# Substance Use Disorders

This is a PDF version of the following document:
Module 2: Basic HIV Primary Care
Lesson 7: Substance Use Disorders

You can always find the most up-to-date version of this document at https://www.hiv.uw.edu/go/basic-primary-care/substance-use-disorders/core-concept/all.

---

## Background

### Overview

Substance use disorders (SUDs) are common among persons with HIV, and active substance use can have a major impact on multiple aspects of HIV care, including retention in medical care, adherence with antiretroviral therapy, ability to sustain virologic suppression, transmission of HIV to others, and food and housing security.[1] Therefore, awareness of and addressing SUDs is an important component of HIV care. This Core Concept will review the epidemiology of SUDs in the United States, data for SUDs in persons with HIV, examine the risk factors that predispose individuals to develop SUDs, and discuss current diagnostic and treatment paradigms for the most commonly identified substance use disorders among people with HIV in the United States.

### Definitions and Terminology

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines substance use disorders as a constellation of recurrent cognitive, behavioral, and physiological symptoms arising from the ongoing use of a substance.[2,3] Note the previously used terms of abuse and dependence are not recommended when describing persons with SUDs. The DSM-5 recognizes substance use disorders resulting from the use of 10 separate classes of drugs (listed in alphabetical order):

- Alcohol
- Caffeine
- Cannabis
- Hallucinogens
- Inhalants
- Opioids
- Sedatives
- Hypnotics, or anxiolytics
- Tobacco
- Stimulants

### DSM-5 Diagnostic Criteria for Substance Use Disorder

The DSM-5 has combined the DSM-IV categories of substance abuse and substance dependence under the single heading of SUDs.[2,3] The diagnosis of substance use disorder is based on scoring from a total of 11 symptom criteria included in four major groups: Impaired Control, Social Impairment, Risk Use of a Substance,

and Pharmacologic Criteria.[2,3]

Table 1.

**DSM-5 Diagnostic Criteria for Substance Use Disorders**

| |
|---|
| **Scoring System**: The diagnosis of substance use disorder is based on scoring from a total of 11 symptom criteria (listed below). The severity of the substance use disorder is based on the number of symptom criteria that are met:<br><br>• Mild Substance Use Disorder: 2 to 3 criteria met<br>• Moderate Substance Use Disorder: 4 to 5 criteria met<br>• Severe Substance Use Disorder: more than 6 criteria met |
| **A. Impaired Control**<br><br>(1) Taking the substance in larger amounts and for longer than intended<br><br>(2) Wanting to cut down or quit but not being able to do it<br><br>(3) Spending a lot of time obtaining, using, or recovering from use of the substance<br><br>(4) Craving or a strong desire to use the substance |
| **B. Social Impairment**<br><br>(5) Repeatedly unable to carry out major obligations at work, school, or home due to substance use<br><br>(6) Continued substance use despite persistent or recurring social or interpersonal problems caused or made worse by substance use<br><br>(7) Stopping or reducing important social, occupational, or recreational activities due to substance use |
| **C. Risk Use of the Substance**<br><br>(8) Recurrent use of the substance in physically hazardous situations<br><br>(9) Consistent use of the substance despite acknowledgment of persistent or recurrent physical or psychological difficulties from using the substance |
| **D. Pharmacologic Criteria**<br><br>(10) Tolerance as defined by either a need for markedly increased amounts to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount (does not apply for diminished effect when used appropriately under medical supervision)<br><br>(11) Withdrawal manifesting as either characteristic syndrome or the substance is used to avoid withdrawal (does not apply when used appropriately under medical supervision) |

Source:


- Hasin DS, O'Brien CP, Auriacombe M, et al. DSM-5 criteria for substance use disorders: recommendations and rationale. Am J Psychiatry. 2013;170:834-51. [PubMed Abstract]

