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Substance-Related and Addictive Disorders

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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, or 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 the ability to directly activate the brain reward systems, which are involved in the reinforcement of behaviors and establishment of memories. Instead of achieving reward system activation through adaptive behaviors, these substances produce such an intense activation of the reward system that normal activities may be neglected. 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, studies suggest that the neurobiological roots of substance use disorders for some individuals can be seen in their behaviors long before the onset of actual substance use (e.g., lower levels of self-control may reflect impairments of brain inhibitory mechanisms); research also suggests the negative impact of substance use itself on brain inhibitory mechanisms. Note that the phrase “drug 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 pattern of drug taking. Some clinicians will choose to use the phrase “drug addiction” to describe more severe presentations, but that wording is omitted from the official DSM-5 substance use disorder diagnostic terminology because of its uncertain definition and its potentially negative connotation. 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 that produce some behavioral symptoms that appear comparable to those produced by the substance use disorders. Other excessive

behavioral patterns, such as Internet gaming (see “Conditions for Further Study”), have also been described, but the research on these and other behavioral syndromes is less clear. Thus, groups of repetitive behaviors, sometimes termed behavioral addictions (with subcategories such as “sex addiction,” “exercise addiction,” and “shopping addiction”), are not included because 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: substance intoxication, substance withdrawal, and substance/medication-induced mental

disorders (diagnostic criteria and text are provided in this manual for substance/medicationinduced psychotic disorders, bipolar and related disorders, depressive disorders, anxiety disorders, obsessive-compulsive and related disorders, sleep disorders, sexual dysfunctions, delirium, and neurocognitive disorders in their respective chapters). The term substance/medication-induced mental disorder refers to symptomatic presentations that are due to the physiological effects of an exogenous substance on the central nervous system and includes typical intoxicants (e.g., alcohol, inhalants, cocaine), psychotropic medications (e.g., stimulants, sedative-hypnotics), other medications, (e.g., steroids), and environmental toxins (e.g., organophosphate insecticides). The current section begins with a general discussion of criteria sets for substance use disorder, substance intoxication, substance withdrawal, and 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 substance class. To facilitate differential diagnosis, the diagnostic criteria and text for the 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”). Note that only certain classes of drugs are capable of causing particular types of substance-induced disorders. The substance-related diagnostic categories associated with specific drug classes are shown in Table 1. TABLE 1 Diagnoses associated with substance class Psychotic disorders Bipolar and related disorders Depressive disorders Anxiety disorders Obsessivecompulsive and related disorders Sleep disorders dy Alcohol I/W I/W I/W I/W I/W Caffeine I I/W Cannabis I I I/W Hallucinogens Phencyclidine I I I I Other hallucinogens I* I I I Inhalants I I I Opioids I/W W I/W Sedatives, hypnotics, or anxiolytics I/W I/W I/W W I/W Stimulants** I I/W I/W I/W I/W I/W Tobacco W

Other (or unknown) I/W I/W I/W I/W I/W I/W 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. Major = major neurocognitive disorder; mild = mild neurocognitive disorder. *Also hallucinogen persisting perception disorder (flashbacks). **Includes amphetamine-type substances, cocaine, and other or unspecified stimulants. Substance-Related Disorders Substance Use Disorders Diagnostic 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 substance 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). Of note, the consumption of substances, including prescribed medications, may depend in part on cultural background, substance availability, and specific local drug regulations. Thus, there can be significant local or cultural variation in exposure (e.g., countries with cultural prohibitions against alcohol or other substance use may have a lower prevalence of substance-related disorders). 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, the diagnostic items making up Criterion A 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 might be queried by asking if there has ever been a time when there were such strong urges to take the drug that the individual 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 (amphetamine-type substances, cocaine, other or unspecified stimulants), 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 use of prescribed medications given as part of medical treatment (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 The clinician should use the code that applies to the substance class but record the name of the specific substance. For example, the clinician should record F13.20 moderate alprazolam use disorder (rather than moderate sedative, hypnotic, or anxiolytic use disorder) or F15.10 mild methamphetamine use disorder (rather than mild amphetamine-type substance use disorder). For substances that do not fit into any of the classes (e.g., anabolic steroids), the ICD-10-CM code for other (or unknown)

substance use disorder should be used and the specific substance indicated (e.g., F19.10 mild anabolic steroid use disorder). If the substance taken by the individual is unknown, the same ICD-10-CM code (i.e., for “other [or unknown] substance use disorder”) should be used (e.g., F19.20 severe unknown substance use disorder). If criteria are met for more than one substance use disorder, each should be diagnosed (e.g., F11.20 severe heroin use disorder; 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 substance intoxication and substance withdrawal). In the first example in the paragraph above, 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 the 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. Substance-Induced Disorders The overall category of substance-induced disorders includes substance intoxication, substance withdrawal, and substance/medication-induced mental disorders (e.g., substance-induced psychotic disorder, substance-induced depressive disorder). While substance intoxication and substance withdrawal are recognized as mental disorders, for purposes of clarity of reference in discussions across this chapter, the term substance/medication-induced mental disorder (e.g., alcohol-induced depressive disorder, methamphetamine-induced anxiety disorder) is used to distinguish these disorders from substance intoxication and substance withdrawal. Substance Intoxication and Substance Withdrawal Criteria for the substance-specific intoxication syndromes are included within the substancespecific 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 (CNS) and develop during or shortly after use of the substance (Criterion B) and are accompanied by substance-specific signs and symptoms (Criterion C). 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 individuals with a substance use disorder but also occurs frequently in persons who use substances but do not have a substance use disorder. This category does not apply to tobacco. The most common changes in substance intoxication involve disturbances of perception, wakefulness, attention, thinking, judgment, psychomotor behavior, and interpersonal behavior. Short-term, or “acute,” substance intoxications may have different signs and symptoms from sustained, or “chronic,” substance 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 the diagnosis of substance intoxication as defined in this manual. Many substances may produce physiological or psychological changes that are not necessarily problematic. For example, an individual with tachycardia from substance use is experiencing a physiological effect from the substance, but if

this is the only symptom in the absence of problematic behavior, the diagnosis of substance intoxication would not apply. Intoxication may sometimes persist beyond the time when the substance is detectable in the body. This may be attributable to enduring CNS effects, from which

the recovery 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 also 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 (Criterion B) 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. Also, it is important to emphasize that symptoms of withdrawal occurring during appropriate use of medications given as part of medical treatment with prescribed medications (e.g., opioid analgesics, sedatives, stimulants) are specifically not counted when diagnosing a substance use disorder. Most individuals with withdrawal have an urge to readminister 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 duration of withdrawal symptoms. 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 Substance Intoxication and Substance 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 F13.230 secobarbital withdrawal (rather than sedative, hypnotic, or anxiolytic withdrawal) or F15.120 methamphetamine intoxication (rather than amphetamine-type substance intoxication). Note that the appropriate ICD-10-CM diagnostic codes for substance intoxication and substance withdrawal

depend on whether there is a comorbid substance use disorder. In this case, the F15.120 code for methamphetamine intoxication indicates the presence of a comorbid mild methamphetamine use disorder. If there had been no comorbid methamphetamine use disorder (and no perceptual disturbances), the diagnostic code would have been F15.920. 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 ICD-10-CM code for other (or unknown) substance intoxication or other (or unknown) substance withdrawal should be used and the specific substance indicated (e.g., F19.920 anabolic steroid intoxication). If the substance taken by the individual is unknown, the same code (i.e., for the class "other [or unknown] substance") should be used (e.g., F19.920 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., 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 for heroin withdrawal is given to cover both presentations. 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 CNS syndromes that develop in the context of the effects of substances of abuse, medications, and some 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 any of the 10 classes of substances that produce substance use disorders, or by a great variety of other medications used in medical treatment. Each substance/medication-induced mental disorder is described in the relevant chapter (e.g., substance/medication-induced depressive disorder is located in "Depressive 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. A clinically significant presentation of symptoms characteristic of disorders in the relevant diagnostic class predominates in the clinical picture. B. There is evidence from the history, physical examination, or laboratory findings of both of the following:

1. The symptoms in Criterion A developed during or soon after substance intoxication, substance withdrawal, or exposure to or withdrawal from a medication; and
2. The involved substance/medication is capable of producing the symptoms in Criterion A. C. The disturbance 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:
3. The disturbance preceded the onset of severe intoxication or withdrawal or exposure to the medication; or
4. The disturbance 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 disturbance does not occur exclusively during the course of a delirium. E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning. Diagnostic and Associated 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, and with substance-induced major depressive episodes observed during withdrawal. Both the more sedating and the 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 symptoms being observed are not likely to be better explained by an independent mental disorder. The latter is more likely to be the case if the symptoms were present before the severe intoxication or withdrawal or medication administration, or, with the exception of several substance-induced persisting disorders listed in 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 substance-induced delirium (e.g., alcohol withdrawal delirium), only the delirium should be diagnosed, and other psychiatric symptoms occurring during the delirium should not also be diagnosed separately, as many of these symptoms (e.g., disturbances in mood, anxiety, 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 with or withdrawal from substances of abuse, whereas medication-induced mental disorders can be seen with prescribed or over-the-counter medications that are taken at the suggested doses.

552 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 anxiolyticinduced neurocognitive disorder; and hallucinogen persisting perception disorder (“flashbacks”; see the section “Hallucinogen-Related Disorders” later in this chapter). However, most 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 developing 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 of 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 were 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 symptoms of the preexisting mental disorder. 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 crosssectionally 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 substanceinduced mental disorders. Recording Procedures for Substance/Medication-Induced Mental Disorders Diagnostic criteria, coding notes, and recording procedures for the specific substance/medication-induced mental disorders are provided in chapters of the manual corresponding with disorders of shared 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,” “ObsessiveCompulsive and Related Disorders,” “Sleep-Wake Disorders,” “Sexual Dysfunctions,” and “Neurocognitive Disorders”). When recording a substance/medication-induced mental disorder that is comorbid with a substance use disorder, only a single diagnosis is given that reflects both the type of substance and the type of mental

disorder induced by the substance, as well as the severity of the comorbid substance use disorder (e.g., cocaine-induced psychotic disorder with severe cocaine use disorder). For a substance-induced mental disorder occurring in the absence of comorbid substance use disorder (e.g., when the disorder is induced by one-time use of a substance or medication), only the substance/medication-induced mental disorder is recorded (e.g., corticosteroid-induced depressive disorder). 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 Alcohol-Induced Mental 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 12month 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). 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/remission: 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/remission: F10.10 Mild: Presence of 2–3 symptoms. F10.11 Mild, In early remission F10.11 Mild, In sustained remission F10.20 Moderate: Presence of 4–5 symptoms. F10.21 Moderate, In early remission F10.21 Moderate, In sustained remission F10.20 Severe: Presence of 6 or more symptoms. F10.21 Severe, In early remission F10.21 Severe, In sustained remission 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) 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, such as 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 their 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 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 increased 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, such as severe memory impairment and degenerative changes in the cerebellum. These effects are related to the direct effects of alcohol, trauma, or 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 WernickeKorsakoff 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 or bipolar disorder. There is an increased rate of suicidal behavior as well as of suicide among individuals with the disorder. Prevalence Alcohol use disorder is common. In the United States, lifetime prevalence rates of DSM-5 alcohol use disorder among adults were estimated to be 29.1% overall with severity specified as follows: 8.6% mild, 6.6% moderate, and 13.9% severe. Among Australian adults, the estimated lifetime prevalence of DSM-5 alcohol use disorder was 31.0%. Rates of disorder vary by gender and age. In the United States, rates were greater among men (36.0% lifetime prevalence) than among women (22.7%). Twelve-month prevalence of DSM-IV alcohol use disorders in the United States was 4.6% among individuals ages 12–17 years, 16.2% among individuals ages 18–29 years, and 1.5% among individuals 65 years and older. Twelve-month prevalence of alcohol use disorders varies across U.S. ethnoracial groups as well. For individuals ages 12–17 years, prevalence of DSM-IV alcohol use disorders was greatest among Native Americans (2.8%) and non-Latinx Whites (2.2%), relative to Asian Americans (1.6%), individuals reporting two or more racialized backgrounds (1.6%), Hispanics (1.5%), and African Americans (0.8%). Among adults, data from a large U.S. population-based study indicated that the 12-month prevalence of DSM-5 alcohol use disorder was 14.4% in African Americans, 14.0% in non-Hispanic Whites, 13.6% in Hispanics, and 10.6% in Asian Americans and Pacific Islanders. Data from a large community-based survey of Native Americans from Southwestern and Northern Plains tribal nations showed that the 12-month prevalence of DSM-IV alcohol abuse and dependence ranged from 4.1% to 9.8%. There is extensive diversity in the rates and patterns of alcohol abuse and dependence across the more than 570 American Indian and Alaska Native communities in the United States, as well as high rates of abstinence from alcohol use in some of these communities. Historical experiences of dispossession and subjugation and ongoing discrimination have been associated with increased risk of symptom onset. Given the diversity of tribal communities, prevalence estimates for alcohol use disorder among Native Americans should be interpreted with caution. 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 before 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

Environmental. Genetic and physiological. 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 minority 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, as suggested by a prospective study in California. 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 risk and prognostic factors may include poverty and discrimination (including structural inequities such as differential incarceration rates and differential access to medications for addiction treatment), unemployment and low levels of education, 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. 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 individual, and higher severity of the alcohol-related problems in those relatives. A significantly higher rate of alcohol use disorder 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. Advances in understanding the 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 is the acute alcohol-related skin flush (seen more commonly in persons of Asian descent). 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

Course modifiers. sensitivity) to alcohol. A number of gene variations may account for low response to alcohol or modulate the dopamine reward systems; however, any single gene variant is likely to explain only 1%–2% of the risk for these disorders. Gene-environment interactions modulate the impact of genetic variations; for example, genetic effects on alcohol use are more pronounced when social constraints are minimized (e.g., low parental monitoring) or when the environment permits easy access to alcohol or encourages its use (e.g., high peer deviance). 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. Globally, 2.8 million deaths were attributed to alcohol use, which corresponds to 2.2% of total age-standardized deaths among women and 6.8% among men. Globally, an estimated 237 million men and 46 million women have alcohol use disorder, with the highest prevalence being among men and women in the European Region (14.8% and 3.5%) and the Region of the Americas (11.5% and 5.1%); in general, high-income countries have the highest prevalence. Greater acculturation to U.S. society among immigrants is associated with rising prevalence of alcohol use disorder, especially among women. Ethnic density (greater proportion of people from the same background) may decrease the risk of alcohol use disorder because of greater social support and buffering against the effects of discrimination. However, neighborhood segregation may increase the risk for disorders because of the association with other risk factors, such as higher concentration of alcohol advertising and retail outlets in lowincome areas. Genetic polymorphisms for the alcohol-metabolizing enzymes alcohol dehydrogenase and aldehyde dehydrogenase may affect the response to alcohol. When consuming alcohol, individuals with certain polymorphisms 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. For example, these gene variations are seen in as many as 40% of Japanese, Chinese, and Korean individuals and are related to lower risks for the disorder. However, this protective effect may be modulated by sociocultural factors, as shown by rising prevalence of alcohol use disorder in Japan, China, and South Korea over the last decades associated with increasing westernization and changing cultural attitudes about women’s drinking. Despite small variations regarding individual criterion items, the diagnostic criteria perform equally well across most race/ethnicity groups. Sex- and Gender-Related Diagnostic Issues Men have higher rates of drinking and alcohol use disorder than women, although the gender gap is narrowing as women are initiating alcohol use at a younger age. 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 alcohol-related blackouts and liver disease. Additionally, while genetic-related mechanisms for alcohol risk overlap for males and females, the specific environmental components that add to the risk may differ across sexes, especially during adolescence. Drinking during pregnancy, which tends to decrease overall, may be a sign of an alcohol use disorder. 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. Given that 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 individual 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 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 highnormal 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 bloating

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. Association With Suicidal Thoughts or Behavior Most studies on suicidality and alcohol address alcohol consumption rather than alcohol use disorder. However, a psychological autopsy study in Australia found that aggression, psychiatric comorbidity, and recent interpersonal conflicts are suicide risk factors in individuals with alcohol use disorder. A review of studies from 1999 through 2014 conducted in several countries, including the United States, reported that both intoxication and chronic heavy alcohol use are associated with suicide, extensive population-level data link alcohol with suicide, and there is evidence suggesting that restrictive alcohol policies may help prevent suicide on a general population level. A meta-analysis of studies conducted in the United States and several other countries from 1996 through 2015 found that compared with nondrinking individuals, the acute use of alcohol was associated with a nearly sevenfold increase in risk of suicide attempt. Moreover, in this meta-

analysis, as well as in U.S.- based case-control crossover studies, heavier alcohol use within 24 hours was a much more potent risk factor for suicide attempt than lower alcohol use. In a cohort of patients in Mississippi, acute co-use of alcohol and sedatives had an even stronger association with suicide attempt compared with alcohol use alone. A systematic review and meta-analysis of studies from 1975 through 2014 in several countries, including the United States, found that alcohol use is associated with possession of firearms, that alcohol drinkers are four to six times more likely to die by suicide with a gun than nondrinkers, and that heavy drinkers are more likely to choose firearms over other suicide methods compared with nondrinkers. 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

Nonpathological use of alcohol. Alcohol intoxication, alcohol withdrawal, and alcohol-induced mental disorders. Sedative, hypnotic, or anxiolytic use disorder. Conduct disorder in childhood and antisocial personality disorder. 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 suicide. 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 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 (< 20%) ever develop alcohol use disorder. Therefore, drinking, even daily, in low doses and occasional intoxication do not by themselves make this diagnosis. Alcohol use disorder is differentiated from alcohol intoxication, alcohol withdrawal, and alcohol induced mental disorders (e.g., alcohol-induced depressive disorder) in that alcohol use disorder describes a problematic pattern of alcohol use that involves impaired control over alcohol use, social impairment due to alcohol use, risky alcohol use (e.g., driving while intoxicated), and pharmacological symptoms (the development of tolerance or withdrawal), whereas alcohol intoxication, alcohol withdrawal, and alcohol-induced mental disorders describe psychiatric syndromes that develop in the context of heavy use. Alcohol intoxication, alcohol withdrawal, and alcohol-induced mental disorders occur frequently in individuals with alcohol use disorder. In such cases, a diagnosis of alcohol intoxication, alcohol withdrawal, or an alcohol-induced mental disorder should be given in addition to a diagnosis of alcohol use disorder, the presence of which is indicated in the diagnostic code. 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. Alcohol use disorder, along with other substance use disorders, is

seen in the majority of individuals with antisocial personality disorder 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 alcohol

use disorder, and most anxiety and depressive disorders are associated with 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, although this point has long been debated. 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-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 F10.120, and if a moderate or severe alcohol use disorder is comorbid, the ICD-10CM code is F10.220. If there is no comorbid alcohol use disorder, then the ICD-10CM code is F10.920. Diagnostic Features The essential feature of alcohol intoxication is the presence of clinically significant and sometimes life-threatening problematic behavioral or psychological changes (e.g., inappropriate sexual or aggressive behavior, mood lability, impaired judgment and decision-making, difficulties with complex tasks such as driving, and 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 vehicle crashes or other events resulting in injury. 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 Signs and symptoms of intoxication are likely to be more intense when the blood alcohol level is rising than when it is falling. 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. 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 reflect stimulation (e.g., talkativeness, a sensation of well-being, 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. Alcohol intoxication is sometimes associated with amnesia for the events that occurred during the course of the intoxication ("blackouts"). This phenomenon is related to a relatively high blood alcohol level and, perhaps, to the rapidity with which this level is reached. Acute alcohol intoxication may cause metabolic alterations (e.g., hypoglycemia, electrolyte disturbances) and may have severe cardiovascular, respiratory, and/or gastrointestinal effects. 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. Alcohol intoxication is an important contributor to interpersonal violence and suicidal behavior. Among individuals intoxicated by alcohol, there appears to be an increased rate of accidental injury (including death due to behaviors associated with altered judgment, self-harm, and violence), suicidal behavior, and suicide. 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 2018, 43% of 12th-grade students in the United States reported having "been drunk" at least once in their lifetime, and 17.5% of them reported that they had gotten drunk at least once in the prior 30 days. Using a definition of intoxication of four or more standard drinks on any day for women and five or more

563 standard drinks on any day for men, the 12-month prevalence of high-risk drinking in U.S. adults is 17.4% for Native Americans, 15.1% for African Americans, 13.5% for Latinx, 12.3% for nonLatinx Whites, and 7.2% for Asians and Pacific Islanders. Development and Course Intoxication usually occurs as an episode 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 having heavy-drinking peers, holding beliefs that heavy drinking is an important component of having fun, and using alcohol to cope with stress. Culture-Related Diagnostic Issues The major issues parallel the cultural differences regarding the use of alcohol overall. For example, some college fraternities and sororities 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). Sex- and Gender-Related Diagnostic Issues Historically, in many Western societies, acceptance of drinking and drunkenness is more tolerated for men, but such gender differences may be much less prominent in recent years, especially during adolescence and young adulthood. In general, women are less

tolerant of the same amount of alcohol than men. 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.

Other medical conditions. Alcohol-induced mental disorders. Sedative, hypnotic, or anxiolytic intoxication. Association With Suicidal Thoughts or Behavior A collaborative, international study in emergency departments in 17 countries found that acute alcohol use, independent of chronic use, increases the risk of suicide attempt, with each drink raising the risk by 30%. For more information, see "Association With Suicidal Thoughts or Behavior" in the Alcohol Use Disorder section. Functional Consequences of Alcohol Intoxication Alcohol intoxication contributed to the more than 95,000 deaths and 2.8 million years of potential life lost each year in the United States from 2011 through 2015, shortening the lives of those who died by an average of 30 years. In addition, intoxication with this drug contributes to huge costs associated with drunk driving and lost time from school or work, as well as interpersonal arguments and physical fights. Differential Diagnosis Several medical (e.g., diabetic acidosis) and neurological conditions (e.g., cerebellar ataxia, multiple sclerosis) can temporarily resemble alcohol intoxication. Alcohol intoxication is distinguished from alcohol-induced mental disorders (e.g., alcohol-induced depressive disorder, with onset during intoxication) because the symptoms (e.g., depressed mood) in these latter disorders are in excess of those usually associated with alcohol intoxication, predominate in the clinical presentation, and are severe enough to warrant clinical attention. 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. Given the typical overlap of alcohol intoxication with alcohol use disorder, see "Comorbidity" under Alcohol Use Disorder for more details about co-occurring conditions that are likely to be encountered.

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-10-CM code depends on whether or not there is a comorbid alcohol use disorder and whether or not there are perceptual disturbances. For alcohol withdrawal, without perceptual disturbances: If a mild alcohol use disorder is comorbid, the ICD-10-CM code is F10.130, and if a moderate or severe alcohol use disorder is comorbid, the ICD-10-CM code is F10.230. If there is no comorbid alcohol use disorder, then the ICD-10-CM code is F10.930. For alcohol withdrawal, with perceptual disturbances: If a mild alcohol use disorder is comorbid, the ICD-10-CM code is F10.132, and if a moderate or severe alcohol use disorder is comorbid, the ICD-10-CM code is F10.232. If there is no comorbid alcohol use disorder, then the ICD-10-CM code is F10.932. 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). Tonicclonic seizures occur in fewer than 3% of individuals. Associated Features 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 in the United States 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

Environmental. Other medical conditions. ever demonstrate alcohol withdrawal delirium or withdrawal seizures. The prevalence of alcohol withdrawal symptoms does not seem to vary across U.S. ethnoracial groups. 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 Alcohol 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 individuals who are also dependent on other depressant drugs (sedative-hypnotics) and individuals who have had more alcohol withdrawal experiences in the past. Predictors of severe alcohol withdrawal include alcohol withdrawal delirium, prior histories of severe withdrawal syndromes, low blood potassium levels, decreased platelet counts, and systolic hypertension. 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 among individuals with alcohol use disorder. Differential Diagnosis 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.

Alcohol-induced mental disorders. Sedative, hypnotic, or anxiolytic withdrawal. Alcohol withdrawal is distinguished from alcohol-induced mental disorders (e.g., alcohol-induced anxiety disorder, with onset during withdrawal) because the symptoms (e.g., anxiety) in these latter disorders are in excess of those usually associated with alcohol withdrawal, predominate in the clinical presentation, and are severe enough to warrant clinical attention. Sedative, hypnotic, or anxiolytic withdrawal produces a syndrome very similar to that of alcohol withdrawal. Comorbidity Given the typical overlap of alcohol withdrawal with alcohol use disorder, see “Comorbidity” under Alcohol Use Disorder for more details about co-occurring conditions that are likely to be encountered. Alcohol-Induced Mental Disorders The following alcohol-induced mental 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 and related 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 mental disorders are diagnosed instead of alcohol intoxication or alcohol withdrawal only when the symptoms are sufficiently severe to warrant independent clinical attention. Diagnostic and Associated Features The symptom profiles for an alcohol-induced condition resemble the corresponding independent mental disorders as described elsewhere in this manual. Moreover, while alcohol-induced conditions can have the same severe consequences as independent mental disorders (e.g., suicide attempts), they 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. These alcohol-induced mental disorders must have developed in the context of severe alcohol intoxication and/or alcohol withdrawal. Given that the presentation of an alcohol-induced mental disorder symptomatically resembles the presentations of independent mental disorders from the same diagnostic class, they must be differentiated based on the temporal relationship between the alcohol use and the psychiatric symptoms. Individuals with alcohol-induced mental disorders are likely to also demonstrate the associated features seen with an alcohol use disorder, as listed in that subsection. There must be evidence that the disorder being observed is not likely to be better explained

by an independent mental disorder. The latter is likely to occur if the mental disorder was present before the severe intoxication or withdrawal, or continued for more than 1 month after the cessation of severe intoxication 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 mental disorder must be clinically relevant, causing significant 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. Rates of alcohol-induced mental 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 alcoholinduced sleep and anxiety disorders are likely, but alcohol-induced psychotic episodes are estimated to be seen in less than 5% of individuals with alcohol use disorder. Development and Course Once present, the symptoms of an alcohol-induced mental disorder are likely to remain clinically relevant as long as the individual continues to experience severe intoxication or withdrawal. While the symptoms may 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), all alcohol-induced mental disorders 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 mental 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 mental disorders, 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 mental 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

F15.920 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 Caffeine-Induced Mental Disorders Unspecified Caffeine-Related Disorder Caffeine Intoxication Diagnostic Criteria 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, 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 in the United States consume caffeine. 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 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, typical dietary 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

Environmental. Genetic and physiological. Independent mental disorders. 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. Consumption of caffeinated energy drinks, often together with alcohol, leading to caffeine intoxication, has increased among adolescents and young adults in high-income countries, resulting in the doubling of U.S. emergency department visits related to caffeinated energy drinks between 2007 and 2011. 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 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 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 Caffeine intoxication may be characterized by symptoms (e.g., panic attacks) that resemble independent 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.

