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Wolters Kluwer

Methamphetamine use disorder: Epidemiology, clinical features, and diagnosis

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INTRODUCTION

Methamphetamine is a psychostimulant that causes the release and blocks the reuptake of monoamine neurotransmitters, including dopamine, norepinephrine, and serotonin. Methamphetamine is most often smoked or snorted and is less commonly injected or ingested orally.

Clinical manifestations of methamphetamine use include increased energy and alertness, euphoria, sympathetic nervous system activation, decreased need for sleep, weight loss, dry mouth leading to tooth decay, and chronic adverse mood and cognitive changes, including irritability, anxiety, aggression, panic, suspiciousness, and/or paranoia, hallucinations, executive dysfunction, and memory impairment. Methamphetamine can also exacerbate existing psychiatric symptoms [1].

The psychiatric diagnoses, methamphetamine abuse and methamphetamine dependence, were replaced by a single diagnosis, amphetamine-type substance and are found under the broader category of stimulant use disorders in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) [2]. Although the crosswalk between the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) and DSM-5-TR disorders is imprecise, methamphetamine dependence is approximately comparable to amphetamine-type substance use disorder, moderate to severe subtype, while methamphetamine abuse is similar to the mild subtype.

This topic describes the epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis of methamphetamine use disorder. The epidemiology, pathogenesis, clinical manifestations, course, assessment, diagnosis, and treatment of other stimulant use disorders are discussed separately. (See "[Cocaine use disorder: Epidemiology, clinical features, and diagnosis](#)" and "[Stimulant use disorder: Treatment overview](#)".)

EPIDEMIOLOGY

Methamphetamine use varies geographically, but overall, amphetamine-type stimulants, which include methamphetamine, are the fastest rising drug of abuse worldwide [3,4]. Amphetamine-type stimulants have become the second most widely used class of illicit drugs worldwide, with use increasing in Asia and Oceania [5].

Prevalence — An estimated 4.7 million Americans (2.1 percent of the United States population) have reportedly tried methamphetamine at some time in their lives [6]. The rate of methamphetamine use in the United States appears to be similar among males and females (0.32 versus 0.23 percent) [7].

Methamphetamine use in the United States increased in the 1990s, reaching epidemic proportions in the early 2000s in the western and midwestern parts of the United States [8]. As a consequence of regulations reducing access to methamphetamine precursors (eg, [pseudoephedrine](#)), United States prevalence indicators for the drug began to decrease in the mid-2000s [9]. Between 2008 and 2014, the United States prevalence rate was found to be stable, with approximately 569,000 current users [10-12].

Evidence suggests that in the United States, the use of methamphetamine and overdose deaths due to methamphetamine are on the rise again [13]. In the past decade, there have been alarming trends in the epidemiology and mortality of methamphetamine use in the United States. For example, a study investigating the trends in methamphetamine related deaths reported a 58-fold increase in methamphetamine-related deaths and a more than 50-fold increase in the age-adjusted mortality rate [14]. This escalation is further complicated by the co-involvement of heroin or [fentanyl](#), ranging from 7 to 61 percent, with stark increases observed over the last decade. The co-use of methamphetamine and opioids contributed significantly to this mortality trend.

In addition, according to a national survey, while past-year methamphetamine use increased by 43 percent (1.4 million [95% CI 1.2-1.6 million] to 2 million [95% CI 1.7-2.3 million]) in a five-year period ending in 2019, overdose deaths attributed to psychostimulants other than cocaine

(largely methamphetamine) increased by 180 percent (ie, 5524 to 15,489) in the same time period [13]. Data from law enforcement groups, welfare agencies, and substance use treatment programs indicate that methamphetamine continues to be a significant public health problem [15].

During the coronavirus disease (COVID-19) pandemic, increased emergency department visits provide further evidence of increased methamphetamine use [16].