# Screening for Substance Use Disorders

## USPSTF Recommendations for Substance Use Disorder Screening

- **Screening for Alcohol Misuse**: The United States Preventive Services Task Force (USPSTF) recommends screening all persons aged 18 years and older for alcohol misuse in the primary care setting.[4] The USPSTF recommends using 1- to 3-item screening instruments, including the Alcohol Use Disorders Identification Test-Concise AUDIT-C) or the Single Alcohol Screening Question recommended by the National Institute on Alcohol Abuse and Alcoholism (NIAAA).[4] If a patient screens positive for alcohol misuse on a 1- to 3-item brief screening instrument, the USPSTF recommends brief behavioral counseling interventions.[4] Follow-up with an in-depth risk assessment, such as the 10-question AUDIT, may also be helpful.[4]
- **Screening for Unhealthy Drug Use**: In 2020, the USPSTF released an updated position statement on screening for unhealthy drug use in adults and adolescents.[5] In this statement, they recommended screening by asking questions about unhealthy drug use in adults 18 years of age and older.[5] In particular, screening should be implemented when resources are available for accurate diagnosis, effective treatment, and appropriate referral can be offered. For adolescents aged 12 to 17 years, the USPSTF concluded that the benefits and harms of screening for unhealthy drug use were uncertain.[5] Although the USPSTF does not make specific recommendations regarding which screening tool to use to assess for unhealthy drug use, in primary care, brief tools, such as the National Institute on Drug Abuse Quick Screen (4-item screening tool), may be most convenient. In addition, several other longer tools are available, including the 8-item Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) and the Tobacco, Alcohol, Prescription Medication, and Other Substance Use (TAPS) tool.[5,6] It should be noted that the tools to screen for unhealthy drug use are not substance specific but rather can be applied across a range of different drug use disorders.

## Screening Resources for Unhealthy Alcohol and Drug Use

The following summarizes available resources (listed in alphabetical order) for alcohol and drug use screening, with most having direct links to screening tools that can potentially be used to evaluate for different types of substance us disorders. Screening for tobacco use is outlined in a separate section below.

### Tools Specific to Alcohol Use

- **AUDIT**: The Alcohol Use Disorders Identification Test (AUDIT) is a 10-item questionnaire that was developed specifically to screen for unhealthy alcohol use.[7] The AUDIT better identifies at-risk, harmful, or hazardous drinking patterns.[8] Developed initially by the World Health Organization, the test has been shown to correctly identify 92% of persons with hazardous drinking and 94% of those without hazardous drinking.[7] A shorter 3-question version, known as the AUDIT-C, has also been validated and performs similarly to the AUDIT for detecting heavy drinking and/or active alcohol use problems.[9]
- **AUDIT-C**: A brief, 3-item version of the full AUDIT, called AUDIT-C, has been found to have similar sensitivity and specificity as the full AUDIT for detecting hazardous drinking.[8,9]
- **CAGE**: The CAGE is a 4-question screening test that works well at detecting lifetime alcohol use problems, but is not sensitive for detecting heavy drinking and does not distinguish between past and present alcohol use.[[8,9]
- **NIAAA Single Alcohol Screening Question**: The National Institute of Alcohol Abuse and Alcoholism (NIAAA) recommends a single prescreening question about binge drinking for individuals who drink any alcohol at all: How many times in the past year have you had 5 (for men) or 4 (for women and all adults older than 65 years) or more drinks in a day? Any individual with one or more days of heavy drinking in the past year is considered at-risk for alcohol use disorder.[10]

### Screening Tools for Unhealthy Drug Use

- **ASSIST**: The World Health Organization (WHO) has also developed the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) to detect substance use and related problems in the primary care setting.[11] The ASSIST covers 12 items related to recent and lifetime use, dependence symptoms, substance-related problems, and intravenous use; it addresses 10 categories of substances: tobacco, alcohol, cannabis, cocaine, stimulants, inhalants, sedatives/hypnotics, hallucinogens, opiates, and other drugs. This tool is lengthy, but it has been effectively modified and condensed for use as a routine screening tool in some clinical settings, and it may be especially useful for screening patient populations with heavier polysubstance use, such as persons with HIV. New technologies that allow for patient-reported outcomes may facilitate incorporating these types of screening tools into busy HIV primary care clinics.[12,13,14]
- **NIDA Quick Screen**: The National Institute on Drug Abuse (NIDA) Quick Screen is a 4-item screening tool that asks about the frequency of use of alcohol, tobacco, prescription drugs for nonmedical reasons, and illegal drugs in the past year.[15] If a patient reports the use of illegal drugs or prescription drugs for nonmedical reasons in the past year, this tool can be used in conjunction with the NIDA-Modified ASSIST tool.[15]
- **TICS**: This brief, two-item conjoint screening, known as TICS, has a sensitivity and specificity of nearly 80% in detecting current substance use problems.[16] A single-question screen—“How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”— has been shown to accurately identify drug use.[17]
- **SUBS**: The 4-item Substance Use Brief Screen (SUBS) can be used with& patients in a primary care setting for tobacco, alcohol, and other drug use.[18] This is the only brief, self-administered, comprehensive screening instrument test that has been validated in the primary care setting and may facilitate the screening of primary care populations.[18]