Caffeine-induced mental disorders. F15.93 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/MedicationInduced Sleep Disorder” in the chapter “Sleep-Wake Disorders”), because the symptoms (e.g., anxiety and insomnia, respectively) in these latter disorders are in excess of those usually associated with caffeine intoxication, predominate in the clinical presentation, 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 substancerelated disorders, whereas individuals with anxiety disorders are more likely to avoid caffeine. Caffeine Withdrawal Diagnostic Criteria 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). Because individuals may be unaware of the wide array of sources of caffeine beyond coffee, colas, and energy drinks (e.g., over-the-counter analgesics and cold remedies, weight loss aids, chocolate), they may not connect ingestion of these substances with symptoms of caffeine withdrawal. 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 clinically 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, mate, 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 Caffeine abstinence has been shown to be associated with impaired behavioral and cognitive performance (e.g., sustained attention), as well as with increased total sleep time, sleep efficiency, and slow-wave sleep. 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

Temperamental. Environmental. Genetic and physiological. 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 in a U.S. metropolitan county reported at least one caffeine withdrawal symptom (47% experienced headache), and 24% experienced headache plus one or more other symptoms as well as functional impairment due to withdrawal. Among individuals who abstained from caffeine for at least 24 hours but were not trying to permanently stop caffeine use, 11% experienced 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. Doses of caffeine significantly less than the individual’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). Caffeine is unique in that it is a behaviorally active

drug that is consumed by individuals of nearly all ages, with rates of caffeine consumption and overall level of caffeine consumption increasing with age. 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 in young people, which could increase the risk for caffeine withdrawal. Risk and Prognostic Factors Heavy caffeine use has been observed among individuals with mental disorders, including eating disorders and alcohol and other substance use disorders, as well as among individuals who smoke cigarettes and those who are incarcerated. Thus, these individuals could be at higher risk for caffeine withdrawal upon acute caffeine abstinence. 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 participation. These external environmental circumstances may precipitate a withdrawal syndrome in vulnerable individuals. Genetic factors appear to increase vulnerability to caffeine withdrawal, but no specific genes have been identified. Culture-Related Diagnostic Issues

Other medical conditions and medication side effects. Caffeine-induced sleep disorder. Habitual caffeine consumers who fast for religious reasons may be at increased risk for caffeine withdrawal. Sex- and Gender-Related Diagnostic Issues Metabolism of caffeine is slower in females who use oral contraceptives and in the luteal phase of the menstrual cycle, and caffeine metabolism becomes progressively slower in the second and third trimesters of pregnancy compared with the first trimester and the nonpregnant state. These features reduce the rate of clearance and may diminish withdrawal, although they can also lengthen the duration of caffeine-associated adverse symptoms. It is unlikely that doses < 300 mg/day are associated with adverse reproductive outcomes in pregnancy. Functional Consequences of Caffeine Withdrawal Caffeine withdrawal symptoms can vary from mild to extreme, at times causing functional impairment in normal daily activities. Rates of functional impairment in studies conducted largely in the United States 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 canceling 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 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. Caffeine withdrawal is distinguished from caffeine-induced sleep disorder (e.g., caffeine-induced sleep disorder, insomnia type, with onset during withdrawal) because the sleep symptoms are in excess of those usually associated caffeine withdrawal, predominate in the clinical presentation, and are severe enough to warrant clinical attention. Comorbidity Caffeine withdrawal may be associated with major depressive disorder, generalized anxiety disorder, panic disorder, antisocial personality disorder, moderate to severe alcohol use disorder, and cannabis and cocaine use. Caffeine-Induced Mental Disorders

The following caffeine-induced mental 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 mental 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 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 Cannabis-Induced Mental 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 12month 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). 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/remission: 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 cannabisinduced 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/remission: F12.10 Mild: Presence of 2–3 symptoms. F12.11 Mild, In early remission F12.11 Mild, In sustained remission F12.20 Moderate: Presence of 4–5 symptoms. F12.21 Moderate, In early remission F12.21 Moderate, In sustained remission F12.20 Severe: Presence of 6 or more symptoms. F12.21 Severe, In early remission F12.21 Severe, In sustained remission 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 includes problems associated with use of substances derived from the cannabis plant and chemically similar synthetic compounds. In these substances, the primary component with psychoactive effects (and hence, addiction potential) is the cannabinoid delta-9tetrahydrocannabinol (delta-9-THC or THC). Cannabinoids have diverse effects in the brain, prominent among which are actions on CB1 and CB2 cannabinoid receptors found throughout the central nervous system. Cannabis is used in many forms. It is most commonly smoked in a cigarette-like form (often

called “joints” or “reefers”), and also in pipes, water pipes (bongs or hookahs), or hollowed-out cigars (“blunts”). More recently developed methods include “vaping” (vaporizing) by heating without combustion plant cannabis material to release psychoactive components for inhalation, and “dabbing,” in which a concentrated cannabis product (butane hash oil, known as “dabs”), created through butane extraction of THC from cannabis plant material, is heated and inhaled. Vaping and dabbing are gaining popularity, particularly among youth. Cannabis can also be ingested orally in food (edibles) or beverages. Inhalation typically produces more rapid and intense onset of effects than oral administration. Hashish or hash oil, a concentrated extraction of the cannabis plant, is also used. Across products, cannabis potency (THC concentration) varies greatly, averaging 10%–15% in typical cannabis plant material, 30%–40% in hashish, and 50%– 55% in hash oil. During the past two decades, the potency of seized illegal plant cannabis has steadily increased, and legal cannabis products may have even higher THC potency (e.g., 20% for plant material and 68% for cannabis extracts). Synthetic oral THC formulations (pill/capsules/sprays) are also available for various medical uses (e.g., chronic pain; nausea and vomiting caused by chemotherapy or ano-rexia; weight loss among those with AIDS). Other entirely illicit synthetic cannabinoid compounds (e.g., K2, Spice, JWH-018, JWH-073) are in the form of plant material sprayed with a cannabinoid formulation. Although such synthetic cannabinoids are designed to

mimic cannabis effects, their chemical composition, potency, effects, and duration of action are unpredictable, and they may cause more severe adverse effects than cannabis plant products, including seizures, cardiac conditions, psychosis, and even death. In the United States, cannabis remains an illegal substance under federal law, while the legal status of cannabis varies by state. Thus, cannabis use under state law can involve an illicit product, a product authorized for medical purposes, or a completely legal product. The most common medical purpose for cannabis use is chronic pain, and the conditions approved for medicinal cannabis use vary from state to state. When cannabis or a cannabinoid is taken as indicated for a medical condition, tolerance and withdrawal (physiological dependence) may occur but should not be the primary basis for diagnosing cannabis use disorder. The efficacy of cannabis for different medical conditions continues to be debated, and cannabis use as medically advised should be taken into account when a cannabis use disorder diagnosis is being considered. Patterns of cannabis use can range from light, infrequent use to heavy, frequent use. Individuals with DSM-5 cannabis use disorder use cannabis frequently (on average, 4 or more days a week), and some individuals may use cannabis throughout the day over a period of months or years. Because of the increasingly common perception that cannabis use is harmless, individuals may not recognize that symptoms of cannabis use disorder (e.g., withdrawal symptoms) are cannabis related. Additionally, among individuals with multiple substance use disorders, lack of clarity about whether symptoms are caused by cannabis or by other substances may lead to underreporting of cannabis use disorder symptoms. Cannabis use disorder is defined by the same 11 criteria that define the other substance use disorders, as supported by considerable empirical evidence. These criteria, a cluster of behavioral and physical symptoms, lead to clinically significant impairment or distress and can include withdrawal, tolerance, craving, spending a great deal of time in activities related to the substance, and hazardous use (e.g., driving while under its influence). Some individuals who use cannabis multiple times per day do not perceive themselves as spending excessive time under the influence of cannabis or recovering from its effects, despite being intoxicated from cannabis or coming down from its effects most of the time, most days. An important marker of a severe

cannabis use disorder is continued use despite negative effects on other important activities or relationships (e.g., school, work, sports, partner or parent relationship). Regular cannabis users become tolerant to many acute cannabis effects, and cessation of regular cannabis use generally leads to a cannabis withdrawal syndrome. Cannabis withdrawal can cause significant distress, leading to continued use to relieve the symptoms and difficulty quitting use or relapse. Associated Features Individuals who regularly use cannabis often report using it to cope with mood, insomnia, anger, pain, or other physiological or psychological problems, and individuals diagnosed with cannabis use disorder frequently have other concurrent mental disorders. Careful assessment can reveal that cannabis use contributes to exacerbation of these symptoms, as well as other reasons for frequent use (e.g., the coping motives listed above; to experience euphoria; as an enjoyable social activity). Chronic intake of cannabis can produce a lack of motivation that resembles persistent depressive disorder. Because some individuals may underreport the amount or frequency of their cannabis use, provider awareness of common signs and symptoms of cannabis use and intoxication facilitates better assessment of cannabis use disorder. Some additional signs of acute and chronic use are red eyes (conjunctival injection), cannabis odor on clothing, yellowing of fingertips (from smoking joints), chronic cough, burning of incense (to hide the odor), and exaggerated craving and impulse for specific foods, sometimes at odd times of the day or night. Prevalence Cannabinoids, especially cannabis, are the most widely used illicit psychoactive

substances in the United States. The following prevalence data are drawn from U.S.-based studies, unless otherwise noted. Among youth (ages 12–17 years), the past-year prevalence of DSM-IV cannabis use disorder is 2.7%–3.1%. Among adults age 18 years and older, the prevalence is 1.5%–2.9%. Among cannabis users, the prevalence of DSM-IV cannabis use disorder is 20.4% among youth and 30.6% among adults. For DSM-5 cannabis use disorder, 12-month prevalence is approximately 2.5% among adults (1.4%, 0.6%, and 0.6% at mild, moderate, and severe levels, respectively). During the past decade, the prevalence of cannabis use disorder has decreased among adolescents. In contrast, among adults, some studies suggest that the prevalence of cannabis use disorder has either remained stable or increased—for example, among adults in the general population, patients in inpatient settings, and patients in the Veterans Health Administration. Globally, the age-standardized rate of cannabis use disorders was 289.7 per 100,000 people in 2016, a 25.6% increase over 1990. Prevalence varies widely across geographic regions, being lowest in Western Sub-Saharan Africa and highest in North America. According to age, the prevalence of cannabis use disorder in the United States is highest among individuals ages 18–29 years (6.9%) and lowest among individuals age 45 years and older (0.8%). Rates of cannabis use disorder are greater in men than in women (3.5% vs. 1.7%) and in boys than in girls ages 12–17 years (3.4% vs. 2.8%), although gender differences have

been narrowing in recent birth cohorts across several countries. Regarding ethnoracial differences, for adolescents ages 12–17 years, rates are highest among Hispanics (3.8%), followed by Whites (3.1%), African Americans (2.9%), and other ethnoracial groups (2.3%). Among adults, the prevalence of cannabis use disorder is 5.3% in American Indians and Alaska Natives, 4.5% in African Americans, 2.6% in Hispanics, 2.2% in Whites, and 1.3% in Asians and Pacific Islanders. In the United States and other high-income countries, the number of individuals seeking treatment for cannabis-related problems has increased since the 1990s. However, among adults with cannabis use disorder, only 7%–8% received any type of cannabisspecific treatment in the past year, indicating that cannabis use disorder is a seriously undertreated condition. Development and Course The onset of cannabis use disorder can occur at any age but is most common during adolescence or young adulthood. The increasing acceptability and availability of medical and recreational marijuana may impact the development and course of cannabis use disorder, with increased onset among older adults. Generally, cannabis use disorder develops over an extended period of time, although the progression may be more rapid in adolescents, particularly in those with conduct problems. Most individuals who develop a cannabis use disorder establish a pattern of cannabis use that gradually increases in frequency and amount. Beginning around 2010, cannabis has increasingly displaced alcohol and tobacco in the United States as the first psychoactive substance used during adolescence. This may be attributable to the decrease in perceived harmfulness of cannabis use among adolescents and adults and the fact that many now perceive cannabis use as less harmful than alcohol or tobacco use. Cannabis use disorder among preteens, adolescents, and young adults is associated with preferences for novelty-seeking and risk-taking, norm-violating or other illegal behaviors, and conduct disorder. Milder cases of cannabis use disorder in youth primarily reflect continued use despite problems related to disapproval of use by peers, school administration, or family, and can place youths at risk for physical or behavioral consequences. In more severe cases, progression to using alone or using throughout the day interferes with daily functioning and takes the place of previously established, prosocial activities. Cannabis use disorder among adults typically involves well-established patterns of daily cannabis use that continue despite clear psychosocial or medical problems. Many adults experience

repeated desire to stop or have failed at repeated cessation attempts. Milder adult cases may resemble mild 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 U.S. middle-age and older adults is increasing, which may be atributable to increased availability and acceptability, along with a possible “baby boomer” cohort effect resulting from high prevalence of use among those who were young adults 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 often concurrent with other externalizing

Temperamental. Environmental. Genetic and physiological. problems (e.g., symptoms of conduct disorder). However, early onset is also a predictor of internalizing problems and as such may reflect a general risk factor for the development of mental disorders. Risk and Prognostic Factors A history of conduct disorder in childhood or adolescence and antisocial personality disorder are risk factors for the development of many substance use disorders, including cannabis use disorder. Other risk factors include externalizing or internalizing disorders during childhood or adolescence. Youth with high behavioral disinhibition scores show early-onset substance use disorders, including cannabis use disorder and multiple substance involvement, and early conduct problems. Risk factors include unstable or abusive family situations, use of cannabis among immediate family members, a childhood history of emotional or physical abuse or the violent death of a close family member or friend, a family history of substance use disorders, 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. Increasingly permissive U.S. state medical and recreational marijuana laws have reduced barriers to obtaining cannabis in about two-thirds of U.S. states. Living in a U.S. state that has legalized recreational marijuana use increases the risk for adult cannabis use disorder. The risk of the disorder among past-year cannabis users is higher among Black, Native American, Hispanic, and Asian American adults and adolescents, relative to non-Hispanic Whites. 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, although studies have not yet definitively identified the specific genetic variants involved. Genetic and environmental influences shared between cannabis and other types of substance use disorders suggest a general common basis for substance use disorders that includes cannabis use disorder. Culture-Related Diagnostic Issues The acceptability of cannabis for medical and recreational use has varied widely over time and across cultural contexts. Currently, cannabis is one of the world’s most commonly used psychoactive substances. In some cultural settings, cannabis use is influenced by ethnicity, religion, and sociocultural practices, such as political movements. Sex- and Gender-Related Diagnostic Issues Compared with men, women report more severe cannabis withdrawal symptoms, especially mood symptoms such as irritability, restlessness, and anger, and gastrointestinal symptoms such as stomachache and nausea, which may contribute to potential telescoping (faster transition from first cannabis use to cannabis use disorder).

Past-month cannabis use was reported by 7.0% of pregnant women in a nationally representative U.S. survey in 2016–2017. The rate of cannabis use is lower in pregnant compared with nonpregnant women, but resumption of use following delivery occurs in the majority who attain abstinence in pregnancy. Diagnostic Markers Detection of 11-nor-9-carboxy-delta-9-

tetrahydrocannabinol (THCCOOH) in urine is often used as a biological marker of cannabis use. In frequent users, urine tests for THCCOOH often remain positive for weeks after last use, limiting the uses for these tests (e.g., remission status), and expertise in urine testing methods is needed to reliably interpret results. However, a positive result can be useful in working with individuals who deny all use despite concerns of family or friends. Tests for the presence of cannabinoids in blood that give more fine-grained results are under active development, and the development of detection using oral fluids may eventually offer the possibility of roadside tests to use in driving safety efforts. Association With Suicidal Thoughts or Behavior In a study of Iraq/Afghanistan-era veterans, after adjustment for multiple sociodemographic factors, psychiatric and other substance comorbidities, and past trauma, including combat, cannabis use disorder was still associated with increased risk of both suicidal and nonsuicidal self-injury. In a study of all U.S. Veterans Health Administration patients in 2005, any current substance use disorder was associated with increased suicide risk in both sexes but especially among women. In particular, men with cannabis use disorder had a suicide rate of 79 per 100,000 person-years, and women with cannabis use disorder had a suicide rate of 47 per 100,000 person-years. A review and meta-analysis of the international literature from 1990 through 2015 found evidence that chronic cannabis use, but not acute cannabis use, is associated with suicidal thoughts and behavior. 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. Although it can be difficult to distinguish the short-term impairments due to cannabis intoxication from the longer-term functional consequences of cannabis use disorder, cognitive function (particularly higher executive function) even while unintoxicated may become compromised in cannabis users in a cumulative dose-dependent relationship, which may contribute to difficulty at school or work. Accidents due to potentially dangerous activities while under the influence (e.g., driving, sports, at work) are also of concern. In particular, placebocontrolled studies and large-scale epidemiological studies show that cannabis use impairs driver reaction time, spatial perceptions, and decision-making. Cannabis use has also been linked to a reduction in goal-directed activity and decreased self-efficacy, labeled an amotivational syndrome, that manifests itself in poor school or work performance. Similarly, cannabisassociated problems with social relationships are commonly reported in those with cannabis use

Nonproblematic use of cannabis. Cannabis intoxication, cannabis withdrawal, and cannabis-induced mental disorders. disorder. Cannabis use is associated with poorer life satisfaction and increased treatment and hospitalization for mental health problems. Differential Diagnosis Although the majority of individuals who use cannabis do not have problems related to its use, 20%–30% of cannabis users do experience symptoms and associated consequences consistent with a cannabis use disorder. Differentiating nonproblematic use of cannabis and cannabis use disorder can be challenging because individuals may not attribute cannabis-related social, behavioral, or psychological problems to the substance, especially in the context of polysubstance use. Also, failure to acknowledge heavy cannabis use and its role in associated problems is common among individuals referred to treatment by others (i.e., school, family, employer, criminal justice system). Cannabis use disorder is differentiated from cannabis intoxication, cannabis withdrawal, and cannabis-induced mental disorders (e.g., cannabis-induced anxiety disorder) in that cannabis use disorder describes a problematic pattern of cannabis use that involves impaired control over cannabis use, social impairment due to cannabis use, risky cannabis use (e.g., driving while

intoxicated), and pharmacological symptoms (the development of tolerance or withdrawal), whereas cannabis intoxication, cannabis withdrawal, and cannabis-induced mental disorders describe psychiatric syndromes that develop in the context of heavy use. Cannabis intoxication, cannabis withdrawal, and cannabis-induced mental disorders occur frequently in individuals with cannabis use disorder. In such cases, a diagnosis of cannabis intoxication, cannabis withdrawal, or a cannabisinduced mental disorder should be given in addition to a diagnosis of cannabis use disorder, the presence of which is indicated in the diagnostic code. Comorbidity Cannabis use disorder is highly comorbid with other substance use disorders (e.g., alcohol, cocaine, opioids). For example, compared with adults without cannabis use disorder, having a cannabis use disorder multiplies the risk for any other substance disorder by a factor of about nine. Cannabis has been commonly considered as a “gateway” drug because individuals who use cannabis have a substantially greater lifetime probability than nonusers of subsequently using other, more risky substances (e.g., opioids or cocaine). Among adults seeking treatment for a cannabis use disorder, many (63%) report problematic use of secondary or tertiary substances, including alcohol, cocaine, methamphetamine/amphetamine, and heroin or other opiates, and cannabis use disorder is often a secondary or tertiary problem among those with a primary diagnosis of other substance use disorders. Among adolescents in treatment, cannabis is frequently the primary substance of abuse (76%). Among adults with DSM-5 cannabis use disorder, 64% had a past-year tobacco use disorder, and the odds of a comorbid tobacco disorder increased sharply as the severity of cannabis use disorder increased. Co-occurring mental disorders are also common among those with cannabis use disorder and

include major depressive disorder, bipolar I and II disorders, anxiety disorders, posttraumatic stress disorder, and personality disorders. In a Minnesota twin study, about half of adolescents with cannabis use disorder had internalizing disorders (e.g., anxiety, depression, posttraumatic stress disorder), and 64% had externalizing disorders (e.g., conduct disorder, attentiondeficit/hyperactivity disorder). Considerable concern has been raised about cannabis use as a risk factor in schizophrenia and other psychotic disorders. Cannabis use in critical periods is consistently associated with a threefold increase in the risk for psychosis. Differences in frequency of daily cannabis use and use of high-potency varieties of cannabis may have contributed to the striking variation in the incidence of psychotic disorder across 11 European sites. The population attributable fraction from regular cannabis in explaining hospital admissions for psychosis was estimated to be 17.7% (95% CI: 1.2%–45.5%) in Chile. On the other hand, some data suggest that childhood abuse may be the determining factor that increases the risk for cannabis abuse and for psychosis. Overall, cannabis use may contribute to the onset of an acute psychotic episode, can exacerbate some symptoms, and can adversely affect treatment of a major psychotic illness. Regarding medical conditions, cannabinoid hyperemesis syndrome is a syndrome of nausea and cyclic vomiting associated with regular cannabis use that is increasingly seen in emergency departments as the prevalence of cannabis use increases. In addition, respiratory disorders (e.g., asthma, chronic obstructive pulmonary disease, pneumonia) are associated with regular cannabis use (by smoking, vaping, or e-cigarettes) regardless of tobacco co-use, as are some adverse cardiovascular outcomes. 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-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 F12.120, and if a moderate or severe cannabis use disorder is comorbid, the ICD-10-CM code is F12.220. If there is no comorbid cannabis use disorder, then the ICD-10-CM code is F12.920. 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 shortterm 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 plant cannabis is smoked, and may take a few hours to develop when the cannabis is ingested orally. The effects usually last 3–4 hours, with duration 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-9THC), 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. Synthetic cannabinoids (e.g., Spice), whose use has become more common in recent years,

Other substance intoxication. Cannabis-induced mental disorders. also produce rapid effects, including euphoria, talkativeness, feelings of joy and laughter, and relaxation. In terms of psychoactive effects, low doses of synthetic cannabinoids and other cannabis products are similar. At higher doses of synthetic cannabinoids, delusional and hallucinatory symptoms are more likely to occur. Prevalence The prevalence of episodes of cannabis intoxication in the general population is unknown. However, it is probable that most individuals using cannabis would at some time experience symptoms that meet criteria for cannabis intoxication. Given this, the prevalence of individuals using cannabis 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. 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. Cannabis intoxication is distinguished from cannabis-induced mental disorders (e.g., cannabis-induced anxiety disorder, with onset during intoxication) because the symptoms (e.g., anxiety) in these latter disorders are in excess of those usually associated with cannabis intoxication, predominate in the clinical presentation, and are severe enough to warrant independent clinical attention. Comorbidity Given the typical overlap of cannabis intoxication with cannabis use disorder, see “Comorbidity” under Cannabis Use Disorder for more details about co-occurring conditions that are likely to be encountered. Cannabis Withdrawal

Diagnostic Criteria 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-10-CM code depends on whether or not there is a comorbid cannabis use disorder. If a mild cannabis use disorder is comorbid, the ICD-10-CM code is F12.13, and if a moderate or severe cannabis use disorder is comorbid, the ICD-10-CM code is F12.23. For cannabis withdrawal occurring in the absence of a cannabis use disorder (e.g., in a patient taking cannabis solely under appropriate medical supervision), the ICD-10-CM code is F12.93. Diagnostic Features The essential feature of cannabis withdrawal is the presence of a characteristic withdrawal syndrome that develops after the cessation of regular cannabis use. Regular users become tolerant to many acute cannabis effects, and cessation of regular use can lead to a cannabis withdrawal syndrome. Common cannabis withdrawal symptoms include irritability, depressed mood, anxiety, restlessness, sleep difficulty, and

decreased appetite or weight loss. Cannabis withdrawal can cause significant distress, leading to continued use to relieve the symptoms, difficulty in quitting, and relapse. Unlike withdrawal from other substances (i.e., opioids, alcohol, sedatives), behavioral and emotional symptoms (e.g., nervousness, irritability, sleep difficulty) are often more common than physical symptoms (e.g., shakiness, sweating). Associated Features

Cannabis withdrawal may be accompanied by observed fatigue, yawning, difficulty concentrating, and rebound periods of increased appetite and hypersomnia that follow initial periods of loss of appetite and insomnia. Prevalence Among adult and adolescent cannabis users, prevalence estimates of cannabis withdrawal symptoms vary widely, from 35% to 95%, based on research in the United States and other countries. Some of the variation in rates is likely attributable to assessment methods, and some to differences between samples. Among adult regular cannabis users in the general population, 12% reported signs and symptoms that met criteria for the full syndrome of DSM-5 cannabis withdrawal, with substantial differences in prevalence among non-Latinx Whites (10%), African Americans (15.3%), and Asian Americans, Native Hawaiians, and Pacific Islanders (31%). Among adults and adolescents who are enrolled in treatment or are 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 Withdrawal onset typically occurs within 24–48 hours after cessation of use. It peaks within 2–5 days and resolves within 1–2 weeks, although sleep disturbance can persist longer. The amount, duration, and frequency of cannabis smoking required to produce cannabis withdrawal are unknown, but more chronic and frequent cannabis use is associated with greater quantity and severity of withdrawal symptoms. Cannabis withdrawal can occur in adults and adolescents. Women may experience more severe cannabis withdrawal symptoms than men. Risk and Prognostic Factors Among cannabis users, the propensity to experience cannabis withdrawal is moderately heritable, indicating genetic influences. The prevalence and severity of cannabis withdrawal are greater among heavier cannabis users, particularly those seeking treatment for cannabis use disorder. Withdrawal severity may also be related to the presence and severity of comorbid symptoms of mental disorders. Functional Consequences of Cannabis Withdrawal Cannabis users report using cannabis to relieve withdrawal symptoms, making cannabis withdrawal a contributor to the persistence of cannabis use disorder. This makes cannabis withdrawal a current target for medication development. Worse outcomes may be associated with greater withdrawal. Sleep difficulty has been reported as the withdrawal symptom most often associated with relapse to cannabis use. Cannabis users report having relapsed to cannabis use or initiating use of other drugs (e.g., tranquilizers) to provide relief from cannabis withdrawal symptoms.