In a United Nations report, the rates of methamphetamine use in other countries ranged from 0.2 to 1.3 percent of the population aged 15 to 64 years [5]. This is similar to the rates in the United States. Over the past two decades, the use of amphetamine and methamphetamine became quite widespread in different regions across the world but was particularly dominant in East and Southeast Asia and North America [17].

Comorbidity — Individuals with diagnosed chronic methamphetamine use show high rates of comorbid psychiatric disorders. For example, in a study of 189 individuals with methamphetamine dependence, co-occurring primary psychotic disorders were found among 29 percent, primary mood disorders were found among 32 percent and primary anxiety disorders were found among 27 percent [18]. Further data supporting relationships between methamphetamine use disorder and psychiatric comorbidity include:

- In a cohort study, an increased risk of psychotic symptoms was found in individuals who use methamphetamine versus the general population (odds ratio 1.3, 95% CI 1.03-1.72) [19].
- In a sample of 214 individuals who used methamphetamine at least weekly and were enrolled in a clinical trial of a psychotherapeutic treatment for methamphetamine use, more than 70 percent had depressive symptoms of a severity meeting diagnostic criteria for major depression. Greater depressive symptom severity in the sample was associated with greater methamphetamine use [20].
- In one population-based sampling, elevated rates of panic disorder (adjusted prevalence ratio 4.7, 95% CI 1.1-19.0) and posttraumatic stress disorder (adjusted prevalence ratio 1.7, 95% CI 1.1-2.6) were found in individuals using methamphetamine compared with those who do not use methamphetamine [21].
- Approximately one-third to 40 percent of individuals with methamphetamine use disorder in samples studied have been assigned a lifetime diagnosis of attention deficit hyperactivity disorder [22].

- According to a national survey, the percentage of individuals using heroin who report use of methamphetamine increased from 9 percent to 44 percent over a five-year period ending in 2019 [23].

HEALTH CONSEQUENCES

Mortality

All-cause mortality and suicide — Methamphetamine use has been associated with increased risk of early mortality and suicide attempts [24-26]. As examples:

- In a retrospective study of 1254 subjects with methamphetamine dependence who were admitted to a psychiatric center, the five-year rate of all-cause mortality was approximately 5 percent, an observed death rate 26 times greater than expected in females and six times greater than expected in males [24].
- Rates of self-reported suicide attempts have been found to be much higher in problem amphetamine users compared with non-drug-using peers of the same age, sex, and socioeconomic status [25].

Fatal overdose/fentanyl contamination — Methamphetamine and cocaine users face a growing risk of fatal overdose from [fentanyl](#) contamination of the stimulants. Fentanyl, a highly potent synthetic opioid, can cause death via respiratory depression, particularly in opioid naïve people who have not developed tolerance. A study of a randomly selected national sample of one million urine drug test results from a wide variety of health care settings in the United States found that, in comparison with 2013, the rate of tests positive for cocaine that were also positive for nonprescribed fentanyl increased by 1850 percent, from 0.9 percent (95% CI 0.7-1.1) to 17.6 percent (95% CI 16.1-19.1) [27]. The rate of tests positive for methamphetamine that were also positive for fentanyl increased by 798 percent, from 0.9 percent (95% CI 0.6-1.2) in 2013 to 7.9 percent (95% CI 7.1-8.7) in 2018.

Cardiovascular disease — Cardiovascular complications such as malignant hypertension, arrhythmias, aortic dissection, myocardial infarction secondary to vasospasm, stroke, and cardiomyopathy are the leading causes of death among methamphetamine users [28,29].

Among patients with cardiomyopathy in one hospital system, the proportion of cases associated with methamphetamine increased from 1.8 (in 2009) to 5.6 percent (in 2014) [30]. In a retrospective cohort analysis, as many as 72 percent of methamphetamine users showed

electrocardiogram abnormalities including tachyarrhythmias, right axis deviation, left ventricular hypertrophy, and QTc prolongation [31].