# Epidemiology of Substance Use in United States

## Data Sources for Substance Use in the United States

The primary source of statistical information for SUDs in the general United States population originates from the National Survey on Drug Use and Health (NSDUH), which is an annual survey of the civilian, noninstitutionalized population of the United States aged 12 years and older. The survey is sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA) within the Department of Health and Human Services, and was most recently conducted in 2021, with results published in December 2022.[19] A major limitation of the NSDUH is that it does not sample persons living unhoused or those from jails or prisons, and is, therefore, likely to underestimate the prevalence of SUDs in the United States. Historically, data collection for the NSDUH has been done in person, but, in 2021, due to the COVID-19 pandemic, data collection occurred both in person and via the web.[19] Due to these differences in methodology, 2021 data are not comparable to prior years.[19] Prevalence estimates for substance use disorders in persons with HIV are derived from several published studies, as there is no comparable annual survey for the population of individuals with HIV.

## Estimates of Substance Use Disorders in the United States

Data from the 2021 NSDUH found that in the United States, approximately 46.3 million people aged 12 years and older, or 16.5% of the population, had an SUD in the past year (Figure 1).[19,20] This included 29.5 million people with an alcohol use disorder, 24.0 million people with a drug use disorder, and 7.3 million people with both an alcohol and drug use disorder.[19] The proportion of people 12 years of age and older with an SUD was highest for Native American/Alaska Native persons (27.6%), followed by multiracial persons (25.9%), Black persons (17.2%), White persons (17.0%), Hispanic persons (15.7%), and Asian persons (8%).[19] In addition to alcohol and other drugs, the NSDUH reported that 61.6 million people, or 22.0% of the population 12 years of age and older, had used tobacco or nicotine in the past month.[19]

## Predictors of Substance Use Disorders

Risk factors for SUDs are complex and likely to include a combination of biologic and social factors.

- **Family History**: Studies indicate that a family history of an SUD is a strong risk factor for the development of SUD among individuals, influenced by both genetic and shared environmental factors.[21,22,23]
- **Mental Health Conditions**: Co-occurring mental health conditions have also been linked to a higher incidence of SUD in both adolescents and adults.[24,25]
- **Social Factors**: Multiple social structural factors, such as one's social network and lived environment, have been identified as risk factors for the development of an SUD, and likely interact with genetic and other familial factors.[26,27,28] A strong body of literature has linked adverse childhood experiences with SUDs, highlighting the way in which addiction can result as a consequence of harmful events incurred during one's formative years.[29] Other social factors such as lower socioeconomic status, lower education, and non-White race, while not impacting the prevalence of SUDs, are associated with increased consequences of addiction, especially criminal justice consequences.[30]
- **Neurobiological Differences**: Although different drugs produce different effects on an individual, dysregulation of brain reward pathways in conjunction with an overactive brain stress system reinforces the use of the substance to achieve a pleasurable high or to not feel pain, even if pursuing these effects incurs great cost or negative consequences for the individual.[31] Neurobiological differences in self-control often become evident in early childhood and may correlate with the subsequent development of an SUD.[32] Although no specific neurological testing, imaging, or laboratory evaluation can accurately predict who will develop an SUD, accurate identification of predictive markers remains an area of active investigation.

