syndrome. Common symptoms of withdrawal include irritability, anger or aggression, anxiety, depressed mood, restlessness, sleep difficulty, and decreased appetite or weight loss. Although typically not as severe as alcohol or opiate withdrawal, the cannabis withdrawal syndrome can cause significant distress and contribute to difficulty quitting or relapse among those trying to abstain.

Individuals with cannabis use disorder may use cannabis throughout the day over a period of months or years, and thus may spend many hours a day under the influence. Others may use less frequently, but their use causes recurrent problems related to family, school, work, or other important activities (e.g., repeated absences at work; neglect of family obligations). Periodic cannabis use and intoxication can negatively affect behavioral and cognitive functioning and thus interfere with optimal performance at work or school, or place the individual at increased physical risk when performing activities that could be physically hazardous (e.g., driving a car; playing certain sports; performing manual work activities, including operating machinery). Arguments with spouses or parents over the use of cannabis in the home, or its use in the presence of children, can adversely impact family functioning and are common features of those with cannabis use disorder. Last, individuals with cannabis use disorder may continue using despite knowledge of physical problems (e.g., chronic cough related to smoking) or psychological problems (e.g., excessive sedation or exacerbation of other mental health problems) associated with its use.

Whether or not cannabis is being used for legitimate medical reasons may also affect diagnosis. When a substance is taken as indicated for a medical condition, symptoms of

tolerance and withdrawal will naturally occur and should not be used as the primary criteria for determining a diagnosis of a substance use disorder. Although medical uses of cannabis remain controversial and equivocal, use for medical circumstances should be considered when a diagnosis is being made.

Associated Features Supporting Diagnosis

Individuals who regularly use cannabis often report that it is being used to cope with mood, sleep, pain, or other physiological or psychological problems, and those diagnosed with cannabis use disorder frequently do have concurrent other mental disorders. Careful assessment typically reveals reports of cannabis use contributing to exacerbation of these same symptoms, as well as other reasons for frequent use (e.g., to experience euphoria, to forget about problems, in response to anger, as an enjoyable social activity). Related to this issue, some individuals who use cannabis multiple times per day for the aforementioned reasons do not perceive themselves as (and thus do not report) spending an excessive amount of time under the influence or recovering from the effects of cannabis, despite being intoxicated on cannabis or coming down from it effects for the majority of most days. An important marker of a substance use disorder diagnosis, particularly in milder cases, is continued use despite a clear risk of negative consequences to other valued activities or relationships (e.g., school, work, sport activity, partner or parent relationship).

Because some cannabis users are motivated to minimize their amount or frequency of use, it is important to be aware of common signs and symptoms of cannabis use and intoxication so as to better assess the extent of use. As with other substances, experienced users of cannabis develop behavioral and pharmacological tolerance such that it can be difficult to detect when they are under the influence. Signs of acute and chronic use include red eyes (conjunctival injection), cannabis odor on clothing, yellowing of finger tips (from smoking joints), chronic cough, burning of incense (to hide the odor), and exaggerated craving and impulse for specific foods, sometimes at unusual times of the day or night.

Prevalence

Cannabinoids, especially cannabis, are the most widely used illicit psychoactive substances in the United States. The 12-month prevalence of cannabis use disorder (DSM-IV abuse and dependence rates combined) is approximately 3.4% among 12- to 17-year-olds and 1.5% among adults age 18 years and older. Rates of cannabis use disorder are greater among adult males (2.2%) than among adult females (0.8%) and among 12- to 17-year-old males (3.8%) than among 12- to 17-year-old females (3.0%). Twelve-month prevalence rates of cannabis use disorder among adults decrease with age, with rates highest among 18- to 29-year-olds (4.4%) and lowest among individuals age 65 years and older (0.01%). The high prevalence of cannabis use disorder likely reflects the much more widespread use of cannabis relative to other illicit drugs rather than greater addictive potential.

Ethnic and racial differences in prevalence are moderate. Twelve-month prevalences of cannabis use disorder vary markedly across racial-ethnic subgroups in the United States. For 12- to 17-year-olds, rates are highest among Native American and Alaska Natives (7.1%) compared with Hispanics (4.1%), whites (3.4%), African Americans (2.7%), and Asian Americans and Pacific Islanders (0.9%). Among adults, the prevalence of cannabis use disorder is also highest among Native Americans and Alaska Natives (3.4%) relative to rates among African Americans (1.8%), whites (1.4%), Hispanics (1.2%), and Asian and Pacific Islanders (1.2%). During the past decade the prevalence of cannabis use disorder has increased among adults and adolescents. Gender differences in cannabis use disorder generally are concordant with those in other substance use disorders. Cannabis use disorder is more commonly observed in males, although the magnitude of this difference is less among adolescents.

Development and Course

The onset of cannabis use disorder can occur at any time during or following adolescence, but onset is most commonly during adolescence or young adulthood. Although much less frequent, onset of cannabis use disorder in the preteen years or in the late 20s or older can occur. Recent acceptance by some of the use and availability of "medical marijuana" may increase the rate of onset of cannabis use disorder among older adults.

Generally, cannabis use disorder develops over an extended period of time, although the progression appears to be more rapid in adolescents, particularly those with pervasive conduct problems. Most people who develop a cannabis use disorder typically establish a pattern of cannabis use that gradually increases in both frequency and amount. Cannabis, along with tobacco and alcohol, is traditionally the first substance that adolescents try. Many perceive cannabis use as less harmful than alcohol or tobacco use, and this perception likely contributes to increased use. Moreover, cannabis intoxication does not typically result in as severe behavioral and cognitive dysfunction as does significant alcohol intoxication, which may increase the probability of more frequent use in more diverse situations than with alcohol. These factors likely contribute to the potential rapid transition from cannabis use to a cannabis use disorder among some adolescents and the common pattern of using throughout the day that is commonly observed among those with more severe cannabis use disorder.

Cannabis use disorder among preteens, adolescents, and young adults is typically expressed as excessive use with peers that is a component of a pattern of other delinquent behaviors usually associated with conduct problems. Milder cases primarily reflect continued use despite clear problems related to disapproval of use by other peers, school administration, or family, which also places the youth at risk for physical or behavioral consequences. In more severe cases, there is a progression to using alone or using throughout the day such that use interferes with daily functioning and takes the place of previously established, prosocial activities.

With adolescent users, changes in mood stability, energy level, and eating patterns are commonly observed. These signs and symptoms are likely due to the direct effects of cannabis use (intoxication) and the subsequent effects following acute intoxication (coming down), as well as attempts to conceal use from others. School-related problems are commonly associated with cannabis use disorder in adolescents, particularly a dramatic drop in grades, truancy, and reduced interest in general school activities and outcomes.

Cannabis use disorder among adults typically involves well-established patterns of daily cannabis use that continue despite clear psychosocial or medical problems. Many adults have experienced repeated desire to stop or have failed at repeated cessation attempts. Milder adult cases may resemble the more common adolescent cases in that cannabis use is not as frequent or heavy but continues despite potential significant consequences of sustained use. The rate of use among middle-age and older adults appears to be increasing, likely because of a cohort effect resulting from high prevalence of use in the late 1960s and the 1970s.

Early onset of cannabis use (e.g., prior to age 15 years) is a robust predictor of the development of cannabis use disorder and other types of substance use disorders and mental disorders during young adulthood. Such early onset is likely related to concurrent other externalizing problems, most notably conduct disorder symptoms. However, early onset is also a predictor of internalizing problems and as such probably reflects a general risk factor for the development of mental health disorders.

Risk and Prognostic Factors

Temperamental. A history of conduct disorder in childhood or adolescence and antisocial personality disorder are risk factors for the development of many substance-related disorders, including cannabis-related disorders. Other risk factors include externalizing

or internalizing disorders during childhood or adolescence. Youths with high behavioral disinhibition scores show early-onset substance use disorders, including cannabis use disorder, multiple substance involvement, and early conduct problems.

Environmental. Risk factors include academic failure, tobacco smoking, unstable or abusive family situation, use of cannabis among immediate family members, a family history of a substance use disorder, and low socioeconomic status. As with all substances of abuse, the ease of availability of the substance is a risk factor; cannabis is relatively easy to obtain in most cultures, which increases the risk of developing a cannabis use disorder.

Genetic and physiological. Genetic influences contribute to the development of cannabis use disorders. Heritable factors contribute between 30% and 80% of the total variance in risk of cannabis use disorders. It should be noted that common genetic and shared environmental influences between cannabis and other types of substance use disorders suggest a common genetic basis for adolescent substance use and conduct problems.

Culture-Related Diagnostic Issues

Cannabis is probably the world's most commonly used illicit substance. Occurrence of cannabis use disorder across countries is unknown, but the prevalence rates are likely similar among developed countries. It is frequently among the first drugs of experimentation (often in the teens) of all cultural groups in the United States.

Acceptance of cannabis for medical purposes varies widely across and within cultures. Cultural factors (acceptability and legal status) that might impact diagnosis relate to differential consequences across cultures for detection of use (i.e., arrest, school suspensions, or employment suspension). The general change in substance use disorder diagnostic criteria from DSM-IV to DSM-5 (i.e., removal of the recurrent substance-related legal problems criterion) mitigates this concern to some degree.

Diagnostic Markers

Biological tests for cannabinoid metabolites are useful for determining if an individual has recently used cannabis. Such testing is helpful in making a diagnosis, particularly in milder cases if an individual denies using while others (family, work, school) purport concern about a substance use problem. Because cannabinoids are fat soluble, they persist in bodily fluids for extended periods of time and are excreted slowly. Expertise in urine testing methods is needed to reliably interpret results.

Functional Consequences of Cannabis Use Disorder

Functional consequences of cannabis use disorder are part of the diagnostic criteria. Many areas of psychosocial, cognitive, and health functioning may be compromised in relation to cannabis use disorder. Cognitive function, particularly higher executive function, appears to be compromised in cannabis users, and this relationship appears to be dose dependent (both acutely and chronically). This may contribute to increased difficulty at school or work. Cannabis use has been related to a reduction in prosocial goal-directed activity, which some have labeled an *amotivational syndrome,* that manifests itself in poor school performance and employment problems. These problems may be related to pervasive intoxication or recovery from the effects of intoxication. Similarly, cannabis-associated problems with social relationships are commonly reported in those with cannabis use disorder. Accidents due to engagement in potentially dangerous behaviors while under the influence (e.g., driving, sport, recreational or employment activities) are also of concern. Cannabis smoke contains high levels of carcinogenic compounds that place chronic users at risk for respiratory illnesses similar to those experienced by tobacco smokers. Chronic cannabis use may contribute to the onset or exacerbation of many other mental disorders. In particular, concern has been raised about cannabis use as a causal factor in schizophrenia and other psychotic disorders. Cannabis use can contribute to the onset of an acute psy-

chotic episode, can exacerbate some symptoms, and can adversely affect treatment of a major psychotic illness.

Differential Diagnosis

Nonproblematic use of cannabis. The distinction between nonproblematic use of cannabis and cannabis use disorder can be difficult to make because social, behavioral, or psychological problems may be difficult to attribute to the substance, especially in the context of use of other substances. Also, denial of heavy cannabis use and the attribution that cannabis is related to or causing substantial problems are common among individuals who are referred to treatment by others (i.e., school, family, employer, criminal justice system).

Other mental disorders. Cannabis-induced disorder may be characterized by symptoms (e.g., anxiety) that resemble primary mental disorders (e.g., generalized anxiety disorder vs. cannabis-induced anxiety disorder, with generalized anxiety, with onset during intoxication). Chronic intake of cannabis can produce a lack of motivation that resembles persistent depressive disorder (dysthymia). Acute adverse reactions to cannabis should be differentiated from the symptoms of panic disorder, major depressive disorder, delusional disorder, bipolar disorder, or schizophrenia, paranoid type. Physical examination will usually show an increased pulse and conjunctival injection. Urine toxicological testing can be helpful in making a diagnosis.

Comorbidity

Cannabis has been commonly thought of as a "gateway" drug because individuals who frequently use cannabis have a much greater lifetime probability than nonusers of using what are commonly considered more dangerous substances, like opioids or cocaine. Cannabis use and cannabis use disorder are highly comorbid with other substance use disorders. Co-occurring mental conditions are common in cannabis use disorder. Cannabis use has been associated with poorer life satisfaction; increased mental health treatment and hospitalization; and higher rates of depression, anxiety disorders, suicide attempts, and conduct disorder. Individuals with past-year or lifetime cannabis use disorder have high rates of alcohol use disorder (greater than 50%) and tobacco use disorder (53%). Rates of other substance use disorders are also likely to be high among individuals with cannabis use disorder. Among those seeking treatment for a cannabis use disorder, 74% report problematic use of a secondary or tertiary substance: alcohol (40%), cocaine (12%), methamphetamine (6%), and heroin or other opiates (2%). Among those younger than 18 years, 61% reported problematic use of a secondary substance: alcohol (48%), cocaine (4%), methamphetamine (2%), and heroin or other opiates (2%). Cannabis use disorder is also often observed as a secondary problem among those with a primary diagnosis of other substance use disorders, with approximately 25%–80% of those in treatment for another substance use disorder reporting use of cannabis.

Individuals with past-year or lifetime diagnoses of cannabis use disorder also have high rates of concurrent mental disorders other than substance use disorders. Major depressive disorder (11%), any anxiety disorder (24%), and bipolar I disorder (13%) are quite common among individuals with a past-year diagnosis of a cannabis use disorder, as are antisocial (30%), obsessive-compulsive, (19%), and paranoid (18%) personality disorders. Approximately 33% of adolescents with cannabis use disorder have internalizing disorders (e.g., anxiety, depression, posttraumatic stress disorder), and 60% have externalizing disorders (e.g., conduct disorder, attention-deficit/hyperactivity disorder).

Although cannabis use can impact multiple aspects of normal human functioning, including the cardiovascular, immune, neuromuscular, ocular, reproductive, and respiratory systems, as well as appetite and cognition/perception, there are few clear medical conditions that commonly co-occur with cannabis use disorder. The most significant health

effects of cannabis involve the respiratory system, and chronic cannabis smokers exhibit high rates of respiratory symptoms of bronchitis, sputum production, shortness of breath, and wheezing.

Cannabis Intoxication

Diagnostic Criteria

A. Recent use of cannabis.
B. Clinically significant problematic behavioral or psychological changes (e.g., impaired motor coordination, euphoria, anxiety, sensation of slowed time, impaired judgment, social withdrawal) that developed during, or shortly after, cannabis use.
C. Two (or more) of the following signs or symptoms developing within 2 hours of cannabis use:
    1. Conjunctival injection.
    2. Increased appetite.
    3. Dry mouth.
    4. Tachycardia.
D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance.