In a systematic review of 21 observational studies, methamphetamine-associated heart failure showed an increasing prevalence while affecting various racial, ethnic, and sociodemographic groups [29]. Males were predominant in this group; up to 44 percent having preserved left ventricular ejection fraction. Methamphetamine-associated heart failure was found to be associated with elevated morbidity and worse heart failure symptoms as compared with non-methamphetamine-related heart failure. Positive predictors of recovery included female sex, methamphetamine abstinence, and guideline-directed heart failure therapy. Specific echocardiography chamber dimensions indicating lack of chronicity and degree of fibrosis on biopsy were associated with increased odds of improvement.

Stroke — Adults who use methamphetamine have an approximately fivefold increased risk of a hemorrhagic stroke. As examples:

A study described 250 adults who presented at a United States emergency department of a university medication center with an intracerebral hemorrhage between 2013 and 2015 [32]. Forty-one of the patients had a positive toxicology test for methamphetamine. Hemorrhagic stroke patients who used methamphetamine were younger than stroke patients who did not (a mean of 52 versus 67 years) and had less premorbid neurologic disability but had higher diastolic blood pressure, longer intensive care unit and hospital stays, and no difference in neurologic disability from non-methamphetamine users at hospital discharge. Intracerebral hemorrhage is an important cause of premature disability and death associated with the methamphetamine use.

Another review article described 98 published case reports of strokes in adults younger than 45 years associated with methamphetamine use [33]. Outcomes of younger adults with methamphetamine-associated strokes were generally poor.

Renal dysfunction — Methamphetamine use appears to be associated with increased risk of renal dysfunction. In a meta-analysis including 9 trials and a total of 1884 subjects, methamphetamine use was found to increase both blood urea nitrogen and creatinine, respectively, raising the possibility that methamphetamine intoxication is linked with increased risk of renal dysfunction, potentially leading to organ failure [34].

Prenatal methamphetamine exposure — Prenatal methamphetamine exposure is associated with lower birth weight [35], shorter body length, smaller head circumference [36], and neurocognitive abnormalities [37].

Risky sexual behaviors — Users of methamphetamine typically have more sexual partners and are more likely to engage in risky sexual behaviors compared with controls [38-40], partly because methamphetamine enhances libido. The odds of risky sex for heterosexual methamphetamine users is, on average, between 37 and 72 percent greater compared with non-methamphetamine users [41].

Some researchers suggest that risky behaviors and methamphetamine use are associative but not causal [30]; however, other data are cause for concern. The number of reported primary and secondary syphilis cases associated with, among other drugs, methamphetamine more than doubled from 2013 to 2017 [42]. A representative sample of 9th to 12th grade high school students in the United States found that lifetime methamphetamine use was associated with greater likelihoods of recent sexual intercourse, multiple recent sexual partners, and pregnancy [40].

PATHOGENESIS

Methamphetamine is a psychostimulant that causes an increase in the synapse of monoamine neurotransmitters including dopamine, norepinephrine, and serotonin via the following molecular mechanisms [43]:

- Redistribution of catecholamines from synaptic vesicles to the cytosol
- Reversal of transport of neurotransmitter through plasma membrane transporters
- Blocking the activity of monoamine transporters
- Decreasing the expression of dopamine transporters at the cell surface
- Inhibiting monoamine oxidase activity
- Increasing the activity and expression of tyrosine hydroxylase, the critical enzyme for synthesizing dopamine

Methamphetamine use exerts its effects largely via the dopamine system. The consequence of the above processes is that dopamine becomes highly concentrated in the synaptic cleft and is available to postsynaptic uptake and subsequent signaling ([figure 1](#)). A figure depicts the chemical structure of methamphetamine ([figure 2](#)).

Neuroimaging studies have shown that methamphetamine dependent individuals have:

- Lower striatal and orbitofrontal dopamine D₂/D₃ receptor availability [44,45], which is associated with higher impulsivity [46].