# Substance Use Disorders in People with HIV

## Estimates of Substance Use Disorders in People with HIV

Multiple studies and surveys have demonstrated high rates of substance use among persons with HIV in the United States.[33,34,35] For example, in 2021, the Medical Monitoring Project (a CDC surveillance system that assesses behaviors and clinical characteristics of persons with HIV who have received outpatient medical care) estimated that 29% of people with HIV currently smoked, including an estimated 23% who smoked daily.[35] In addition, the use of alcohol and other substances is higher in persons with HIV compared to use in the general population. The 2021 Medical Monitoring Project estimated that 48% of persons with HIV had used one or more noninjection drugs in the prior 12 months for recreational purposes, 3% had used injection drugs in the prior 12 months, and 16% had engaged in binge drinking in the past 30 days.[35]

## Substance Use Disorders and Impact on HIV Transmission

Recent studies have provided overwhelming evidence that persons with HIV who take antiretroviral therapy and consistently maintain undetectable plasma HIV RNA levels do not transmit HIV sexually to others, even with condomless sex.[36,37,38] Thus, any substance use disorder that interferes with antiretroviral medication adherence can impact the transmission of HIV and have significant public health consequences. Certain substance use disorders in persons with HIV have been consistently linked to decreased antiretroviral medication adherence and to activities that enhance the likelihood of HIV transmission to sex partners and needle-sharing partners who do not have HIV.[1,39,40,41]

- **Medical Monitoring Project**: The 2021 data from the Medical Monitoring Project noted that among people with HIV, 11% reported alcohol or drug use as the reason for missing their last dose of antiretroviral medications.[35]
- **Multicenter AIDS Cohort Study**: The Multicenter AIDS Cohort Study reported that methamphetamine use increased the number of condomless anal receptive sex partners, and several other studies, including a review of 61 studies, confirmed that men with HIV who have sex with men and use methamphetamine are more likely to report sex activities, such as condomless anal intercourse, that place them at higher risk of transmitting HIV to a sex partner.[42,43,44]

## Substance Use Disorders and Impact on HIV Care

Substance use can create a barrier to care for individuals with HIV.[41,45,46] Several studies have shown that persons with HIV who have substance use disorders are more likely to miss clinic appointments, use the emergency room for care, have poor medication adherence, and experience food and housing insecurity.[47,48,49] Antiretroviral medication adherence problems in individuals with a substance use disorder may have serious consequences, including suboptimal virologic control and the potential emergence of virologic resistance. Studies have shown that persons with HIV can improve healthcare utilization and antiretroviral adherence patterns through the treatment of substance use disorders, particularly opioid use disorders; medications for opioid use disorder (MOUD) have been shown to increase rates of viral suppression, improved adherence to antiretrovirals, and lower overall mortality.[48,50,51]

## Substance Use and HIV Disease Progression

Alcohol, tobacco smoking, and drug use can also impact HIV disease progression independent of antiretroviral adherence patterns. Tobacco smoking has been shown to increase immune activation and decrease T-cell function in persons with HIV.[52,53] Heavy alcohol use, crack cocaine, and heroin use each have been linked to immune dysregulation, lower CD4 cell counts, impaired viral control, and higher AIDS-related mortality.[54,55,56,57,58,59,60] Furthermore, methamphetamine has been shown to increase HIV replication in animal models.[61]

# Alcohol Use Disorder

## Prevalence of Alcohol Use Disorder in the United States

In 2021, the National Survey on Drug Use and Health estimated that 133.1 million people had used alcohol in the past month, equating to approximately 48% of the total adult and adolescent population in the United States. Among those who consumed alcohol in the past month, 45.1% (60 million people) were current binge alcohol users, and 12.3% (16.3 million) were heavy alcohol users (Figure 2).[19,20] In 2021, 10.6% of the United States population 12 years of age or older had an alcohol use disorder, which corresponds to an estimated 29.5 million people.[19] The prevalence of alcohol use disorder was highest for persons 18 to 25 years of age, among whom 15%, or 5 million people, were estimated to have alcohol use disorder.[19]

## Prevalence of Alcohol Use Disorder in Adults with HIV

As in the general population, hazardous drinking is common among persons with HIV.[62] The 2021 Medical Monitoring Project found that 65% of people diagnosed with HIV had consumed any alcohol in the past 12 months, with 8% reporting daily consumption of alcohol.[35] In this same survey, 16% of persons diagnosed with HIV were classified as having engaged in binge drinking in the past 30 days, which equates to greater than or equal to 5 alcoholic beverages in a single sitting for men and 4 or more for women.[35]