Specify if:

With perceptual disturbances: Hallucinations with intact reality testing or auditory, visual, or tactile illusions occur in the absence of a delirium.

Coding note: The ICD-9-CM code is **292.89.** The ICD-10-CM code depends on whether or not there is a comorbid cannabis use disorder and whether or not there are perceptual disturbances.

For cannabis intoxication, without perceptual disturbances: If a mild cannabis use disorder is comorbid, the ICD-10-CM code is **F12.129,** and if a moderate or severe cannabis use disorder is comorbid, the ICD-10-CM code is **F12.229.** If there is no comorbid cannabis use disorder, then the ICD-10-CM code is **F12.929.**

For cannabis intoxication, with perceptual disturbances: If a mild cannabis use disorder is comorbid, the ICD-10-CM code is **F12.122,** and if a moderate or severe cannabis use disorder is comorbid, the ICD-10-CM code is **F12.222.** If there is no comorbid cannabis use disorder, then the ICD-10-CM code is **F12.922.**

Specifiers

When hallucinations occur in the absence of intact reality testing, a diagnosis of substance/medication-induced psychotic disorder should be considered.

Diagnostic Features

The essential feature of cannabis intoxication is the presence of clinically significant problematic behavioral or psychological changes that develop during, or shortly after, cannabis use (Criterion B). Intoxication typically begins with a "high" feeling followed by symptoms that include euphoria with inappropriate laughter and grandiosity, sedation, lethargy, impairment in short-term memory, difficulty carrying out complex mental processes, impaired judgment, distorted sensory perceptions, impaired motor performance, and the sensation that time is passing slowly. Occasionally, anxiety (which can be severe),

dysphoria, or social withdrawal occurs. These psychoactive effects are accompanied by two or more of the following signs, developing within 2 hours of cannabis use: conjunctival injection, increased appetite, dry mouth, and tachycardia (Criterion C).

Intoxication develops within minutes if the cannabis is smoked but may take a few hours to develop if the cannabis is ingested orally. The effects usually last 3–4 hours, with the duration being somewhat longer when the substance is ingested orally. The magnitude of the behavioral and physiological changes depends on the dose, the method of administration, and the characteristics of the individual using the substance, such as rate of absorption, tolerance, and sensitivity to the effects of the substance. Because most cannabinoids, including delta-9-tetrahydrocannabinol (delta-9-THC), are fat soluble, the effects of cannabis or hashish may occasionally persist or reoccur for 12–24 hours because of the slow release of psychoactive substances from fatty tissue or to enterohepatic circulation.

Prevalence

The prevalence of actual episodes of cannabis intoxication in the general population is unknown. However, it is probable that most cannabis users would at some time meet criteria for cannabis intoxication. Given this, the prevalence of cannabis users and the prevalence of individuals experiencing cannabis intoxication are likely similar.

Functional Consequences of Cannabis Intoxication

Impairment from cannabis intoxication may have serious consequences, including dysfunction at work or school, social indiscretions, failure to fulfill role obligations, traffic accidents, and having unprotected sex. In rare cases, cannabis intoxication may precipitate a psychosis that may vary in duration.

Differential Diagnosis

Note that if the clinical presentation includes hallucinations in the absence of intact reality testing, a diagnosis of substance/medication-induced psychotic disorder should be considered.

Other substance intoxication. Cannabis intoxication may resemble intoxication with other types of substances. However, in contrast to cannabis intoxication, alcohol intoxication and sedative, hypnotic, or anxiolytic intoxication frequently decrease appetite, increase aggressive behavior, and produce nystagmus or ataxia. Hallucinogens in low doses may cause a clinical picture that resembles cannabis intoxication. Phencyclidine, like cannabis, can be smoked and also causes perceptual changes, but phencyclidine intoxication is much more likely to cause ataxia and aggressive behavior.

Other cannabis-induced disorders. Cannabis intoxication is distinguished from the other cannabis-induced disorders (e.g., cannabis-induced anxiety disorder, with onset during intoxication) because the symptoms in these latter disorders predominate the clinical presentation and are severe enough to warrant independent clinical attention.

Cannabis Withdrawal

Diagnostic Criteria **292.0 (F12.288)**

A. Cessation of cannabis use that has been heavy and prolonged (i.e., usually daily or almost daily use over a period of at least a few months).

B. Three (or more) of the following signs and symptoms develop within approximately 1 week after Criterion A:

1. Irritability, anger, or aggression.
2. Nervousness or anxiety.
3. Sleep difficulty (e.g., insomnia, disturbing dreams).
4. Decreased appetite or weight loss.
5. Restlessness.
6. Depressed mood.
7. At least one of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache.

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

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

Coding note: The ICD-9-CM code is 292.0. The ICD-10-CM code for cannabis withdrawal is F12.288. Note that the ICD-10-CM code indicates the comorbid presence of a moderate or severe cannabis use disorder, reflecting the fact that cannabis withdrawal can only occur in the presence of a moderate or severe cannabis use disorder. It is not permissible to code a comorbid mild cannabis use disorder with cannabis withdrawal.

Diagnostic Features

The essential feature of cannabis withdrawal is the presence of a characteristic withdrawal syndrome that develops after the cessation of or substantial reduction in heavy and prolonged cannabis use. In addition to the symptoms in Criterion B, the following may also be observed postabstinence: fatigue, yawning, difficulty concentrating, and rebound periods of increased appetite and hypersomnia that follow initial periods of loss of appetite and insomnia. For the diagnosis, withdrawal symptoms must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion C). Many cannabis users report smoking cannabis or taking other substances to help relieve withdrawal symptoms, and many report that withdrawal symptoms make quitting difficult or have contributed to relapse. The symptoms typically are not of sufficient severity to require medical attention, but medication or behavioral strategies may help alleviate symptoms and improve prognosis in those trying to quit using cannabis.

Cannabis withdrawal is commonly observed in individuals seeking treatment for cannabis use as well as in heavy cannabis users who are not seeking treatment. Among individuals who have used cannabis regularly during some period of their lifetime, up to one-third report having experienced cannabis withdrawal. Among adults and adolescents enrolled in treatment or heavy cannabis users, 50%–95% report cannabis withdrawal. These findings indicate that cannabis withdrawal occurs among a substantial subset of regular cannabis users who try to quit.

Development and Course

The amount, duration, and frequency of cannabis smoking that is required to produce an associated withdrawal disorder during a quit attempt are unknown. Most symptoms have their onset within the first 24–72 hours of cessation, peak within the first week, and last approximately 1–2 weeks. Sleep difficulties may last more than 30 days. Cannabis withdrawal has been documented among adolescents and adults. Withdrawal tends to be more common and severe among adults, most likely related to the more persistent and greater frequency and quantity of use among adults.

Risk and Prognostic Factors

Environmental. Most likely, the prevalence and severity of cannabis withdrawal are greater among heavier cannabis users, and particularly among those seeking treatment for cannabis use disorders. Withdrawal severity also appears to be positively related to the severity of comorbid symptoms of mental disorders.

Functional Consequences of Cannabis Withdrawal

Cannabis users report using cannabis to relieve withdrawal symptoms, suggesting that withdrawal might contribute to ongoing expression of cannabis use disorder. Worse outcomes may be associated with greater withdrawal. A substantial proportion of adults and adolescents in treatment for moderate to severe cannabis use disorder acknowledge moderate to severe withdrawal symptoms, and many complain that these symptoms make cessation more difficult. Cannabis users report having relapsed to cannabis use or initiating use of other drugs (e.g., tranquilizers) to provide relief from cannabis withdrawal symptoms. Last, individuals living with cannabis users observe significant withdrawal effects, suggesting that such symptoms are disruptive to daily living.

Differential Diagnosis

Because many of the symptoms of cannabis withdrawal are also symptoms of other substance withdrawal syndromes or of depressive or bipolar disorders, careful evaluation should focus on ensuring that the symptoms are not better explained by cessation from another substance (e.g., tobacco or alcohol withdrawal), another mental disorder (generalized anxiety disorder, major depressive disorder), or another medical condition.

Other Cannabis-Induced Disorders

The following cannabis-induced disorders are described in other chapters of the manual with disorders with which they share phenomenology (see the substance/medication-induced mental disorders in these chapters): cannabis-induced psychotic disorder ("Schizophrenia Spectrum and Other Psychotic Disorders"); cannabis-induced anxiety disorder ("Anxiety Disorders"); and cannabis-induced sleep disorder ("Sleep-Wake Disorders"). For cannabis intoxication delirium, see the criteria and discussion of delirium in the chapter "Neurocognitive Disorders." These cannabis-induced disorders are diagnosed instead of cannabis intoxication or cannabis withdrawal when the symptoms are sufficiently severe to warrant independent clinical attention.

Unspecified Cannabis-Related Disorder

292.9 (F12.99)

This category applies to presentations in which symptoms characteristic of a cannabis-related 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 specific cannabis-related disorder or any of the disorders in the substance-related and addictive disorders diagnostic class.

Hallucinogen-Related Disorders

Phencyclidine Use Disorder
Other Hallucinogen Use Disorder
Phencyclidine Intoxication
Other Hallucinogen Intoxication
Hallucinogen Persisting Perception Disorder
Other Phencyclidine-Induced Disorders
Other Hallucinogen-Induced Disorders
Unspecified Phencyclidine-Related Disorder
Unspecified Hallucinogen-Related Disorder

Phencyclidine Use Disorder

Diagnostic Criteria

A. A pattern of phencyclidine (or a pharmacologically similar substance) use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Phencyclidine is often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control phencyclidine use.
3. A great deal of time is spent in activities necessary to obtain phencyclidine, use the phencyclidine, or recover from its effects.
4. Craving, or a strong desire or urge to use phencyclidine.
5. Recurrent phencyclidine use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences from work or poor work performance related to phencyclidine use; phencyclidine-related absences, suspensions, or expulsions from school; neglect of children or household).
6. Continued phencyclidine use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the phencyclidine (e.g., arguments with a spouse about consequences of intoxication; physical fights).
7. Important social, occupational, or recreational activities are given up or reduced because of phencyclidine use.
8. Recurrent phencyclidine use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by a phencyclidine).
9. Phencyclidine use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the phencyclidine.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of the phencyclidine to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of the phencyclidine.

Note: Withdrawal symptoms and signs are not established for phencyclidines, and so this criterion does not apply. (Withdrawal from phencyclidines has been reported in animals but not documented in human users.)

Specify if:

In early remission: After full criteria for phencyclidine use disorder were previously met, none of the criteria for phencyclidine use disorder have been met for at least 3 months but for less than 12 months (with the exception that Criterion A4, "Craving, or a strong desire or urge to use the phencyclidine," may be met).

In sustained remission: After full criteria for phencyclidine use disorder were previously met, none of the criteria for phencyclidine use disorder have been met at any time during a period of 12 months or longer (with the exception that Criterion A4, "Craving, or a strong desire or urge to use the phencyclidine," may be met).

Specify if:

In a controlled environment: This additional specifier is used if the individual is in an environment where access to phencyclidines is restricted.

Coding based on current severity: Note for ICD-10-CM codes: If a phencyclidine intoxication or another phencyclidine-induced mental disorder is also present, do not use the codes below for phencyclidine use disorder. Instead, the comorbid phencyclidine use disorder is indicated in the 4th character of the phencyclidine-induced disorder code (see the coding note for phencyclidine intoxication or a specific phencyclidine-induced mental disorder). For example, if there is comorbid phencyclidine-induced psychotic disorder, only the phencyclidine-induced psychotic disorder code is given, with the 4th character indicating whether the comorbid phencyclidine use disorder is mild, moderate, or severe: F16.159 for mild phencyclidine use disorder with phencyclidine-induced psychotic disorder or F16.259 for a moderate or severe phencyclidine use disorder with phencyclidine-induced psychotic disorder.

Specify current severity:

305.90 (F16.10) Mild: Presence of 2–3 symptoms.

304.60 (F16.20) Moderate: Presence of 4–5 symptoms.

304.60 (F16.20) Severe: Presence of 6 or more symptoms.

Specifiers

"In a controlled environment" applies as a further specifier of remission if the individual is both in remission and in a controlled environment (i.e., in early remission in a controlled environment or in sustained remission in a controlled environment). Examples of these environments are closely supervised and substance-free jails, therapeutic communities, and locked hospital units.

Diagnostic Features

The phencyclidines (or phencyclidine-like substances) include phencyclidine (e.g., PCP, "angel dust") and less potent but similarly acting compounds such as ketamine, cyclohexamine, and dizocilpine. These substances were first developed as dissociative anesthetics in the 1950s and became street drugs in the 1960s. They produce feelings of separation from mind and body (hence "dissociative") in low doses, and at high doses, stupor and coma can result. These substances are most commonly smoked or taken orally, but they may also be snorted or injected. Although the primary psychoactive effects of PCP last for a few hours, the total elimination rate of this drug from the body typically extends 8 days or longer. The hallucinogenic effects in vulnerable individuals may last for weeks and may precipitate a persistent psychotic episode resembling schizophrenia. Ketamine has been observed to have utility in the treatment of major depressive disorder. Withdrawal symp-

toms have not been clearly established in humans, and therefore the withdrawal criterion is not included in the diagnosis of phencyclidine use disorder.

Associated Features Supporting Diagnosis

Phencyclidine may be detected in urine for up to 8 days or even longer at very high doses. In addition to laboratory tests to detect its presence, characteristic symptoms resulting from intoxication with phencyclidine or related substances may aid in its diagnosis. Phencyclidine is likely to produce dissociative symptoms, analgesia, nystagmus, and hypertension, with risk of hypotension and shock. Violent behavior can also occur with phencyclidine use, as intoxicated persons may believe that they are being attacked. Residual symptoms following use may resemble schizophrenia.

Prevalence

The prevalence of phencyclidine use disorder is unknown. Approximately 2.5% of the population reports having ever used phencyclidine. The proportion of users increases with age, from 0.3% of 12- to 17-year-olds, to 1.3% of 18- to 25-year-olds, to 2.9% of those age 26 years and older reporting ever using phencyclidine. There appears to have been an increase among 12th graders in both ever used (to 2.3% from 1.8%) and past-year use (to 1.3% from 1.0%) of phencyclidine. Past-year use of ketamine appears relatively stable among 12th graders (1.6%–1.7% over the past 3 years).

Risk and Prognostic Factors

There is little information about risk factors for phencyclidine use disorder. Among individuals admitted to substance abuse treatment, those for whom phencyclidine was the primary substance were younger than those admitted for other substance use, had lower educational levels, and were more likely to be located in the West and Northeast regions of the United States, compared with other admissions.

