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]).