## Risk Factors

Alcohol use disorder has a significant genetic component, with rates three to four times higher in individuals with a close relative with alcohol use disorder.[63] The risk for developing alcohol use disorder also depends on personal experiences with alcohol, peer influences, cultural attitudes toward drinking, and personal strategies for coping with stress.[3] Individuals with bipolar disorder, impulsivity, schizophrenia, personality disorders, anxiety, and depression are also at increased risk for developing an alcohol use disorder. For individuals with HIV, hazardous and heavy drinking has been associated with the use of other substances, such as heroin, cocaine, marijuana, and tobacco.[62]

## Screening Recommendations

The United States Preventive Services Task Force (USPSTF) recommends screening all patients aged 18 years and older for alcohol misuse in the primary care setting.[4] The USPSTF recommends using 1- to 3-item screening instruments, including the AUDIT-C or the Single Alcohol Screening Question recommended by the NIAAA.[4] If a patient screens positive for alcohol misuse on a 1- to 3-item brief screening instrument, the USPSTF recommends brief behavioral counseling interventions.[4] Follow-up with an in-depth risk assessment, such as the 10-question AUDIT, may also be helpful.[4]

## Diagnostic Criteria

The National Institute of Alcohol Abuse and Alcoholism (NIAAA) recommends that women of all ages and men older than 65 years consume no more than seven alcoholic drinks per week and no more than three per day; the recommendations for men 65 years of age and younger are to consume no more than 14 drinks per week and no more than 4 drinks per day).[10] These guidelines underscore that people who drink over recommended limits, even if they do not meet the criteria for alcohol use disorder, are at significant risk for alcohol-related problems.[10,64] The DSM-5 defines alcohol use disorder by the presence of at least two symptoms (from a list of 11 symptoms) related to evidence of impaired control, social impairment, risky use, and pharmacological criteria.[2]

Table 2.

**DSM-5 Diagnostic Criteria for Alcohol Use Disorder**

| |
|---|
| **A maladaptive pattern of alcohol use leading to clinically significant** |

| **impairment or distress, as manifested by 2 (or more) of the following, occurring within a 12-month period:** | |
|---|---|
| 1. Had times when the patient drank more, or longer, than intended | |
| 2. More than once wanted to cut down or stop, tried it, but could not | |
| 3. Spent a lot of time drinking or being sick/getting over the aftereffects of drinking | |
| 4. Wanted to drink so badly that they could not think of anything else | |
| 5. Found that drinking (or being sick from drinking) often interfered with taking care of home or family responsibilities, caused problems at work, or caused problems at school | |
| 6. Continued to drink even though it was causing trouble with family and friends | |
| 7. Given up or cut back on activities that were important, interesting, or pleasurable in order to drink | |
| 8. More than once gotten into situations while or after drinking that increased the chances of getting hurt (e.g., driving, swimming, unsafe sexual behavior) | |
| 9. Continued to drink even though it was causing depression or anxiety, other health problems, or causing memory blackouts | |
| 10. Had to drink much more than previously in order to get the desired effect, or finding that the usual number of drinks had much less effect than previously | |
| 11. Experienced symptoms of withdrawal after the effects of alcohol were wearing off, such as trouble sleeping, shakiness, restlessness, nausea, sweating, racing heart, or seizure Severity is determined based on the number of symptoms present:<br>• Mild: 2 to 3 symptoms<br>• Moderate: 4 to 5 symptoms<br>• Severe: more than 6 symptoms | |

Source:

- US Preventive Services Task Force, Curry SJ, Krist AH, et al. Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2018;320:1899-1909. [PubMed Abstract]

## Behavioral Counseling

The USPSTF recommends that persons who screen positive for unhealthy alcohol use be assessed for alcohol use disorder. Those with unhealthy drinking but without an alcohol use disorder, should receive brief behavioral counseling, which may include giving general feedback to patients regarding their drinking, how it relates to recommended limits, and how to cut back on drinking.[4] Another commonly employed method is the use of personalized normative feedback, where individuals are given information on how their alcohol use compares to that of their peers. Other forms of behavioral counseling interventions include web-based, telephonic, or written counseling materials. The use of behavioral counseling improves behavioral outcomes, including reducing overall consumption as well as reducing heavy drinking days.[65,66] Persons with an alcohol use disorder should receive more intensive behavioral interventions, which may include motivational interviewing, cognitive behavioral therapy, residential treatment, mutual help groups (e.g., 12-step programs), mindfulness-based approaches, contingency management, or a combination of behavioral

treatments.[67,68]