Culture-Related Diagnostic Issues

Ketamine use in youths ages 16–23 years has been reported to be more common among whites (0.5%) than among other ethnic groups (range 0%–0.3%). Among individuals admitted to substance abuse treatment, those for whom phencyclidine was the primary substance were predominantly black (49%) or Hispanic (29%).

Gender-Related Diagnostic Issues

Males make up about three-quarters of those with phencyclidine-related emergency room visits.

Diagnostic Markers

Laboratory testing may be useful, as phencyclidine is present in the urine in intoxicated individuals up to 8 days after ingestion. The individual's history, along with certain physical signs, such as nystagmus, analgesia and prominent hypertension, may aid in distinguishing the phencyclidine clinical picture from that of other hallucinogens.

Functional Consequences of Phencyclidine Use Disorder

In individuals with phencyclidine use disorder, there may be physical evidence of injuries from accidents, fights, and falls. Chronic use of phencyclidine may lead to deficits in memory, speech, and cognition that may last for months. Cardiovascular and neurological toxicities (e.g., seizures, dystonias, dyskinesias, catalepsy, hypothermia or hyperthermia) may result from intoxication with phencyclidine. Other consequences include intracranial hemorrhage, rhabdomyolysis, respiratory problems, and (occasionally) cardiac arrest.

Differential Diagnosis

Other substance use disorders. Distinguishing the effects of phencyclidine from those of other substances is important, since it may be a common additive to other substances (e.g., cannabis, cocaine).

Schizophrenia and other mental disorders. Some of the effects of phencyclidine and related substance use may resemble symptoms of other psychiatric disorders, such as psychosis (schizophrenia), low mood (major depressive disorder), violent aggressive behaviors (conduct disorder, antisocial personality disorder). Discerning whether these behaviors occurred before the intake of the drug is important in the differentiation of acute drug effects from preexisting mental disorder. Phencyclidine-induced psychotic disorder should be considered when there is impaired reality testing in individuals experiencing disturbances in perception resulting from ingestion of phencyclidine.

Other Hallucinogen Use Disorder

Diagnostic Criteria

A. A problematic pattern of hallucinogen (other than phencyclidine) use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. The hallucinogen is often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control hallucinogen use.
3. A great deal of time is spent in activities necessary to obtain the hallucinogen, use the hallucinogen, or recover from its effects.
4. Craving, or a strong desire or urge to use the hallucinogen.
5. Recurrent hallucinogen use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences from work or poor work performance related to hallucinogen use; hallucinogen-related absences, suspensions, or expulsions from school; neglect of children or household).
6. Continued hallucinogen use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the hallucinogen (e.g., arguments with a spouse about consequences of intoxication; physical fights).
7. Important social, occupational, or recreational activities are given up or reduced because of hallucinogen use.
8. Recurrent hallucinogen use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by the hallucinogen).
9. Hallucinogen use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the hallucinogen.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of the hallucinogen to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of the hallucinogen.

Note: Withdrawal symptoms and signs are not established for hallucinogens, and so this criterion does not apply.

Specify **the particular hallucinogen.**

Specify if:

In early remission: After full criteria for other hallucinogen use disorder were previously met, none of the criteria for other hallucinogen use disorder have been met for at least 3 months but for less than 12 months (with the exception that Criterion A4, "Craving, or a strong desire or urge to use the hallucinogen," may be met).

In sustained remission: After full criteria for other hallucinogen use disorder were previously met, none of the criteria for other hallucinogen use disorder have been met at any time during a period of 12 months or longer (with the exception that Criterion A4, "Craving, or a strong desire or urge to use the hallucinogen," may be met).

Specify if:

In a controlled environment: This additional specifier is used if the individual is in an environment where access to hallucinogens is restricted.

Coding based on current severity: Note for ICD-10-CM codes: If a hallucinogen intoxication or another hallucinogen-induced mental disorder is also present, do not use the codes below for hallucinogen use disorder. Instead, the comorbid hallucinogen use disorder is indicated in the 4th character of the hallucinogen-induced disorder code (see the coding note for hallucinogen intoxication or specific hallucinogen-induced mental disorder). For example, if there is comorbid hallucinogen-induced psychotic disorder and hallucinogen use disorder, only the hallucinogen-induced psychotic disorder code is given, with the 4th character indicating whether the comorbid hallucinogen use disorder is mild, moderate, or severe: F16.159 for mild hallucinogen use disorder with hallucinogen-induced psychotic disorder or F16.259 for a moderate or severe hallucinogen use disorder with hallucinogen-induced psychotic disorder.

Specify current severity:

305.30 (F16.10) Mild: Presence of 2–3 symptoms.

304.50 (F16.20) Moderate: Presence of 4–5 symptoms.

304.50 (F16.20) Severe: Presence of 6 or more symptoms.

Specifiers

"In a controlled environment" applies as a further specifier of remission if the individual is both in remission and in a controlled environment (i.e., in early remission in a controlled environment or in sustained remission in a controlled environment). Examples of these environments are closely supervised and substance-free jails, therapeutic communities, and locked hospital units.

Diagnostic Features

Hallucinogens comprise a diverse group of substances that, despite having different chemical structures and possibly involving different molecular mechanisms, produce similar alterations of perception, mood, and cognition in users. Hallucinogens included are phenylalkylamines (e.g., mescaline, DOM [2,5-dimethoxy-4-methylamphetamine], and MDMA [3,4-methylenedioxymethamphetamine; also called "ecstasy"]); the indoleamines, including psilocybin (i.e., psilocin) and dimethyltryptamine (DMT); and the ergolines, such as LSD (lysergic acid diethylamide) and morning glory seeds. In addition, miscellaneous other ethnobotanical compounds are classified as "hallucinogens," of which *Salvia divinorum* and jimsonweed are two examples. Excluded from the hallucinogen group are cannabis and its active compound, delta-9-tetrahydrocannabinol (THC) (see the section "Cannabis-Related Disorders"). These substances can have hallucinogenic effects but are diagnosed separately because of significant differences in their psychological and behavioral effects.

Hallucinogens are usually taken orally, although some forms are smoked (e.g., DMT, salvia) or (rarely) taken intranasally or by injection (e.g., ecstasy). Duration of effects varies

across types of hallucinogens. Some of these substances (i.e., LSD, MDMA) have a long half-life and extended duration such that users may spend hours to days using and/or recovering from the effects of these drugs. However, other hallucinogenic drugs (e.g., DMT, salvia) are short acting. Tolerance to hallucinogens develops with repeated use and has been reported to have both autonomic and psychological effects. Cross-tolerance exists between LSD and other hallucinogens (e.g., psilocybin, mescaline) but does not extend to other drug categories such as amphetamines and cannabis.

MDMA/ecstasy as a hallucinogen may have distinctive effects attributable to both its hallucinogenic and its stimulant properties. Among heavy ecstasy users, continued use despite physical or psychological problems, tolerance, hazardous use, and spending a great deal of time obtaining the substance are the most commonly reported criteria—over 50% in adults and over 30% in a younger sample, while legal problems related to substance use and persistent desire/inability to quit are rarely reported. As found for other substances, diagnostic criteria for other hallucinogen use disorder are arrayed along a single continuum of severity.

One of the generic criteria for substance use disorders, a clinically significant withdrawal syndrome, has not been consistently documented in humans, and therefore the diagnosis of hallucinogen withdrawal syndrome is not included in DSM-5. However, there is evidence of withdrawal from MDMA, with endorsement of two or more withdrawal symptoms observed in 59%–98% in selected samples of ecstasy users. Both psychological and physical problems have been commonly reported as withdrawal problems.

Associated Features Supporting Diagnosis

The characteristic symptom features of some of the hallucinogens can aid in diagnosis if urine or blood toxicology results are not available. For example, individuals who use LSD tend to experience visual hallucinations that can be frightening. Individuals intoxicated with hallucinogens may exhibit a temporary increase in suicidality.

Prevalence

Of all substance use disorders, other hallucinogen use disorder is one of the rarest. The 12-month prevalence is estimated to be 0.5% among 12- to 17-year-olds and 0.1% among adults age 18 and older in the United States. Rates are higher in adult males (0.2%) compared with females (0.1%), but the opposite is observed in adolescent samples ages 12–17, in which the 12-month rate is slightly higher in females (0.6%) than in males (0.4%). Rates are highest in individuals younger than 30 years, with the peak occurring in individuals ages 18–29 years (0.6%) and decreasing to virtually 0.0% among individuals age 45 and older.

There are marked ethnic differences in 12-month prevalence of other hallucinogen use disorder. Among youths ages 12–17 years, 12-month prevalence is higher among Native Americans and Alaska Natives (1.2%) than among Hispanics (0.6%), whites (0.6%), African Americans (0.2%), and Asian Americans and Pacific Islanders (0.2%). Among adults, 12-month prevalence of other hallucinogen use disorder is similar for Native Americans and Alaska Natives, whites, and Hispanics (all 0.2%) but somewhat lower for Asian Americans and Pacific Islanders (0.07%) and African Americans (0.03%). Past-year prevalence is higher in clinical samples (e.g., 19% in adolescents in treatment). Among individuals currently using hallucinogens in the general population, 7.8% (adult) to 17% (adolescent) had a problematic pattern of use that met criteria for past-year other hallucinogen use disorder. Among select groups of individuals who use hallucinogens (e.g., recent heavy ecstasy use), 73.5% of adults and 77% of adolescents have a problematic pattern of use that may meet other hallucinogen use disorder criteria.

Development and Course

Unlike most substances where an early age at onset is associated with elevations in risk for the corresponding use disorder, it is unclear whether there is an association of an early age

at onset with elevations in risk for other hallucinogen use disorder. However, patterns of drug consumption have been found to differ by age at onset, with early-onset ecstasy users more likely to be polydrug users than their later-onset counterparts. There may be a disproportionate influence of use of specific hallucinogens on risk of developing other hallucinogen use disorder, with use of ecstasy/MDMA increasing the risk of the disorder relative to use of other hallucinogens.

Little is known regarding the course of other hallucinogen use disorder, but it is generally thought to have low incidence, low persistence, and high rates of recovery. Adolescents are especially at risk for using these drugs, and it is estimated that 2.7% of youths ages 12–17 years have used one or more of these drugs in the past 12 months, with 44% having used ecstasy/MDMA. Other hallucinogen use disorder is a disorder observed primarily in individuals younger than 30 years, with rates vanishingly rare among older adults.

Risk and Prognostic Factors

Temperamental. In adolescents but not consistently in adults, MDMA use is associated with an elevated rate of other hallucinogen use disorder. Other substance use disorders, particularly alcohol, tobacco, and cannabis, and major depressive disorder are associated with elevated rates of other hallucinogen use disorder. Antisocial personality disorder may be elevated among individuals who use more than two other drugs in addition to hallucinogens, compared with their counterparts with less extensive use history. The influence of adult antisocial behaviors—but not conduct disorder or antisocial personality disorder—on other hallucinogen use disorder may be stronger in females than in males. Use of specific hallucinogens (e.g., salvia) is prominent among individuals ages 18–25 years with other risk-taking behaviors and illegal activities. Cannabis use has also been implicated as a precursor to initiation of use of hallucinogens (e.g., ecstasy), along with early use of alcohol and tobacco. Higher drug use by peers and high sensation seeking have also been associated with elevated rates of ecstasy use. MDMA/ecstasy use appears to signify a more severe group of hallucinogen users.

Genetic and physiological. Among male twins, total variance due to additive genetics has been estimated to range from 26% to 79%, with inconsistent evidence for shared environmental influences.

Culture-Related Diagnostic Issues

Historically, hallucinogens have been used as part of established religious practices, such as the use of peyote in the Native American Church and in Mexico. Ritual use by indigenous populations of psilocybin obtained from certain types of mushrooms has occurred in South America, Mexico, and some areas in the United States, or of ayahuasca in the Santo Daime and União de Vegetal sects. Regular use of peyote as part of religious rituals is not linked to neuropsychological or psychological deficits. For adults, no race or ethnicity differences for the full criteria or for any individual criterion are apparent at this time.

Gender-Related Diagnostic Issues

In adolescents, females may be less likely than males to endorse "hazardous use," and female gender may be associated with increased odds of other hallucinogen use disorder.

Diagnostic Markers

Laboratory testing can be useful in distinguishing among the different hallucinogens. However, because some agents (e.g., LSD) are so potent that as little as 75 micrograms can produce severe reactions, typical toxicological examination will not always reveal which substance has been used.

Functional Consequences of Other Hallucinogen Use Disorder

There is evidence for long-term neurotoxic effects of MDMA/ecstasy use, including impairments in memory, psychological function, and neuroendocrine function; serotonin system dysfunction; and sleep disturbance; as well as adverse effects on brain microvasculature, white matter maturation, and damage to axons. Use of MDMA/ecstasy may diminish functional connectivity among brain regions.

Differential Diagnosis

Other substance use disorders. The effects of hallucinogens must be distinguished from those of other substances (e.g., amphetamines), especially because contamination of the hallucinogens with other drugs is relatively common.

Schizophrenia. Schizophrenia also must be ruled out, as some affected individuals (e.g., individuals with schizophrenia who exhibit paranoia) may falsely attribute their symptoms to use of hallucinogens.

Other mental disorders or medical conditions. Other potential disorders or conditions to consider include panic disorder, depressive and bipolar disorders, alcohol or sedative withdrawal, hypoglycemia and other metabolic conditions, seizure disorder, stroke, ophthalmological disorder, and central nervous system tumors. Careful history of drug taking, collateral reports from family and friends (if possible), age, clinical history, physical examination, and toxicology reports should be useful in arriving at the final diagnostic decision.

Comorbidity

Adolescents who use MDMA/ecstasy and other hallucinogens, as well as adults who have recently used ecstasy, have a higher prevalence of other substance use disorders compared with nonhallucinogen substance users. Individuals who use hallucinogens exhibit elevations of nonsubstance mental disorders (especially anxiety, depressive, and bipolar disorders), particularly with use of ecstasy and salvia. Rates of antisocial personality disorder (but not conduct disorder) are significantly elevated among individuals with other hallucinogen use disorder, as are rates of adult antisocial behavior. However, it is unclear whether the mental illnesses may be precursors to rather than consequences of other hallucinogen use disorder (see the section "Risk and Prognostic Factors" for this disorder). Both adults and adolescents who use ecstasy are more likely than other drug users to be polydrug users and to have other drug use disorders.

Phencyclidine Intoxication

Diagnostic Criteria

A. Recent use of phencyclidine (or a pharmacologically similar substance).
B. Clinically significant problematic behavioral changes (e.g., belligerence, assaultiveness, impulsiveness, unpredictability, psychomotor agitation, impaired judgment) that developed during, or shortly after, phencyclidine use.
C. Within 1 hour, two (or more) of the following signs or symptoms:

   Note: When the drug is smoked, "snorted," or used intravenously, the onset may be particularly rapid.