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 of another substance (e.g., tobacco or alcohol withdrawal), another mental disorder (generalized anxiety disorder, major depressive disorder), or another medical condition. Given the increasingly common belief that cannabis use is harmless, regular cannabis users experiencing cannabis withdrawal may not realize that their withdrawal symptoms are due to the effects of cannabis wearing off, and continue to use cannabis as a form of self-medication. Comorbidity Among adult frequent cannabis users, cannabis withdrawal is associated with comorbid depression, anxiety, and antisocial personality disorder. Given the typical overlap of cannabis withdrawal with cannabis use disorder,

see “Comorbidity” under Cannabis Use Disorder for more details about co-occurring conditions that are likely to be encountered. Cannabis-Induced Mental Disorders The following cannabis-induced mental 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 and delirium induced by pharmaceutical cannabis receptor agonists taken as prescribed, see the criteria and discussion of delirium in the chapter “Neurocognitive Disorders.” These cannabis-induced mental 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 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 Phencyclidine-Induced Mental Disorders Hallucinogen-Induced Mental 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. Code based on current severity/remission: 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 phencyclidineinduced 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/remission: F16.10 Mild: Presence of 2–3 symptoms. F16.11 Mild, In early remission F16.11 Mild, In sustained remission F16.20 Moderate: Presence of 4–5 symptoms. F16.21 Moderate, In early remission F16.21 Moderate, In sustained remission F16.20 Severe: Presence of 6 or more symptoms. F16.21 Severe, In early remission F16.21 Severe, In sustained remission 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 phencyclidine 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 symptoms have not been clearly established in

humans, and therefore the withdrawal criterion is not included in the diagnosis of phencyclidine use disorder. Associated Features 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, risk of hypertension/hypotension and shock, euphoria, visual/auditory hallucinations, derealization, and unusual thought content.

Other substance use disorders. Phencyclidine intoxication and phencyclidine-induced mental disorders. Violent behavior can also occur with phencyclidine use, as intoxicated individuals may believe that they are being attacked. Prevalence Data on the prevalence of phencyclidine use disorder are not available, but rates appear to be low (based on rates of the overall category of hallucinogen use disorder, which includes phencyclidine, of about 0.1% among individuals age 12 and older in the United States). Furthermore, among U.S. substance use treatment facility admissions, only 0.3% of the admitted individuals endorsed phencyclidine as their primary drug. Risk and Prognostic Factors In a general population study in Australia, ketamine users were more likely to be men and to have consumed more than 11 standard drinks per day. Sex- and Gender-Related Diagnostic Issues The gender ratio for phencyclidine use disorder is not known, but among U.S. substance use treatment facility admissions endorsing phencyclidine as the primary drug, 62% were men. 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 (e.g., nystagmus, analgesia, 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 can lead to acute and persistent cognitive impairment; urinary tract and intestinal symptoms; abdominal pain, chest pain, palpitations, and tachycardia; respiratory depression; sleep disorders; and depression. Differential Diagnosis Distinguishing the effects of phencyclidine from those of other substances may be important, because phencyclidine can be an additive to other substances (e.g., cannabis, cocaine). Phencyclidine use disorder is differentiated from phencyclidine intoxication and phencyclidine-induced mental disorders (e.g., phencyclidine-induced psychotic disorder) in that phencyclidine use disorder describes a problematic pattern of phencyclidine use that involves impaired control over phencyclidine use, social impairment attributable to phencyclidine use, risky phencyclidine use (e.g., driving while intoxicated), and pharmacological symptoms (the development of tolerance), whereas

Independent mental disorders. phencyclidine intoxication and phencyclidine-induced mental disorders describe psychiatric syndromes that occur in the context of heavy use. Phencyclidine intoxication and phencyclidineinduced mental disorders occur frequently in individuals with phencyclidine use disorder. In such cases, a diagnosis of phencyclidine intoxication or a phencyclidine-induced mental disorder should be given in addition to a diagnosis of phencyclidine use disorder, the presence of which is indicated in the diagnostic code. Some of the effects of phencyclidine use may resemble symptoms of independent mental disorders, such as psychosis (schizophrenia); low mood (major depressive disorder); and 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 a preexisting mental

disorder. Comorbidity Conduct disorder in adolescents and antisocial personality disorder may be associated with phencyclidine use. Other substance use disorders, especially alcohol, cocaine, and amphetamine use disorders, are common among those with phencyclidine use disorder. 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. Code based on current severity/remission: 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/remission: F16.10 Mild: Presence of 2–3 symptoms. F16.11 Mild, In early remission F16.11 Mild, In sustained remission F16.20 Moderate: Presence of 4–5 symptoms. F16.21 Moderate, In early remission F16.21 Moderate, In sustained remission F16.20 Severe: Presence of 6 or more symptoms. F16.21 Severe, In early remission F16.21 Severe, In sustained remission 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 [3,4methylenedioxymethamphetamine; also called “ecstasy” or “molly”]); the indoleamines, including psilocybin (and its metabolite psilocin, the compound primarily responsible for the psychedelic effects of hallucinogenic mushrooms) 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.

Temperamental. MDMA/ecstasy as a hallucinogen may have distinctive effects attributable to both its hallucinogenic and its stimulant properties. Ecstasy users have a higher risk of developing a hallucinogen use disorder than those using other hallucinogens. Among both adolescent and adult ecstasy users and users of other hallucinogens, the most frequently reported hallucinogen use disorder criteria are tolerance, hazardous use, use despite emotional or health problems, giving up activities in favor of use, and spending a lot of time obtaining, using, or recovering from the effects of use. As found for other substances, diagnostic criteria for other hallucinogen use disorder are arrayed along a single continuum of severity. Given that a clinically significant withdrawal syndrome has not been consistently documented in humans, the diagnosis of hallucinogen

withdrawal syndrome is not included in this manual and therefore is not part of the hallucinogen use disorder diagnostic criteria. However, there may be evidence of withdrawal from MDMA, with endorsement of any two or more withdrawal symptoms (e.g., malaise, appetite disturbance, mood changes [anxious, depressed, irritable], poor concentration, sleep disruption) or withdrawal avoidance observed in more than half of individuals in diverse samples of ecstasy users in the United States and internationally. Associated Features The characteristic symptom features of use of some 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. Prevalence Other hallucinogen use disorder is rare. In the U.S. general population, about 0.1% of individuals age 12 or older endorsed the symptoms of past 12-month hallucinogen use disorder in 2018. The rate was 0.2% among those ages 12–17, 0.4% among those ages 18–25, and < 0.1% among those age 26 and older. Prevalence is higher in U.S. clinical samples (e.g., 19% in adolescents in treatment), and among select groups of individuals who use hallucinogens frequently (e.g., recent heavy ecstasy use) in the United States and Australia, 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 Prevalence of other hallucinogen use disorder by age among adolescents is unknown. Among U.S. adults age 18 years and older, most (90%) of those with other hallucinogen use disorder are ages 18–29, suggesting that the disorder is not often persistent and is concentrated in young adults. Risk and Prognostic Factors The use of specific hallucinogens (i.e., ecstasy, salvia) has been linked with high

Environmental. Genetic and physiological. sensation-seeking. On the basis of research in the United States, environmental risk factors of other hallucinogen use disorder include higher income, lower education, being never married, and residing in urban areas. Early onset of hallucinogen use has also been linked to transition to hallucinogen use disorder. Peer use of other drugs is also highly associated with ecstasy and salvia use. 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 or spiritual 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 religious groups. Sex- and Gender-Related Diagnostic Issues Among U.S. adolescents, boys have greater 12-month prevalence rates of other hallucinogen use than girls, and these gender differences extend to specific hallucinogens, including LSD, MDMA, psilocybin, and salvia divinorum. Among U.S. adults, 60% of individuals with other hallucinogen use disorder are men. International research suggests that women administered MDMA may have greater subjective effects, such as altered state of consciousness, anxiety, and depression. No information from international studies is available regarding gender differences for 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 Although insufficient information exists to clearly note the functional consequences of other hallucinogen use disorder, complications of use of these substances have been identified. Adverse effects of other hallucinogen use include those related to intoxication, such as hyperthermia, cardiac tachyarrhythmias, pneumothorax

hypernatremia, motor incoordination, nystagmus, restlessness, hallucinations/delusions, mydriasis, increased alertness, and high blood pressure. Other more serious reactions related to consequences of repeated use of other hallucinogens include renal failure, hepatic failure, seizures, cerebral infarction, rhabdomyolysis,

Other substance disorders. Hallucinogen intoxication and hallucinogen-induced mental disorders. Independent mental disorders. cardiac complications, and hepatotoxicity. There is evidence for persisting 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. Differential Diagnosis The effects of hallucinogen use must be distinguished from those of other substances (e.g., amphetamine use disorder, alcohol or sedative withdrawal), especially because contamination of the hallucinogens with other drugs is relatively common. Hallucinogen use disorder is differentiated from hallucinogen intoxication and hallucinogen-induced mental disorders (e.g., hallucinogen-induced psychotic disorder) in that hallucinogen use disorder describes a problematic pattern of hallucinogen use that involves impaired control over hallucinogen use, social impairment attributable to hallucinogen use, risky hallucinogen use (e.g., driving while intoxicated), and pharmacological symptoms (the development of tolerance), whereas hallucinogen intoxication and hallucinogen-induced mental disorders describe psychiatric syndromes that occur in the context of heavy use. Hallucinogen intoxication and hallucinogeninduced mental disorders occur frequently in individuals with hallucinogen use disorder. In such cases, a diagnosis of hallucinogen intoxication or a hallucinogen-induced mental disorder should be given in addition to a diagnosis of hallucinogen use disorder, the presence of which is indicated in the diagnostic code. Some of the effects of hallucinogen use may resemble symptoms of independent psychiatric disorders, such as schizophrenia and depressive and bipolar disorders. Discerning whether symptoms occurred before the intake of the drug is important in the differentiation of acute drug effects from a preexisting mental disorder. In particular, schizophrenia should be ruled out, as some affected individuals (e.g., individuals with schizophrenia who exhibit paranoia) may falsely attribute their symptoms to use of hallucinogens. Comorbidity Other hallucinogen use disorder is highly associated with cocaine use disorder, stimulant use disorder, other substance use disorder, tobacco (nicotine) use disorder, any personality disorder, posttraumatic stress disorder, and panic attacks. 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-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 F16.120, and if a moderate or severe phencyclidine use disorder is comorbid, the ICD-10-CM code is F16.220. If there is no comorbid phencyclidine use disorder, then the ICD-10-CM code is F16.920. 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; nystagmus; numbness or diminished responsiveness to pain; ataxia; dysarthria; muscle rigidity; hyperacusis; and coma of varying severity. Other clinically significant behavioral changes associated with phencyclidine intoxication include violent behavior, extreme agitation, persecutory delusions, euphoria, retrograde amnesia, and hypertension. Prevalence Use of phencyclidine or related substances (e.g., ketamine) may be taken as an estimate of the prevalence of intoxication. Phencyclidine use is rare, with < 0.1% of the U.S. population age 12 and older reporting past 12-month use in 2018. In surveys of U.S. students and young adults followed up from high school, past 12-month prevalence of ketamine use, which is assessed

Other substance intoxication. Phencyclidine-induced mental disorders. Other medical conditions. separately from other substances, was estimated at about 1.2% among 12th graders and 0.5% among young adults, ages 19–28 years. 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 that the perceptual abnormalities are drug induced), an additional diagnosis of phencyclidine-induced psychotic disorder should be considered. Phencyclidine intoxication should be differentiated from intoxication due to other substances, including other hallucinogens; amphetamine, cocaine, 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. However, the weak correlation between quantitative toxicology levels of phencyclidine and clinical presentation may diminish the utility of the laboratory findings for patient management. Phencyclidine intoxication is distinguished from phencyclidine-induced mental disorders (e.g., phencyclidine-induced depressive disorder, with onset during intoxication) because the symptoms (e.g., depressed mood) in the latter disorders are in excess of those usually associated with phencyclidine intoxication, predominate in the clinical presentation, and are severe enough to warrant clinical attention. Medical conditions to be considered include certain metabolic disorders like hypoglycemia and

hyponatremia, central nervous system tumors, seizure disorders, sepsis, neuroleptic malignant syndrome, and vascular insults. Comorbidity Given the typical overlap of phencyclidine intoxication with phencyclidine use disorder, see “Comorbidity” under Phencyclidine Use Disorder for more details about co-occurring conditions that are likely to be encountered. 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-10-CM code depends on whether there is a comorbid hallucinogen use disorder. If a mild hallucinogen use disorder is comorbid, the ICD10-CM code is F16.120, and if a moderate or severe hallucinogen use disorder is comorbid, the ICD-10-CM code is F16.220. If there is no comorbid hallucinogen use disorder, then the ICD-10-CM code is F16.920. Note: For information on Associated Features 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

Other substance intoxication. Other conditions. Hallucinogen persisting perception disorder. The prevalence of other hallucinogen intoxication is not fully known but may be approximated based on the prevalence of use of the substances. In 2018, 1.5% of individuals ages 12–17 years in the United States reported use of hallucinogens in the past year; among individuals ages 18– 25, the rate was 6.9%, and among those age 26 or older, the rate was 1.3%. Rates were consistently higher for boys and men than for girls and women in every age group. Association With Suicidal Thoughts or Behavior Other hallucinogen intoxication may lead to increased suicidal thoughts or behavior, although suicide is rare among individuals who use hallucinogens. Of note, a study of more than 135,000 randomly selected U.S. adults, including more than 19,000 individuals who use psychedelics, did not find evidence, after adjustment for sociodemographics, other drug use, and childhood depression, that lifetime psychedelic use is an independent risk factor for mental health

problems, suicidal thoughts, or suicide attempts. In addition, one large U.S. population survey found that a lifetime history of hallucinogen use was associated with lower odds of mental distress and suicidal thoughts or behavior, although a causal relationship between hallucinogenic drugs and lower distress cannot be inferred from this study. On the basis of these findings, the relationship of other hallucinogen use to suicidal thoughts and behaviors is uncertain. 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., cuts or falls from impaired depth perception). When other hallucinogens are consumed in combination with other drugs (including alcohol), coma can occur, with the duration and profundity of coma greater than when other hallucinogens are taken alone. Continued use of hallucinogens, particularly MDMA, has also been linked with neurotoxic effects. Adverse effects of other hallucinogen use include hyperthermia, cardiac tachyarrhythmias, pneumothorax hypernatremia, motor incoordination, nystagmus, restlessness, hallucinations/delusions, mydriasis, increased alertness, and high blood pressure. More serious reactions include renal failure, hepatic failure, seizures, cerebral infarction, rhabdomyolysis, cardiac complications, and hepatotoxicity. Differential Diagnosis Other hallucinogen intoxication should be differentiated from intoxication with amphetamine-type substances, 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 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. Other hallucinogen intoxication is distinguished from

Hallucinogen-induced mental disorders. F16.983 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 intoxication is distinguished from hallucinogen-induced mental disorders (e.g., hallucinogen-induced anxiety disorder, with onset during intoxication) because the symptoms (e.g., anxiety) in these latter disorders are in excess of those usually associated with other hallucinogen intoxication, predominate in the clinical presentation, and are severe enough to warrant independent clinical attention. Comorbidity Given the typical overlap of other hallucinogen intoxication with other hallucinogen use disorder, see “Comorbidity” under Other Hallucinogen Use Disorder for more details about cooccurring conditions that are likely to be encountered. Hallucinogen Persisting Perception Disorder Diagnostic Criteria 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, visual snow, positive afterimages (i.e., a samecolored 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), adaptation to dark environments, exercise, and exposure to noise and photophobia. Associated Features 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, major depressive disorder, bipolar I disorder, and schizophrenia spectrum disorders. Phencyclidine-Induced Mental Disorders Other phencyclidine-induced mental 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 and related disorder (“Bipolar and Related Disorders”); phencyclidine-induced depressive disorder (“Depressive Disorders”); and phencyclidine-induced anxiety disorder (“Anxiety Disorders”). For phencyclidine-induced intoxication delirium and delirium induced by ketamine taken as prescribed, see the criteria and discussion of delirium in the chapter “Neurocognitive Disorders.” These phencyclidine-induced mental disorders are diagnosed instead of phencyclidine intoxication only when the symptoms are sufficiently severe to warrant independent clinical attention. Hallucinogen-Induced Mental Disorders The following other hallucinogen-induced mental disorders are described in other chapters of the manual with disorders with which they share phenomenology (see the substance/medicationinduced mental disorders in these chapters): other hallucinogen–induced psychotic disorder (“Schizophrenia Spectrum and Other Psychotic Disorders”); other hallucinogen–induced bipolar and related 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 and delirium induced by other hallucinogens taken as prescribed, see the criteria and discussion of delirium in the chapter “Neurocognitive Disorders.” These hallucinogen-induced mental disorders are diagnosed instead of other hallucinogen intoxication only when the symptoms are sufficiently severe to warrant independent clinical attention. Unspecified Phencyclidine-Related Disorder

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 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 Inhalant-Induced Mental 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. Code based on current severity/remission: 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/remission: F18.10 Mild: Presence of 2–3 symptoms. F18.11 Mild, In early remission F18.11 Mild, In sustained remission F18.20 Moderate: Presence of 4–5 symptoms. F18.21 Moderate, In early remission F18.21 Moderate, In sustained remission F18.20 Severe: Presence of 6 or more symptoms. F18.21 Severe, In early remission F18.21 Severe, In sustained remission 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. 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 Examples of inhalant substances include volatile hydrocarbons, which comprise 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. 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) is reported by about 10% of individuals who use inhalants. Because a clinically significant withdrawal syndrome has not been established with inhalant use, neither a diagnosis of inhalant withdrawal nor a corresponding diagnostic criterion for withdrawal complaints for inhalant use disorder is included. However, withdrawal symptoms may occur among inhalant users and individuals with moderate to severe inhalant use disorder, and these symptoms appear to be similar in frequency to withdrawal symptoms among those with moderate to severe cocaine use disorder. Associated Features 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 other substance use disorders. Individuals with inhalant use disorder may present with symptoms of pernicious anemia, subacute combined degeneration of the spinal cord, major or mild neurocognitive disorder, brain atrophy, leukoencephalopathy, and many other nervous system disorders. Prevalence About 2.3% of American youth ages 12–17 years have used inhalants in the past 12 months, with 0.1% having a pattern of use that meets criteria for inhalant use disorder. Among U.S. adults, age 18 years and older, past 12-month prevalence of inhalant use is about 0.21%, with 0.04% having a pattern of use that meets criteria for an inhalant use disorder. Among youth, the prevalence of past 12-month inhalant use is highest among non-Hispanic Whites and individuals reporting more than one racialized identity and lowest among American Indians/Alaska Natives. Twelvemonth prevalence rates of inhalant use and inhalant use disorder among adults are highest among non-Hispanic Whites and lowest among non-Hispanic Blacks and American Indians/Alaska Natives. Development and Course

Temperamental. Environmental. Genetic and physiological. The declining prevalence in the United States of inhalant use and inhalant use disorder after adolescence (from 2.3% during adolescence to 0.1% in early adulthood for inhalant use and from 0.1% to 0.04% for inhalant use disorder) indicates that the disorder usually remits in early adulthood. Inhalant 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. Those with inhalant use disorder extending into adulthood demonstrate earlier onset of inhalant use, use of multiple inhalants, and more frequent inhalant use. Risk and Prognostic Factors Predictors of inhalant use disorder include sensation seeking and impulsivity. 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. 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 use and antisocial behaviors are at elevated risk for inhalant use disorder. Culture-Related Diagnostic Issues Internationally, certain isolated Indigenous communities have experienced a high prevalence of inhalant problems. Also, in some low- and middle-income countries, groups of homeless children living on the streets have extensive inhalant use problems because of the effects of poverty and the availability and affordability of the substances, and as a way to cope with homelessness. Sex- and Gender-Related Diagnostic Issues Although the past 12-month prevalence of inhalant use disorder in the United States is almost identical among adolescent boys and girls, the disorder is very rare among adult women. 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. Association With Suicidal Thoughts or Behavior

Inhalant exposure (unintentional) from industrial or other accidents. Inhalant intoxication, without meeting criteria for inhalant use disorder. Inhalant intoxication meeting criteria for inhalant use disorder, and inhalant-induced mental disorders. Other substance use disorders, especially those involving sedating substances (e.g., alcohol, benzodiazepines, barbiturates). In the United States, adolescent and adult inhalant use and inhalant use disorder are associated with suicidal thoughts and behavior, especially among individuals reporting symptoms of anxiety and depression and histories of trauma. Functional Consequences of Inhalant Use Disorder Because of inherent toxicity, use of inhalants can be fatal. Death can occur from anoxia, cardiac dysfunction, extreme allergic reaction, severe injury to the lungs, vomiting, accidents or injury, or central nervous system depression. Moreover, any inhaled volatile hydrocarbons may produce “sudden sniffing death” from cardiac arrhythmia. Inhalant 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. Differential Diagnosis A diagnosis of inhalant use disorder only applies if the inhalant exposure is intentional. Inhalant intoxication occurs frequently during inhalant use disorder but also may occur among individuals whose use does not meet criteria for inhalant use disorder. Inhalant use disorder is differentiated from inhalant intoxication and inhalant-induced mental disorders (e.g., inhalant-induced depressive disorder) in that inhalant use disorder describes a problematic pattern of inhalant use that involves impaired control over inhalant use, social impairment attributable to inhalant use, risky inhalant use (e.g., inhalant use despite medical complications), and pharmacological symptoms (the development of tolerance), whereas inhalant intoxication and inhalant-induced mental disorders describe psychiatric syndromes that develop in the context of heavy use. Inhalant intoxication and inhalant-induced mental disorders occur frequently in individuals with inhalant use disorder. In such cases, a diagnosis of inhalant intoxication or an inhalant-induced mental disorder should be given in addition to a diagnosis of inhalant use disorder, the presence of which is indicated in the diagnostic code. 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. Comorbidity Individuals with inhalant use disorder receiving clinical care often have numerous other substance use, mood, anxiety, and personality disorders. Inhalant use disorder commonly co-

occurs with conduct disorder in adolescents and with antisocial personality disorder. Individuals with inhalant use disorder may have comorbid symptoms of hepatic or renal damage, rhabdomyolysis, methemoglobinemia, or symptoms of other gastrointestinal, cardiovascular, or pulmonary diseases. 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-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 F18.120, and if a moderate or severe inhalant use disorder is comorbid, the ICD-10-CM code is F18.220. If there is no comorbid inhalant use disorder, then the ICD-10-CM code is F18.920.