## Pharmacologic Therapy for Alcohol Use Disorder

There are currently three United States Food and Drug Administration (FDA)-approved medications for the treatment of alcohol use disorder: acamprosate, disulfiram, and naltrexone (oral naltrexone and extended-release naltrexone injection).[69,70] In a 2014 meta-analysis, based on 122 randomized, controlled trials evaluating the benefits and harms of medications for adults with alcohol use disorder, authors reported acamprosate and oral naltrexone were associated with similar reductions in return to drinking.[71] In a similar meta-analysis of acamprosate and naltrexone, authors found that acamprosate was more effective in preventing a lapse in sobriety, whereas naltrexone was more effective in preventing relapse to heavy drinking following a lapse in sobriety.[72] The following summarizes available FDA-approved therapies for alcohol use disorder, as well as information on two medications (gabapentin and topiramate) that sometimes are used to treat alcohol use disorder but do not have FDA-approval for this indication.

Table 3.

| Medication | Typical Dose | Comment |
|---|---|---|
| Acamprosate | 666 mg three times daily | Dose reduction required with renal impairment |
| Disulfiram | 500 mg once daily for 1-2 weeks, then decrease to maintenance dose (range 125-500 once daily) | Not for use in persons actively drinking alcohol; avoid alcohol in other products |
| Oral Naltrexone | 50 mg once daily | Cannot be given to patients taking opioids |
| Extended-Release Naltrexone | 380 mg IM every 4 weeks; administer in gluteal area with 1.5 inch 20-gauge needle | Cannot be given to patients taking opioids |

Source:

- Substance Abuse and Mental Health Services Administration and National Institute on Alcohol Abuse and Alcoholism. Medication for the treatment of alcohol use disorder: a brief guide. HHS Publication No. (SMA) 15-4907. Rockville, MD: Substance Abuse and Mental Health Services Administration,

October, 2015. [SAMHSA]

### Naltrexone Oral and Extended-Release Injectable Naltrexone

Oral naltrexone was approved by the U.S. FDA in 1994 for the treatment of alcohol use disorder. Advantages observed with naltrexone include mild side effects (most commonly nausea) and low potential for misuse.

- **Mechanism**: Naltrexone is an opioid antagonist that mediates the rewarding effects of alcohol and attenuates cravings (Figure 3).[73,74] Although the exact mechanism of how naltrexone works to reduce alcohol consumption is not completely understood, the presumed major effect is via blockade of opioid receptors that play a role in the reward effects of alcohol.[70]
- **Dosing**: Naltrexone is currently available both as an oral tablet (50 mg once daily) and as an extended-release injectable (380 mg IM every 4 weeks).[73]
- **Adverse Effects**: The most common adverse effect of naltrexone is nausea. There was a prior FDA black box warning regarding the potential for hepatotoxicity when naltrexone is given in excessive doses, but this warning was removed in 2013.[75] Since naltrexone works by blocking opioid receptors, neither oral nor injectable naltrexone should be used in patients who use opioids or receive treatment with methadone or buprenorphine. Naltrexone given to someone actively using opioids could precipitate sudden drug withdrawal. In addition, persons who discontinue naltrexone can subsequently have enhanced effects of opioids.
- **Treatment Data**: In a large meta-analysis of randomized, placebo-controlled trials, oral naltrexone was found to have a small but significant effect in reducing craving and relapse.[76] Most of the studies in this meta-analysis were published prior to the U.S. FDA approval in 2006 of extended-release injectable naltrexone. Subsequently, two multicenter, double-blind, placebo-controlled trials in the United States confirmed that extended-release injectable naltrexone can reduce heavy drinking and increase abstinence rates (Figure 4).[77,78] In these trials, however, the secondary outcomes in each trial were not as promising: one trial showed no difference in the time study subjects returned to heavy drinking, and the other trial showed no reduction in risky drinking.[77,78,79]
- **Potential Drug Interactions**: There are no clinically significant drug interactions between naltrexone and antiretroviral medications used for the treatment of HIV.