   1. Vertical or horizontal nystagmus.
   2. Hypertension or tachycardia.

3. Numbness or diminished responsiveness to pain.
4. Ataxia.
5. Dysarthria.
6. Muscle rigidity.
7. Seizures or coma.
8. Hyperacusis.

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance.

Coding note: The ICD-9-CM code is **292.89.** The ICD-10-CM code depends on whether there is a comorbid phencyclidine use disorder. If a mild phencyclidine use disorder is comorbid, the ICD-10-CM code is **F16.129,** and if a moderate or severe phencyclidine use disorder is comorbid, the ICD-10-CM code is **F16.229.** If there is no comorbid phencyclidine use disorder, then the ICD-10-CM code is **F16.929.**

Note: In addition to the section "Functional Consequences of Phencyclidine Intoxication," see the corresponding section in phencyclidine use disorder.

Diagnostic Features

Phencyclidine intoxication reflects the clinically significant behavioral changes that occur shortly after ingestion of this substance (or a pharmacologically similar substance). The most common clinical presentations of phencyclidine intoxication include disorientation, confusion without hallucinations, hallucinations or delusions, a catatonic-like syndrome, and coma of varying severity. The intoxication typically lasts for several hours but, depending on the type of clinical presentation and whether other drugs besides phencyclidine were consumed, may last for several days or longer.

Prevalence

Use of phencyclidine or related substances may be taken as an estimate of the prevalence of intoxication. Approximately 2.5% of the population reports having ever used phencyclidine. Among high school students, 2.3% of 12th graders report ever using phencyclidine, with 57% having used in the past 12 months. This represents an increase from prior to 2011. Past-year use of ketamine, which is assessed separately from other substances, has remained stable over time, with about 1.7% of 12th graders reporting use.

Diagnostic Markers

Laboratory testing may be useful, as phencyclidine is detectable in urine for up to 8 days following use, although the levels are only weakly associated with an individual's clinical presentation and may therefore not be useful for case management. Creatine phosphokinase and aspartate aminotransferase levels may be elevated.

Functional Consequences of Phencyclidine Intoxication

Phencyclidine intoxication produces extensive cardiovascular and neurological (e.g., seizures, dystonias, dyskinesias, catalepsy, hypothermia or hyperthermia) toxicity.

Differential Diagnosis

In particular, in the absence of intact reality testing (i.e., without insight into any perceptual abnormalities), an additional diagnosis of phencyclidine-induced psychotic disorder should be considered.

Other substance intoxication. Phencyclidine intoxication should be differentiated from intoxication due to other substances, including other hallucinogens; amphetamine, co-

caine, or other stimulants; and anticholinergics, as well as withdrawal from benzodiazepines. Nystagmus and bizarre and violent behavior may distinguish intoxication due to phencyclidine from that due to other substances. Toxicological tests may be useful in making this distinction, since phencyclidine is detectable in urine for up to 8 days after use. However, there is a weak correlation between quantitative toxicology levels of phencyclidine and clinical presentation that diminishes the utility of the laboratory findings for patient management.

Other conditions. Other conditions to be considered include schizophrenia, depression, withdrawal from other drugs (e.g., sedatives, alcohol), certain metabolic disorders like hypoglycemia and hyponatremia, central nervous system tumors, seizure disorders, sepsis, neuroleptic malignant syndrome, and vascular insults.

Other Hallucinogen Intoxication

Diagnostic Criteria

A. Recent use of a hallucinogen (other than phencyclidine).
B. Clinically significant problematic behavioral or psychological changes (e.g., marked anxiety or depression, ideas of reference, fear of "losing one's mind," paranoid ideation, impaired judgment) that developed during, or shortly after, hallucinogen use.
C. Perceptual changes occurring in a state of full wakefulness and alertness (e.g., subjective intensification of perceptions, depersonalization, derealization, illusions, hallucinations, synesthesias) that developed during, or shortly after, hallucinogen use.
D. Two (or more) of the following signs developing during, or shortly after, hallucinogen use:
    1. Pupillary dilation.
    2. Tachycardia.
    3. Sweating.
    4. Palpitations.
    5. Blurring of vision.
    6. Tremors.
    7. Incoordination.
E. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance.

Coding note: The ICD-9-CM code is **292.89.** The ICD-10-CM code depends on whether there is a comorbid hallucinogen use disorder. If a mild hallucinogen use disorder is comorbid, the ICD-10-CM code is **F16.129,** and if a moderate or severe hallucinogen use disorder is comorbid, the ICD-10-CM code is **F16.229.** If there is no comorbid hallucinogen use disorder, then the ICD-10-CM code is **F16.929.**

Note: For information on Associated Features Supporting Diagnosis and Culture-Related Diagnostic Issues, see the corresponding sections in other hallucinogen use disorder.

Diagnostic Features

Other hallucinogen intoxication reflects the clinically significant behavioral or psychological changes that occur shortly after ingestion of a hallucinogen. Depending on the specific hallucinogen, the intoxication may last only minutes (e.g., for salvia) or several hours or longer (e.g., for LSD [lysergic acid diethylamide] or MDMA [3,4-methylenedioxymethamphetamine]).

Prevalence

The prevalence of other hallucinogen intoxication may be estimated by use of those substances. In the United States, 1.8% of individuals age 12 years or older report using hallucinogens in the past year. Use is more prevalent among younger individuals, with 3.1% of 12- to 17-year-olds and 7.1% of 18- to 25-year-olds using hallucinogens in the past year, compared with only 0.7% of individuals age 26 years or older. Twelve-month prevalence for hallucinogen use is more common in males (2.4%) than in females (1.2%), and even more so among 18- to 25-year-olds (9.2% for males vs. 5.0% for females). In contrast, among individuals ages 12–17 years, there are no gender differences (3.1% for both genders). These figures may be used as proxy estimates for gender-related differences in the prevalence of other hallucinogen intoxication.

Suicide Risk

Other hallucinogen intoxication may lead to increased suicidality, although suicide is rare among users of hallucinogens.

Functional Consequences of Other Hallucinogen Intoxication

Other hallucinogen intoxication can have serious consequences. The perceptual disturbances and impaired judgment associated with other hallucinogen intoxication can result in injuries or fatalities from automobile crashes, physical fights, or unintentional self-injury (e.g., attempts to "fly" from high places). Environmental factors and the personality and expectations of the individual using the hallucinogen may contribute to the nature of and severity of hallucinogen intoxication. Continued use of hallucinogens, particularly MDMA, has also been linked with neurotoxic effects.

Differential Diagnosis

Other substance intoxication. Other hallucinogen intoxication should be differentiated from intoxication with amphetamines, cocaine, or other stimulants; anticholinergics; inhalants; and phencyclidine. Toxicological tests are useful in making this distinction, and determining the route of administration may also be useful.

Other conditions. Other disorders and conditions to be considered include schizophrenia, depression, withdrawal from other drugs (e.g., sedatives, alcohol), certain metabolic disorders (e.g., hypoglycemia), seizure disorders, tumors of the central nervous system, and vascular insults.

Hallucinogen persisting perception disorder. Other hallucinogen intoxication is distinguished from hallucinogen persisting perception disorder because the symptoms in the latter continue episodically or continuously for weeks (or longer) after the most recent intoxication.

Other hallucinogen-induced disorders. Other hallucinogen intoxication is distinguished from the other hallucinogen-induced disorders (e.g., hallucinogen-induced anxiety disorder, with onset during intoxication) because the symptoms in these latter disorders predominate the clinical presentation and are severe enough to warrant independent clinical attention.

Hallucinogen Persisting Perception Disorder

Diagnostic Criteria **292.89 (F16.983)**

A. Following cessation of use of a hallucinogen, the reexperiencing of one or more of the perceptual symptoms that were experienced while intoxicated with the hallucinogen (e.g., geometric hallucinations, false perceptions of movement in the peripheral visual fields, flashes of color, intensified colors, trails of images of moving objects, positive afterimages, halos around objects, macropsia and micropsia).
B. The symptoms in Criterion A cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
C. The symptoms are not attributable to another medical condition (e.g., anatomical lesions and infections of the brain, visual epilepsies) and are not better explained by another mental disorder (e.g., delirium, major neurocognitive disorder, schizophrenia) or hypnopompic hallucinations.

Diagnostic Features

The hallmark of hallucinogen persisting perception disorder is the reexperiencing, when the individual is sober, of the perceptual disturbances that were experienced while the individual was intoxicated with the hallucinogen (Criterion A). The symptoms may include any perceptual perturbations, but visual disturbances tend to be predominant. Typical of the abnormal visual perceptions are geometric hallucinations, false perceptions of movement in the peripheral visual fields, flashes of color, intensified colors, trails of images of moving objects (i.e., images left suspended in the path of a moving object as seen in stroboscopic photography), perceptions of entire objects, positive afterimages (i.e., a same-colored or complementary-colored "shadow" of an object remaining after removal of the object), halos around objects, or misperception of images as too large (macropsia) or too small (micropsia). Duration of the visual disturbances may be episodic or nearly continuous and must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion B). The disturbances may last for weeks, months, or years. Other explanations for the disturbances (e.g., brain lesions, preexisting psychosis, seizure disorders, migraine aura without headaches) must be ruled out (Criterion C).

Hallucinogen persisting perception disorder occurs primarily after LSD (lysergic acid diethylamide) use, but not exclusively. There does not appear to be a strong correlation between hallucinogen persisting perception disorder and number of occasions of hallucinogen use, with some instances of hallucinogen persisting perception disorder occurring in individuals with minimal exposure to hallucinogens. Some instances of hallucinogen persisting perception disorder may be triggered by use of other substances (e.g., cannabis or alcohol) or in adaptation to dark environments.

Associated Features Supporting Diagnosis

Reality testing remains intact in individuals with hallucinogen persisting perception disorder (i.e., the individual is aware that the disturbance is linked to the effect of the drug). If this is not the case, another disorder might better explain the abnormal perceptions.

Prevalence

Prevalence estimates of hallucinogen persisting perception disorder are unknown. Initial prevalence estimates of the disorder among individuals who use hallucinogens is approximately 4.2%.

Development and Course

Little is known about the development of hallucinogen persisting perception disorder. Its course, as suggested by its name, is persistent, lasting for weeks, months, or even years in certain individuals.

Risk and Prognostic Factors

There is little evidence regarding risk factors for hallucinogen persisting perception disorder, although genetic factors have been suggested as a possible explanation underlying the susceptibility to LSD effects in this condition.

Functional Consequences of Hallucinogen Persisting Perception Disorder

Although hallucinogen persisting perception disorder remains a chronic condition in some cases, many individuals with the disorder are able to suppress the disturbances and continue to function normally.

Differential Diagnosis

Conditions to be ruled out include schizophrenia, other drug effects, neurodegenerative disorders, stroke, brain tumors, infections, and head trauma. Neuroimaging results in hallucinogen persisting perception disorder cases are typically negative. As noted earlier, reality testing remains intact (i.e., the individual is aware that the disturbance is linked to the effect of the drug); if this is not the case, another disorder (e.g., psychotic disorder, another medical condition) might better explain the abnormal perceptions.

Comorbidity

Common comorbid mental disorders accompanying hallucinogen persisting perception disorder are panic disorder, alcohol use disorder, and major depressive disorder.

Other Phencyclidine-Induced Disorders

Other phencyclidine-induced disorders are described in other chapters of the manual with disorders with which they share phenomenology (see the substance/medication-induced mental disorders in these chapters): phencyclidine-induced psychotic disorder ("Schizophrenia Spectrum and Other Psychotic Disorders"); phencyclidine-induced bipolar disorder ("Bipolar and Related Disorders"); phencyclidine-induced depressive disorder ("Depressive Disorders"); and phencyclidine-induced anxiety disorder ("Anxiety Disorders"). For phencyclidine-induced intoxication delirium, see the criteria and discussion of delirium in the chapter "Neurocognitive Disorders." These phencyclidine-induced disorders are diagnosed instead of phencyclidine intoxication only when the symptoms are sufficiently severe to warrant independent clinical attention.

Other Hallucinogen-Induced Disorders

The following other hallucinogen-induced disorders are described in other chapters of the manual with disorders with which they share phenomenology (see the substance/medication-induced mental disorders in these chapters): other hallucinogen–induced psychotic disorder ("Schizophrenia Spectrum and Other Psychotic Disorders"); other hallucinogen–induced bipolar disorder ("Bipolar and Related Disorders"); other hallucinogen–induced

depressive disorder ("Depressive Disorders"); and other hallucinogen–induced anxiety disorder ("Anxiety Disorders"). For other hallucinogen intoxication delirium, see the criteria and discussion of delirium in the chapter "Neurocognitive Disorders." These hallucinogen-induced disorders are diagnosed instead of other hallucinogen intoxication only when the symptoms are sufficiently severe to warrant independent clinical attention.

Unspecified Phencyclidine-Related Disorder

292.9 (F16.99)

This category applies to presentations in which symptoms characteristic of a phencyclidine-related 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 specific phencyclidine-related disorder or any of the disorders in the substance-related and addictive disorders diagnostic class.

Unspecified Hallucinogen-Related Disorder

292.9 (F16.99)

This category applies to presentations in which symptoms characteristic of a hallucinogen-related 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 specific hallucinogen-related disorder or any of the disorders in the substance-related and addictive disorders diagnostic class.

Inhalant-Related Disorders

Inhalant Use Disorder
Inhalant Intoxication
Other Inhalant-Induced Disorders
Unspecified Inhalant-Related Disorder

Inhalant Use Disorder

Diagnostic Criteria

A. A problematic pattern of use of a hydrocarbon-based inhalant substance leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. The inhalant substance is often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control use of the inhalant substance.

3. A great deal of time is spent in activities necessary to obtain the inhalant substance, use it, or recover from its effects.
4. Craving, or a strong desire or urge to use the inhalant substance.
5. Recurrent use of the inhalant substance resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued use of the inhalant substance despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of its use.
7. Important social, occupational, or recreational activities are given up or reduced because of use of the inhalant substance.
8. Recurrent use of the inhalant substance in situations in which it is physically hazardous.
9. Use of the inhalant substance is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of the inhalant substance to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of the inhalant substance.

Specify **the particular inhalant:** When possible, the particular substance involved should be named (e.g., "solvent use disorder").

Specify if:

In early remission: After full criteria for inhalant use disorder were previously met, none of the criteria for inhalant use disorder have been met for at least 3 months but for less than 12 months (with the exception that Criterion A4, "Craving, or a strong desire or urge to use the inhalant substance," may be met).

In sustained remission: After full criteria for inhalant use disorder were previously met, none of the criteria for inhalant use disorder have been met at any time during a period of 12 months or longer (with the exception that Criterion A4, "Craving, or a strong desire or urge to use the inhalant substance," may be met).