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 The essential feature of inhalant intoxication is the presence of clinically significant problematic behavioral or psychological changes that develop during, or immediately after, intended or unintended inhalation of a volatile hydrocarbon substance. When possible, the particular substance involved should be named (e.g., toluene intoxication). 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 with further inhalant use. Associated Features Inhalant intoxication may be indicated by evidence of possession, or lingering odors, of inhalant substances (e.g., glue, paint thinner, gasoline, butane lighters); other features may include euphoria, relaxation, headache, rapid heartbeat, confusion, talkativeness, blurred vision, amnesia, slurred

speech, irritability, nausea, fatigue, burning in eyes or throat, grandiosity, chest pain, auditory or visual hallucinations, and dissociation. Prevalence The prevalence of actual episodes of inhalant intoxication in the general population is unknown, but it is probable that a majority of inhalant users would at some time exhibit behavioral or psychological changes and symptoms that would meet criteria for inhalant intoxication. Therefore, the prevalence of inhalant use and the prevalence of inhalant intoxication are likely similar. In 2017, inhalant use in the past year was reported by 0.6% of all Americans older than 12 years; the prevalence was highest in younger age groups (2.3% for individuals ages 12 –17 years, 1.6% for individuals ages 18–25 years, and 0.3% for individuals age 26 and older). Sex- and Gender-Related Diagnostic Issues Gender differences in the prevalence of inhalant intoxication in the general population are unknown. Regarding gender differences in the prevalence of inhalant use in the United States, 0.8% of boys/men older than 12 years and 0.5% of girls/women older than 12 years have used inhalants in the previous year, but in the younger age groups differences are minimal or girls may have slightly higher prevalence (e.g., among adolescents ages 12–17 years, 2.4% of girls and 2.2% of boys have used inhalants in the past year). 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

Intoxication from other substances, especially from sedating substances (e.g., alcohol, benzodiazepines, barbiturates). Inhalant-induced mental disorders. Other toxic, metabolic, traumatic, neoplastic, or infectious disorders that impair brain function and cognition. 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. Clinically significant correlates of inhalant intoxication include reckless behaviors (e.g., taking foolish risks, getting into fights, having unprotected sex), antisocial behaviors (cruelty, damaging property, arrests), and having serious accidents. Differential Diagnosis These disorders may have similar signs and symptoms, but intoxication attributable to other intoxicants 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; or apparent intoxication despite negative results on standard drug screens (which usually fail to identify inhalants). Inhalant intoxication is distinguished from inhalant-induced mental disorders (e.g., inhalant-induced anxiety disorder, with onset during intoxication) because the symptoms (e.g., anxiety) in these latter disorders are in excess of those usually associated with inhalant intoxication, predominate in the clinical presentation, and are severe enough to warrant independent clinical attention. 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. Comorbidity Given the typical overlap of inhalant intoxication with inhalant use disorder, see “Comorbidity” under Inhalant Use Disorder for more details about co-occurring conditions that are likely to be encountered. Inhalant-Induced Mental Disorders The following inhalant-induced mental 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 mental disorders are diagnosed instead of inhalant intoxication only when symptoms are sufficiently severe to warrant independent clinical attention. Unspecified Inhalant-Related Disorder 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 Opioid-Induced Mental 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 12month 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). 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 individuals 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. Code based on current severity/remission: 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/remission: F11.10 Mild: Presence of 2–3 symptoms. F11.11 Mild, In early remission F11.11 Mild, In sustained remission F11.20 Moderate: Presence of 4–5 symptoms. F11.21 Moderate, In early remission F11.21 Moderate, In sustained remission F11.20 Severe: Presence of 6 or more symptoms. F11.21 Severe, In early remission F11.21 Severe, In sustained remission 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 substancefree 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 The opioids include natural opioids (e.g., morphine, codeine), semisynthetics (e.g., heroin, oxycodone, hydrocodone, hydromorphone, oxymorphone), and synthetics with morphine-like action (e.g., methadone, meperidine, tramadol, fentanyl, carfentanil). Medications such as pentazocine and buprenorphine that have both opiate agonist and antagonist effects are also included in this class because, especially at lower doses, their agonist properties produce similar physiological and behavioral effects as classic opioid agonists. Opioids are prescribed as analgesics, anesthetics, antidiarrheal agents, or cough suppressants. Heroin is one of the most commonly misused drugs of this class and is usually taken by injection, although it can be smoked or “snorted,” especially when very pure heroin is available. Fentanyl is typically injected, both medically and nonmedically, and is used medically in transdermal and transmucosal formulations, whereas cough suppressants and antidiarrheal agents

are taken orally. The other opioids are generally taken both by injection and orally. Opioid use disorder can arise from prescription opioids or illicit opioids (e.g., heroin and, especially in recent years, fentanyl-related synthetic opioids). Opioid use disorder consists of signs and symptoms reflecting compulsive, prolonged self-administration of opioid substances either for a purpose other than a legitimate medical one or for use in a “non-medical” manner (i.e., greatly exceeding the amount prescribed for a medical condition). For example, an individual with adequate doses of prescribed analgesic opioid medication for pain relief who uses significantly more of the medication than prescribed, and not only because of persistent pain, is engaging in nonmedical opioid use and may have an opioid use disorder. Most individuals with opioid use disorder have tolerance and experience withdrawal on abrupt cessation or reduction in opioid use. Similar to processes that occur with other psychoactive substances, individuals with opioid use disorder often develop conditioned responses to drugrelated stimuli (e.g., cue-reactive craving on seeing drug images or paraphernalia). These responses probably contribute to relapse, are difficult to extinguish, and typically persist long after withdrawal is completed. 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. Prescription opioids used nonmedically can be obtained from family or friends, from physicians by falsifying or exaggerating medical problems, by receiving simultaneous prescriptions from several physicians, or via purchase on the illegal market. Health care professionals with opioid use disorder can obtain opioids by writing prescriptions for themselves or by diverting opioids that have been prescribed for individuals or from pharmacy supplies. Associated Features An attempt to achieve opioid intoxication may result in fatal or nonfatal opioid overdose. Opioid overdose is characterized by unconsciousness, respiratory depression, and pinpoint pupils. However, opioid overdoses can also occur in the absence of intoxication-seeking drug use.

Opioid overdoses have increased exponentially in the United States since 1999. Up to 2009, opioid overdoses were mainly due to prescribed opioids, but since 2010, overdoses due to heroin began a sharp rise, and additionally, since 2015, fatal overdoses due to synthetic opioids other than methadone (generally fentanyl) have outnumbered overdoses due to prescribed opioids. 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, a different pattern of illegal activities may involve problems with state licensing boards, professional staffs of hospitals, or other administrative agencies. Marital difficulties (including divorce), unemployment, and irregular employment can be associated with opioid use disorder at all socioeconomic levels. Prevalence The prevalence of nonmedical prescription opioid use among U.S. adults age 18 and older is 4.1%–4.7%, with rates of use higher in adults ages 18–25 than in those age 26 and older (5.5% vs. 3.4%, respectively). The prevalence of heroin use in the United States is 0.3%–0.4% and is higher among adults ages 18–25 (0.5%–0.7%) than in other age groups. In U.S. adolescents ages 12–17, 2.8%–3.9% use prescription opioids nonmedically, with higher rates in older adolescents than in younger adolescents. Heroin use in adolescents is quite low (< 0.05%–0.1%). The prevalence of prescription opioid use disorder among U.S. adults age 18 and older (DSM-IV or DSM-5 criteria) is 0.6%–0.9%, and the prevalence of heroin use disorder (DSM-IV or DSM-5 criteria) is 0.1%–0.3%. Among those ages 12–17, prevalence of prescription opioid use disorder is 0.4%, and heroin use disorder is rare (essentially 0%). In the United States, rates of opioid use disorder (prescription opioids and heroin) are higher among men than women, among young adults than

older adults, and among those with lower income or education. Among U.S. adults in 2012–2013, the prevalence of nonmedical prescription opioid use disorder varied by ethnoracial group: 1.42% in Native Americans, 1.04% in African Americans, 0.96% in nonLatinx Whites, 0.70% in Latinx, and 0.16% in Asian Americans or Pacific Islanders. Rates based on household surveys may underestimate national prevalence by omitting individuals in institutions and jail or prison, whose rates are likely to be much higher. Globally in 2016, there were 26.8 million cases of DSM-IV opioid dependence, with an agestandardized prevalence of 353.0 cases per 100,000 people; prevalence of opioid dependence across geographic regions ranged from 0.14% to 0.46%. Development and Course Opioid use disorder can begin at any age. In the United States, problems associated with opioid use are most commonly first observed in the late teens or early 20s, with a longer interval between first opioid use and onset of disorder for prescription opioids than for heroin. Early use can reflect a desire for relief from life stressors or psychological pain. Longterm studies show that once an opioid use disorder that requires treatment develops, it can continue over many years, with brief periods of abstinence in some individuals but long-term

abstinence only in a minority. An exception occurred among U.S. soldiers who became dependent on opioids while serving in the Vietnam War; over 90% had long-term abstinence from opioids after returning to the United States, although many subsequently experienced problems with alcohol, amphetamines, or suicidal thoughts or behavior. Risk and Prognostic Factors In addition to an association with more frequent nonmedical prescription opioid use, adult prescription opioid use disorder is associated with most other substance use disorders. Opioid use disorder is highly associated with externalizing traits such as novelty-seeking, impulsivity, and disinhibition. Family, peer, and social environmental factors all increase the risk for opioid use disorder. Family and twin studies also indicate a strong genetic contribution to the risk for opioid use disorders, although identifying the specific genetic variants contributing to genetic risk has been slow. Peer factors may relate to genetic predisposition in terms of how individuals select their environments, including their peers. Culture-Related Diagnostic Issues Individuals from socially oppressed ethnoracial groups were historically overrepresented among individuals with opioid use disorder. However, over time, opioid use disorder has become more common among White individuals, suggesting that the widespread availability of opioids and other social factors (e.g., changes in rates of poverty and unemployment) have an impact on prevalence. Consistent with these factors, despite small variations between ethnoracial groups in the psychometric performance of opioid use disorder criterion items, the criteria for opioid use disorder perform equally well across ethnoracial groups. Sex- and Gender-Related Diagnostic Issues Women with opioid use disorder appear more likely than men to have initiated opioid use in response to sexual abuse and violence, and they are more likely than men to be introduced to the drug by a partner. There is substantial evidence of telescoping among women in that they progress to a use disorder more quickly than men after first use; women also appear to be more ill when entering treatment facilities than are men, as noted in a large sample of heroin users in Italy. 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. Some opioids, such as fentanyl and oxycodone, are not detected by standard urine tests (which test for morphine), but can be identified by more specialized procedures for several days after use. Similarly, methadone and buprenorphine (or buprenorphine/naloxone combinations) will not cause a positive result on routine tests for opiates; they require specific tests that can detect these substances for several days up to more than 1

week. Although not specific markers of opioid use disorder, laboratory evidence of the presence of other substances (e.g., cocaine, marijuana, alcohol, amphetamines, benzodiazepines) is common

in heroin users. In addition, screening test results for hepatitis A, B, and C virus are often positive in injection opioid users, either for hepatitis antigen (signifying active infection) or for hepatitis antibody (signifying past infection). 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. HIV is also prevalent in injection opioid users. Subtle changes in cortisol secretion patterns and body temperature regulation have been observed for up to 6 months following opioid withdrawal. Association With Suicidal Thoughts or Behavior Opioid use disorder is associated with a heightened risk for suicide attempts and suicide. 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 suicide. Nonfatal accidental opioid overdose and attempted suicide are distinct phenomena that can be difficult to differentiate but should not be mistaken for each other, if possible. Findings from the Global Burden of Disease Study 2010 showed that among drugs of abuse, suicide is a common cause of death among regular users of opioids. Evidence suggests that suicides are undercounted or often misclassified in opioid-poisoning data. In a study of the Veterans Health Administration (VHA) national medical records, after adjustment for psychiatric comorbidity, opioid use disorder elevated the risk for suicide mortality, with greater increase in risk among women than among men. In another study also using VHA national medical records, among veterans prescribed opioids for chronic pain, suicide mortality increased with higher opioid doses, even after demographic and clinical factors were taken into account. A follow-up of a U.S. national cohort of adults with a history of an opioid overdose found that the standardized mortality ratio (SMR; the ratio between the observed number of deaths in a study population and the number of deaths that would be expected) was 25.9 for suicide, with a higher SMR for women than for men. A review posited that the reasons for the increased risk for suicide among opioid users were related to shared risk factors, namely, comorbid mental disorders and pain. Functional Consequences of Opioid Use Disorder Physiologically, 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 rare but serious consequences of injecting opioids, especially with contaminated needles.

Opioid intoxication, opioid withdrawal, and opioid-induced mental disorders. 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 individuals who inject opioids. In addition, the prevalence of HIV infection is high among individuals who inject drugs, a large proportion of whom are individuals with opioid use disorder. For example, HIV infection rates are as high as 60% among heroin users in some areas of the United States and the Russian Federation. However, the

incidence may be much lower in areas 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 or tuberculosis blood test (interferon gamma release assay). 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 (insufflation, or “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. Although acute opioid use produces analgesia, chronic use can produce hyperalgesia (opioidinduced hyperalgesia), a condition characterized by increased sensitivity to pain. 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 in the neonate requiring medical treatment and has increased markedly in prevalence. The mortality rate in individuals with opioid use disorder is 6–20 times greater than in the general population. Fatal overdoses due to prescription opioids increased dramatically in the United States since 1999, with almost 400,000 such deaths occurring since then, and the rate of such overdoses is now five times higher than in 1999. Fatal overdoses due to heroin began a sharp increase in 2010, and since 2013, fatal overdoses due to synthetic opioids (e.g., fentanyl) increased so sharply that these rates were almost double the rates for prescription opioid or heroin overdoses by 2017. Nonfatal opioid overdoses resulting in hospitalization and emergency department visits have increased as well. Although not all risk factors for opioid use disorder and opioid overdose are the same, substantial overlap exists, making the risk for overdose one of the most serious potential consequences of opioid use disorder. Individuals with opioid use disorder are also at increased risk for mortality from many medical conditions (e.g., hepatitis, HIV infection, tuberculosis, cardiovascular disease). Death can also result from accidents, injuries, or other general medical complications. Differential Diagnosis Opioid use disorder is differentiated from opioid intoxication, opioid withdrawal, and opioid-induced mental disorders

Other substance intoxication. Other withdrawal disorders. Independent mental disorders. (e.g., opioid-induced depressive disorder) in that opioid use disorder describes a problematic pattern of opioid use that involves impaired control over opioid use, social impairment attributable to opioid use, risky opioid use (e.g., continued opioid use despite medical complications), and pharmacological symptoms (the development of tolerance or withdrawal), whereas opioid intoxication, opioid withdrawal, and opioid-induced mental disorders describe psychiatric syndromes that occur in the context of heavy use. Opioid intoxication, opioid withdrawal, and opioid-induced mental disorders occur frequently in individuals with opioid use disorder. In such cases, a diagnosis of opioid intoxication, opioid withdrawal, or opioid-induced mental disorder should be given in addition to a diagnosis of opioid use disorder, the presence of which is indicated in the diagnostic code. Alcohol intoxication and sedative, hypnotic, or anxiolytic intoxication can cause a clinical picture that resembles that of 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. 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 sedativetype 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. Some of the effects of opioid use may resemble symptoms (e.g., depressed mood) of an independent mental disorder (e.g., persistent depressive disorder). Opioids are less likely to produce symptoms of mental disturbance than are most other drugs of abuse. Comorbidity Other than overdose, the most common medical comorbidities associated with opioid use disorder are viral (e.g., HIV, hepatitis C virus) and bacterial infections, particularly among injection heroin users. These infections are less common in prescription opioid use disorder. Research with nationally representative samples of the U.S. population has found that opioid use disorder is often associated with other substance use disorders, especially those involving tobacco, alcohol, cannabis, stimulants, and benzodiazepines. Individuals with opioid use disorder are at risk for the development of persistent depressive disorder or major depressive disorder. These symptoms may represent an opioid-induced depressive disorder or an exacerbation of a preexisting independent depressive disorder. Periods of depression are especially common during chronic intoxication or in association with physical or psychosocial stressors related to the opioid use disorder. Insomnia is also common, especially during withdrawal. Opioid use disorder is also associated with bipolar I disorder, posttraumatic stress disorder, and antisocial, borderline,

and schizotypal personality disorders. A history of conduct disorder in childhood or adolescence has also been identified as a significant risk factor for substance-related disorders, especially opioid use disorder. Further, prescription opioid use disorder and heroin use disorder are generally associated with serious mental illness, defined as a mental disorder other than a substance use disorder that results in serious functional impairment substantially limiting or interfering with major life activities. 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-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 F11.120, and if a moderate or severe opioid use disorder is comorbid, the ICD-10-CM code is F11.220. If there is no comorbid opioid use disorder, then the ICD-10-CM code

is F11.920. 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.

Other substance intoxication. 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 of opioid intoxication must not be attributable to another medical condition and are not better explained by another mental disorder (Criterion D). Up to 2009, opioid overdoses were mainly due to prescribed opioids, but starting in 2010, overdoses due to heroin began a sharp rise, and additionally, since 2015, fatal overdoses due to synthetic opioids other than methadone (generally fentanyl) have outnumbered overdoses due to prescribed opioids. Associated Features Opioid intoxication can include decreases in respiratory rate and blood pressure, and mild hypothermia. The duration of opioid intoxication can vary as a function of the pharmacokinetics of the opioid ingested. Opioid intoxication may result in fatal or nonfatal opioid overdose. Opioid overdose is characterized by unconsciousness, respiratory depression, and pinpoint pupils. Fatal opioid overdoses have increased exponentially in the United States since 1999. Development and Course Opioid intoxication can occur in an individual who is opioid naïve, an individual who uses opioids sporadically, and an individual who is physically dependent on opioids. The dose of opioid consumed relative to the likelihood of experiencing opioid intoxication will vary as a function of the status and history of the individual’s opioid exposure (i.e., tolerance). Individuals often report that the qualitative pleasurable experience of opioid intoxication diminishes after repeated use of an opioid. Differential Diagnosis 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, naloxone administration will not reverse all of the sedative effects. While response to administration of

Opioid-induced mental disorders. naloxone can support the diagnosis of opioid intoxication, nonresponse may be due to the coingestion of an opioid with another drug (e.g., a benzodiazepine, alcohol) or to ingestion of a higher dose of and/or higher-potency opioid (e.g., fentanyl). Opioid intoxication is distinguished from opioid-induced mental disorders (e.g., opioid-induced depressive disorder, with onset during intoxication) because the symptoms (e.g., depressed mood) in the latter disorders are in excess of those usually associated with opioid intoxication, predominate in the clinical presentation, and are severe enough to warrant clinical attention. Comorbidity Given the typical overlap of opioid intoxication with opioid use disorder, see “Comorbidity” under Opioid Use Disorder for more details about co-occurring conditions that are likely to be encountered. Opioid Withdrawal Diagnostic Criteria 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:
3. Dysphoric mood.
4. Nausea or vomiting.
5. Muscle aches.
6. Lacrimation or rhinorrhea.
7. Pupillary dilation, piloerection, or sweating.
8. Diarrhea.
9. Yawning.
10. Fever.
11. 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-10-CM code depends on whether or not there is a comorbid

opioid use disorder. If a mild opioid use disorder is comorbid, the ICD-10-CM code is F11.13, and if a moderate or severe opioid use disorder is comorbid, the ICD-10-CM code is F11.23. For opioid withdrawal occurring in the absence of an opioid use disorder (e.g., in a patient taking opioids solely under appropriate medical supervision), the ICD-10-CM code is F11.93. 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) prolonged opioid use (Criterion A1). The opioids used may be illicit or licitly obtained drugs prescribed to treat pain. A withdrawal syndrome can also be precipitated by administration of an opioid antagonist (e.g., naloxone, naltrexone, nalmefene) after a period of opioid use (Criterion A2); it can also occur after administration of an opioid partial agonist (e.g., buprenorphine) to an individual currently using a full opioid agonist. Opioid withdrawal has a characteristic pattern of signs and symptoms. 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). Having symptoms that meet 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. Associated Features 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 illicit use, or following attempts to self-treat symptoms of mental disorders with opioids. Opioid withdrawal is a distinct condition from opioid addiction or

opioid use disorder and does not necessarily require the drug-seeking behaviors associated with opioid use disorder to be diagnosed. Thus, opioid withdrawal may occur in individuals without opioid use disorder and should not be confused with it. Males with opioid withdrawal may experience piloerection, sweating, and spontaneous ejaculations while awake. Prevalence

Other withdrawal disorders. Other substance intoxication. Opioid-induced mental disorders. Among individuals from various U.S. clinical settings, opioid withdrawal occurred in 60% of individuals who had used heroin at least once in the prior 12 months. Individuals regularly using opioids (e.g., prescription opioids for pain, illicit opioids) for a period of time are at risk for developing physical dependence, including withdrawal, on cessation or marked reduction in use. Development and Course 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 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. More chronic symptoms (e.g., anxiety, dysphoria, anhedonia, craving, insomnia) can last for weeks to months. The severity of opioid withdrawal also varies depending on the duration of opioid use. Opioid withdrawal symptoms among individuals receiving long-term prescription opioid treatment for pain can be minimized by tapering the drug slowly. Among those with an opioid use disorder, opioid withdrawal and attempts to relieve withdrawal are typical. The course of withdrawal can be part of an escalating pattern in which an opioid is used to reduce withdrawal symptoms, in turn leading to recurrent episodes of withdrawal at a later time. Differential Diagnosis 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 sedativetype 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, and lacrimation, are not present. Opioid withdrawal is distinguished from opioid-induced mental disorders (e.g., opioid-induced depressive disorder, with onset during withdrawal) because the symptoms (e.g., depressed mood) in these latter disorders are in excess of those usually associated with opioid withdrawal, predominate in the clinical presentation, and are severe enough to warrant clinical attention. Comorbidity Given the typical overlap of opioid withdrawal with opioid use disorder, see “Comorbidity” under Opioid Use Disorder for more details about co-occurring conditions that are likely to be encountered.

Opioid-Induced Mental Disorders The following opioid-induced mental 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, opioid withdrawal delirium, and delirium induced by opioids taken as prescribed, see the criteria and discussion of delirium in the chapter “Neurocognitive Disorders.” These opioid-induced mental 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 F11.99 This category applies to presentations in which symptoms characteristic of an opioidrelated 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 Sedative-, Hypnotic-, or Anxiolytic-Induced Mental 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).

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. Code based on current severity/remission: 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/remission: F13.10 Mild: Presence of 2–3 symptoms. F13.11 Mild, In early remission F13.11 Mild, In sustained remission F13.20 Moderate: Presence of 4–5 symptoms. F13.21 Moderate, In early remission

F13.21 Moderate, In sustained remission F13.20 Severe: Presence of 6 or more symptoms. F13.21 Severe, In early remission F13.21 Severe, In sustained remission 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, propofol). This class of substances includes most prescription sleeping medications and most 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 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 during periods of active use or during periods of abstinence, is a typical feature of sedative, hypnotic, or anxiolytic use disorder. Misuse of substances from this class may occur 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; the continued use of the substances despite arguments with a spouse about consequences of intoxication or despite physical fights (Criterion A6) may also occur. 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 machinery when impaired by such use (Criterion A8) are also seen in sedative, hypnotic, or anxiolytic use disorder. Very significant levels of tolerance and withdrawal can develop to sedative, hypnotic, or

anxiolytic substances. 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 withdrawal. 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 count toward the diagnosis of a substance use disorder. However, it is necessary to determine whether the drugs were inappropriately 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). 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 Research with nationally representative samples of the U.S. population has found that 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 sedative, hypnotic, or anxiolytic, 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 suicide. Prevalence The 12-month prevalence of DSM-IV sedative, hypnotic, or anxiolytic use disorder in the United States is estimated to be 0.3% among adolescents ages 12–17 years and adults age 18 years and older, and this prevalence has remained stable nationally despite increases in rates of prescription of these medications. Rates of DSM-IV sedative, hypnotic, or anxiolytic use disorder in the United States have not been shown to vary consistently by gender,

but data from other countries have generally found higher rates among girls and women than boys and men. The 12-month prevalence of DSM-IV sedative, hypnotic, or anxiolytic use disorder in the United States decreases as a function of age and is greatest among individuals ages 18–29 years (0.5%) and lowest among individuals 65 years and older (0.04%). Twelve-month prevalence of sedative, hypnotic, or anxiolytic use, misuse (e.g., use without a prescription), or disorder varies across U.S. ethnoracial groups. For instance, 12-month prevalence estimates for sedative, hypnotic, or anxiolytic misuse across ethnoracial groups range from 0.6% to 2.5% for adolescents ages 12–17 years and 0.7% to 10.1% for adults.

Temperamental. Environmental. 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 can be expected, as well as increasingly severe episodes of cognitive dysfunction and physiological withdrawal. 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 original anxiety or insomnia symptoms, 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. Although the risk for misuse and use disorder decreases with age after about age 30, side effects associated with psychoactive substances may increase 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 are more likely to develop intoxication and impaired physiological functioning at lower doses. Because sedatives, hypnotics, and anxiolytics are often used in combination with other psychoactive substances, it can be difficult to ascertain whether the functional consequences are attributable to a single substance (e.g., sedative) or to the use of multiple substances. 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 major neurocognitive disorder. Risk and Prognostic Factors Impulsivity and novelty seeking are individual temperaments that relate to the propensity to develop a substance use disorder but may themselves be genetically determined. Personality disorders can also increase the risk of sedative, hypnotic, or anxiolytic misuse or use disorder. Because sedatives, hypnotics, or anxiolytics are all medications, a key risk factor

Genetic and physiological. Course modifiers. relates to availability of the substances, both through an individual's own prescriptions and from prescriptions dispensed to family and friends. In the United States, the historical patterns of sedative, hypnotic, or anxiolytic misuse relate to broad prescribing patterns. For instance, a marked decrease in prescription of barbiturates was associated with an increase in benzodiazepine prescriptions. 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. As with other substance use disorders, the risk for sedative, hypnotic, or anxiolytic use disorder has been found in U.S.-based twin registry studies to 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. In nationally representative U.S. studies, early onset of use is associated with greater likelihood for developing a sedative, hypnotic, or anxiolytic use disorder. Culture-Related Diagnostic Issues Prescription patterns (and availability) of this class of substances vary across countries and populations, which may lead to variations in prevalence of sedative, hypnotic, or anxiolytic use disorder. In the United States, use of benzodiazepines has been more frequently reported by nonLatinx Whites than Latinx or African Americans. However, risk of the disorder may vary within populations exposed to these substances. For example, the 12-month prevalence of DSM-IV benzodiazepine use disorder among U.S. individuals who used benzodiazepines was higher among African Americans (3.0%) and non-Latinx "others" (2.6%) than among non-Latinx Whites (1.3%). Sex- and Gender-Related Diagnostic Issues Although estimates from individual studies vary, there appear to be no gender differences in the prevalence of sedative, hypnotic, or anxiolytic use disorder. 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 test results are likely to remain positive for up to approximately 1 week after the use of long-acting substances, such as diazepam or flurazepam. Association With Suicidal Thoughts or Behavior U.S. epidemiological studies show that hypnotics are associated with suicide, but it is unclear if this association is attributable to underlying psychiatric conditions such as depression and insomnia, which are themselves risk factors for suicide.