- Lower dopamine transporter and vesicular monoamine transporter type-2 in the striatum [47] as well as in orbitofrontal and dorsolateral prefrontal cortex [48], which persists even after protracted sobriety [49].

Neurotoxicity — Methamphetamine use may lead to death of nerve cells as a consequence of multiple intracellular processes, but the evidence to date has not been conclusive.

Research in animals suggests that human brain structures that are highly sensitive to oxidative stress, such as the hippocampus, may be affected by chronic methamphetamine use. Extensive studies in animals have shown that methamphetamine increases the blood brain barrier permeability, which most sensitively affects hippocampus [50]. Several molecular mechanisms have been proposed to contribute to methamphetamine-induced neurotoxicity, including [51]:

- Oxidative stress (eg, free radicals in the intracellular space)
- Excitotoxic mechanisms (eg, excessive glutamate)
- Neuroinflammation (eg, inflammation of the glia)
- Ubiquitin proteasome system, dysfunctional recycling of proteins
- Mitochondrial dysfunction (eg, abnormal carbohydrate metabolism)
- Protein nitration
- Endoplasmatic reticulum stress
- Microtubule deacetylation
- Neurotrophic factor dysfunction (eg, altered growth or development of neurons and glia)

Changes in the blood brain barrier may enable the entry of pathogens into the brain parenchyma, thus decreasing the endogenous brain repair resources [52].

Postmortem studies of brains of methamphetamine users have found some evidence of neurotoxicity [53,54].

Inflammation — Methamphetamine may directly affect inflammatory processes via its binding to the toll-like receptor 4 (TLR-4) [55]. This activation results in nuclear factor kappa B activation of microglia and proinflammatory cytokine response such as TNF-alpha, IL-6, and IL-1beta, which can be observed in increased levels in the central nervous system after acute or repeated drug use [56]. These and other findings have been used to propose that inflammatory processes may play a significant role in the development of methamphetamine use disorder [57].

CLINICAL MANIFESTATIONS

The clinical effects of methamphetamine use are almost immediate, in part due to the routes of administration. The drug has been found most often to be smoked (68 percent) or snorted (31 percent), and less commonly to be injected (7 percent) or orally ingested (3 percent) [58].

Methamphetamine rapidly enters well-perfused organs, including the brain, and has a half-life of approximately 9 to 13 hours [59]. Methamphetamine can accumulate in the brain in concentrations up to 10 times greater than those in the plasma [60].

The acute behavioral effects of methamphetamine include [61]:

- Increased energy and alertness
- Decreased need for sleep
- Euphoria
- Increased sexuality
- Excessive talking
- Sweating
- Disrupted sleep patterns
- Tightened jaw muscles
- Grinding teeth
- Loss of appetite, contributing to weight loss with chronic use
- Disorganized thinking
- Itching
- Gastrointestinal symptoms such as nausea, vomiting, or diarrhea
- Dry mouth leading to serious tooth decay with chronic use
- Changes in mood consisting of irritability, anxiety, aggression, or panic
- Other signs of sympathetic nervous system activation including pupillary dilatation, increased heart rate and other cardiovascular changes

Psychosis — A meta-analysis estimates that between 37 and 43 percent of individuals exposed to methamphetamine develop methamphetamine-induced psychotic disorder [62]. Other studies suggest a bidirectional relationship between methamphetamine use and psychosis [63]. (See 'Comorbidity' above.)

The predominant symptoms are paranoia, persecutory delusions, auditory, visual, and tactile hallucinations. Methamphetamine-associated psychosis is often characterized by relatively long duration of psychosis and recurrence during periods of abstinence from the drug [64-67].

Catatonia — A systematic review concluded that clinicians should consider the potential relationship between methamphetamine use and catatonia [68].