Specify if:

In a controlled environment: This additional specifier is used if the individual is in an environment where access to inhalant substances is restricted.

Coding based on current severity: Note for ICD-10-CM codes: If an inhalant intoxication or another inhalant-induced mental disorder is also present, do not use the codes below for inhalant use disorder. Instead, the comorbid inhalant use disorder is indicated in the 4th character of the inhalant-induced disorder code (see the coding note for inhalant intoxication or a specific inhalant-induced mental disorder). For example, if there is comorbid inhalant-induced depressive disorder and inhalant use disorder, only the inhalant-induced depressive disorder code is given, with the 4th character indicating whether the comorbid inhalant use disorder is mild, moderate, or severe: F18.14 for mild inhalant use disorder with inhalant-induced depressive disorder or F18.24 for a moderate or severe inhalant use disorder with inhalant-induced depressive disorder.

Specify current severity:

305.90 (F18.10) Mild: Presence of 2–3 symptoms.

304.60 (F18.20) Moderate: Presence of 4–5 symptoms.

304.60 (F18.20) Severe: Presence of 6 or more symptoms.

Specifiers

This manual recognizes volatile hydrocarbon use meeting the above diagnostic criteria as inhalant use disorder. Volatile hydrocarbons are toxic gases from glues, fuels, paints, and other volatile compounds. When possible, the particular substance involved should be named (e.g., "toluene use disorder"). However, most compounds that are inhaled are a mixture of several substances that can produce psychoactive effects, and it is often difficult to ascertain the exact substance responsible for the disorder. Unless there is clear evidence that a single, unmixed substance has been used, the general term inhalant should be used in recording the diagnosis. Disorders arising from inhalation of nitrous oxide or of amyl-, butyl-, or isobutylnitrite are considered as other (or unknown) substance use disorder.

"In a controlled environment" applies as a further specifier of remission if the individual is both in remission and in a controlled environment (i.e., in early remission in a controlled environment or in sustained remission in a controlled environment). Examples of these environments are closely supervised and substance-free jails, therapeutic communities, and locked hospital units.

The severity of individuals' inhalant use disorder is assessed by the number of diagnostic criteria endorsed. Changing severity of individuals' inhalant use disorder across time is reflected by reductions in the frequency (e.g., days used per month) and/or dose (e.g., tubes of glue per day) used, as assessed by the individual's self-report, report of others, clinician's observations, and biological testing (when practical).

Diagnostic Features

Features of inhalant use disorder include repeated use of an inhalant substance despite the individual's knowing that the substance is causing serious problems for the individual (Criterion A9). Those problems are reflected in the diagnostic criteria.

Missing work or school or inability to perform typical responsibilities at work or school (Criterion A5), and continued use of the inhalant substance even though it causes arguments with family or friends, fights, and other social or interpersonal problems (Criterion A6), may be seen in inhalant use disorder. Limiting family contact, work or school obligations, or recreational activities (e.g., sports, games, hobbies) may also occur (Criterion A7). Use of inhalants when driving or operating dangerous equipment (Criterion A8) is also seen.

Tolerance (Criterion A10) and mild withdrawal are each reported by about 10% of individuals who use inhalants, and a few individuals use inhalants to avoid withdrawal. However, because the withdrawal symptoms are mild, this manual neither recognizes a diagnosis of inhalant withdrawal nor counts withdrawal complaints as a diagnostic criterion for inhalant use disorder.

Associated Features Supporting Diagnosis

A diagnosis of inhalant use disorder is supported by recurring episodes of intoxication with negative results in standard drug screens (which do not detect inhalants); possession, or lingering odors, of inhalant substances; peri-oral or peri-nasal "glue-sniffer's rash"; association with other individuals known to use inhalants; membership in groups with prevalent inhalant use (e.g., some native or aboriginal communities, homeless children in street gangs); easy access to certain inhalant substances; paraphernalia possession; presence of the disorder's characteristic medical complications (e.g., brain white matter pathology, rhabdomyolysis); and the presence of multiple substance use disorders. Inhalant use and inhalant use disorder are associated with past suicide attempts, especially among adults reporting previous episodes of low mood or anhedonia.

Prevalence

About 0.4% of Americans ages 12–17 years have a pattern of use that meets criteria for inhalant use disorder in the past 12 months. Among those youths, the prevalence is highest

in Native Americans and lowest in African Americans. Prevalence falls to about 0.1% among Americans ages 18–29 years, and only 0.02% when all Americans 18 years or older are considered, with almost no females and a preponderance of European Americans. Of course, in isolated subgroups, prevalence may differ considerably from these overall rates.

Development and Course

About 10% of 13-year-old American children report having used inhalants at least once; that percentage remains stable through age 17 years. Among those 12- to 17-year-olds who use inhalants, the more-used substances include glue, shoe polish, or toluene; gasoline or lighter fluid; or spray paints.

Only 0.4% of 12- to 17-year-olds progress to inhalant use disorder; those youths tend to exhibit multiple other problems. The declining prevalence of inhalant use disorder after adolescence indicates that this disorder usually remits in early adulthood.

Volatile hydrocarbon use disorder is rare in prepubertal children, most common in adolescents and young adults, and uncommon in older persons. Calls to poison-control centers for "intentional abuse" of inhalants peak with calls involving individuals at age 14 years. Of adolescents who use inhalants, perhaps one-fifth develop inhalant use disorder; a few die from inhalant-related accidents, or "sudden sniffing death". But the disorder apparently remits in many individuals after adolescence. Prevalence declines dramatically among individuals in their 20s. Those with inhalant use disorder extending into adulthood often have severe problems: substance use disorders, antisocial personality disorder, and suicidal ideation with attempts.

Risk and Prognostic Factors

Temperamental. Predictors of progression from nonuse of inhalants, to use, to inhalant use disorder include comorbid non-inhalant substance use disorders and either conduct disorder or antisocial personality disorder. Other predictors are earlier onset of inhalant use and prior use of mental health services.

Environmental. Inhalant gases are widely and legally available, increasing the risk of misuse. Childhood maltreatment or trauma also is associated with youthful progression from inhalant non-use to inhalant use disorder.

Genetic and physiological. *Behavioral disinhibition* is a highly heritable general propensity to not constrain behavior in socially acceptable ways, to break social norms and rules, and to take dangerous risks, pursuing rewards excessively despite dangers of adverse consequences. Youths with strong behavioral disinhibition show risk factors for inhalant use disorder: early-onset substance use disorder, multiple substance involvement, and early conduct problems. Because behavioral disinhibition is under strong genetic influence, youths in families with substance and antisocial problems are at elevated risk for inhalant use disorder.

Culture-Related Diagnostic Issues

Certain native or aboriginal communities have experienced a high prevalence of inhalant problems. Also, in some countries, groups of homeless children in street gangs have extensive inhalant use problems.

Gender-Related Diagnostic Issues

Although the prevalence of inhalant use disorder is almost identical in adolescent males and females, the disorder is very rare among adult females.

Diagnostic Markers

Urine, breath, or saliva tests may be valuable for assessing concurrent use of non-inhalant substances by individuals with inhalant use disorder. However, technical problems and

the considerable expense of analyses make frequent biological testing for inhalants themselves impractical.

Functional Consequences of Inhalant Use Disorder

Because of inherent toxicity, use of butane or propane is not infrequently fatal. Moreover, any inhaled volatile hydrocarbons may produce "sudden sniffing death" from cardiac arrhythmia. Fatalities may occur even on the first inhalant exposure and are not thought to be dose-related. Volatile hydrocarbon use impairs neurobehavioral function and causes various neurological, gastrointestinal, cardiovascular, and pulmonary problems.

Long-term inhalant users are at increased risk for tuberculosis, HIV/AIDS, sexually transmitted diseases, depression, anxiety, bronchitis, asthma, and sinusitis. Deaths may occur from respiratory depression, arrhythmias, asphyxiation, aspiration of vomitus, or accident and injury.

Differential Diagnosis

Inhalant exposure (unintentional) from industrial or other accidents. This designation is used when findings suggest repeated or continuous inhalant exposure but the involved individual and other informants deny any history of purposeful inhalant use.

Inhalant use (intentional), without meeting criteria for inhalant use disorder. Inhalant use is common among adolescents, but for most of those individuals, the inhalant use does not meet the diagnostic standard of two or more Criterion A items for inhalant use disorder in the past year.

Inhalant intoxication, without meeting criteria for inhalant use disorder. Inhalant intoxication occurs frequently during inhalant use disorder but also may occur among individuals whose use does not meet criteria for inhalant use disorder, which requires at least two of the 10 diagnostic criteria in the past year.

Inhalant-induced disorders (i.e., inhalant-induced psychotic disorder, depressive disorder, anxiety disorder, neurocognitive disorder, other inhalant-induced disorders) without meeting criteria for inhalant use disorder. Criteria are met for a psychotic, depressive, anxiety, or major neurocognitive disorder, and there is evidence from history, physical examination, or laboratory findings that the deficits are etiologically related to the effects of inhalant substances. Yet, criteria for inhalant use disorder may not be met (i.e., fewer than 2 of the 10 criteria were present).

Other substance use disorders, especially those involving sedating substances (e.g., alcohol, benzodiazepines, barbiturates). Inhalant use disorder commonly co-occurs with other substance use disorders, and the symptoms of the disorders may be similar and overlapping. To disentangle symptom patterns, it is helpful to inquire about which symptoms persisted during periods when some of the substances were not being used.

Other toxic, metabolic, traumatic, neoplastic, or infectious disorders impairing central or peripheral nervous system function. Individuals with inhalant use disorder may present with symptoms of pernicious anemia, subacute combined degeneration of the spinal cord, psychosis, major or minor cognitive disorder, brain atrophy, leukoencephalopathy, and many other nervous system disorders. Of course, these disorders also may occur in the absence of inhalant use disorder. A history of little or no inhalant use helps to exclude inhalant use disorder as the source of these problems.

Disorders of other organ systems. Individuals with inhalant use disorder may present with symptoms of hepatic or renal damage, rhabdomyolysis, methemoglobinemia, or symptoms of other gastrointestinal, cardiovascular, or pulmonary diseases. A history of little or no inhalant use helps to exclude inhalant use disorder as the source of such medical problems.

Comorbidity

Individuals with inhalant use disorder receiving clinical care often have numerous other substance use disorders. Inhalant use disorder commonly co-occurs with adolescent conduct disorder and adult antisocial personality disorder. Adult inhalant use and inhalant use disorder also are strongly associated with suicidal ideation and suicide attempts.

Inhalant Intoxication

Diagnostic Criteria

A. Recent intended or unintended short-term, high-dose exposure to inhalant substances, including volatile hydrocarbons such as toluene or gasoline.

B. Clinically significant problematic behavioral or psychological changes (e.g., belligerence, assaultiveness, apathy, impaired judgment) that developed during, or shortly after, exposure to inhalants.

C. Two (or more) of the following signs or symptoms developing during, or shortly after, inhalant use or exposure:

1. Dizziness.
2. Nystagmus.
3. Incoordination.
4. Slurred speech.
5. Unsteady gait.
6. Lethargy.
7. Depressed reflexes.
8. Psychomotor retardation.
9. Tremor.
10. Generalized muscle weakness.
11. Blurred vision or diplopia.
12. Stupor or coma.
13. Euphoria.

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance.

Coding note: The ICD-9-CM code is **292.89.** The ICD-10-CM code depends on whether there is a comorbid inhalant use disorder. If a mild inhalant use disorder is comorbid, the ICD-10-CM code is **F18.129,** and if a moderate or severe inhalant use disorder is comorbid, the ICD-10-CM code is **F18.229.** If there is no comorbid inhalant use disorder, then the ICD-10-CM code is **F18.929.**

Note: For information on Development and Course, Risk and Prognostic Factors, Culture-Related Diagnostic Issues, and Diagnostic Markers, see the corresponding sections in inhalant use disorder.

Diagnostic Features

Inhalant intoxication is an inhalant-related, clinically significant mental disorder that develops during, or immediately after, intended or unintended inhalation of a volatile hydrocarbon substance. Volatile hydrocarbons are toxic gases from glues, fuels, paints, and other volatile compounds. When it is possible to do so, the particular substance involved should be named (e.g., toluene intoxication). Among those who do, the intoxication clears within a few minutes to a few hours after the exposure ends. Thus, inhalant intoxication usually occurs in brief episodes that may recur.

Associated Features Supporting Diagnosis

Inhalant intoxication may be indicated by evidence of possession, or lingering odors, of inhalant substances (e.g., glue, paint thinner, gasoline, butane lighters); apparent intoxication occurring in the age range with the highest prevalence of inhalant use (12–17 years); and apparent intoxication with negative results from the standard drug screens that usually fail to identify inhalants.

Prevalence

The prevalence of actual episodes of inhalant intoxication in the general population is unknown, but it is probable that most inhalant users would at some time exhibit use that would meet criteria for inhalant intoxication disorder. Therefore, the prevalence of inhalant use and the prevalence of inhalant intoxication disorder are likely similar. In 2009 and 2010, inhalant use in the past year was reported by 0.8% of all Americans older than 12 years; the prevalence was highest in younger age groups (3.6% for individuals 12 to 17 years old, and 1.7% for individuals 18 to 25 years old).

Gender-Related Diagnostic Issues

Gender differences in the prevalence of inhalant intoxication in the general population are unknown. However, if it is assumed that most inhalant users eventually experience inhalant intoxication, gender differences in the prevalence of inhalant *users* likely approximate those in the proportions of males and females experiencing inhalant intoxication. Regarding gender differences in the prevalence of inhalant users in the United States, 1% of males older than 12 years and 0.7% of females older than 12 years have used inhalants in the previous year, but in the younger age groups more females than males have used inhalants (e.g., among 12- to 17-year-olds, 3.6% of males and 4.2% of females).

Functional Consequences of Inhalant Intoxication

Use of inhaled substances in a closed container, such as a plastic bag over the head, may lead to unconsciousness, anoxia, and death. Separately, "sudden sniffing death," likely from cardiac arrhythmia or arrest, may occur with various volatile inhalants. The enhanced toxicity of certain volatile inhalants, such as butane or propane, also causes fatalities. Although inhalant intoxication itself is of short duration, it may produce persisting medical and neurological problems, especially if the intoxications are frequent.

Differential Diagnosis

Inhalant exposure, without meeting the criteria for inhalant intoxication disorder. The individual intentionally or unintentionally inhaled substances, but the dose was insufficient for the diagnostic criteria for inhalant use disorder to be met.