Sedative, hypnotic, or anxiolytic intoxication; sedative, hypnotic, or anxiolytic withdrawal; and sedative-, hypnotic-, or anxiolytic-induced mental disorders. 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, and interference with work or school performance are common outcomes. The disinhibiting effects of these agents, like alcohol, may potentially contribute to overly aggressive behavior and arguments or fights, with subsequent interpersonal and legal problems. 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). Acute intoxication can result in accidental injuries and automobile accidents. There may be consequences of trauma (e.g., internal bleeding, a subdural hematoma) from accidents that occur while intoxicated. For elderly individuals, even short-term use of these sedating medications at prescribed doses may be associated with an increased risk for cognitive problems and falls. The

association of sedative, hypnotic, or anxiolytic medications with increased risk of major neurocognitive disorder remains unclear. At high doses, sedative, hypnotic, or anxiolytic substances can be lethal, particularly when mixed with other central nervous system depressants, such as opioids or alcohol, although the lethal dosage varies considerably among the specific substances. Intravenous use of these substances can result in medical complications related to the use of contaminated needles (e.g., hepatitis, HIV). Accidental or deliberate overdoses, similar to those observed for alcohol use disorder or repeated alcohol intoxication, can occur. Overdoses may be associated with a deterioration in vital signs that signals an impending medical emergency (e.g., respiratory arrest from barbiturates). In contrast to their wide margin of safety when used alone, benzodiazepines taken in combination with opioids and alcohol can be particularly dangerous, and accidental overdoses are reported commonly in U.S. data. Accidental overdoses have also been reported in individuals who deliberately misuse barbiturates and other nonbenzodiazepine sedatives (e.g., methaqualone), but because these agents are much less available than the benzodiazepines, the frequency of overdosing is low in most settings. Differential Diagnosis Sedative, hypnotic, or anxiolytic use disorder is differentiated from sedative, hypnotic, or anxiolytic intoxication; sedative, hypnotic, or anxiolytic withdrawal; and sedative-, hypnotic-, or anxiolytic-induced mental disorders (e.g., sedative-, hypnotic-, or anxiolytic-induced depressive disorder) in that sedative, hypnotic, or anxiolytic use disorder describes a problematic pattern of sedative, hypnotic, or anxiolytic use that involves impaired control over such use; social impairment attributable to this use; risky sedative, hypnotic, or anxiolytic use (e.g., driving while intoxicated); and pharmacological symptoms (the development of tolerance or withdrawal); whereas sedative, hypnotic, or anxiolytic intoxication; sedative, hypnotic, or anxiolytic

Other medical conditions. Alcohol use disorder. Clinically appropriate use of sedative, hypnotic, or anxiolytic medications. withdrawal; and sedative-, hypnotic-, or anxiolytic-induced mental disorders describe psychiatric syndromes that occur in the context of heavy use. Sedative, hypnotic, or anxiolytic intoxication; sedative, hypnotic, or anxiolytic withdrawal; and sedative-, hypnotic-, or anxiolytic-induced mental disorders occur frequently in individuals with sedative, hypnotic, or anxiolytic use disorder. In such cases, a diagnosis of sedative, hypnotic, or anxiolytic intoxication; sedative, hypnotic, or anxiolytic withdrawal; or a sedative-, hypnotic-, or anxiolytic-induced mental disorder should be given in addition to a diagnosis of sedative, hypnotic, and anxiolytic use disorder, the presence of which is indicated in the diagnostic code. 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). Sedative, hypnotic, or anxiolytic use disorder must be differentiated from alcohol use disorder. The differential diagnosis is determined mostly through clinical history, although liver damage and other potential signs of chronic alcohol toxicity (e.g., cardiomyopathy) can also be more suggestive of alcohol use disorder than of sedative, hypnotic, or anxiolytic use disorder. 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 overlap between sedative, hypnotic, or anxiolytic

use disorder and antisocial personality disorder; depressive, bipolar, and anxiety disorders; and other substance use disorders, such as alcohol use disorder and illicit drug use disorders. Antisocial behavior and antisocial personality disorder are especially associated with sedative, hypnotic, or anxiolytic use disorder when the substances are obtained illegally. Comorbidity with other substance use disorders and other psychiatric disorders increases the risk of transition from sedative, hypnotic, or anxiolytic use to use disorder and decreases the probability of remission. Sedative, Hypnotic, or Anxiolytic Intoxication Diagnostic Criteria A. Recent use of a sedative, hypnotic, or anxiolytic. B. Clinically significant maladaptive behavioral or psychological changes (e.g.,

inappropriate sexual or aggressive behavior, mood lability, impaired judgment) that developed during, or shortly after, sedative, hypnotic, or anxiolytic use. C. One (or more) of the following signs or symptoms developing during, or shortly after, sedative, hypnotic, or anxiolytic use:

1. Slurred speech.
2. Incoordination.
3. Unsteady gait.
4. Nystagmus.
5. Impairment in cognition (e.g., attention, 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-10-CM code depends on whether there is a comorbid sedative, hypnotic, or anxiolytic use disorder. If a mild sedative, hypnotic, or anxiolytic use disorder is comorbid, the ICD-10-CM code is F13.120, and if a moderate or severe sedative, hypnotic, or anxiolytic use disorder is comorbid, the ICD-10-CM code is F13.220. If there is no comorbid sedative, hypnotic, or anxiolytic use disorder, then the ICD-10-CM code is F13.920. Note: For information on Development and Course; Risk and Prognostic Factors; Culture-Related Diagnostic Issues; Diagnostic Markers; Functional Consequences of Sedative, Hypnotic, or Anxiolytic Intoxication; and Comorbidity, see the corresponding sections in Sedative, Hypnotic, or Anxiolytic Use Disorder. Diagnostic Features The essential feature of sedative, hypnotic, or anxiolytic intoxication is the presence of clinically significant maladaptive 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, use of a sedative, hypnotic, or anxiolytic (Criteria A and B). As with other brain depressants, such as alcohol, these behaviors may be accompanied by slurred speech, incoordination (at levels that can interfere with driving abilities and with performing usual activities to the point of causing falls or automobile accidents), an unsteady gait, nystagmus, impairment in cognition (e.g., attentional or memory problems), and stupor or coma (Criterion C). Memory impairment is a prominent feature of sedative, hypnotic, or anxiolytic intoxication and is most often characterized by an anterograde amnesia that resembles “alcoholic blackouts,” which can be disturbing to the individual. The symptoms must not be attributable to another medical condition and are not better explained by another mental disorder (Criterion D). Intoxication may occur in individuals who are receiving these substances by prescription, are borrowing the medication from friends or relatives, or are deliberately taking

Alcohol use disorder. Alcohol intoxication. Sedative-, hypnotic-, or anxiolytic-induced mental disorders. Neurocognitive disorders. the substance to achieve intoxication. Because sedatives, hypnotics, and anxiolytics are often used in combination with other psychoactive substances, it can be difficult to ascertain whether the functional consequences are attributable to a sedative, hypnotic, or anxiolytic or to the use of multiple substances. Associated Features Associated features include taking more medication than prescribed, taking multiple different medications, or mixing sedative, hypnotic, or anxiolytic agents with alcohol, which can markedly increase the effects of these agents. Prevalence The prevalence of sedative, hypnotic, or anxiolytic intoxication in the general population is unknown. However, it is probable that most nonmedical users of sedatives, hypnotics, or anxiolytics would at some time have signs or symptoms that meet criteria for sedative, hypnotic, or anxiolytic intoxication; if so, then the prevalence of nonmedical sedative, hypnotic, or anxiolytic use in the general population may be similar to the prevalence of sedative, hypnotic, or anxiolytic intoxication. For example, in 2018, tranquilizers or sedative were used nonmedically in the United States by 2.4% of individuals age 12 or older and 4.9% of those ages 18–25. Differential Diagnosis Because the clinical presentations may be identical, distinguishing sedative, hypnotic, or anxiolytic intoxication from alcohol use disorder requires evidence for recent ingestion of sedative, hypnotic, or anxiolytic medications by self-report, informant report, or toxicological testing. Many individuals who misuse sedatives, hypnotics, or anxiolytics may also misuse alcohol and other substances, and so multiple intoxication diagnoses are possible. Alcohol intoxication may be distinguished from sedative, hypnotic, or anxiolytic intoxication by the smell of alcohol on the breath. Otherwise, the features of the two disorders may be similar. Sedative, hypnotic, or anxiolytic intoxication is distinguished from sedative-, hypnotic-, or anxiolytic-induced mental disorders (e.g., sedative-, hypnotic-, or anxiolytic-induced anxiety disorder, with onset during withdrawal) because the symptoms (e.g., anxiety) in the latter disorders are in excess of those usually associated with sedative, hypnotic, or anxiolytic intoxication; predominate in the clinical presentation; and are severe enough to warrant clinical attention. In situations of cognitive impairment, traumatic brain injury, and delirium from other causes, sedatives, hypnotics, or anxiolytics may be intoxicating at quite low dosages. The differential diagnosis in these complex settings is based on the predominant syndrome. An additional diagnosis of sedative, hypnotic, or anxiolytic intoxication may be appropriate even if the substance has been ingested at a low dosage in the setting of these other

(or similar) co-occurring conditions. Comorbidity Given the typical overlap of sedative, hypnotic, or anxiolytic intoxication with sedative, hypnotic, or anxiolytic use disorder, see “Comorbidity” under Sedative, Hypnotic, or Anxiolytic Use Disorder for more details about co-occurring conditions that are likely to be encountered. Sedative, Hypnotic, or Anxiolytic Withdrawal Diagnostic Criteria A. Cessation of (or reduction in) sedative, hypnotic, or anxiolytic use that has been prolonged. B. Two (or more) of the following, developing within several hours to a few days after the cessation of (or reduction in) sedative, hypnotic, or anxiolytic use described in Criterion A:

1. Autonomic hyperactivity (e.g., sweating or pulse rate greater than 100 bpm).
2. Hand tremor.
3. Insomnia.
4. Nausea or vomiting.
5. Transient visual, tactile, or auditory hallucinations or illusions.
6. Psychomotor agitation.

7. Anxiety.
8. Grand mal 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 may be noted when hallucinations with intact reality testing or auditory, visual, or tactile illusions occur in the absence of a delirium. Coding note: The ICD-10-CM code depends on whether or not there is a comorbid sedative, hypnotic, or anxiolytic use disorder and whether or not there are perceptual disturbances. For sedative, hypnotic, or anxiolytic withdrawal, without perceptual

disturbances: If a mild sedative, hypnotic, or anxiolytic use disorder is comorbid, the ICD-10-CM code is F13.130, and if a moderate or severe sedative, hypnotic, or anxiolytic use disorder is comorbid, the ICD-10-CM code is F13.230. If there is no comorbid sedative, hypnotic, or anxiolytic use disorder (e.g., in a patient taking sedatives, hypnotics, or anxiolytics solely under appropriate medical supervision), then the ICD-10-CM code is F13.930. For sedative, hypnotic, or anxiolytic withdrawal, with perceptual disturbances: If a mild sedative, hypnotic, or anxiolytic use disorder is comorbid, the ICD-10-CM code is F13.132, and if a moderate or severe sedative, hypnotic, or anxiolytic use disorder is comorbid, the ICD-10-CM code is F13.232. If there is no comorbid sedative, hypnotic, or anxiolytic use disorder (e.g., in a patient taking sedatives, hypnotics, or anxiolytics solely under appropriate medical supervision), then the ICD-10-CM code is F13.932. Note: For information on Development and Course; Risk and Prognostic Factors; Culture-Related Diagnostic Issues; Functional Consequences of Sedative, Hypnotic, or Anxiolytic Withdrawal; and Comorbidity, see the corresponding sections in Sedative, Hypnotic, or Anxiolytic Use Disorder. Diagnostic Features The essential feature of sedative, hypnotic, or anxiolytic withdrawal is the presence of a characteristic syndrome that develops after a marked decrease in or cessation of intake after several weeks or more of regular use (Criteria A and B). This withdrawal syndrome is characterized by two or more symptoms (similar to alcohol withdrawal) that include autonomic hyperactivity (e.g., increases in heart rate, respiratory rate, blood pressure, or body temperature, along with sweating); a tremor of the hands; insomnia; nausea, sometimes accompanied by vomiting; anxiety; and psychomotor agitation. A grand mal seizure may occur in perhaps as many as 20%–30% of individuals undergoing untreated withdrawal from these substances. In severe withdrawal, visual, tactile, or auditory hallucinations or illusions can occur but are usually in the context of a withdrawal delirium. If the individual’s reality testing is intact (i.e., knows the substance is causing the hallucinations) and the illusions occur in a clear sensorium, the specifier “with perceptual disturbances” can be noted. When hallucinations occur in the absence of intact reality testing, a diagnosis of substance/medication-induced psychotic disorder should be considered. The 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., alcohol withdrawal, generalized anxiety disorder) (Criterion D). Relief of withdrawal symptoms with administration of any sedative-hypnotic agent would support a diagnosis of sedative, hypnotic, or anxiolytic withdrawal.

Other medical conditions. Associated Features The timing and severity of the withdrawal syndrome will differ depending on the specific substance and its pharmacokinetics and pharmacodynamics. For example, withdrawal from shorter-acting substances that are rapidly absorbed and that have no active metabolites (e.g., triazolam) can begin within hours after the substance is stopped; withdrawal from substances with long-acting metabolites (e.g., diazepam) may not begin for 1–2 days or longer. The withdrawal syndrome produced by substances in this class may be characterized by the development of a delirium that can be life-threatening. There may be evidence of tolerance and withdrawal in the absence of a diagnosis of a benzodiazepine use disorder in an individual who has abruptly discontinued benzodiazepines that were taken for long periods of time at prescribed and therapeutic doses. The time course of the withdrawal syndrome is generally predicted by the half-life of the substance. Medications whose actions typically last about 10 hours or less (e.g., lorazepam, oxazepam, temazepam) produce withdrawal symptoms within 6–8 hours of decreasing blood levels that peak in intensity on the second day and improve markedly by the fourth or fifth day. For substances with longer half-lives (e.g., diazepam), symptoms may not develop for more than 1 week, peak in intensity during the second week, and decrease markedly during the third or fourth week. There may be additional longer-term symptoms at a much lower level of intensity that persist for several months. The longer the substance has been taken and the higher the dosages used, the more likely there will be severe withdrawal. However, withdrawal has been reported with as little as 15 mg of diazepam (or its equivalent in other benzodiazepines) when taken daily for several months. Doses of approximately 40 mg of diazepam (or its equivalent) daily are more likely to produce clinically relevant withdrawal symptoms, and even higher doses (e.g., 100 mg of diazepam) are more likely to be followed by withdrawal seizures or delirium. Sedative, hypnotic, or anxiolytic withdrawal delirium is characterized by disturbances in consciousness and cognition, with visual, tactile, or auditory hallucinations. When present, sedative, hypnotic, or anxiolytic withdrawal delirium should be diagnosed instead of withdrawal. Prevalence The prevalence of sedative, hypnotic, or anxiolytic withdrawal is unknown. Diagnostic Markers Seizures and autonomic instability in the setting of a history of prolonged exposure to sedative, hypnotic, or anxiolytic medications suggest a high likelihood of sedative, hypnotic, or anxiolytic withdrawal. Differential Diagnosis The symptoms of sedative, hypnotic, or anxiolytic withdrawal may be mimicked by other medical conditions (e.g., hypoglycemia, diabetic ketoacidosis). If seizures are a feature of the sedative, hypnotic, or anxiolytic withdrawal, the

Essential tremor. Alcohol withdrawal. Sedative-, hypnotic-, or anxiolytic-induced mental disorders. Anxiety disorders. differential diagnosis includes the various causes of seizures (e.g., infections, head injury, poisonings). Essential tremor, a neurological condition that frequently runs in families, may erroneously suggest the tremulousness associated with sedative, hypnotic, or anxiolytic withdrawal. Alcohol withdrawal produces a syndrome very similar to that of sedative, hypnotic, or anxiolytic withdrawal. The differential diagnosis is determined mostly through clinical history, although liver damage and other potential signs of chronic alcohol toxicity (e.g., cardiomyopathy) can also be more suggestive of alcohol withdrawal than of sedative, hypnotic, or anxiolytic withdrawal. Sedative, hypnotic, or anxiolytic withdrawal is distinguished from sedative-, hypnotic-, or anxiolytic-induced mental disorders (e.g., sedative-, hypnotic-, or anxiolytic-induced anxiety disorder, with onset during withdrawal) because the symptoms (e.g., anxiety) in the latter disorders are in excess of those usually associated with sedative, hypnotic, or anxiolytic withdrawal; predominate in the clinical presentation; and are severe enough to warrant clinical attention.

Recurrence or worsening of an underlying anxiety disorder produces a syndrome similar to sedative, hypnotic, or anxiolytic withdrawal, although the most extreme manifestations of withdrawal, such as delirium tremens or true seizures, are not symptoms of any anxiety disorder. Withdrawal would be suspected with an abrupt reduction in the dosage of a sedative, hypnotic, or anxiolytic medication. When a taper is under way, distinguishing the withdrawal syndrome from the underlying anxiety disorder can be difficult. As with alcohol, lingering withdrawal symptoms (e.g., anxiety, moodiness, trouble sleeping) can be mistaken for independent anxiety or depressive disorders (e.g., generalized anxiety disorder). Comorbidity Given the typical overlap of sedative, hypnotic, or anxiolytic withdrawal with sedative, hypnotic, or anxiolytic use disorder, see "Comorbidity" under Sedative, Hypnotic, or Anxiolytic Use Disorder for more details about co-occurring conditions that are likely to be encountered. Sedative-, Hypnotic-, or Anxiolytic-Induced Mental Disorders The following sedative-, hypnotic-, or anxiolytic-induced mental 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): sedative-, hypnotic-, or anxiolytic-induced psychotic disorder ("Schizophrenia Spectrum and Other Psychotic Disorders"); sedative-, hypnotic-, or anxiolytic-induced bipolar and related disorder ("Bipolar and Related Disorders"); sedative-, hypnotic-, or anxiolytic-induced depressive disorder ("Depressive Disorders"); sedative-, hypnotic-, or anxiolytic-induced anxiety disorder ("Anxiety Disorders"); sedative-, hypnotic-, or anxiolytic-induced sleep disorder ("Sleep-Wake Disorders"); sedative-, hypnotic-, or anxiolytic-induced sexual dysfunction ("Sexual

Dysfunctions"); and sedative-, hypnotic-, or anxiolytic-induced major or mild neurocognitive disorder ("Neurocognitive Disorders"). For sedative, hypnotic, or anxiolytic intoxication delirium; sedative, hypnotic, or anxiolytic withdrawal delirium; and delirium induced by sedatives, hypnotics, or anxiolytics taken as prescribed, see the criteria and discussion of delirium in the chapter "Neurocognitive Disorders." These sedative-, hypnotic-, or anxiolytic-induced mental disorders are diagnosed instead of sedative, hypnotic, or anxiolytic intoxication or sedative, hypnotic, or anxiolytic withdrawal only when the symptoms are sufficiently severe to warrant independent clinical attention. Unspecified Sedative-, Hypnotic-, or Anxiolytic-Related Disorder F13.99 This category applies to presentations in which symptoms characteristic of a sedative-, hypnotic-, or anxiolytic-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 sedative-, hypnotic-, or anxiolytic-related disorder or any of the disorders in the substance-related and addictive disorders diagnostic class. Stimulant-Related Disorders Stimulant Use Disorder Stimulant Intoxication Stimulant Withdrawal Stimulant-Induced Mental Disorders Unspecified Stimulant-Related Disorder Stimulant Use Disorder Diagnostic Criteria A. A pattern of amphetamine-type substance, cocaine, or other stimulant 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 stimulant 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 stimulant use.
3. A great deal of time is spent in activities necessary to obtain the stimulant, use the stimulant, or recover from its effects.
4. Craving, or a strong desire or urge to use the stimulant.

5. Recurrent stimulant use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued stimulant use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the stimulant.
7. Important social, occupational, or recreational activities are given up or reduced because of stimulant use.
8. Recurrent stimulant use in situations in which it is physically hazardous.
9. Stimulant 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 stimulant.
10. Tolerance, as defined by either of the following: a. A need for markedly increased amounts of the stimulant to achieve intoxication or desired effect. b. A markedly diminished effect with continued use of the same amount of the stimulant. Note: This criterion is not considered to be met for those taking stimulant medications solely under appropriate medical supervision, such as medications for attention-deficit/hyperactivity disorder or narcolepsy.
11. Withdrawal, as manifested by either of the following: a. The characteristic withdrawal syndrome for the stimulant (refer to Criteria A and B of the criteria set for stimulant withdrawal). b. The stimulant (or a closely related substance) is taken to relieve or avoid withdrawal symptoms. Note: This criterion is not considered to be met for those taking stimulant medications solely under appropriate medical supervision, such as medications for attention-deficit/hyperactivity disorder or narcolepsy. Specify if: In early remission: After full criteria for stimulant use disorder were previously met, none of the criteria for stimulant 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 stimulant,” may be met). In sustained remission: After full criteria for stimulant use disorder were previously met, none of the criteria for stimulant 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 stimulant,” may be met). Specify if: In a controlled environment: This additional specifier is used if the individual is in an environment where access to stimulants is restricted. Code based on current severity/remission: If an amphetamine-type substance intoxication, amphetamine-type substance withdrawal, or amphetamine-type substance-induced mental disorder is also present, do not use the codes below for amphetamine-type substance use disorder. Instead, the comorbid amphetaminetype substance use disorder is indicated in the 4th character of the amphetaminetype substance-induced disorder code (see the coding note for amphetamine-type substance intoxication, amphetamine-type substance withdrawal, or a specific amphetamine-type substance-induced mental disorder). For example, if there is comorbid amphetamine-induced depressive disorder and amphetamine use disorder, only the amphetamine-induced depressive disorder code is given, with the 4th character indicating whether the comorbid amphetamine use disorder is mild, moderate, or severe: F15.14 for mild amphetamine use disorder with amphetamineinduced depressive disorder or F15.24 for a moderate or severe amphetamine use disorder with amphetamine-induced depressive disorder. (The instructions for amphetamine-type substance also apply to other or unspecified stimulant intoxication, other or unspecified stimulant withdrawal, and other or unspecified stimulant-induced mental disorder.) Similarly, if there is comorbid cocaine-induced depressive disorder and cocaine

use disorder, only the cocaine-induced depressive disorder code is given, with the 4th character indicating whether the comorbid cocaine use disorder is mild, moderate, or severe: F14.14 for a mild cocaine use disorder with cocaine-induced depressive disorder or F14.24 for a moderate or severe cocaine use disorder with cocaineinduced depressive disorder. Specify current severity/remission: Mild: Presence of 2–3 symptoms. F15.10 Amphetamine-type substance F14.10 Cocaine F15.10 Other or unspecified stimulant Mild, In early remission F15.11 Amphetamine-type substance F14.11 Cocaine

F15.11 Other or unspecified stimulant Mild, In sustained remission F15.11 Amphetamine-type substance F14.11 Cocaine F15.11 Other or unspecified stimulant Moderate: Presence of 4–5 symptoms. F15.20 Amphetamine-type substance F14.20 Cocaine F15.20 Other or unspecified stimulant Moderate, In early remission F15.21 Amphetamine-type substance F14.21 Cocaine F15.21 Other or unspecified stimulant Moderate, In sustained remission F15.21 Amphetamine-type substance F14.21 Cocaine F15.21 Other or unspecified stimulant Severe: Presence of 6 or more symptoms. F15.20 Amphetamine-type substance F14.20 Cocaine F15.20 Other or unspecified stimulant Severe, In early remission F15.21 Amphetamine-type substance F14.21 Cocaine F15.21 Other or unspecified stimulant Severe, In sustained remission F15.21 Amphetamine-type substance F14.21 Cocaine F15.21 Other or unspecified stimulant 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 Stimulants are a type of psychoactive substance that increases activity in the brain and can temporarily elevate alertness, mood, and awareness. Stimulants covered in this chapter include amphetamine and prescription stimulants with similar effects (e.g., methylphenidate) and cocaine. Substance-related disorders involving certain other substances with stimulant properties are classified in other sections of this chapter. These include caffeine (in caffeine-related disorders), nicotine (in tobacco-related disorders), and MDMA (3,4methylenedioxymethamphetamine; in other hallucinogen-related disorders), which has both stimulant and hallucinogenic effects. Given that the effects of amphetamine-type substances are similar to those of cocaine, amphetamine-related disorders and cocaine-related disorders are grouped under the single rubric “stimulant-related disorders.” Amphetamine-type substances (and other or unspecified stimulants) and cocaine have different ICD-10-CM codes (e.g., F15.10 mild amphetamine-type substance use disorder, F14.10 mild cocaine use disorder). The particular stimulant used by the individual is recorded in the diagnosis (e.g., “methamphetamine withdrawal,” “methylphenidate use disorder,” “cocaine intoxication”). The amphetamine-type substances include stimulants with a substituted phenylethylamine structure, such as amphetamine, dextroamphetamine, and methamphetamine. Also included are substances that are structurally different but have similar effects, such as methylphenidate, modafinil, and armodafinil. These amphetamine-type substances are usually taken orally or intravenously, although methamphetamine is also taken by the nasal route. In addition to the synthetic amphetamine-type compounds, there are naturally occurring, plant-derived stimulants such as khât, as well as synthetic chemical khât analogs, called cathinones. Amphetamines and other stimulants may be obtained by prescription for the treatment of obesity, attention-deficit/hyperactivity disorder, and narcolepsy. Consequently, prescribed stimulants may be diverted into the illegal market. Cocaine,

a naturally occurring substance produced by the coca plant, is consumed in several preparations (e.g., coca leaves, coca paste, cocaine hydrochloride, and cocaine alkaloids such as freebase and crack) that differ in potency because of varying levels of purity and speed of onset. However, in all of the forms, cocaine is the active ingredient. Cocaine hydrochloride powder is usually “snorted” through the nostrils or dissolved in water and injected intravenously. Crack and other cocaine alkaloids are easily vaporized and inhaled, and thus their effects have an extremely rapid onset. Individuals exposed to amphetamine-type substances or cocaine can develop stimulant use disorder as rapidly as 1 week, although the onset is not always this rapid. Regardless of the route of administration, tolerance occurs with repeated use. Withdrawal symptoms, particularly hypersomnia, increased appetite, and dysphoria, can occur and can enhance craving. Most individuals with stimulant use disorder have experienced tolerance or withdrawal. Use patterns and course are similar for disorders involving amphetamine-type substances and cocaine, as both are potent central nervous system stimulants with similar psychoactive and sympathomimetic effects. Amphetamine-type substances are longer acting than cocaine and thus are used fewer times per day. Usage may be chronic or episodic, with binges punctuated by brief non-use periods. Aggressive or violent behavior is common when high doses are smoked, ingested, or administered intravenously. Intense temporary anxiety resembling panic disorder or