Cognitive effects — Evidence of the effect of chronic methamphetamine use on cognition is mixed [69-73]. A longitudinal study of drug users in China suggested methamphetamine use was associated with increased cognitive impairment [74]. Furthermore, a meta-analysis examining the neuropsychological effects of methamphetamine use disorder reported medium effect-sized deficits in episodic memory, executive functions, information processing, motor skills, language and visuoconstructional abilities (eg, having difficulties copying geometric figures) [75]. Evidence suggests that cognitive measures of impulsivity associated with methamphetamine use do not improve with early abstinence [76].

The clinical significance of cognitive impairments associated with long-term methamphetamine use is uncertain. Cognitive functioning in methamphetamine users has been found to fall overwhelmingly within the normal range when compared against normative data [69].

Abstinence syndrome — Individuals experience an early abstinence syndrome after cessation of methamphetamine use, which manifests as one or more symptoms including [77]:

- Anhedonia
- Irritability
- Poor concentration
- Hyperphagia
- Insomnia or hypersomnia
- Psychomotor agitation or retardation

Most of these symptoms appear to resolve within two weeks, although sleep disruption was reported for as long as four weeks in a small sample [78]. This is consistent with 2016 findings suggesting rapid recovery of stored dopamine in some methamphetamine users who become abstinent [79].

ONSET AND COURSE

In a nationally representative United States survey, approximately five percent of respondents who used nonprescribed stimulants were estimated to become stimulant-dependent (DSM-IV) over a two-year period [80]. Methamphetamine users were more likely to become dependent soon after onset of use compared with users of other stimulants.

Furthermore, a six-year longitudinal study including 5034 12th grade students found that cocaine use or prescription stimulant misuse by age 18 years, but not a prior history of prescriptions stimulant use as prescribed for attention deficit hyperactivity disorder, are associated with onset of methamphetamine (or cocaine) use during you adulthood (age 19 to

24 years) [81]. (See "[Cocaine use disorder: Epidemiology, clinical features, and diagnosis](#)", section on 'Epidemiology'.)

Little is known about the factors that influence the transition from use of methamphetamine to methamphetamine use disorder.

Methamphetamine addiction is often characterized by repeated periods of intense use with intermittent sobriety and relapse [82,83]. Although there are few long-term studies, an analysis of methamphetamine use in 474 individuals with chronic use over a 10-year period following initiation found that subjects used the drug an average of approximately 12 days per month [84]. Analyses revealed five distinct trajectories of drug use:

- Increasing use, 15 percent
- Decreasing use, 21 percent
- High use, 22 percent
- Moderate use, 35 percent
- Low use, 7 percent

There has been limited study of patient characteristics associated with treatment completion or outcome. In an analysis of 113,575 outpatient or residential treatment episodes for methamphetamine abuse or dependence from 1992 to 2002, noncompletion of treatment was associated with patient and clinical characteristics including [85]:

- Less than a high school education
- Younger age at treatment admission
- Concurrent disability
- Greater severity of methamphetamine use prior to treatment
- Methamphetamine injection

Individuals who inject methamphetamine have been found to have particularly poor treatment outcomes in other studies. As an example, in a study of 974 methamphetamine users in outpatient treatment, patients who injected the drug, relative to those using other routes of administration, had [86]:

- Poorer treatment engagement
- Greater drug use during treatment
- Lower rates of treatment completion
- Greater methamphetamine use 12 months following treatment

Social pressure to use methamphetamine is a leading antecedent of relapse, based on our experience as well as a study of 60 patients in Taiwan [87]. These interactions may be mediated by social adaptation, emotional stability, and education level.