Intoxication and other substance/medication-induced disorders from other substances, especially from sedating substances (e.g., alcohol, benzodiazepines, barbiturates). These disorders may have similar signs and symptoms, but the intoxication is attributable to other intoxicants that may be identified via a toxicology screen. Differentiating the source of the intoxication may involve discerning evidence of inhalant exposure as described for inhalant use disorder. A diagnosis of inhalant intoxication may be suggested by possession, or lingering odors, of inhalant substances (e.g., glue, paint thinner, gasoline, butane lighters,); paraphernalia possession (e.g., rags or bags for concentrating glue fumes); perioral or perinasal "glue-sniffer's rash"; reports from family or friends that the intoxicated individual possesses or uses inhalants; apparent intoxication despite negative results on standard drug screens (which usually fail to identify inhalants); apparent intoxication occurring in that age range with the highest prevalence of inhalant use (12–17

years); association with others known to use inhalants; membership in certain small communities with prevalent inhalant use (e.g., some native or aboriginal communities, homeless street children and adolescents); or unusual access to certain inhalant substances.

Other inhalant-related disorders. Episodes of inhalant intoxication do occur during, but are not identical with, other inhalant-related disorders. Those inhalant-related disorders are recognized by their respective diagnostic criteria: inhalant use disorder, inhalant-induced neurocognitive disorder, inhalant-induced psychotic disorder, inhalant-induced depressive disorder, inhalant-induced anxiety disorder, and other inhalant-induced disorders.

Other toxic, metabolic, traumatic, neoplastic, or infectious disorders that impair brain function and cognition. Numerous neurological and other medical conditions may produce the clinically significant behavioral or psychological changes (e.g., belligerence, assaultiveness, apathy, impaired judgment) that also characterize inhalant intoxication.

Other Inhalant-Induced Disorders

The following inhalant-induced disorders are described in other chapters of the manual with disorders with which they share phenomenology (see the substance/medication-induced mental disorders in these chapters): inhalant-induced psychotic disorder ("Schizophrenia Spectrum and Other Psychotic Disorders"); inhalant-induced depressive disorder ("Depressive Disorders"); inhalant-induced anxiety disorder ("Anxiety Disorders"); and inhalant-induced major or mild neurocognitive disorder ("Neurocognitive Disorders"). For inhalant intoxication delirium, see the criteria and discussion of delirium in the chapter "Neurocognitive Disorders." These inhalant-induced disorders are diagnosed instead of inhalant intoxication only when symptoms are sufficiently severe to warrant independent clinical attention.

Unspecified Inhalant-Related Disorder

292.9 (F18.99)

This category applies to presentations in which symptoms characteristic of an inhalant-related 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 specific inhalant-related disorder or any of the disorders in the substance-related and addictive disorders diagnostic class.

Opioid-Related Disorders

Opioid Use Disorder
Opioid Intoxication
Opioid Withdrawal
Other Opioid-Induced Disorders
Unspecified Opioid-Related Disorder

Opioid Use Disorder

Diagnostic Criteria

A. A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of an opioid.

    Note: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.
11. Withdrawal, as manifested by either of the following:
    a. The characteristic opioid withdrawal syndrome (refer to Criteria A and B of the criteria set for opioid withdrawal, pp. 547–548).
    b. Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.

    Note: This criterion is not considered to be met for those individuals taking opioids solely under appropriate medical supervision.

Specify if:

In early remission: After full criteria for opioid use disorder were previously met, none of the criteria for opioid use disorder have been met for at least 3 months but for less than 12 months (with the exception that Criterion A4, "Craving, or a strong desire or urge to use opioids," may be met).

In sustained remission: After full criteria for opioid use disorder were previously met, none of the criteria for opioid use disorder have been met at any time during a period of 12 months or longer (with the exception that Criterion A4, "Craving, or a strong desire or urge to use opioids," may be met).

Specify if:

On maintenance therapy: This additional specifier is used if the individual is taking a prescribed agonist medication such as methadone or buprenorphine and none of the criteria for opioid use disorder have been met for that class of medication (except tolerance to, or withdrawal from, the agonist). This category also applies to those individ-

uals being maintained on a partial agonist, an agonist/antagonist, or a full antagonist such as oral naltrexone or depot naltrexone.

In a controlled environment: This additional specifier is used if the individual is in an environment where access to opioids is restricted.

Coding based on current severity: Note for ICD-10-CM codes: If an opioid intoxication, opioid withdrawal, or another opioid-induced mental disorder is also present, do not use the codes below for opioid use disorder. Instead, the comorbid opioid use disorder is indicated in the 4th character of the opioid-induced disorder code (see the coding note for opioid intoxication, opioid withdrawal, or a specific opioid-induced mental disorder). For example, if there is comorbid opioid-induced depressive disorder and opioid use disorder, only the opioid-induced depressive disorder code is given, with the 4th character indicating whether the comorbid opioid use disorder is mild, moderate, or severe: F11.14 for mild opioid use disorder with opioid-induced depressive disorder or F11.24 for a moderate or severe opioid use disorder with opioid-induced depressive disorder.

Specify current severity:

305.50 (F11.10) Mild: Presence of 2–3 symptoms.

304.00 (F11.20) Moderate: Presence of 4–5 symptoms.

304.00 (F11.20) Severe: Presence of 6 or more symptoms.

Specifiers

The "on maintenance therapy" specifier applies as a further specifier of remission if the individual is both in remission and receiving maintenance therapy. "In a controlled environment" applies as a further specifier of remission if the individual is both in remission and in a controlled environment (i.e., in early remission in a controlled environment or in sustained remission in a controlled environment). Examples of these environments are closely supervised and substance-free jails, therapeutic communities, and locked hospital units.

Changing severity across time in an individual is also reflected by reductions in the frequency (e.g., days of use per month) and/or dose (e.g., injections or number of pills) of an opioid, as assessed by the individual's self-report, report of knowledgeable others, clinician's observations, and biological testing.

Diagnostic Features

Opioid use disorder includes signs and symptoms that reflect compulsive, prolonged self-administration of opioid substances that are used for no legitimate medical purpose or, if another medical condition is present that requires opioid treatment, that are used in doses greatly in excess of the amount needed for that medical condition. (For example, an individual prescribed analgesic opioids for pain relief at adequate dosing will use significantly more than prescribed and not only because of persistent pain.) Individuals with opioid use disorder tend to develop such regular patterns of compulsive drug use that daily activities are planned around obtaining and administering opioids. Opioids are usually purchased on the illegal market but may also be obtained from physicians by falsifying or exaggerating general medical problems or by receiving simultaneous prescriptions from several physicians. Health care professionals with opioid use disorder will often obtain opioids by writing prescriptions for themselves or by diverting opioids that have been prescribed for patients or from pharmacy supplies. Most individuals with opioid use disorder have significant levels of tolerance and will experience withdrawal on abrupt discontinuation of opioid substances. Individuals with opioid use disorder often develop conditioned responses to drug-related stimuli (e.g., craving on seeing any heroin powder–like substance)—a phenomenon that occurs with most drugs that cause intense psychological changes. These responses probably contribute to relapse, are difficult to extinguish, and typically persist long after detoxification is completed.

Associated Features Supporting Diagnosis

Opioid use disorder can be associated with a history of drug-related crimes (e.g., possession or distribution of drugs, forgery, burglary, robbery, larceny, receiving stolen goods). Among health care professionals and individuals who have ready access to controlled substances, there is often a different pattern of illegal activities involving problems with state licensing boards, professional staffs of hospitals, or other administrative agencies. Marital difficulties (including divorce), unemployment, and irregular employment are often associated with opioid use disorder at all socioeconomic levels.

Prevalence

The 12-month prevalence of opioid use disorder is approximately 0.37% among adults age 18 years and older in the community population. This may be an underestimate because of the large number of incarcerated individuals with opioid use disorders. Rates are higher in males than in females (0.49% vs. 0.26%), with the male-to-female ratio typically being 1.5:1 for opioids other than heroin (i.e., available by prescription) and 3:1 for heroin. Female adolescents may have a higher likelihood of developing opioid use disorders. The prevalence decreases with age, with the prevalence highest (0.82%) among adults age 29 years or younger, and decreasing to 0.09% among adults age 65 years and older. Among adults, the prevalence of opioid use disorder is lower among African Americans at 0.18% and overrepresented among Native Americans at 1.25%. It is close to average among whites (0.38%), Asian or Pacific Islanders (0.35%), and Hispanics (0.39%).

Among individuals in the United States ages 12–17 years, the overall 12-month prevalence of opioid use disorder in the community population is approximately 1.0%, but the prevalence of heroin use disorder is less than 0.1%. By contrast, analgesic use disorder is prevalent in about 1.0% of those ages 12–17 years, speaking to the importance of opioid analgesics as a group of substances with significant health consequences.

The 12-month prevalence of problem opioid use in European countries in the community population ages 15–64 years is between 0.1% and 0.8%. The average prevalence of problem opioid use in the European Union and Norway is between 0.36% and 0.44%.

Development and Course

Opioid use disorder can begin at any age, but problems associated with opioid use are most commonly first observed in the late teens or early 20s. Once opioid use disorder develops, it usually continues over a period of many years, even though brief periods of abstinence are frequent. In treated populations, relapse following abstinence is common. Even though relapses do occur, and while some long-term mortality rates may be as high as 2% per year, about 20%–30% of individuals with opioid use disorder achieve long-term abstinence. An exception concerns that of military service personnel who became dependent on opioids in Vietnam; over 90% of this population who had been dependent on opioids during deployment in Vietnam achieved abstinence after they returned, but they experienced increased rates of alcohol or amphetamine use disorder as well as increased suicidality.

Increasing age is associated with a decrease in prevalence as a result of early mortality and the remission of symptoms after age 40 years (i.e., "maturing out"). However, many individuals continue have presentations that meet opioid use disorder criteria for decades.

Risk and Prognostic Factors

Genetic and physiological. The risk for opiate use disorder can be related to individual, family, peer, and social environmental factors, but within these domains, genetic factors play a particularly important role both directly and indirectly. For instance, impulsivity and novelty seeking are individual temperaments that relate to the propensity to develop

a substance use disorder but may themselves be genetically determined. Peer factors may relate to genetic predisposition in terms of how an individual selects his or her environment.

Culture-Related Diagnostic Issues

Despite small variations regarding individual criterion items, opioid use disorder diagnostic criteria perform equally well across most race/ethnicity groups. Individuals from ethnic minority populations living in economically deprived areas have been overrepresented among individuals with opioid use disorder. However, over time, opioid use disorder is seen more often among white middle-class individuals, especially females, suggesting that differences in use reflect the availability of opioid drugs and that other social factors may impact prevalence. Medical personnel who have ready access to opioids may be at increased risk for opioid use disorder.

Diagnostic Markers

Routine urine toxicology test results are often positive for opioid drugs in individuals with opioid use disorder. Urine test results remain positive for most opioids (e.g., heroin, morphine, codeine, oxycodone, propoxyphene) for 12–36 hours after administration. Fentanyl is not detected by standard urine tests but can be identified by more specialized procedures for several days. Methadone, buprenorphine (or buprenorphine/naloxone combination), and LAAM (L-alpha-acetylmethadol) have to be specifically tested for and will not cause a positive result on routine tests for opiates. They can be detected for several days up to more than 1 week. Laboratory evidence of the presence of other substances (e.g., cocaine, marijuana, alcohol, amphetamines, benzodiazepines) is common. Screening test results for hepatitis A, B, and C virus are positive in as many as 80%–90% of injection opioid users, either for hepatitis antigen (signifying active infection) or for hepatitis antibody (signifying past infection). HIV is prevalent in injection opioid users as well. Mildly elevated liver function test results are common, either as a result of resolving hepatitis or from toxic injury to the liver due to contaminants that have been mixed with the injected opioid. Subtle changes in cortisol secretion patterns and body temperature regulation have been observed for up to 6 months following opioid detoxification.

Suicide Risk

Similar to the risk generally observed for all substance use disorders, opioid use disorder is associated with a heightened risk for suicide attempts and completed suicides. Particularly notable are both accidental and deliberate opioid overdoses. Some suicide risk factors overlap with risk factors for an opioid use disorder. In addition, repeated opioid intoxication or withdrawal may be associated with severe depressions that, although temporary, can be intense enough to lead to suicide attempts and completed suicides. Available data suggest that nonfatal accidental opioid overdose (which is common) and attempted suicide are distinct clinically significant problems that should not be mistaken for each other.

Functional Consequences of Opioid Use Disorder

Opioid use is associated with a lack of mucous membrane secretions, causing dry mouth and nose. Slowing of gastrointestinal activity and a decrease in gut motility can produce severe constipation. Visual acuity may be impaired as a result of pupillary constriction with acute administration. In individuals who inject opioids, sclerosed veins (“tracks”) and puncture marks on the lower portions of the upper extremities are common. Veins sometimes become so severely sclerosed that peripheral edema develops, and individuals switch to injecting in veins in the legs, neck, or groin. When these veins become unusable, individuals often inject directly into their subcutaneous tissue (“skin-popping”), resulting

in cellulitis, abscesses, and circular-appearing scars from healed skin lesions. Tetanus and *Clostridium botulinum* infections are relatively rare but extremely serious consequences of injecting opioids, especially with contaminated needles. Infections may also occur in other organs and include bacterial endocarditis, hepatitis, and HIV infection. Hepatitis C infections, for example, may occur in up to 90% of persons who inject opioids. In addition, the prevalence of HIV infection can be high among individuals who inject drugs, a large proportion of whom are individuals with opioid use disorder. HIV infection rates have been reported to be as high as 60% among heroin users with opioid use disorder in some areas of the United States or the Russian Federation. However, the incidence may also be 10% or less in other areas, especially those where access to clean injection material and paraphernalia is facilitated.

Tuberculosis is a particularly serious problem among individuals who use drugs intravenously, especially those who are dependent on heroin; infection is usually asymptomatic and evident only by the presence of a positive tuberculin skin test. However, many cases of active tuberculosis have been found, especially among those who are infected with HIV. These individuals often have a newly acquired infection but also are likely to experience reactivation of a prior infection because of impaired immune function.

Individuals who sniff heroin or other opioids into the nose ("snorting") often develop irritation of the nasal mucosa, sometimes accompanied by perforation of the nasal septum. Difficulties in sexual functioning are common. Males often experience erectile dysfunction during intoxication or chronic use. Females commonly have disturbances of reproductive function and irregular menses.

In relation to infections such as cellulitis, hepatitis, HIV infection, tuberculosis, and endocarditis, opioid use disorder is associated with a mortality rate as high as 1.5%–2% per year. Death most often results from overdose, accidents, injuries, AIDS, or other general medical complications. Accidents and injuries due to violence that is associated with buying or selling drugs are common. In some areas, violence accounts for more opioid-related deaths than overdose or HIV infection. Physiological dependence on opioids may occur in about half of the infants born to females with opioid use disorder; this can produce a severe withdrawal syndrome requiring medical treatment. Although low birth weight is also seen in children of mothers with opioid use disorder, it is usually not marked and is generally not associated with serious adverse consequences.