Stimulant use disorder: amphetamine-type substances. generalized anxiety disorder, as well as paranoid ideation and psychotic episodes that resemble schizophrenia, is seen with high-dose use. Withdrawal states are associated with temporary but intense depressive symptoms that can resemble a major depressive episode; the depressive symptoms usually resolve within 1 week. Tolerance to amphetamine-type substances develops and leads to escalation of the dose. Conversely, some users of amphetamine-type substances develop sensitization, characterized by enhanced effects. Associated Features When injected or smoked, stimulants typically produce an instant feeling of well-being, confidence, and euphoria. Dramatic behavioral changes can rapidly develop with stimulant use disorder. Chaotic behavior, social isolation, aggressive behavior, and sexual dysfunction can result from long-term stimulant use disorder. Individuals with acute intoxication may present with rambling speech, headache, transient ideas of reference, and tinnitus. There may be paranoid ideation, auditory hallucinations in a clear sensorium, and tactile hallucinations, which the individual usually recognizes as drug effects. Threats or acting out of aggressive behavior may occur. Depression, suicidal thoughts, irritability, anhedonia, emotional lability, or disturbances in attention and concentration commonly occur during withdrawal. Mental disturbances associated with cocaine use usually resolve hours to days after cessation of use but can persist for 1 month. Physiological changes during stimulant withdrawal are opposite to those of the intoxication phase, sometimes including bradycardia. Temporary depressive symptoms may meet symptomatic and duration criteria for major depressive episode. Histories consistent with repeated panic attacks, social anxiety disorder–like behavior, and generalized anxiety–like syndromes are common, as are eating disorders. One extreme instance of stimulant toxicity is stimulant-induced psychotic disorder, a disorder that resembles schizophrenia, with delusions and hallucinations. Individuals with stimulant use disorder often develop conditioned responses to drug-related stimuli (e.g., craving on seeing any white powderlike substance). These responses contribute to relapse, are difficult to extinguish, and persist after detoxification. Depressive symptoms with suicidal thoughts or behavior can occur and are generally the most serious problems seen during stimulant withdrawal. Prevalence Estimated 12-month prevalence of amphetamine-type substance use disorder in the United States is 0.4% among individuals 12 years

and older. Twelve-month prevalence is 0.1% among individuals ages 12–17 years, 0.5% among those ages 18–25, and 0.4% among those age 26 and older. Rates are 0.5% for men and 0.2% for women, overall. Rates are approximately 0.4% among Hispanics and non-Hispanic Whites and 0.1% among African Americans and Asian Americans. Prevalence estimates for American Indian/Alaskan Natives and Native Hawaiian/Pacific Islander populations are difficult to determine, given small sample sizes, but there is some evidence for higher rates in American

Stimulant use disorder: cocaine. Temperamental. Indians/Alaskan Natives. Among U.S. adults, 6.6% (annual average) used prescription stimulants overall; 4.5% used without misuse, 1.9% misused without use disorders, and 0.2% had use disorders. While nonHispanic Whites are more likely to use prescription stimulants nonmedically, Hispanics tend to use them more frequently and have higher rates of prescription stimulant use disorder. Estimated 12-month prevalence of cocaine use disorder in the United States is 0.4% among individuals 12 years and older. Rates are 0.1% among individuals ages 12–17 years, 0.7% among those ages 18–25 years, and 0.3% among those age 26 and older. Rates are 0.5% for men and 0.2% for women, overall. Rates are 0.4% among African Americans and non-Hispanic Whites, 0.3% in Hispanics, and < 0.1% among Asian Americans. Development and Course In the United States, stimulant use disorder occurs throughout all levels of society and is more common among individuals ages 18–25 years compared with individuals ages 12–17 or 26 years and older. On average, first regular use among individuals in treatment occurs at approximately age 23 years. For primary methamphetamine treatment admissions, the average age is 34 years, and for primary cocaine treatment admissions, the average age is 44 years for smoked cocaine and 37 years for other routes. Some persons begin stimulant use to control weight or to improve performance in school, work, or athletics. Initial use may include obtaining medications such as methylphenidate or amphetamine salts prescribed to others for the treatment of attention-deficit/hyperactivity disorder. Among primary treatment admissions for amphetamine-type substance use in the United States, 61% reported smoking, 26% reported injecting, and 9% reported snorting, suggesting that stimulant use disorder can develop from multiple modes of administration. Patterns of stimulant administration include episodic or daily (or almost daily) use. Episodic use (e.g., intense use over a weekend or on one or more weekdays) tends to be separated by 2 or more days of nonuse. “Binges” involve continuous high-dose use over hours or days and are often associated with physical dependence. Binges usually terminate only when stimulant supplies are depleted or exhaustion ensues. Chronic daily use may involve high or low doses, often with an increase in dose over time. Stimulant smoking and intravenous use are associated with rapid progression to severe-level stimulant use disorder, often occurring over weeks to months. Intranasal use of cocaine and oral use of amphetamine-type substances result in more gradual progression occurring over months to years. With continued use, there is a diminution of pleasurable effects because of tolerance and an increase in dysphoric effects. Risk and Prognostic Factors Comorbid bipolar disorder, schizophrenia, antisocial personality disorder, and other substance use disorders are risk factors for developing stimulant use disorder and for relapse to cocaine use in treatment samples. Higher stress reactivity has been correlated with frequency of cocaine use in some U.S. treatment samples. Conduct disorder in childhood and antisocial personality disorder are associated with the development of stimulant-related

Environmental. disorders. In the United States, previous use of another substance, being male, having a Cluster B personality disorder, family history of substance use disorder, and being separated, divorced, or widowed all result in increased risk of using cocaine. Men who have sex

with men are also at higher risk for methamphetamine use. Predictors of cocaine use among a cohort of U.S. teenagers include prenatal cocaine exposure, postnatal cocaine use by parents, and exposure to community violence during childhood. Research in industrialized countries suggests that exposure to intimate partner violence or childhood mistreatment often co-occurs with stimulant use, especially in women. In a cohort of U.S. women followed up longitudinally, socioeconomic status, including food insecurity, had a dose-dependent effect on risk of stimulant use. For youth, especially girls, risk factors include living in an unstable home environment, having a psychiatric condition, criminal behavior, and associating with dealers and users. Culture-Related Diagnostic Issues The prevalence of cocaine use in the United States increased between 2001–2002 and 2012– 2013 among non-Latinx Whites, African Americans, and Latinx, but the prevalence of cocaine use disorder increased only among Whites. Despite small variations, cocaine and other stimulant use disorder diagnostic criteria perform equally across gender and ethnoracial groups. In limited data on prevalence estimates, it appears that American Indian/Alaskan Native populations are at higher risk for methamphetamine use disorder, and, to a lesser degree, cocaine use disorder, than are non-Hispanic Whites, while native Hawaiian/Pacific Islanders appear to have similar risks to non-Hispanic Whites. Approximately 64% of individuals admitted to publicly funded substance abuse treatment programs for primary methamphetamine/amphetamine-related disorders are non-Hispanic White, followed by 20% of Hispanic origin, 3% Asian and Pacific Islander, and 6% non-Hispanic Black. Among individuals admitted for primary treatment related to smoked cocaine, 51% were non-Hispanic Black, 35% non-Hispanic White, 8% Hispanic, and 1% Asian/Pacific Islander. For admissions related to other routes of cocaine administration, 47% were non-Hispanic White, 31% were non-Hispanic Black, 17% were of Hispanic origin, and 1% were Asian/Pacific Islander. Rates of disorders in clinical samples should be interpreted with caution because they may be affected by differential access to and utilization of services, pathways to care, criminalization, stigma, and racial bias in diagnosis and referral for treatment. Sex- and Gender-Related Diagnostic Issues In the United States, women with cocaine use disorder more frequently have comorbid psychiatric disorders, such as depression and posttraumatic stress disorder (PTSD), compared with men. Gonadal hormones affect a male’s responses to cocaine. Females with cocaine use disorder and higher levels of progesterone have lower stress-induced and cue-induced cocaine craving and lower cue-induced changes in blood pressure than females with cocaine use disorder and lower levels of progesterone. This may explain why use of cocaine in pregnant females is lower than in nonpregnant females.

Diagnostic Markers Benzoylecgonine, a metabolite of cocaine, typically remains in the urine for 1–3 days after a single dose and may be present for 7–12 days in individuals using repeated high doses. Mildly elevated liver function tests can be present in cocaine injectors or users with concomitant alcohol use. There are no neurobiological markers of diagnostic utility. Discontinuation of chronic cocaine use may be associated with electroencephalographic changes, suggesting persistent abnormalities; alterations in secretion patterns of prolactin; and downregulation of dopamine receptors. Short-half-life amphetamine-type substances (e.g., methamphetamine) can be detected for 1– 3 days, and possibly up to 4 days depending on dosage and metabolism. Hair samples can be used to detect presence of amphetamine-type substances for up to 90 days. Other laboratory findings, as well as physical findings and other medical conditions (e.g., weight loss, malnutrition; poor hygiene), are similar for both cocaine and amphetamine-type substance use disorder. Association With Suicidal Thoughts or Behavior Few data on the association of stimulant use disorders and suicide are available because most studies examining suicidal thoughts and

behavior examine use of stimulants rather than stimulant use disorders. One systematic review found that regular or problem amphetamine use (examining primarily individuals who inject amphetamines and/or individuals admitted to treatment for use of amphetamines) is associated with increased suicide mortality. A general population study of adults in the United States found an association of prescription stimulant use disorder with suicidal thoughts. In a study of individuals admitted to substance use treatment, those with cocaine use disorder were much more likely to report suicidal thoughts than those with other substance use disorders. In a study of both men and women in the U.S. Veterans Administration health care system, cocaine and amphetamine use disorders were each associated with increased rates of suicide deaths. Functional Consequences of Stimulant Use Disorder Various medical conditions may occur depending on the route of administration. Intranasal users often develop sinusitis, irritation, bleeding of the nasal mucosa, and a perforated nasal septum. Individuals who smoke stimulants are at increased risk for respiratory problems (e.g., coughing, bronchitis, and pneumonitis). Injectors have puncture marks and “tracks,” most commonly on their forearms. Risk of HIV and hepatitis C infection increases with frequent intravenous injections and unsafe sexual activity. Other sexually transmitted diseases, hepatitis B, and tuberculosis and other lung infections are also seen. Weight loss and malnutrition are common. Chest pain may be a common symptom during stimulant intoxication. Myocardial infarction, palpitations and arrhythmias, sudden death from respiratory or cardiac arrest, and stroke have been associated with stimulant use among young and otherwise healthy individuals. Pneumothorax can result from performing Valsalva-like maneuvers done to better absorb inhaled

Phencyclidine intoxication. Stimulant intoxication, stimulant withdrawal, and stimulant-induced mental disorders. Independent mental disorders. smoke. Cocaine use is associated with irregularities in placental blood flow, abruptio placentae, premature labor and delivery, and an increased prevalence of infants with very low birth weights. Individuals with stimulant use disorder may become involved in theft, prostitution, or drug dealing in order to acquire drugs or money for drugs. Traumatic injuries due to violent behavior are common among individuals trafficking drugs. Neurocognitive impairment is common among both methamphetamine and cocaine users, including deficits related to attention, impulsivity, verbal learning/memory, working memory, and executive functioning. Transient psychosis and seizure have also been reported with chronic use of either cocaine or methamphetamine, possibly related to patterns of use or the exacerbation of preexisting vulnerabilities. Amphetamine use can cause toxic effects related to elevated body temperature, and there is some evidence that chronic use causes neuroinflammation and neurotoxicity in dopaminergic neurons. Oral health problems include “meth mouth” with gum disease, tooth decay, and mouth sores related to the toxic effects of smoking the drug and to bruxism while intoxicated. Adverse pulmonary effects appear to be less common for amphetamine-type substances because they are smoked fewer times per day, although methamphetamine use is still associated with a risk of pulmonary arterial hypertension. Emergency department visits are common for stimulant-related mental disorder symptoms, injury, skin infections, and dental pathology. In the United States, diagnosis of a stimulant use disorder is associated with a 20% increase in 30-day readmission rates in assessment of followup after hospitalization for “any cause” (a standard measure of overall hospital quality of care). Differential Diagnosis Intoxication with phencyclidine (PCP or “angel dust”) or synthetic “designer drugs” such as mephedrone (known by different names, including “bath salts”) may cause a similar clinical picture and can only be distinguished from stimulant intoxication by the presence of cocaine or amphetamine-type substance metabolites in a urine or plasma sample. Stimulant use disorder is differentiated from

stimulant intoxication, stimulant withdrawal, and stimulantinduced mental disorders (e.g., stimulant-induced depressive disorder) in that stimulant use disorder describes a problematic pattern of stimulant use that involves impaired control over stimulant use, social impairment attributable to stimulant use, risky stimulant use (e.g., continued stimulant use despite medical complications), and pharmacological symptoms (the development of tolerance or withdrawal), whereas stimulant intoxication, stimulant withdrawal, and stimulant-induced mental disorders describe psychiatric syndromes that occur in the context of heavy use. Stimulant intoxication, stimulant withdrawal, and stimulant-induced mental disorders occur frequently in individuals with stimulant use disorder. In such cases, a diagnosis of stimulant intoxication, stimulant withdrawal, or a stimulant-induced mental disorder should be given in addition to a diagnosis of stimulant use disorder, the presence of which is indicated in the diagnostic code. Some of the effects of stimulant use may resemble symptoms of independent mental disorders, such as psychosis (schizophrenia) and low mood (major

depressive disorder). Discerning whether these behaviors occurred before the intake of the drug is important in the differentiation of acute drug effects from a preexisting mental disorder. Comorbidity Stimulant-related disorders often co-occur with other substance use disorders, especially those involving substances with sedative properties, which are often taken to reduce insomnia, nervousness, and other unpleasant side effects. Individuals admitted to treatment for cocaine use are likely to also use heroin, PCP, or alcohol, and individuals admitted for amphetamine-type substance use disorder are likely to use marijuana, heroin, or alcohol. Stimulant use disorder may be associated with posttraumatic stress disorder, antisocial personality disorder, attentiondeficit/hyperactivity disorder, and gambling disorder. Cardiopulmonary problems are often present in individuals seeking treatment for cocaine-related problems, with chest pain being the most common. Medical problems occur in response to adulterants used as “cutting” agents. Cocaine users who ingest cocaine cut with levamisole, an antimicrobial and veterinary medication, may experience agranulocytosis and febrile neutropenia. Stimulant Intoxication Diagnostic Criteria A. Recent use of an amphetamine-type substance, cocaine, or other stimulant. B. Clinically significant problematic behavioral or psychological changes (e.g., euphoria or affective blunting; changes in sociability; hypervigilance; interpersonal sensitivity; anxiety, tension, or anger; stereotyped behaviors; impaired judgment) that developed during, or shortly after, use of a stimulant. C. Two (or more) of the following signs or symptoms, developing during, or shortly after, stimulant use:

1. Tachycardia or bradycardia.
2. Pupillary dilation.
3. Elevated or lowered blood pressure.
4. Perspiration or chills.
5. Nausea or vomiting.
6. Evidence of weight loss.
7. Psychomotor agitation or retardation.
8. Muscular weakness, respiratory depression, chest pain, or cardiac arrhythmias.
9. Confusion, seizures, dyskinesias, dystonias, 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.

641 Specify the particular intoxicant (i.e., amphetamine-type substance, cocaine, or other stimulant). Specify if: With perceptual disturbances: This specifier may be noted when hallucinations with intact reality testing or auditory, visual, or tactile illusions occur in the absence of a delirium. Coding note: The ICD-10-CM code depends on whether the stimulant is an amphetamine-type substance, cocaine, or other stimulant; whether there is a comorbid amphetamine-type substance, cocaine, or other stimulant use disorder; and whether or not there are perceptual disturbances. For amphetamine-type substance, cocaine, or other stimulant intoxication, without perceptual disturbances: If a mild amphetamine-type substance or other stimulant use disorder is comorbid, the ICD-10-CM code is F15.120, and if a moderate or severe amphetamine-type substance or other stimulant use disorder is comorbid, the ICD-10-CM code is F15.220. If there is no comorbid amphetamine-type substance or other stimulant use disorder, then the ICD-10CM code is F15.920. Similarly, if a mild cocaine use disorder is comorbid, the ICD-10-CM code is F14.120, and if a moderate or severe cocaine use disorder is comorbid, the ICD-10-CM code is F14.220. If there is no comorbid cocaine use disorder, then the ICD-10-CM code is F14.920. For amphetamine-type substance, cocaine, or other stimulant intoxication, with perceptual disturbances: If a mild amphetamine-type substance or other stimulant use disorder is comorbid, the ICD-10-CM code is F15.122, and if a moderate or severe amphetamine-type substance or other stimulant use disorder is comorbid, the ICD-10-CM code is F15.222. If there is no comorbid amphetamine-type substance or other stimulant use disorder, then the ICD-10CM code is F15.922. Similarly, if a mild cocaine use disorder is comorbid, the ICD-10-CM code is F14.122, and if a moderate or severe cocaine use disorder is comorbid, the ICD-10-CM code is F14.222. If there is no comorbid cocaine use disorder, then the ICD-10-CM code is F14.922. Diagnostic Features The essential feature of stimulant intoxication, related to amphetamine-type substances and cocaine, is the presence of clinically significant behavioral or psychological changes that develop during, or shortly after, use of stimulants (Criteria A and B). Auditory hallucinations may be prominent, as may paranoid ideation, and these symptoms must be distinguished from an independent psychotic disorder such as schizophrenia. Stimulant intoxication usually begins with a “high” feeling and includes one or more of the following: euphoria with enhanced vigor, gregariousness, hyperactivity, restlessness, hypervigilance, interpersonal sensitivity, talkativeness, anxiety, tension, alertness, grandiosity, stereotyped and repetitive behavior, anger, impaired judgment, and, in the case of chronic intoxication, affective blunting with fatigue or

sadness and social withdrawal. These behavioral and psychological changes are accompanied by two or more of the following signs and symptoms that develop during or shortly after stimulant use: tachycardia or bradycardia; pupillary dilation; elevated or lowered blood pressure; perspiration or chills; nausea or vomiting; evidence of weight loss; psychomotor agitation or retardation; muscular weakness, respiratory depression, chest pain, or cardiac arrhythmias; and confusion, seizures, dyskinesias, dystonias, or coma (Criterion C). Intoxication, either acute or chronic, is often associated with impaired social or occupational functioning. Severe intoxication can lead to convulsions, cardiac arrhythmias, hyperpyrexia, and death. For the diagnosis of stimulant intoxication to be made, the symptoms must not be attributable to another medical condition and are not better explained by another mental disorder (Criterion D). While stimulant intoxication occurs in individuals with stimulant use disorders, intoxication is not a criterion for stimulant use disorder, which is confirmed by the presence of 2 of the 11 diagnostic criteria for use disorder. Associated Features The magnitude and direction of the behavioral and physiological changes depend on many variables, including the dose used and the characteristics of the individual using

the substance or the context (e.g., tolerance, rate of absorption, chronicity of use, context in which taken). Stimulant effects such as euphoria, increased pulse and blood pressure, and psychomotor activity are most commonly seen. Depressant effects such as sadness, bradycardia, decreased blood pressure, and decreased psychomotor activity are less common and generally emerge only with chronic high-dose use. Prevalence Although prevalence of stimulant intoxication is not known, prevalence of stimulant use can be used as a proxy. Many individuals who use stimulants may not have symptoms that fully meet the criteria for stimulant intoxication, which requires “clinically significant problematic behavioral or psychological changes.” Thus, rates of stimulant use can be considered the upper bounds of the likely prevalence of stimulant intoxication. Estimated 12-month prevalence of cocaine use in the United States is 2.2% for individuals age 12 and older (0.5% among individuals ages 12–17-years, 6.2% among individuals ages 18– 25 years, and 1.7% among individuals age 26 and older); 3% of men/boys and 1.4% of women/girls used cocaine in the last 12 months. Twelve-month prevalence of cocaine use is 2.3% among Whites, 2.2% among Hispanics, 1.7% among African Americans, and 1% among Asian Americans. Estimated 12-month prevalence of methamphetamine use in the United States is 0.6% for individuals age 12 and older (0.2% among individuals ages 12–17 years, 1.1% among individuals ages 18–25 years, and 0.6% among individuals age 26 and older). Twelve-month prevalence of methamphetamine use is 0.8% among men/boys and 0.4% among women/girls. Twelve-month prevalence of methamphetamine use is 0.7% among Whites, 0.6% among Hispanics, 0.2% among African Americans, and 0.1% among Asian Americans. Small sample

Stimulant-induced mental disorders. Independent mental disorders. sizes make estimating rates among American Indians/Alaskan Natives difficult. Differential Diagnosis Stimulant intoxication is distinguished from stimulant-induced mental disorders (e.g., stimulant-induced anxiety disorder, with onset during intoxication) because the symptoms (e.g., anxiety) in the latter disorders are in excess of those usually seen in stimulant intoxication, predominate in the clinical presentation, and meet full criteria for the relevant disorder. Salient mental disturbances associated with stimulant intoxication should be distinguished from the symptoms of schizophrenia, bipolar and depressive disorders, generalized anxiety disorder, and panic disorder as described in this manual. Comorbidity Given the typical overlap of stimulant intoxication with stimulant use disorder, see “Comorbidity” under Stimulant Use Disorder for more details about co-occurring conditions that are likely to be encountered. Stimulant Withdrawal Diagnostic Criteria A. Cessation of (or reduction in) prolonged amphetamine-type substance, cocaine, or other stimulant use. B. Dysphoric mood and two (or more) of the following physiological changes, developing within a few hours to several days after Criterion A:

1. Fatigue.
2. Vivid, unpleasant dreams.
3. Insomnia or hypersomnia.
4. Increased appetite.
5. Psychomotor retardation or 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 or withdrawal from another substance. Specify the particular substance that causes the withdrawal syndrome (i.e., amphetamine-type substance, cocaine, or other stimulant).

Coding note: The ICD-10-CM code depends on whether the stimulant is an

Stimulant-induced mental disorders. amphetamine-type substance, cocaine, or other stimulant and on whether or not there is a comorbid amphetamine-type substance, cocaine, or other stimulant use disorder. If mild amphetamine-type substance or other stimulant use disorder is comorbid, the ICD-10-CM code is F15.13. If moderate or severe amphetamine-type substance or other stimulant use disorder is comorbid, the ICD-10-CM code is F15.23. For amphetamine-type substance or other stimulant withdrawal occurring in the absence of amphetamine-type substance or other stimulant use disorder (e.g., in a patient taking amphetamine solely under appropriate medical supervision), the ICD-10-CM code is F15.93. If mild cocaine use disorder is comorbid, the ICD-10-CM code is F14.13. If moderate or severe cocaine use disorder is comorbid, the ICD-10CM code is F14.23. For cocaine withdrawal occurring in the absence of a cocaine use disorder, the ICD-10-CM code is F14.93. Diagnostic Features The essential feature of stimulant withdrawal is the presence of a characteristic withdrawal syndrome that develops within a few hours to several days after the cessation of (or marked reduction in) stimulant use (generally high dose) that has been prolonged (Criterion A). The withdrawal syndrome is characterized by the development of dysphoric mood accompanied by two or more of the following physiological changes: fatigue, vivid and unpleasant dreams, insomnia or hypersomnia, increased appetite, and psychomotor retardation or agitation (Criterion B). Bradycardia is often present and is a reliable measure of stimulant withdrawal. Anhedonia and drug craving can often be present but are not part of the diagnostic criteria. These 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 (Criterion D). Associated Features Acute withdrawal symptoms (“a crash”) are often seen after periods of repetitive high-dose use (“runs” or “binges”). These symptoms are characterized by intense and unpleasant feelings of lassitude and depression and increased appetite, generally requiring several days of rest and recuperation. Depressive symptoms with suicidal thoughts or behavior can occur and are generally the most serious problems seen during “crashing” or other forms of stimulant withdrawal. Many individuals with stimulant use disorder may experience a withdrawal syndrome at some point. Differential Diagnosis Stimulant withdrawal is distinguished from stimulant-induced mental disorders (e.g., stimulant-induced depressive disorder, with onset during withdrawal) because the symptoms (e.g., depressed mood) in these latter disorders are in excess of those usually associated with stimulant withdrawal, predominate in the clinical presentation, and are severe enough to warrant clinical attention.