ASSESSMENT

The initial examination of the patient should focus on the characteristics of current use (ie, the pattern, amount, and progression of recent use, and the route of administration). Given the clinical effects of methamphetamine use, the significant comorbidity of other psychiatric disorders, and the medical consequences of methamphetamine use, patients should also be assessed for:

- Presence of depression, anxiety, psychosis, and suicidality.
 - Use of other substances.
 - Personality disorders.
 - Medical conditions, including cardiovascular and central nervous system disease. Risk of stroke, seizures, heart disease (including cardiac valve abnormalities, angina, arrhythmias) should be evaluated. An electrocardiogram should be performed.
 - Socio-cultural context of methamphetamine use, which is important for identifying factors that might predict relapse (eg, regular contact with peers or partners who continue to use the drug). Evidence from 2016 suggests that the experience of childhood physical abuse may be means through which family history of substance use is associated with an earlier age of first drug use [88].
 - Urine toxicology tests can identify whether or not methamphetamine has been used, but no current laboratory or neuroimaging tests can be useful in diagnosing methamphetamine use disorder. No clinical tests can predict outcomes of these disorders following treatment.
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DIAGNOSIS

The psychiatric diagnoses, methamphetamine abuse and methamphetamine dependence, were replaced by a single diagnosis, amphetamine-type substance and are found under the broader category of stimulant use disorders in DSM-5-TR [2]. DSM-5-TR diagnostic criteria for methamphetamine use disorder are described below.

DSM-5-TR criteria — A problematic pattern of amphetamine-type substance, cocaine or other stimulant use (eg, methamphetamine use) leading to clinically significant impairment or distress, as manifested by two or more of the following within a 12-month period:

- Methamphetamine is often taken in larger amounts or over a longer period than was intended
- There is a persistent desire or unsuccessful efforts to cut down or control methamphetamine use
- A great deal of time is spent in activities necessary to obtain methamphetamine, use methamphetamine, or recover from its effects
- Craving, or a strong desire or urge to use methamphetamine
- Recurrent methamphetamine use resulting in a failure to fulfill major role obligations at work, school, or home
- Continued methamphetamine use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of methamphetamine
- Important social, occupational, or recreational activities are given up or reduced because of methamphetamine use
- Recurrent methamphetamine use in situations in which it is physically hazardous
- Continued methamphetamine use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by methamphetamine
- Tolerance*
- Withdrawal*

*These criteria are not considered to be met for those taking methamphetamine solely under appropriate medical supervision, such as for attention deficit hyperactivity disorder or narcolepsy.

Specifiers for the diagnosis include:

- In early remission – After full criteria for methamphetamine use disorder were previously met, none of the criteria for methamphetamine use disorder have been met (with the exception of craving) for at least three months but less than 12 months

- In sustained remission – After full criteria for methamphetamine use disorder were previously met, none of the criteria for methamphetamine use disorder have been met (with the exception of craving) during a period of 12 months or longer
- In a controlled environment – If the individual is in an environment where access to methamphetamine is restricted

The severity of methamphetamine use disorder at the time of diagnosis can be specified as a subtype based on the number of symptoms present:

- Mild: Two to three symptoms
- Moderate: Four to five symptoms
- Severe: Six or more symptoms

Most clinical trials of treatments for methamphetamine use were conducted in samples limited to patients with methamphetamine dependence in DSM-IV-TR or an earlier edition. Applying trial results to patients diagnosed with DSM-5-TR methamphetamine use disorder is imprecise; the most closely comparable patients are those with methamphetamine use disorder, moderate to severe subtype. Methamphetamine abuse is similar to the mild subtype of methamphetamine use disorder.

Comorbid conditions — Diagnosis of a comorbid psychiatric disorder (most commonly, an anxiety, depressive, or psychotic disorder, or attention deficit hyperactivity disorder) may be difficult when the individual is actively using methamphetamine, because methamphetamine use can induce these symptoms. A drug-free period of at least a month is suggested before diagnosing one of these mental disorders [89]. (See '[Comorbidity](#)' above.)

Differential diagnosis — Symptoms related to methamphetamine use need to be distinguished from other mental and substance-use disorders that can present similarly.