Differential Diagnosis

Opioid-induced mental disorders. Opioid-induced disorders occur frequently in individuals with opioid use disorder. Opioid-induced disorders may be characterized by symptoms (e.g., depressed mood) that resemble primary mental disorders (e.g., persistent depressive disorder [dysthymia] vs. opioid-induced depressive disorder, with depressive features, with onset during intoxication). Opioids are less likely to produce symptoms of mental disturbance than are most other drugs of abuse. Opioid intoxication and opioid withdrawal are distinguished from the other opioid-induced disorders (e.g., opioid-induced depressive disorder, with onset during intoxication) because the symptoms in these latter disorders predominate the clinical presentation and are severe enough to warrant independent clinical attention.

Other substance intoxication. Alcohol intoxication and sedative, hypnotic, or anxiolytic intoxication can cause a clinical picture that resembles that for opioid intoxication. A diagnosis of alcohol or sedative, hypnotic, or anxiolytic intoxication can usually be made based on the absence of pupillary constriction or the lack of a response to naloxone challenge. In some cases, intoxication may be due both to opioids and to alcohol or other sedatives. In these cases, the naloxone challenge will not reverse all of the sedative effects.

Other withdrawal disorders. The anxiety and restlessness associated with opioid withdrawal resemble symptoms seen in sedative-hypnotic withdrawal. However, opioid withdrawal is also accompanied by rhinorrhea, lacrimation, and pupillary dilation, which

are not seen in sedative-type withdrawal. Dilated pupils are also seen in hallucinogen intoxication and stimulant intoxication. However, other signs or symptoms of opioid withdrawal, such as nausea, vomiting, diarrhea, abdominal cramps, rhinorrhea, or lacrimation, are not present.

Comorbidity

The most common medical conditions associated with opioid use disorder are viral (e.g., HIV, hepatitis C virus) and bacterial infections, particularly among users of opioids by injection. These infections are less common in opioid use disorder with prescription opioids. Opioid use disorder is often associated with other substance use disorders, especially those involving tobacco, alcohol, cannabis, stimulants, and benzodiazepines, which are often taken to reduce symptoms of opioid withdrawal or craving for opioids, or to enhance the effects of administered opioids. Individuals with opioid use disorder are at risk for the development of mild to moderate depression that meets symptomatic and duration criteria for persistent depressive disorder (dysthymia) or, in some cases, for major depressive disorder. These symptoms may represent an opioid-induced depressive disorder or an exacerbation of a preexisting primary depressive disorder. Periods of depression are especially common during chronic intoxication or in association with physical or psychosocial stressors that are related to the opioid use disorder. Insomnia is common, especially during withdrawal. Antisocial personality disorder is much more common in individuals with opioid use disorder than in the general population. Posttraumatic stress disorder is also seen with increased frequency. A history of conduct disorder in childhood or adolescence has been identified as a significant risk factor for substance-related disorders, especially opioid use disorder.

Opioid Intoxication

Diagnostic Criteria

A. Recent use of an opioid.

B. Clinically significant problematic behavioral or psychological changes (e.g., initial euphoria followed by apathy, dysphoria, psychomotor agitation or retardation, impaired judgment) that developed during, or shortly after, opioid use.

C. Pupillary constriction (or pupillary dilation due to anoxia from severe overdose) and one (or more) of the following signs or symptoms developing during, or shortly after, opioid use:

   1. Drowsiness or coma.
   2. Slurred speech.
   3. Impairment in attention or memory.

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance.

Specify if:

With perceptual disturbances: This specifier may be noted in the rare instance in which hallucinations with intact reality testing or auditory, visual, or tactile illusions occur in the absence of a delirium.

Coding note: The ICD-9-CM code is **292.89.** The ICD-10-CM code depends on whether or not there is a comorbid opioid use disorder and whether or not there are perceptual disturbances.

For opioid intoxication without perceptual disturbances: If a mild opioid use disorder is comorbid, the ICD-10-CM code is **F11.129,** and if a moderate or severe opioid

use disorder is comorbid, the ICD-10-CM code is **F11.229.** If there is no comorbid opioid use disorder, then the ICD-10-CM code is **F11.929.**

For opioid intoxication with perceptual disturbances: If a mild opioid use disorder is comorbid, the ICD-10-CM code is **F11.122,** and if a moderate or severe opioid use disorder is comorbid, the ICD-10-CM code is **F11.222.** If there is no comorbid opioid use disorder, then the ICD-10-CM code is **F11.922.**

Diagnostic Features

The essential feature of opioid intoxication is the presence of clinically significant problematic behavioral or psychological changes (e.g., initial euphoria followed by apathy, dysphoria, psychomotor agitation or retardation, impaired judgment) that develop during, or shortly after, opioid use (Criteria A and B). Intoxication is accompanied by pupillary constriction (unless there has been a severe overdose with consequent anoxia and pupillary dilation) and one or more of the following signs: drowsiness (described as being "on the nod"), slurred speech, and impairment in attention or memory (Criterion C); drowsiness may progress to coma. Individuals with opioid intoxication may demonstrate inattention to the environment, even to the point of ignoring potentially harmful events. The signs or symptoms must not be attributable to another medical condition and are not better explained by another mental disorder (Criterion D).

Differential Diagnosis

Other substance intoxication. Alcohol intoxication and sedative-hypnotic intoxication can cause a clinical picture that resembles opioid intoxication. A diagnosis of alcohol or sedative-hypnotic intoxication can usually be made based on the absence of pupillary constriction or the lack of a response to a naloxone challenge. In some cases, intoxication may be due both to opioids and to alcohol or other sedatives. In these cases, the naloxone challenge will not reverse all of the sedative effects.

Other opioid-related disorders. Opioid intoxication is distinguished from the other opioid-induced disorders (e.g., opioid-induced depressive disorder, with onset during intoxication) because the symptoms in the latter disorders predominate in the clinical presentation and meet full criteria for the relevant disorder.

Opioid Withdrawal

Diagnostic Criteria **292.0 (F11.23)**

A. Presence of either of the following:
   1. Cessation of (or reduction in) opioid use that has been heavy and prolonged (i.e., several weeks or longer).
   2. Administration of an opioid antagonist after a period of opioid use.

B. Three (or more) of the following developing within minutes to several days after Criterion A:
   1. Dysphoric mood.
   2. Nausea or vomiting.
   3. Muscle aches.
   4. Lacrimation or rhinorrhea.
   5. Pupillary dilation, piloerection, or sweating.

6. Diarrhea.
7. Yawning.
8. Fever.
9. Insomnia.

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

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

Coding note: The ICD-9-CM code is 292.0. The ICD-10-CM code for opioid withdrawal is F11.23. Note that the ICD-10-CM code indicates the comorbid presence of a moderate or severe opioid use disorder, reflecting the fact that opioid withdrawal can only occur in the presence of a moderate or severe opioid use disorder. It is not permissible to code a comorbid mild opioid use disorder with opioid withdrawal.

Diagnostic Features

The essential feature of opioid withdrawal is the presence of a characteristic withdrawal syndrome that develops after the cessation of (or reduction in) opioid use that has been heavy and prolonged (Criterion A1). The withdrawal syndrome can also be precipitated by administration of an opioid antagonist (e.g., naloxone or naltrexone) after a period of opioid use (Criterion A2). This may also occur after administration of an opioid partial agonist such as buprenorphine to a person currently using a full opioid agonist.

Opioid withdrawal is characterized by a pattern of signs and symptoms that are opposite to the acute agonist effects. The first of these are subjective and consist of complaints of anxiety, restlessness, and an "achy feeling" that is often located in the back and legs, along with irritability and increased sensitivity to pain. Three or more of the following must be present to make a diagnosis of opioid withdrawal: dysphoric mood; nausea or vomiting; muscle aches; lacrimation or rhinorrhea; pupillary dilation, piloerection, or increased sweating; diarrhea; yawning; fever; and insomnia (Criterion B). Piloerection and fever are associated with more severe withdrawal and are not often seen in routine clinical practice because individuals with opioid use disorder usually obtain substances before withdrawal becomes that far advanced. These symptoms of opioid withdrawal must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion C). The symptoms must not be attributable to another medical condition and are not better explained by another mental disorder (Criterion D). Meeting diagnostic criteria for opioid withdrawal alone is not sufficient for a diagnosis of opioid use disorder, but concurrent symptoms of craving and drug-seeking behavior are suggestive of comorbid opioid use disorder. ICD-10-CM codes only allow a diagnosis of opioid withdrawal in the presence of comorbid moderate to severe opioid use disorder.

The speed and severity of withdrawal associated with opioids depend on the half-life of the opioid used. Most individuals who are physiologically dependent on short-acting drugs such as heroin begin to have withdrawal symptoms within 6–12 hours after the last dose. Symptoms may take 2–4 days to emerge in the case of longer-acting drugs such as methadone, LAAM (L-alpha-acetylmethadol), or buprenorphine. Acute withdrawal symptoms for a short-acting opioid such as heroin usually peak within 1–3 days and gradually subside over a period of 5–7 days. Less acute withdrawal symptoms can last for weeks to months. These more chronic symptoms include anxiety, dysphoria, anhedonia, and insomnia.

Associated Features Supporting Diagnosis

Males with opioid withdrawal may experience piloerection, sweating, and spontaneous ejaculations while awake. Opioid withdrawal is distinct from opioid use disorder and does not necessarily occur in the presence of the drug-seeking behavior associated with opioid use disorder. Opioid withdrawal may occur in any individual after cessation of repeated use of an opioid, whether in the setting of medical management of pain, during opioid agonist therapy for opioid use disorder, in the context of private recreational use, or following attempts to self-treat symptoms of mental disorders with opioids.

Prevalence

Among individuals from various clinical settings, opioid withdrawal occurred in 60% of individuals who had used heroin at least once in the prior 12 months.

Development and Course

Opioid withdrawal is typical in the course of an opioid use disorder. It can be part of an escalating pattern in which an opioid is used to reduce withdrawal symptoms, in turn leading to more withdrawal at a later time. For persons with an established opioid use disorder, withdrawal and attempts to relieve withdrawal are typical.

Differential Diagnosis

Other withdrawal disorders. The anxiety and restlessness associated with opioid withdrawal resemble symptoms seen in sedative-hypnotic withdrawal. However, opioid withdrawal is also accompanied by rhinorrhea, lacrimation, and pupillary dilation, which are not seen in sedative-type withdrawal.

Other substance intoxication. Dilated pupils are also seen in hallucinogen intoxication and stimulant intoxication. However, other signs or symptoms of opioid withdrawal, such as nausea, vomiting, diarrhea, abdominal cramps, rhinorrhea, and lacrimation, are not present.

Other opioid-induced disorders. Opioid withdrawal is distinguished from the other opioid-induced disorders (e.g., opioid-induced depressive disorder, with onset during withdrawal) because the symptoms in these latter disorders are in excess of those usually associated with opioid withdrawal and meet full criteria for the relevant disorder.

Other Opioid-Induced Disorders

The following opioid-induced disorders are described in other chapters of the manual with disorders with which they share phenomenology (see the substance/medication-induced mental disorders in these chapters): opioid-induced depressive disorder ("Depressive Disorders"); opioid-induced anxiety disorder ("Anxiety Disorders"); opioid-induced sleep disorder ("Sleep-Wake Disorders"); and opioid-induced sexual dysfunction ("Sexual Dysfunctions"). For opioid intoxication delirium and opioid withdrawal delirium, see the criteria and discussion of delirium in the chapter "Neurocognitive Disorders." These opioid-induced disorders are diagnosed instead of opioid intoxication or opioid withdrawal only when the symptoms are sufficiently severe to warrant independent clinical attention.

Unspecified Opioid-Related Disorder

292.9 (F11.99)

This category applies to presentations in which symptoms characteristic of an opioid-related 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 specific opioid-related disorder or any of the disorders in the substance-related and addictive disorders diagnostic class.

Sedative-, Hypnotic-, or Anxiolytic-Related Disorders

Sedative, Hypnotic, or Anxiolytic Use Disorder
Sedative, Hypnotic, or Anxiolytic Intoxication
Sedative, Hypnotic, or Anxiolytic Withdrawal
Other Sedative-, Hypnotic-, or Anxiolytic-Induced Disorders
Unspecified Sedative-, Hypnotic-, or Anxiolytic-Related Disorder

Sedative, Hypnotic, or Anxiolytic Use Disorder

Diagnostic Criteria

A. A problematic pattern of sedative, hypnotic, or anxiolytic use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Sedatives, hypnotics, or anxiolytics are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control sedative, hypnotic, or anxiolytic use.
3. A great deal of time is spent in activities necessary to obtain the sedative, hypnotic, or anxiolytic; use the sedative, hypnotic, or anxiolytic; or recover from its effects.
4. Craving, or a strong desire or urge to use the sedative, hypnotic, or anxiolytic.
5. Recurrent sedative, hypnotic, or anxiolytic use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences from work or poor work performance related to sedative, hypnotic, or anxiolytic use; sedative-, hypnotic-, or anxiolytic-related absences, suspensions, or expulsions from school; neglect of children or household).
6. Continued sedative, hypnotic, or anxiolytic use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of sedatives, hypnotics, or anxiolytics (e.g., arguments with a spouse about consequences of intoxication; physical fights).
7. Important social, occupational, or recreational activities are given up or reduced because of sedative, hypnotic, or anxiolytic use.

8. Recurrent sedative, hypnotic, or anxiolytic use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by sedative, hypnotic, or anxiolytic use).
9. Sedative, hypnotic, or anxiolytic use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the sedative, hypnotic, or anxiolytic.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of the sedative, hypnotic, or anxiolytic to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of the sedative, hypnotic, or anxiolytic.

    Note: This criterion is not considered to be met for individuals taking sedatives, hypnotics, or anxiolytics under medical supervision.
11. Withdrawal, as manifested by either of the following:
    a. The characteristic withdrawal syndrome for sedatives, hypnotics, or anxiolytics (refer to Criteria A and B of the criteria set for sedative, hypnotic, or anxiolytic withdrawal, pp. 557–558).
    b. Sedatives, hypnotics, or anxiolytics (or a closely related substance, such as alcohol) are taken to relieve or avoid withdrawal symptoms.

    Note: This criterion is not considered to be met for individuals taking sedatives, hypnotics, or anxiolytics under medical supervision.