Comorbidity Given the typical overlap of stimulant withdrawal with stimulant use disorder, see “Comorbidity” under Stimulant Use Disorder for more details about co-occurring conditions that are likely to be encountered. Stimulant-Induced Mental Disorders The following stimulant-induced mental disorders (which include amphetamine-type substance–, cocaine-, and other stimulant–induced mental disorders) are described in other chapters of the manual with disorders with which they share phenomenology (see the substance/medicationinduced mental disorders in these chapters): stimulant-induced psychotic disorder (“Schizophrenia Spectrum and Other Psychotic Disorders”); stimulant-induced bipolar and related disorder (“Bipolar and Related Disorders”); stimulant-induced depressive disorder (“Depressive Disorders”); stimulant-induced anxiety disorder (“Anxiety Disorders”); stimulantinduced obsessive-compulsive disorder (“Obsessive-Compulsive and Related Disorders”); stimulant-induced sleep disorder (“Sleep-Wake

Disorders”); stimulant-induced sexual dysfunction (“Sexual Dysfunctions”); and stimulant-induced mild neurocognitive disorder (“Neurocognitive Disorders”). For stimulant intoxication delirium and delirium induced by stimulants taken as prescribed, see the criteria and discussion of delirium in the chapter “Neurocognitive Disorders.” These stimulant-induced mental disorders are diagnosed instead of stimulant intoxication or stimulant withdrawal only when the symptoms are sufficiently severe to warrant independent clinical attention. Unspecified Stimulant-Related Disorder This category applies to presentations in which symptoms characteristic of a stimulant-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 stimulant-related disorder or any of the disorders in the substance-related and addictive disorders diagnostic class. Coding note: The ICD-10-CM code depends on whether the stimulant is an amphetamine-type substance, cocaine, or other stimulant. The ICD-10-CM code for an unspecified amphetamine-type substance or other stimulant–related disorder is F15.99. The ICD-10-CM code for an unspecified cocaine-related disorder is F14.99. Tobacco-Related Disorders Tobacco Use Disorder Tobacco Withdrawal

Tobacco-Induced Mental Disorders Unspecified Tobacco-Related Disorder Tobacco Use Disorder Diagnostic Criteria A. A problematic pattern of tobacco use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12month period:

1. Tobacco 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 tobacco use.
3. A great deal of time is spent in activities necessary to obtain or use tobacco.
4. Craving, or a strong desire or urge to use tobacco.
5. Recurrent tobacco use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., interference with work).
6. Continued tobacco use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of tobacco (e.g., arguments with others about tobacco use).
7. Important social, occupational, or recreational activities are given up or reduced because of tobacco use.
8. Recurrent tobacco use in situations in which it is physically hazardous (e.g., smoking in bed).
9. Tobacco 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 tobacco.
10. Tolerance, as defined by either of the following: a. A need for markedly increased amounts of tobacco to achieve the desired effect. b. A markedly diminished effect with continued use of the same amount of tobacco.
11. Withdrawal, as manifested by either of the following: a. The characteristic withdrawal syndrome for tobacco (refer to Criteria A and B of the criteria set for tobacco withdrawal). b. Tobacco (or a closely related substance, such as nicotine) is taken to relieve or avoid withdrawal symptoms. Specify if:

646 In early remission: After full criteria for tobacco use disorder were previously met, none of the criteria for tobacco 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 tobacco,” may be met). In sustained remission: After full criteria for tobacco use disorder were previously met, none of the criteria for tobacco 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 tobacco,” may be met). Specify if: On maintenance therapy: The individual is taking a long-term maintenance medication, such as nicotine replacement medication, and no criteria for tobacco use disorder have been met for that class of medication (except tolerance to, or withdrawal from, the nicotine replacement medication). In a controlled environment: This additional specifier is used if the individual is in an environment where access to tobacco is restricted. Code based on current severity/remission: If a tobacco withdrawal or tobaccoinduced sleep disorder is also present, do not use the codes below for tobacco use disorder. Instead, the comorbid tobacco use disorder is indicated in the 4th character of the tobacco-induced disorder code (see the coding note for tobacco withdrawal or tobacco-induced sleep disorder). For example, if there is comorbid tobacco-induced sleep disorder and tobacco use disorder, only the tobacco-induced sleep disorder code is given, with the 4th character indicating whether the comorbid tobacco use disorder is moderate or severe: F17.208 for moderate or severe tobacco use disorder with tobacco-induced sleep disorder. It is not permissible to code a comorbid mild tobacco use disorder with a tobacco-induced sleep disorder. Specify current severity/remission: Z72.0 Mild: Presence of 2–3 symptoms. F17.200 Moderate: Presence of 4–5 symptoms. F17.201 Moderate, In early remission F17.201 Moderate, In sustained remission F17.200 Severe: Presence of 6 or more symptoms. F17.201 Severe, In early remission F17.201 Severe, In sustained remission Specifiers “On maintenance therapy” applies as a specifier to be added to “in remission” if the individual is both in remission and on 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. Diagnostic Features Tobacco use disorder can develop with use of all forms of tobacco (e.g., cigarettes, chewing tobacco, snuff, pipes, cigars, electronic nicotine delivery devices such as electronic cigarettes [ecigarettes]) and with prescription nicotine-containing medications (nicotine gum and patch). The relative ability of these products to produce tobacco use disorder or to induce withdrawal is associated with the rapidity of the route of administration (smoked over oral over transdermal) and the nicotine content of the product. The name of this substance category was changed from “nicotine” in prior editions of DSM to “tobacco” in DSM-5 on the basis of harms from addiction being associated mostly with tobacco and much less with nicotine. Tobacco use disorder is common among individuals who use cigarettes and smokeless tobacco daily, is less common among individuals who use e-cigarettes, and is uncommon among those who do not use tobacco daily or use nicotine medications. Tolerance to tobacco is exemplified by the disappearance of nausea and dizziness after intake and by a more intense effect of tobacco the first time it is used during the day. Cessation of tobacco use can produce a well-defined withdrawal syndrome. Many individuals with tobacco use disorder use tobacco to relieve or to avoid withdrawal symptoms (e.g., after being in a situation where use is restricted). Many individuals with tobacco use disorder have tobacco-related physical symptoms or diseases and continue to smoke. The large majority report craving when they do not smoke for several hours. Spending excessive time using tobacco can be exemplified by chain-smoking (i.e., smoking one cigarette after another with no time between cigarettes). Because tobacco sources

are readily and legally available, and because tobacco intoxication is very rare, spending a great deal of time attempting to procure tobacco or recovering from its effects is uncommon. Giving up important social, occupational, or recreational activities can occur when an individual forgoes an activity because it occurs in tobacco use–restricted areas. Use of tobacco rarely results in failure to fulfill major role obligations (e.g., interference with work or home responsibilities), but persistent social or interpersonal problems (e.g., having arguments with others about tobacco use, avoiding social situations because of others' disapproval of tobacco use) or use that is physically hazardous (e.g., smoking in bed, smoking around flammable chemicals) occur at an intermediate prevalence. Although these criteria are less often endorsed by tobacco users, if endorsed, they can indicate a more severe disorder. Associated Features Smoking within 30 minutes of waking, smoking daily, smoking more cigarettes per day, and waking at night to smoke are associated with tobacco use disorder. Environmental cues can evoke craving and withdrawal. Serious medical conditions often occur, including lung and other cancers, cardiac and pulmonary disease, perinatal problems, cough, shortness of breath, and accelerated skin aging.

Temperamental. Environmental. Genetic and physiological. Prevalence Although cigarettes are the most commonly used tobacco product, use of other tobacco products (especially e-cigarettes) has become more common. In the United States, 19% of adults used a tobacco product in the last year, 19% used more than one product, 14% used cigarettes, 4% used cigars, 3% used e-cigarettes, and 2% used smokeless tobacco. One fourth (24%) of current U.S. smokers are nondaily smokers. The 12-month prevalence of DSM-5 tobacco use disorder in the United States in 2012–2013 was 20% among adults age 18 years and older and 29.6% among Native Americans, 22.3% among non-Latinx Whites, 20.1% among African Americans, 12.2% among Latinx, and 11.2% among Asian Americans and Pacific Islanders. Prevalence was higher among men; those who were young, unmarried, less educated, poor, or residing in the southern United States; and those with almost any psychiatric disorder. The prevalence among current daily smokers is approximately 50%. Global comparisons show that in all geographic regions of the world, the age-standardized prevalence of daily tobacco smoking is higher in men than in women, but the gender ratio varies greatly, from 16.9:1 in East Asia to 1.2:1 in Australasia. Development and Course About 20% of U.S. high school seniors report having ever smoked cigarettes, and about 5% have used in the past 30 days. Among adolescents who smoke cigarettes at least monthly, most of these individuals will become daily tobacco users in the future. Initiation of smoking after age 21 years is rare. Some of the tobacco use disorder criteria symptoms (e.g., craving) occur soon after beginning tobacco use, suggesting the addiction process begins with initial use; however, fulfilling DSM criteria usually occurs over several years. Nondaily smoking has become more prevalent since the late 1990s in the United States, especially among individuals ages 18–34 years, Blacks, Hispanics, and individuals with at least a college education. Risk and Prognostic Factors Individuals with externalizing personality traits are more likely to initiate tobacco use. Children with attention-deficit/hyperactivity disorder or conduct disorder, and adults with depressive, bipolar, anxiety, personality, psychotic, or other substance use disorders, are at higher risk for starting and continuing tobacco use and of tobacco use disorder. Persons with low incomes and low educational levels are more likely to initiate tobacco use and are less likely to stop. Genetic factors contribute to the onset of tobacco use, the continuation of tobacco use, and the development of tobacco use disorder, with a degree of heritability equivalent to that observed with other substance use disorders (i.e., about 50%). Some of this risk is specific to tobacco, and some is common with the vulnerability to developing any substance use disorder.

Culture-Related Diagnostic Issues Acceptance of tobacco use varies across cultural contexts. Age-standardized prevalence of daily tobacco smoking varies greatly by geographic region, ranging from 4.7% in Western SubSaharan Africa to 24.2% in Eastern Europe. The degree to which these geographic differences are the result of income, education, and tobacco control activities in a country is unclear. Prevalence of tobacco use in the United States varies by age, gender, and ethnoracial background, with lower rates of smoking onset and progression to daily smoking among Black youth, especially young women. Liver enzyme polymorphisms that vary across ethnoracial groups can affect nicotine metabolism, contributing to variation in smoking behavior. Higher tobacco use disorder prevalence is also associated with exposure to racism and ethnic discrimination. Prevalence of DSM-IV nicotine dependence is higher among adult lesbian, gay, and bisexual individuals than among heterosexuals, possibly also due to an association with exposure to sexual orientation–related discrimination. Among individuals with DSM-IV nicotine dependence, lower income and education are associated with disorder persistence. Sex- and Gender-Related Diagnostic Issues The ratio of men to women among U.S. smokers is approximately 1.4:1 and has been stable between 2004 and 2014. This ratio is generally consistent across various income and educational levels. The ratio diminishes in older age groups as fewer men are smoking as age increases. The literature from several U.S. settings suggests that negative reinforcement (i.e., that smoking relieves negative affect) is a greater motivator in women than in men. Menstrual cycle effects on smoking are found inconsistently, but tobacco withdrawal appears worse in the luteal than the follicular phase of the cycle. Pregnant females smoke at a lower rate than nonpregnant females but relapse back to smoking rapidly after delivery. Diagnostic Markers The following biomarkers can be used to measure the extent of tobacco or nicotine use: carbon monoxide in the breath and nicotine and its metabolite cotinine in blood, saliva, or urine; however, these are only weakly associated with tobacco use disorder. Association With Suicidal Thoughts or Behavior National U.S. survey data show that past-year cigarette use is associated with a two- to threefold increased risk of suicidal thoughts and behavior, with earlier age at first tobacco use increasing risk. Evidence from the U.S. Veterans Health Administration shows that even after adjustment for covariates, tobacco use disorder is associated with an increased risk of suicide. A large study of twins in Finland found that the relationship between tobacco use and suicide increased in a dose-response manner, and that for identical twins discordant for tobacco use, tobacco use was associated with a sixfold increased risk for suicide. Functional Consequences of Tobacco Use Disorder Medical consequences of tobacco use often begin when tobacco users are in their 40s and usually

F17.203 become progressively more debilitating over time. One-half of smokers who do not stop using tobacco will die early from a tobacco-related illness, and smoking-related morbidity occurs in more than one-half of tobacco users. Most medical conditions result from exposure to carbon monoxide, tars, and other non-nicotine components of tobacco. The major predictor of reversibility is duration of smoking. Secondhand smoke increases the risk of heart disease and cancer by 30%. Long-term use of nicotine medications does not appear to cause medical harm. Comorbidity The most common medical conditions from smoking are cardiovascular illnesses, chronic obstructive pulmonary disease, and cancers. Smoking also increases perinatal problems, such as low birth weight and miscarriage. Prevalence of smoking is almost twice as high in individuals with major depressive disorder; although the prevalence of smoking in the United States is higher among individuals with low socioeconomic status, the increased prevalence of smoking among those with depression is independent of socioeconomic status. The most common psychiatric comorbidities

associated with smoking are alcohol and other substance, depressive, bipolar, anxiety, personality, and attention-deficit/hyperactivity disorders. In the United States, individuals with a psychiatric disorder are three times more likely than others to have tobacco use disorder. Adults with DSM-5 tobacco use disorder are significantly more likely than other adults to have comorbid psychiatric disorders, including other DSM-5 substance use disorders, major depressive disorder, bipolar I disorder, panic disorder, generalized anxiety disorder, posttraumatic stress disorder, and borderline and antisocial personality disorders. Tobacco Withdrawal Diagnostic Criteria A. Daily use of tobacco for at least several weeks. B. Abrupt cessation of tobacco use, or reduction in the amount of tobacco used, followed within 24 hours by four (or more) of the following signs or symptoms:

1. Irritability, frustration, or anger.
2. Anxiety.
3. Difficulty concentrating.
4. Increased appetite.
5. Restlessness.
6. Depressed mood.
7. 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 attributed to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance. Coding note: The ICD-10-CM code for tobacco withdrawal is F17.203. Note that the ICD-10-CM code indicates the comorbid presence of a moderate or severe tobacco use disorder, reflecting the fact that tobacco withdrawal can only occur in the presence of a moderate or severe tobacco use disorder. Diagnostic Features Withdrawal symptoms impair the ability to stop tobacco use. The symptoms after abstinence from tobacco are in large part due to nicotine deprivation. Tobacco withdrawal is common among daily tobacco users who stop or reduce their use of tobacco. Symptoms are more intense among individuals who smoke cigarettes and also use smokeless tobacco or electronic cigarettes daily. This symptom intensity is likely attributable to the more rapid onset and higher levels of nicotine with cigarette smoking. Significant withdrawal among those who are nondaily cigarette users or use only nicotine medications is uncommon. Typically, heart rate decreases by 5–12 bpm in the first few days after stopping smoking, and weight increases an average of 4–7 lb (2–3 kg) over the first year after stopping smoking. Tobacco withdrawal can produce clinically significant mood changes and functional impairment. Because of conditioning effects, withdrawal can be prompted by environmental cues such as seeing others smoking. Gradual reduction of tobacco decreases the severity of withdrawal. Associated Features Craving for tobacco or nicotine is very common during abstinence and has a large effect on the ability to remain abstinent. Abstinence can increase impulsivity and anhedonia and can decrease positive affect. Abstinence from tobacco or nicotine also appears to increase craving for sweet or sugary foods and impairs performance on tasks requiring vigilance. Smoking increases the metabolism of many medications used to treat mental disorders; thus, cessation of smoking can increase the blood levels of these medications, and this can produce clinically significant outcomes. This effect appears to be due not to nicotine but rather to other compounds in tobacco. Prevalence Approximately 50% of daily smokers who quit for 2 or more days will have four or more symptoms of tobacco withdrawal. The most commonly endorsed signs and symptoms are anxiety, irritability, and difficulty concentrating. The least commonly endorsed symptoms are depression and

insomnia. Development and Course Tobacco withdrawal usually begins within 24 hours of stopping or cutting down tobacco use, peaks at 2–3 days after abstinence, and usually lasts 2–3 weeks. Tobacco withdrawal symptoms can occur among adolescent tobacco users, even prior to daily tobacco use. Prolonged symptoms beyond 1 month can occur but are uncommon.

Temperamental. Genetic and physiological. Risk and Prognostic Factors Smokers with depressive disorders, bipolar disorders, anxiety disorders, attention-deficit/hyperactivity disorder, and other substance use disorders have more severe withdrawal. Genotype can influence the probability of withdrawal upon abstinence. Diagnostic Markers The following biomarkers can be used to measure the extent of tobacco or nicotine use but are only weakly associated with tobacco withdrawal: carbon monoxide in the breath and nicotine and its metabolite cotinine in blood, saliva, or urine. Functional Consequences of Tobacco Withdrawal Tobacco withdrawal can cause significant distress and difficulty functioning in a minority of smokers, but this may be uncommon. Withdrawal impairs the ability to stop or control tobacco use. Whether tobacco withdrawal can prompt the development of a new mental disorder or recurrence of a mental disorder is debatable, but if this occurs, it would be in a small minority of tobacco users. Differential Diagnosis The symptoms of tobacco withdrawal overlap with those of other substance withdrawal syndromes (e.g., alcohol withdrawal; sedative, hypnotic, or anxiolytic withdrawal; stimulant withdrawal; caffeine withdrawal; opioid withdrawal); caffeine intoxication; anxiety, depressive, bipolar, and sleep disorders; and medication-induced akathisia. Admission to smoke-free inpatient units or voluntary smoking cessation can induce withdrawal symptoms that mimic, intensify, or disguise other disorders or adverse effects of medications used to treat mental disorders (e.g., irritability thought to be due to alcohol withdrawal could be due to tobacco withdrawal). Reduction in symptoms with the use of nicotine confirms the diagnosis. Comorbidity Given the typical overlap of tobacco withdrawal with tobacco use disorder, see “Comorbidity” under Tobacco Use Disorder for more details about co-occurring conditions that are likely to be encountered. Tobacco-Induced Mental Disorders Tobacco-induced sleep disorder is discussed in the chapter “Sleep-Wake Disorders” (see “Substance/Medication-Induced Sleep Disorder”). Unspecified Tobacco-Related Disorder

F17.209 This category applies to presentations in which symptoms characteristic of a tobacco-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 tobacco-related disorder or any of the disorders in the substance-related and addictive disorders diagnostic class. Other (or Unknown) Substance–Related Disorders Other (or Unknown) Substance Use Disorder Other (or Unknown) Substance Intoxication Other (or Unknown) Substance Withdrawal Other (or Unknown) Substance–Induced Mental Disorders Unspecified Other (or Unknown) Substance–Related Disorder Other (or Unknown) Substance Use Disorder Diagnostic Criteria A. A problematic pattern of use of an intoxicating substance not able to be classified within the alcohol; caffeine; cannabis; hallucinogen (phencyclidine and others); inhalant; opioid; sedative, hypnotic, or anxiolytic; stimulant; or tobacco categories and leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. The 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 substance.

3. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
4. Craving, or a strong desire or urge to use the substance.
5. Recurrent use of the substance resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued use of the 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 substance.
8. Recurrent use of the substance in situations in which it is physically hazardous.
9. Use of the 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 substance to achieve intoxication or desired effect. b. A markedly diminished effect with continued use of the same amount of the substance.
11. Withdrawal, as manifested by either of the following: a. The characteristic withdrawal syndrome for other (or unknown) substance (refer to Criteria A and B of the criteria sets for other [or unknown] substance withdrawal). b. The substance (or a closely related substance) is taken to relieve or avoid withdrawal symptoms. Specify if: In early remission: After full criteria for other (or unknown) substance use disorder were previously met, none of the criteria for other (or unknown) substance 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 substance,” may be met). In sustained remission: After full criteria for other (or unknown) substance use disorder were previously met, none of the criteria for other (or unknown) substance 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 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 the substance is restricted. Code based on current severity/remission: If an other (or unknown) substance intoxication, other (or unknown) substance withdrawal, or other (or unknown) substance–induced mental disorder is present, do not use the codes below for other (or unknown) substance use disorder. Instead, the comorbid other (or unknown) substance use disorder is indicated in the 4th character of the other (or unknown)

substance–induced disorder code (see the coding note for other [or unknown] substance intoxication, other [or unknown] substance withdrawal, or specific other [or unknown] substance–induced mental disorder). For example, if there is comorbid other (or unknown) substance–induced depressive disorder and other (or unknown) substance use disorder, only the other (or unknown) substance–induced depressive disorder code is given, with the 4th character indicating whether the comorbid other (or unknown) substance use disorder is mild, moderate, or severe: F19.14 for other (or unknown) substance use disorder with other (or unknown) substance–induced depressive disorder or F19.24 for a moderate or severe other (or unknown) substance use disorder with other (or unknown) substance–induced depressive disorder. Specify current severity/remission: F19.10 Mild: Presence of 2–3 symptoms. F19.11 Mild, In early remission

F19.11 Mild, In sustained remission F19.20 Moderate: Presence of 4–5 symptoms. F19.21 Moderate, In early remission F19.21 Moderate, In sustained remission F19.20 Severe: Presence of 6 or more symptoms. F19.21 Severe, In early remission F19.21 Severe, In sustained remission 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 diagnostic class other (or unknown) substance–related disorders applies to substances that are not included within any of the nine substance classes presented earlier in this chapter (i.e., to alcohol; caffeine; cannabis; hallucinogens [phencyclidine and others]; inhalants; opioids; sedatives, hypnotics, or anxiolytics; stimulants; or tobacco). Such substances include anabolic steroids; nonsteroidal anti-inflammatory drugs; corticosteroids; antiparkinsonian medications; antihistamines; nitrous oxide; amyl-, butyl-, or isobutyl-nitrites; betel nut, which is chewed in many geographic regions to produce mild euphoria and a floating sensation; and kava (from a South Pacific pepper plant), which produces mild euphoria, sedation, incoordination, and weight loss, as well as health effects (e.g., mild hepatitis, lung abnormalities). Note that gaseous substances are included with the inhalant category only if they are hydrocarbon agents; other

gaseous substances (including nitrous oxide mentioned above) are included in the other (or unknown) substance category. Unknown substance–related disorders are associated with unidentified substances, such as intoxications in which the individual cannot identify the ingested drug, or substance use disorders involving either new, black market drugs not yet identified or familiar drugs illegally sold under false names. Note that substances included within the scope of one of the substance classes should be coded within that respective substance class and are inappropriate to include in the “other substance” category. For example, the following substances are explicitly included in specific substance classes and should not be included in the “other substance” category: synthetic cannabinoids are included in the cannabis category; propofol is included in the sedative, hypnotic, or anxiolytic category; and cathinones (including khât plant agents and synthetic chemical derivatives) are included in the stimulant category. Other (or unknown) substance use disorder is a mental disorder in which repeated use of an other or unknown substance typically continues, despite the individual’s knowing that the substance is causing serious problems for the individual. Those problems are reflected in the diagnostic criteria. When the substance is known but does not fit within any of the other nine substance classes, it should be reflected when recording and coding the name of the disorder (e.g., “nitrous oxide use disorder,” using the applicable code for other [or unknown] substance use disorder). Associated Features A diagnosis of other (or unknown) substance use disorder is supported by any of the following: the individual’s reported use of a substance that is not among the nine classes listed in this chapter; recurring episodes of intoxication with negative results in standard drug screens, which may not detect new or rarely used substances; and the presence of symptoms characteristic of an unidentified substance that has newly appeared in the individual’s community. Because of access to nitrous oxide (“laughing gas”), membership in certain populations may be associated with frequent use of the substance and possibly with a diagnosis of nitrous oxide use disorder. The role of this gas as an anesthetic agent leads to misuse by some medical and dental professionals, and its use as a propellant for commercial products (e.g., whipped cream dispensers) contributes to misuse by food service workers. Nitrous oxide misuse by adolescents and young adults is significant, and some individuals with very frequent use may present with serious medical

complications and mental conditions, including myeloneuropathy, spinal cord subacute combined degeneration, peripheral neuropathy, and psychosis. Use of amyl-, butyl-, and isobutyl (and similar) nitrite gases is prevalent among homosexual men and some adolescents, especially those with conduct disorder. Substance use disorders generally are associated with elevated risks of suicide, but there is no evidence of unique risk factors for suicide with other (or unknown) substance use disorder. Prevalence Based on extremely limited data, the prevalence of most other (or unknown) substance use disorders is likely lower than that of use disorders involving the nine substance classes in this

Use of other or unknown substances without meeting criteria for other (or unknown) substance use disorder. Substance use disorders. Other (or unknown) substance intoxication, other (or unknown) substance withdrawal, and other (or unknown) substance–induced mental disorders. chapter. For certain gaseous substances, prevalence of use is not rare (lifetime prevalence in the U.S. household population for individuals age 12 and older is estimated at 4.6% for nitrous oxide and 2.5% for nitrites), but how often the patterns of use qualify for a use disorder is unknown. Development and Course No single pattern of development or course characterizes the pharmacologically varied other (or unknown) substance use disorders. Often unknown substance use disorders will be reclassified when the unknown substance eventually is identified. Risk and Prognostic Factors Risk and prognostic factors for other (or unknown) substance use disorders are thought to be similar to those for most substance use disorders and include the presence of any other substance use disorders, conduct disorder, or antisocial personality disorder in the individual or the individual's family; early onset of substance problems; easy availability of the substance in the individual's environment; childhood maltreatment or trauma; and evidence of limited early selfcontrol and behavioral disinhibition. Culture-Related Diagnostic Issues Certain cultures may be associated with other (or unknown) substance use disorders involving specific indigenous substances within the cultural region, such as betel nut. Diagnostic Markers Urine, breath, or saliva tests may correctly identify a commonly used substance falsely sold as a novel product. However, routine clinical tests usually cannot identify truly unusual or new substances, which may require testing in specialized laboratories. Differential Diagnosis Use of unknown substances is not rare among adolescents, but most use does not meet the diagnostic standard of two or more criteria for other (or unknown) substance use disorder in a 12-month period. Other (or unknown) substance use disorder may co-occur with various substance use disorders that involve any of the nine substance classes presented earlier in this chapter, 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 (or unknown) substance use disorder is differentiated from other (or unknown) substance intoxication, other (or unknown) substance withdrawal, and other-(or unknown) substanceinduced mental disorders (e.g., corticosteroid-induced bipolar and related disorder) in that other (or unknown) substance use disorder describes a problematic pattern of use of the other (or unknown) substance that involves impaired control over the use of the substance, social

impairment attributable to use of the substance, risky use of the substance (e.g., continued use despite medical complications), and pharmacological symptoms (the development of tolerance or withdrawal), whereas other (or unknown) substance intoxication, other (or unknown) substance withdrawal, and other (or unknown) substance-induced mental disorders describe psychiatric syndromes that occur in the context of heavy use. Other (or unknown) substance intoxication,

other (or unknown) substance withdrawal, and other (or unknown) substance–induced mental disorders may occur in individuals with other (or unknown) substance use disorder. In such cases, a diagnosis of other (or unknown) substance intoxication, other (or unknown) substance withdrawal, or other (or unknown) substance–induced mental disorder should be given in addition to a diagnosis of other (or unknown) substance use disorder, the presence of which is indicated in the diagnostic code. Comorbidity Substance use disorders, including other (or unknown) substance use disorder, are commonly comorbid with one another, with conduct disorder in adolescence, and with antisocial personality disorder. Other (or Unknown) Substance Intoxication Diagnostic Criteria A. The development of a reversible substance-specific syndrome attributable to recent ingestion of (or exposure to) a substance that is not listed elsewhere or is unknown. B. Clinically significant problematic behavioral or psychological changes that are attributable to the effect of the substance on the central nervous system (e.g., impaired motor coordination, psychomotor agitation or retardation, euphoria, anxiety, belligerence, mood lability, cognitive impairment, impaired judgment, social withdrawal) and develop during, or shortly after, use of the substance. C. 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 when hallucinations with intact reality testing or auditory, visual, or tactile illusions occur in the absence of a delirium. Coding note: The ICD-10-CM code depends on whether there is a comorbid other (or unknown) substance use disorder involving the same substance and whether or not there are perceptual disturbances.