Psychosis — The psychotic symptoms and disorganized thinking that can be seen with methamphetamine use can be indistinguishable from an acute psychotic episode due to other causes, including (see '[Psychosis](#)' above):

- Schizophrenia or schizoaffective disorder (see "[Schizophrenia in adults: Clinical features, assessment, and diagnosis](#)")
- Acute manic episode (see "[Bipolar disorder in adults: Assessment and diagnosis](#)")
- Other stimulant drugs including cocaine, phencyclidine, and synthetic cathinone ('bath salts') (see "[Cocaine use disorder: Epidemiology, clinical features, and diagnosis](#)" and

"Phencyclidine (PCP) intoxication in adults" and "Acute amphetamine and synthetic cathinone ("bath salt") intoxication")

Factors that may be useful in distinguishing methamphetamine-induced psychosis from other causes include:

- Age of onset – Earlier onset more likely to be due to primary psychotic disorder
- Family history – Positive family history for substance use disorder
- Symptom type – Nonauditory hallucinations more common than thought disorder with methamphetamine use

Anxiety — The effects of methamphetamine intoxication or withdrawal can mimic an anxiety disorder.

Other psychiatric disorders — Differentiating a methamphetamine-use disorder from other mental or substance-use disorders can typically be informed by:

- Collateral information from individuals close to the patient
- Detailed history of prior episodes
- Urine toxicology for methamphetamine and other drugs

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "[Society guideline links: Stimulant use disorder and withdrawal](#)".)

SUMMARY AND RECOMMENDATIONS

- **Epidemiology** – Methamphetamine use varies geographically, but overall, amphetamine-type stimulants, which include methamphetamine, are the fastest rising drug of abuse worldwide. (See '[Epidemiology](#)' above.)
- **Cardiovascular disease** – Cardiovascular complications including malignant hypertension, arrhythmias, aortic dissection, myocardial infarction secondary to vasospasm, stroke, and cardiomyopathy are the leading causes of increased mortality in individuals who use methamphetamine. Cessation of methamphetamine use is associated with improvement

in left ventricle function and decreased admission for heart failure at one-year follow-up. (See '[Cardiovascular disease](#)' above.)

- **Pathogenesis** – Methamphetamine has profound and multilevel effects on the dopamine system in the brain and increases the synaptic availability of this neurotransmitter following intake. Inflammatory processes are believed to contribute to the development of methamphetamine use disorder. (See '[Pathogenesis](#)' above.)
- **Clinical manifestations** – Clinical manifestations of methamphetamine use include intense euphoria, energy, increased libido, and excessive talkativeness. Other manifestations may include (see '[Clinical manifestations](#)' above):
 - **Psychosis** – Predominant symptoms include paranoia, persecutory delusions, auditory, visual, and tactile hallucinations. (See '[Psychosis](#)' above.)
 - **Cognitive effects** – Evidence on the effects of methamphetamine on cognitive performance is mixed. While some studies have identified neurocognitive deficits in users, their magnitude has not been clearly shown to be clinically significant. (See '[Cognitive effects](#)' above.)
 - **Abstinence syndrome** – Individuals experience an early abstinence syndrome after cessation of methamphetamine use, which manifests as one or more symptoms including anhedonia, irritability, poor concentration, hyperphagia, sleep disturbance, or psychomotor changes. (See '[Abstinence syndrome](#)' above.)

Additionally, exposure to [fentanyl](#) (via drug contamination) and subsequent apnea and hypoxia, and increased risk of sexually transmitted disease due to risky sexual behavior are seen.

- **Course** – The course of methamphetamine addiction is prolonged and often characterized by repeated episodes of intense use, sobriety, and relapse. Individuals who inject the drug have been found to experience a worse course compared with those with other routes of administration. (See '[Onset and course](#)' above.)
- **Assessment** – Our assessment focuses on the severity of methamphetamine use, comorbid conditions, and psychosocial factors that may contribute to future relapse. (See '[Assessment](#)' above.)
- **Diagnosis** – The diagnoses of methamphetamine abuse and methamphetamine dependence in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) were replaced by the single

diagnosis, amphetamine-type substance use disorder under the broader category of stimulant use disorder. (See '[Diagnosis](#)' above.)

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