Specify if:

In early remission: After full criteria for sedative, hypnotic, or anxiolytic use disorder were previously met, none of the criteria for sedative, hypnotic, or anxiolytic use disorder have been met for at least 3 months but for less than 12 months (with the exception that Criterion A4, "Craving, or a strong desire or urge to use the sedative, hypnotic, or anxiolytic," may be met).

In sustained remission: After full criteria for sedative, hypnotic, or anxiolytic use disorder were previously met, none of the criteria for sedative, hypnotic, or anxiolytic use disorder have been met at any time during a period of 12 months or longer (with the exception that Criterion A4, "Craving, or a strong desire or urge to use the sedative, hypnotic, or anxiolytic," may be met).

Specify if:

In a controlled environment: This additional specifier is used if the individual is in an environment where access to sedatives, hypnotics, or anxiolytics is restricted.

Coding based on current severity: Note for ICD-10-CM codes: If a sedative, hypnotic, or anxiolytic intoxication; sedative, hypnotic, or anxiolytic withdrawal; or another sedative-, hypnotic-, or anxiolytic-induced mental disorder is also present, do not use the codes below for sedative, hypnotic, or anxiolytic use disorder. Instead the comorbid sedative, hypnotic, or anxiolytic use disorder is indicated in the 4th character of the sedative-, hypnotic-, or anxiolytic-induced disorder (see the coding note for sedative, hypnotic, or anxiolytic intoxication; sedative, hypnotic, or anxiolytic withdrawal; or specific sedative-, hypnotic-, or anxiolytic-induced mental disorder). For example, if there is comorbid sedative-, hypnotic-, or anxiolytic-induced depressive disorder and sedative, hypnotic, or anxiolytic use disorder, only the sedative-, hypnotic-, or anxiolytic-induced depressive disorder code is given with the 4th character indicating whether the comorbid sedative, hypnotic, or anxiolytic use disorder is mild, moderate, or severe: F13.14 for mild sedative, hypnotic, or anxiolytic use disorder with sedative-, hypnotic-, or anxiolytic-induced depressive disorder or F13.24 for a moderate or severe sedative, hypnotic, or anxiolytic use disorder with sedative-, hypnotic-, or anxiolytic-induced depressive disorder.

Specify current severity:

305.40 (F13.10) Mild: Presence of 2–3 symptoms.

304.10 (F13.20) Moderate: Presence of 4–5 symptoms.

304.10 (F13.20) Severe: Presence of 6 or more symptoms.

Specifiers

"In a controlled environment" applies as a further specifier of remission if the individual is both in remission and in a controlled environment (i.e., in early remission in a controlled environment or in sustained remission in a controlled environment). Examples of these environments are closely supervised and substance-free jails, therapeutic communities, and locked hospital units.

Diagnostic Features

Sedative, hypnotic, or anxiolytic substances include benzodiazepines, benzodiazepine-like drugs (e.g., zolpidem, zaleplon), carbamates (e.g., glutethimide, meprobamate), barbiturates (e.g., secobarbital), and barbiturate-like hypnotics (e.g., glutethimide, methaqualone). This class of substances includes all prescription sleeping medications and almost all prescription antianxiety medications. Nonbenzodiazepine antianxiety agents (e.g., buspirone, gepirone) are not included in this class because they do not appear to be associated with significant misuse.

Like alcohol, these agents are brain depressants and can produce similar substance/medication-induced and substance use disorders. Sedative, hypnotic, or anxiolytic substances are available both by prescription and illegally. Some individuals who obtain these substances by prescription will develop a sedative, hypnotic, or anxiolytic use disorder, while others who misuse these substances or use them for intoxication will not develop a use disorder. In particular, sedatives, hypnotics, or anxiolytics with rapid onset and/or short to intermediate lengths of action may be taken for intoxication purposes, although longer acting substances in this class may be taken for intoxication as well.

Craving (Criterion A4), either while using or during a period of abstinence, is a typical feature of sedative, hypnotic, or anxiolytic use disorder. Misuse of substances from this class may occur on its own or in conjunction with use of other substances. For example, individuals may use intoxicating doses of sedatives or benzodiazepines to "come down" from cocaine or amphetamines or use high doses of benzodiazepines in combination with methadone to "boost" its effects.

Repeated absences or poor work performance, school absences, suspensions or expulsions, and neglect of children or household (Criterion A5) may be related to sedative, hypnotic, or anxiolytic use disorder, as may the continued use of the substances despite arguments with a spouse about consequences of intoxication or despite physical fights (Criterion A6). Limiting contact with family or friends, avoiding work or school, or stopping participation in hobbies, sports, or games (Criterion A7) and recurrent sedative, hypnotic, or anxiolytic use when driving an automobile or operating a machine when impaired by sedative, hypnotic, or anxiolytic use (Criterion A8) are also seen in sedative, hypnotic, or anxiolytic use disorder.

Very significant levels of tolerance and withdrawal can develop to the sedative, hypnotic, or anxiolytic. There may be evidence of tolerance and withdrawal in the absence of a diagnosis of a sedative, hypnotic, or anxiolytic use disorder in an individual who has abruptly discontinued use of benzodiazepines that were taken for long periods of time at prescribed and therapeutic doses. In these cases, an additional diagnosis of sedative, hypnotic, or anxiolytic use disorder is made only if other criteria are met. That is, sedative, hypnotic, or anxiolytic medications may be prescribed for appropriate medical purposes, and depending on the dose regimen, these drugs may then produce tolerance and with-

drawal. If these drugs are prescribed or recommended for appropriate medical purposes, and if they are used as prescribed, the resulting tolerance or withdrawal does not meet the criteria for diagnosing a substance use disorder. However, it is necessary to determine whether the drugs were appropriately prescribed and used (e.g., falsifying medical symptoms to obtain the medication; using more medication than prescribed; obtaining the medication from several doctors without informing them of the others' involvement).

Given the unidimensional nature of the symptoms of sedative, hypnotic, or anxiolytic use disorder, severity is based on the number of criteria endorsed.

Associated Features Supporting Diagnosis

Sedative, hypnotic, or anxiolytic use disorder is often associated with other substance use disorders (e.g., alcohol, cannabis, opioid, stimulant use disorders). Sedatives are often used to alleviate the unwanted effects of these other substances. With repeated use of the substance, tolerance develops to the sedative effects, and a progressively higher dose is used. However, tolerance to brain stem depressant effects develops much more slowly, and as the individual takes more substance to achieve euphoria or other desired effects, there may be a sudden onset of respiratory depression and hypotension, which may result in death. Intense or repeated sedative, hypnotic, or anxiolytic intoxication may be associated with severe depression that, although temporary, can lead to suicide attempt and completed suicide.

Prevalence

The 12-month prevalences of DSM-IV sedative, hypnotic, or anxiolytic use disorder are estimated to be 0.3% among 12- to 17-year-olds and 0.2% among adults age 18 years and older. Rates of DSM-IV sedative, hypnotic, or anxiolytic use disorder are slightly greater among adult males (0.3%) than among adult females, but for 12- to 17-year-olds, the rate for females (0.4%) exceeds that for males (0.2%). The 12-month prevalence of DSM-IV sedative, hypnotic, or anxiolytic use disorder decreases as a function of age and is greatest among 18- to 29-year-olds (0.5%) and lowest among individuals 65 years and older (0.04%).

Twelve-month prevalence of sedative, hypnotic, or anxiolytic use disorder varies across racial/ethnic subgroups of the U.S. population. For 12- to 17-year-olds, rates are greatest among whites (0.3%) relative to African Americans (0.2%), Hispanics (0.2%), Native Americans (0.1%), and Asian Americans and Pacific Islanders (0.1%). Among adults, 12-month prevalence is greatest among Native Americans and Alaska Natives (0.8%), with rates of approximately 0.2% among African Americans, whites, and Hispanics and 0.1% among Asian Americans and Pacific Islanders.

Development and Course

The usual course of sedative, hypnotic, or anxiolytic use disorder involves individuals in their teens or 20s who escalate their occasional use of sedative, hypnotic, or anxiolytic agents to the point at which they develop problems that meet criteria for a diagnosis. This pattern may be especially likely among individuals who have other substance use disorders (e.g., alcohol, opioids, stimulants). An initial pattern of intermittent use socially (e.g., at parties) can lead to daily use and high levels of tolerance. Once this occurs, an increasing level of interpersonal difficulties, as well as increasingly severe episodes of cognitive dysfunction and physiological withdrawal, can be expected.

The second and less frequently observed clinical course begins with an individual who originally obtained the medication by prescription from a physician, usually for the treatment of anxiety, insomnia, or somatic complaints. As either tolerance or a need for higher doses of the medication develops, there is a gradual increase in the dose and frequency of self-administration. The individual is likely to continue to justify use on the basis of his or her original symptoms of anxiety or insomnia, but substance-seeking behavior becomes

more prominent, and the individual may seek out multiple physicians to obtain sufficient supplies of the medication. Tolerance can reach high levels, and withdrawal (including seizures and withdrawal delirium) may occur.

As with many substance use disorders, sedative, hypnotic, or anxiolytic use disorder generally has an onset during adolescence or early adult life. There is an increased risk for misuse and problems from many psychoactive substances as individuals age. In particular, cognitive impairment increases as a side effect with age, and the metabolism of sedatives, hypnotics, or anxiolytics decreases with age among older individuals. Both acute and chronic toxic effects of these substances, especially effects on cognition, memory, and motor coordination, are likely to increase with age as a consequence of pharmacodynamic and pharmacokinetic age-related changes. Individuals with major neurocognitive disorder (dementia) are more likely to develop intoxication and impaired physiological functioning at lower doses.

Deliberate intoxication to achieve a "high" is most likely to be observed in teenagers and individuals in their 20s. Problems associated with sedatives, hypnotics, or anxiolytics are also seen in individuals in their 40s and older who escalate the dose of prescribed medications. In older individuals, intoxication can resemble a progressive dementia.

Risk and Prognostic Factors

Temperamental. Impulsivity and novelty seeking are individual temperaments that relate to the propensity to develop a substance use disorder but may themselves be genetically determined.

Environmental. Since sedatives, hypnotics, or anxiolytics are all pharmaceuticals, a key risk factor relates to availability of the substances. In the United States, the historical patterns of sedative, hypnotic, or anxiolytic misuse relate to the broad prescribing patterns. For instance, a marked decrease in prescription of barbiturates was associated with an increase in benzodiazepine prescribing. Peer factors may relate to genetic predisposition in terms of how individuals select their environment. Other individuals at heightened risk might include those with alcohol use disorder who may receive repeated prescriptions in response to their complaints of alcohol-related anxiety or insomnia.

Genetic and physiological. As for other substance use disorders, the risk for sedative, hypnotic, or anxiolytic use disorder can be related to individual, family, peer, social, and environmental factors. Within these domains, genetic factors play a particularly important role both directly and indirectly. Overall, across development, genetic factors seem to play a larger role in the onset of sedative, hypnotic, or anxiolytic use disorder as individuals age through puberty into adult life.

Course modifiers. Early onset of use is associated with greater likelihood for developing a sedative, hypnotic, or anxiolytic use disorder.

Culture-Related Diagnostic Issues

There are marked variations in prescription patterns (and availability) of this class of substances in different countries, which may lead to variations in prevalence of sedative, hypnotic, or anxiolytic use disorders.

Gender-Related Diagnostic Issues

Females may be at higher risk than males for prescription drug misuse of sedative, hypnotic, or anxiolytic substances.

Diagnostic Markers

Almost all sedative, hypnotic, or anxiolytic substances can be identified through laboratory evaluations of urine or blood (the latter of which can quantify the amounts of these

agents in the body). Urine tests are likely to remain positive for up to approximately 1 week after the use of long-acting substances, such as diazepam or flurazepam.

Functional Consequences of Sedative, Hypnotic, or Anxiolytic Use Disorder

The social and interpersonal consequences of sedative, hypnotic, or anxiolytic use disorder mimic those of alcohol in terms of the potential for disinhibited behavior. Accidents, interpersonal difficulties (such as arguments or fights), and interference with work or school performance are all common outcomes. Physical examination is likely to reveal evidence of a mild decrease in most aspects of autonomic nervous system functioning, including a slower pulse, a slightly decreased respiratory rate, and a slight drop in blood pressure (most likely to occur with postural changes). At high doses, sedative, hypnotic, or anxiolytic substances can be lethal, particularly when mixed with alcohol, although the lethal dosage varies considerably among the specific substances. Overdoses may be associated with a deterioration in vital signs that signals an impending medical emergency (e.g., respiratory arrest from barbiturates). There may be consequences of trauma (e.g., internal bleeding or a subdural hematoma) from accidents that occur while intoxicated. Intravenous use of these substances can result in medical complications related to the use of contaminated needles (e.g., hepatitis and HIV).

Acute intoxication can result in accidental injuries and automobile accidents. For elderly individuals, even short-term use of these sedating medications at prescribed doses can be associated with an increased risk for cognitive problems and falls. The disinhibiting effects of these agents, like alcohol, may potentially contribute to overly aggressive behavior, with subsequent interpersonal and legal problems. Accidental or deliberate overdoses, similar to those observed for alcohol use disorder or repeated alcohol intoxication, can occur. In contrast to their wide margin of safety when used alone, benzodiazepines taken in combination with alcohol can be particularly dangerous, and accidental overdoses are reported commonly. Accidental overdoses have also been reported in individuals who deliberately misuse barbiturates and other nonbenzodiazepine sedatives (e.g., methaqualone), but since these agents are much less available than the benzodiazepines, the frequency of overdosing is low in most settings.

Differential Diagnosis

Other mental disorders or medical conditions. Individuals with sedative-, hypnotic-, or anxiolytic-induced disorders may present with symptoms (e.g., anxiety) that resemble primary mental disorders (e.g., generalized anxiety disorder vs. sedative-, hypnotic-, or anxiolytic-induced anxiety disorder, with onset during withdrawal). The slurred speech, incoordination, and other associated features characteristic of sedative, hypnotic, or anxiolytic intoxication could be the result of another medical condition (e.g., multiple sclerosis) or of a prior head trauma (e.g., a subdural hematoma).

Alcohol use disorder. Sedative, hypnotic, or anxiolytic use disorder must be differentiated from alcohol use disorder.

Clinically appropriate use of sedative, hypnotic, or anxiolytic medications. Individuals may continue to take benzodiazepine medication according to a physician's direction for a legitimate medical indication over extended periods of time. Even if physiological signs of tolerance or withdrawal are manifested, many of these individuals do not develop symptoms that meet the criteria for sedative, hypnotic, or anxiolytic use disorder because they are not preoccupied with obtaining the substance and its use does not interfere with their performance of usual social or occupational roles.

Comorbidity

Nonmedical use of sedative, hypnotic, or anxiolytic agents is associated with alcohol use disorder, tobacco use disorder, and, generally, illicit drug use. There may also be an over-