For other (or unknown) substance intoxication, without perceptual disturbances: If a mild other (or unknown) substance use disorder is comorbid, the ICD-10-CM code is F19.120, and if a moderate or severe other (or unknown) substance use disorder is comorbid, the ICD-10-CM code is F19.220. If there is no comorbid other (or unknown) substance use disorder, then the ICD-10-CM code is F19.920. For other (or unknown) substance intoxication, with perceptual disturbances: If a mild other (or unknown) substance use disorder is comorbid, the ICD-10-CM code is F19.122, and if a moderate or severe other (or unknown) substance use disorder is comorbid, the ICD-10-CM code is F19.222. If there is no comorbid other (or unknown) substance use disorder, then the ICD-10-CM code is F19.922. Note: For information on Risk and Prognostic Factors, Culture-Related Diagnostic Issues, and Diagnostic Markers, see the corresponding sections in Other (or Unknown) Substance Use Disorder. Diagnostic Features The essential feature of other (or unknown) substance intoxication is the presence of clinically significant behavioral or psychological changes that develop during, or immediately after, use of either a) a substance not included within one of the nine substance classes presented in this chapter (i.e., alcohol; caffeine; cannabis; phencyclidine and other hallucinogens; inhalants; opioids; sedatives, hypnotics, or anxiolytics; stimulants; or tobacco) or b) an unknown substance. If the substance is known, it should be reflected in the name of the disorder upon coding (e.g., “kava intoxication”). Application of the diagnostic criteria for other (or unknown) substance intoxication is very challenging. Criterion A requires development of a reversible “substance-specific syndrome,” but if the substance is unknown, that syndrome usually will be unknown. To resolve this conflict, clinicians may ask the individual or obtain collateral history as to whether the individual has experienced a similar episode after using substances with the same “street” name or from the same source. Similarly, hospital emergency departments sometimes recognize over a few days numerous presentations of a severe, unfamiliar intoxication syndrome from a newly available, previously unknown substance. Because of the great variety of intoxicating substances, Criterion B can provide only broad examples of signs and

symptoms from some intoxications, with no threshold for the number of symptoms required for a diagnosis; clinical judgment guides those decisions. Criterion C requires ruling out other medical conditions, mental disorders, or intoxications. Prevalence The prevalence of other (or unknown) substance intoxication is unknown. Development and Course

Use of other or unknown substance, without meeting criteria for other (or unknown) substance intoxication. Substance intoxication or other substance/medication-induced mental disorders. Other toxic, metabolic, traumatic, neoplastic, vascular, or infectious disorders that impair brain function and cognition. Intoxications usually appear and then peak minutes to hours after use of the substance, but the onset and course vary with the substance and the route of administration. Generally, substances used by pulmonary inhalation and intravenous injection have the most rapid onset of action, whereas those ingested by mouth and requiring metabolism to an active product are much slower. (For example, after ingestion of certain mushrooms, the first signs of an eventually fatal intoxication may not appear for a few days.) Intoxication effects usually resolve within hours to a very few days. However, the body may completely eliminate an anesthetic gas such as nitrous oxide just minutes after use ends. At the other extreme, some “hit-and-run” intoxicating substances poison systems, leaving permanent impairments. For example, MPTP (1-methyl-4phenyl-1,2,3,6-tetrahydropyridine), a contaminating by-product in the synthesis of a certain opioid, kills dopaminergic cells and induces permanent parkinsonism in individuals who had sought opioid intoxication. Functional Consequences of Other (or Unknown) Substance Intoxication Impairment from intoxication with any substance may have serious consequences, including dysfunction at work, social indiscretions, problems in interpersonal relationships, failure to fulfill role obligations, traffic accidents, fighting, high-risk behaviors (i.e., having unprotected sex), and substance or medication overdose. The pattern of consequences will vary with the particular substance. Differential Diagnosis The individual used an other or unknown substance(s), but the dose was insufficient to produce symptoms that meet the diagnostic criteria required for the diagnosis. Familiar substances may be sold in the black market as novel products, and individuals may experience intoxication from those substances. History, toxicology screens, or chemical testing of the substance itself may help to identify it. Other substance intoxication is distinguished from other substance/medication-induced mental disorders (e.g., corticosteroid-induced anxiety disorder) because the symptoms (e.g., anxiety) in these latter disorders are in excess of those (if known) usually associated with the specific substance intoxication, predominate in the clinical presentation, and are severe enough to warrant clinical attention. Numerous neurological and other medical conditions may produce rapid onset of signs and symptoms mimicking those of intoxications, including the examples in Criterion B. Paradoxically, drug withdrawals also must be ruled out; for example, lethargy may indicate withdrawal from one drug or intoxication with another substance. Comorbidity

As with all substance-related disorders, conduct disorder in adolescence, antisocial personality disorder, and other substance use disorders tend to co-occur with other (or unknown) substance intoxication. Other (or Unknown) Substance Withdrawal Diagnostic Criteria A. Cessation of (or reduction in) use of a substance that has been heavy and prolonged. B. The development of a substance-specific syndrome shortly after the cessation of (or reduction in) substance use. C. The substance-specific syndrome causes clinically significant distress or impairment in social, occupational, or other important areas of functioning. D. The symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including

withdrawal from another substance. E. The substance involved cannot be classified under any of the other substance categories (alcohol; caffeine; cannabis; opioids; sedatives, hypnotics, or anxiolytics; stimulants; or tobacco) or is unknown. Specify if: With perceptual disturbances: This specifier may be noted when hallucinations with intact reality testing or auditory, visual, or tactile illusions occur in the absence of a delirium. Coding note: The ICD-10-CM code depends on whether or not there is a comorbid other (or unknown) substance use disorder and whether or not there are perceptual disturbances. For other (or unknown) substance withdrawal, without perceptual disturbances: If a mild other (or unknown) substance use disorder is comorbid, the ICD-10-CM code is F19.130, and if a moderate or severe other (or unknown) substance use disorder is comorbid, the ICD-10-CM code is F19.230. If there is no comorbid other (or unknown) substance use disorder (e.g., in a patient taking an other [or unknown] substance solely under appropriate medical supervision), then the ICD-10-CM code is F19.930. For other (or unknown) substance withdrawal, with perceptual disturbances: If a mild other (or unknown) substance use disorder is comorbid, the ICD-10-CM code is F19.132, and if a moderate or severe other (or unknown) substance use disorder

is comorbid, the ICD-10-CM code is F19.232. If there is no comorbid other (or unknown) substance use disorder (e.g., in a patient taking an other [or unknown] substance solely under appropriate medical supervision), then the ICD-10-CM code is F19.932. Note: For information on Risk and Prognostic Factors and Diagnostic Markers, see the corresponding sections in Other (or Unknown) Substance Use Disorder. Diagnostic Features Other (or unknown) substance withdrawal is a clinically significant syndrome that develops during or within a few hours to days after reducing or terminating dosing with a substance (Criteria A and B). Although recent dose reduction or termination usually is clear in the history, other diagnostic procedures are very challenging if the drug is unknown. Criterion B requires development of a “substance-specific syndrome” (i.e., the individual’s signs and symptoms must correspond with the known withdrawal syndrome for the recently stopped drug)—a requirement that rarely can be met with an unknown substance. Consequently, clinical judgment must guide such decisions when this information is limited. Criterion D requires ruling out other medical conditions, mental disorders, or withdrawals from familiar substances. When the substance is known, it should be reflected in the name of the disorder upon coding (e.g., “betel nut withdrawal”). Prevalence The prevalence of other (or unknown) substance withdrawal is unknown. Development and Course Withdrawal signs commonly appear some hours after use of the substance is terminated, but the onset and course vary greatly, depending on the dose typically used and the rate of elimination of the specific substance from the body. At peak severity, withdrawal symptoms from some substances involve only moderate levels of discomfort, whereas withdrawal from other substances may be fatal. Withdrawal-associated dysphoria often motivates relapse to substance use. Withdrawal symptoms slowly abate over days, weeks, or months, depending on the particular drug and doses to which the individual became tolerant. Functional Consequences of Other (or Unknown) Substance Withdrawal Withdrawal from any substance may have serious consequences, including physical signs and symptoms (e.g., malaise, vital sign changes, abdominal distress, headache), intense drug craving, anxiety, depression, agitation, psychotic symptoms, or cognitive impairments. These consequences may lead to problems such as dysfunction at work, problems in interpersonal relationships, failure to fulfill role obligations, traffic accidents, fighting, high-risk behavior (e.g., having unprotected sex), suicide attempts, and substance or medication overdose. The pattern of consequences will vary with the particular substance.

Dose reduction after extended dosing, but not meeting the criteria for other (or unknown) substance withdrawal. Substance withdrawal or other substance/medication-induced mental disorders. Other toxic, metabolic, traumatic, neoplastic, vascular, or infectious disorders that impair brain function and cognition. Differential Diagnosis The individual used other (or unknown) substances, but the dose that was used was insufficient to produce symptoms that meet the criteria required for the withdrawal diagnosis. Familiar substances may be sold in the black market as novel products, and individuals may experience withdrawal when discontinuing those substances. History, toxicology screens, or chemical testing of the substance itself may help to identify it. Other substance withdrawal is distinguished from other substance/medication-induced mental disorders (e.g., venlafaxineinduced anxiety disorder, with onset during withdrawal) because the symptoms (e.g., anxiety) in these latter disorders are in excess of symptoms (if known) usually associated with the specific substance withdrawal, predominate in the clinical presentation, and are severe enough to warrant clinical attention. Numerous neurological and other medical conditions may produce rapid onset of signs and symptoms mimicking those of withdrawals. Paradoxically, drug intoxications also must be ruled out; for example, lethargy may indicate withdrawal from one drug or intoxication with another substance. Comorbidity As with all substance-related disorders, conduct disorder in adolescence, antisocial personality disorder, and other substance use disorders are likely to co-occur with other (or unknown) substance withdrawal. Other (or Unknown) Substance–Induced Mental Disorders Because the category of other or unknown substances is inherently ill-defined, the extent and range of these substance-induced mental disorders are uncertain. Nevertheless, other (or unknown) substance–induced mental disorders are possible and are described in other chapters of the manual with disorders with which they share phenomenology (see the substance/medicationinduced mental disorders in these chapters): other (or unknown) substance–induced psychotic disorder (“Schizophrenia Spectrum and Other Psychotic Disorders”); other (or unknown) substance–induced bipolar and related disorder (“Bipolar and Related Disorders”); other (or unknown) substance–induced depressive disorder (“Depressive Disorders”); other (or unknown) substance–induced anxiety disorders (“Anxiety Disorders”); other (or unknown) substance– induced obsessive-compulsive disorder (“Obsessive-Compulsive and Related Disorders”); other (or unknown) substance–induced sleep disorder (“Sleep-Wake Disorders”); other (or unknown) substance–induced sexual dysfunction (“Sexual Dysfunctions”); and other (or unknown)

F63.0 substance/medication–induced major or mild neurocognitive disorder (“Neurocognitive Disorders”). For other (or unknown) substance–induced intoxication delirium, other (or unknown) substance–induced withdrawal delirium, and delirium induced by other (or unknown) substance taken as prescribed, see the criteria and discussion of delirium in the chapter “Neurocognitive Disorders.” These other (or unknown) substance–induced mental disorders are diagnosed instead of other (or unknown) substance intoxication or other (or unknown) substance withdrawal only when the symptoms are sufficiently severe to warrant independent clinical attention. Unspecified Other (or Unknown) Substance–Related Disorder F19.99 This category applies to presentations in which symptoms characteristic of an other (or unknown) substance–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 other (or unknown) substance–related disorder or any of the disorders in the substance-related disorders diagnostic class. Non-Substance-Related Disorders Gambling Disorder Diagnostic Criteria A. Persistent and recurrent problematic gambling behavior leading to clinically significant impairment or distress, as

indicated by the individual exhibiting four (or more) of the following in a 12-month period:

1. Needs to gamble with increasing amounts of money in order to achieve the desired excitement.
2. Is restless or irritable when attempting to cut down or stop gambling.
3. Has made repeated unsuccessful efforts to control, cut back, or stop gambling.
4. Is often preoccupied with gambling (e.g., having persistent thoughts of

reliving past gambling experiences, handicapping or planning the next venture, thinking of ways to get money with which to gamble). 5. Often gambles when feeling distressed (e.g., helpless, guilty, anxious, depressed). 6. After losing money gambling, often returns another day to get even ("chasing" one's losses). 7. Lies to conceal the extent of involvement with gambling. 8. Has jeopardized or lost a significant relationship, job, or educational or career opportunity because of gambling. 9. Relies on others to provide money to relieve desperate financial situations caused by gambling. B. The gambling behavior is not better explained by a manic episode. Specify if: Episodic: Meeting diagnostic criteria at more than one time point, with symptoms subsiding between periods of gambling disorder for at least several months. Persistent: Experiencing continuous symptoms, to meet diagnostic criteria for multiple years. Specify if: In early remission: After full criteria for gambling disorder were previously met, none of the criteria for gambling disorder have been met for at least 3 months but for less than 12 months. In sustained remission: After full criteria for gambling disorder were previously met, none of the criteria for gambling disorder have been met during a period of 12 months or longer. Specify current severity: Mild: 4–5 criteria met. Moderate: 6–7 criteria met. Severe: 8–9 criteria met. Note: Although some behavioral conditions that do not involve ingestion of substances have similarities to substance-related disorders, only one disorder—gambling disorder— has sufficient data to be included in this section. Specifiers Severity is based on the number of criteria endorsed. Individuals with mild gambling disorder may exhibit only 4–5 of the criteria, with the most frequently endorsed criteria usually related to preoccupation with gambling and "chasing" losses. Individuals with moderately severe gambling disorder exhibit more of the criteria (i.e., 6–7). Individuals with the most severe form will exhibit

all or most of the nine criteria (i.e., 8–9). Jeopardizing relationships or career opportunities because of gambling and relying on others to provide money for gambling losses are typically the least often endorsed criteria and most often occur among those with more severe gambling disorder. Furthermore, individuals presenting for treatment of gambling disorder typically have moderate to severe forms of the disorder. Diagnostic Features Gambling involves risking something of value in the hopes of obtaining something of greater value. In many cultures, individuals gamble on games and events, and most do so without experiencing problems. However, some individuals develop substantial impairment related to their gambling behaviors. The essential feature of gambling disorder is persistent and recurrent maladaptive gambling behavior that disrupts personal, family, and/or vocational pursuits (Criterion A). Gambling disorder is defined as a cluster of four or more of the symptoms listed in Criterion A occurring at any time in the same 12-month period. A pattern of "chasing one's losses" may develop, with an urgent need to continue gambling (often with placing larger bets or taking greater risks) to undo a loss or series of losses. The individual may abandon a gambling strategy and try to win back losses all at once. Although many gamblers may "chase" for short periods of time, it is the frequent, and often long-term, "chase" that is characteristic of

gambling disorder (Criterion A6). Individuals may lie to family members, therapists, or others to conceal the extent of involvement with gambling; these instances of deceit may also include, but are not limited to, covering up illegal behaviors such as forgery, fraud, theft, or embezzlement to obtain money with which to gamble (Criterion A7). Individuals may also engage in “bailout” behavior, turning to family or others for help with a desperate financial situation that was caused by gambling (Criterion A9). In some cases, symptoms meeting diagnostic criteria for gambling disorder may occur as a direct physiological consequence of taking dopaminergic medications, such as those used to treat Parkinson’s disease. When such symptoms are induced by a medication, these cases would be diagnosed as gambling disorder. Associated Features Distortions in thinking (e.g., denial, superstitions, a sense of power and control over the outcome of chance events, overconfidence) may be present in individuals with gambling disorder. Many individuals with gambling disorder believe that money is both the cause of and the solution to their problems. Some individuals with gambling disorder are impulsive, competitive, energetic, restless, and easily bored; they may be overly concerned with the approval of others and may be generous to the point of extravagance when winning. Other individuals with gambling disorder are depressed and lonely, and they may gamble when feeling helpless, guilty, or depressed. Prevalence The past-year prevalence rate of gambling disorder is about 0.2%–0.3% in the general U.S. population, with a range of 0.1%–0.7% observed across international studies. In the

general U.S. population, the lifetime prevalence rate is about 0.4%–1.0%. For women, the lifetime prevalence rate of gambling disorder is about 0.2%, and for men it is about 0.6%. The 12-month prevalence of DSM-5 gambling disorder varies among ethnoracial groups in the United States: it is 0.52% in African Americans, 0.25% in Latinx, and 0.23% in non-Latinx Whites. Development and Course The onset of gambling disorder can occur during adolescence or young adulthood, but in other individuals it manifests during middle or even older adulthood. Generally, gambling disorder develops over the course of years, although the progression appears to be more rapid in women than in men. National data from the United States and Canada show that most individuals who develop a gambling disorder evidence a pattern of gambling that gradually increases in both frequency and amount of wagering. Certainly, milder forms can develop into more severe cases. Most individuals with gambling disorder report that one or two types of gambling are most problematic for them, although some individuals participate in many forms of gambling. Individuals are likely to engage in certain types of gambling (e.g., buying scratch tickets daily) more frequently than others (e.g., playing slot machines or blackjack at the casino weekly). Frequency of gambling can be related more to the type of gambling than to the severity of the overall gambling disorder. For example, purchasing a single scratch ticket each day may not be problematic, while less frequent casino, sports, or card gambling may be part of a gambling disorder. Similarly, amounts of money spent wagering are not in themselves indicative of gambling disorder. Some individuals can wager thousands of dollars per month and not have a problem with gambling, while others may wager much smaller amounts but experience substantial gambling-related difficulties. Gambling patterns may be regular or episodic, and gambling disorder can be persistent or in remission. Gambling can increase during periods of stress or depression and during periods of substance use or abstinence. There may be periods of heavy gambling and severe problems, times of total abstinence, and periods of nonproblematic gambling. Gambling disorder is sometimes associated with spontaneous, long-term remissions. Nevertheless, some individuals underestimate their vulnerability to develop gambling disorder or to relapse following remission. When in a period of remission, they may incorrectly assume that they will have no problem regulating gambling and

that they can engage in some forms of gambling nonproblematically, only to experience a relapse of gambling disorder. Early expression of gambling disorder is more common among young men (ages 18–21 years) than among young women. Individuals who begin gambling in youth often do so with family members or friends. Development of early-life gambling disorder appears to be associated with impulsivity and substance abuse. Internet gambling has been linked to risky and problematic gambling among youth and may be conducted in a more isolative (i.e., nonpeer) fashion. Some video gaming characteristics (e.g., loot boxes or loot crates containing prizes determined by chance that may be of higher or lower value or desirability) overlap with gambling behavior and may influence the course of gambling disorder. Many high school and college students who develop gambling disorder grow out of the disorder over time, although it remains a lifelong problem for some. Mid- and later-life onset of gambling disorder is more common among women than among men.

Temperamental. Genetic and physiological. Course modifiers. There are age and gender variations in the type of gambling activities and the prevalence rates of gambling disorder. Gambling disorder in the United States is more common among younger and middle-age individuals than among older adults. Among U.S. young adults (ages 18–21 years), the disorder is more prevalent in young men than in young women. Younger individuals prefer different forms of gambling (e.g., sports betting), whereas older adults are more likely to develop problems with slot machine and bingo gambling. Although the proportions of individuals who seek treatment for gambling disorder are low across all age groups in the United States, younger individuals are especially unlikely to present for treatment. Risk and Prognostic Factors Gambling that begins in childhood or early adolescence is associated with increased rates of gambling disorder. Gambling disorder also appears to aggregate with antisocial personality disorder, depressive and bipolar disorders, and other substance use disorders, particularly alcohol use disorder. Gambling disorder can aggregate in families, and this effect appears to relate to both environmental and genetic factors. Gambling problems are more frequent in monozygotic than in dizygotic twins. Gambling disorder is also more prevalent among firstdegree relatives of individuals with moderate to severe alcohol use disorder than among the general population. Many individuals, including adolescents and young adults, are likely to resolve their problems with gambling disorder over time, although a strong predictor of future gambling problems is previous gambling problems. Psychopathology, including attentiondeficit/hyperactivity and anxiety disorders, has been found to be associated with increased risk of onset of gambling disorder among those who gamble and with persistence of gambling disorder symptoms over time. Culture-Related Diagnostic Issues Types of gambling activities vary across cultural contexts and ethnoracial groups (e.g., pai gow, cockfights, blackjack, horse racing). Some Indigenous populations in Canada, New Zealand, and the United States have high prevalence rates of gambling problems, possibly related to limited economic opportunities, the expectation that gambling may help advance social goals, and the location of casinos on some U.S. tribal lands. U.S.-born individuals have higher rates of gambling problems than first-generation immigrants to the United States. Endorsement of specific disorder criteria may vary across ethnoracial groups. For example, among individuals with gambling problems, Asian Americans may be less likely than other groups to endorse being preoccupied with gambling (Criterion A4), while African Americans and Latinx may be more likely to endorse repeated unsuccessful efforts to control gambling (Criterion A3). Sex- and Gender-Related Diagnostic Issues Men develop gambling disorder at higher rates than women, although this gender gap may be narrowing. Data from treatment-seeking populations have suggested that women may develop

Nondisordered gambling. Manic episode. gambling problems more rapidly after the onset of gambling (so-called telescoping), although general population data suggest that men progress more rapidly to disordered gambling than women do. Although women seek treatment sooner than men do, rates of treatment seeking in U.S. national surveys are low (< 10%) among individuals with gambling disorder regardless of gender. Women may gamble as a maladaptive approach to negative affect, whereas men may gamble more for the thrill of it. Compared with men, women may also experience more shame related to gambling. Men tend to wager on different forms of gambling than women, with cards, sports, and horse race gambling more prevalent among men, and slot machine and bingo gambling more common among women. Women with gambling disorder are more likely than men with gambling disorder to have depressive, bipolar, and anxiety disorders. Association With Suicidal Thoughts or Behavior In a U.S. study, up to half of individuals in treatment for gambling disorder in Connecticut reported suicidal thoughts, and about 17% reported attempted suicide. A nationwide register study in Sweden showed that compared with individuals without gambling disorder, individuals ages 20–74 years with gambling disorder have a 15-fold increased suicide mortality rate. Functional Consequences of Gambling Disorder Areas of psychosocial, health, and mental health functioning may be adversely affected by gambling disorder. Specifically, individuals with gambling disorder may, because of their involvement with gambling, jeopardize or lose important relationships with family members or friends. Such problems may occur from repeatedly lying to others to cover up the extent of gambling or from requesting money that is used for gambling or to pay off gambling debts. Employment or educational activities may likewise be adversely impacted by gambling disorder; absenteeism or poor work or school performance can occur with gambling disorder, as individuals may gamble during work or school hours or be preoccupied with gambling or its adverse consequences when they should be working or studying. Individuals with gambling disorder in a U.S. national sample had poor general health and utilized medical services at high rates. Differential Diagnosis Gambling disorder must be distinguished from professional and social gambling. In professional gambling, risks are limited and discipline is central. Social gambling typically occurs with friends or colleagues and lasts for a limited period of time, with acceptable losses. Some persons can experience problems associated with gambling (e.g., short-term chasing behavior and loss of control) that do not meet the full criteria for gambling disorder. Loss of judgment and excessive gambling may occur during a manic episode. An additional diagnosis of gambling disorder should be given only if the gambling behavior is not better explained by manic episodes (e.g., a history of maladaptive gambling behavior at times other than during a manic episode). Alternatively, an individual with gambling disorder may,

Personality disorders. Gambling symptoms due to dopaminergic medications. during a period of gambling, exhibit behavior that resembles a manic episode, but once the individual is away from the gambling, these manic-like features dissipate. Problems with gambling may occur in individuals with antisocial personality disorder and other personality disorders. If the criteria are met for both disorders, both can be diagnosed. Some individuals taking dopaminergic medications (e.g., for Parkinson‘s disease) may experience urges to gamble that might be distressing or impairing enough to meet criteria for gambling disorder. In such cases, a diagnosis of gambling disorder would be warranted. Comorbidity Gambling disorder is associated with poor general health. In addition, some specific medical conditions, such as tachycardia and angina, are more common among individuals with gambling disorder than in the general population, even when other substance use disorders, including tobacco use disorder, are controlled for. In U.S. national surveys, individuals with gambling disorder have high rates of comorbidity with other mental

disorders, such as substance use disorders, depressive disorders, anxiety disorders, and personality disorders. In some individuals, other mental disorders may precede gambling disorder and be either absent or present during the manifestation of gambling disorder. Gambling disorder may also occur prior to the onset of other mental disorders, especially bipolar and related disorders, anxiety disorders, and substance use disorders. In a U.S. national survey, in approximately three-quarters of cases of individuals with gambling disorder and another mental disorder, other psychopathology preceded the gambling disorder.

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