### Acamprosate

Acamprosate is an oral medication approved by the U.S. FDA in 2004 for the maintenance of abstinence from alcohol in patients with alcohol use disorder who are abstinent at treatment initiation. The primary beneficial effect of acamprosate is sustained abstinence (in patients who are abstinent from alcohol at acamprosate treatment initiation).[80,81]

- **Mechanism**: The mechanism of action of acamprosate is not well understood, but it is thought to decrease the activity of glutamate and increase the activity of the GABAergic system, thus restoring balance to GABA and glutamate systems that are disrupted in persons with alcohol use disorder.
- **Dosing**: The recommended dose of acamprosate is 666 mg three times daily (given as two 333 mg delayed-release tablets three times daily). Several advantages of acamprosate include good patient tolerance, ability to use in patients with liver disease, no tapering of doses required at the time of discontinuation, minimal overdose risk, and ability to use concomitantly with opioid therapy.
- **Treatment Data**: Although evidence with acamprosate has been mixed, a large meta-analysis of randomized, placebo-controlled trials found that acamprosate had a small but significant effect on promoting abstinence compared with placebo—calculating that the number needed to treat (NNT) was approximately eight people in order to achieve one additional case of abstinence (NNT=7.5).[76] Trials in Europe have shown more benefit with acamprosate than those conducted in the United States—for unknown reasons (Figure 5).[82,83]
- **Side Effects**: The most common side effect is diarrhea. A baseline evaluation of renal function should be performed prior to prescribing acamprosate, as severe renal impairment (creatinine clearance less

than or equal to 30 mL/min) is a contraindication for the use of acamprosate. For individuals with moderate renal impairment (creatinine clearance 30-50 mL/min), the dose of acamprosate should be reduced to 333 mg three times daily. There are no identified drug interactions between acamprosate and antiretroviral therapies used to treat HIV.
- **Potential Drug Interactions**: No significant drug interactions occur with the use of acamprosate and antiretroviral medications.[84]

### Disulfiram

In 1951, disulfiram was the first FDA-approved medication for the treatment of alcohol use disorder. Disulfiram is taken as an oral medication once daily on a regular basis. The primary beneficial effect of disulfiram is as a deterrent to prevent relapse in persons with alcohol use disorder.

- **Mechanism**: Disulfiram works by blocking the enzyme aldehyde dehydrogenase (Figure 6), which results in acetaldehyde levels rising within 10 to 30 minutes of alcohol ingestion, thereby triggering a highly unpleasant disulfiram-alcohol reaction.[73,85] The nature of this reaction varies based on individual characteristics of the patient, as well as on the amounts of alcohol and disulfiram consumed, and symptoms typically include flushing of the skin, nausea and vomiting, sweating, dizziness, and tachycardia. Severe reactions are possible and may include tachycardia, seizures, respiratory collapse, and even death.
- **Dosing**: The first dose of disulfiram should not be administered until the individual has been abstinent for at least 12 hours or they have a documented blood alcohol level of zero. Induction dosing for disulfiram is 500 mg once daily for 2 weeks, followed by maintenance dosing, typically 250 mg once daily (range is 125 to 500 mg once daily).[69,70]
- **Treatment Data**: Findings from a meta-analysis support the efficacy of disulfiram, but clinical trial data showing a clear benefit are lacking (in trials where adherence was assured, a positive effect was observed).[85,86]
- **Side Effects**: Rare side effects with disulfiram include optic neuritis, peripheral neuropathy, polyneuritis, and hepatitis.[70]
- **Potential Drug Interactions**: There are multiple potential drug interactions that can occur with disulfiram, including medical contraindications to its use, so patients who are considering disulfiram should be carefully screened and counseled about the medication's risks and benefits. Certain antiretroviral medications can alter disulfiram levels—efavirenz has been shown to increase the activity of disulfiram on aldehyde dehydrogenase, and atazanavir may decrease the activity of disulfiram.[87] Disulfiram should not be used in patients taking ritonavir oral solution, as this formulation contains alcohol and may precipitate an alcohol-disulfiram reaction.[88]

### Gabapentin

Although gabapentin is not FDA-approved for the treatment of alcohol use disorder, it may be another effective treatment option. In a 12-week, double-blind, placebo-controlled trial involving 150 participants, gabapentin (900 mg to 1800 mg/day) was found to be safe and effective in treating alcohol dependence, as well as in reducing relapse-related symptoms, including insomnia, dysphoria, and craving.[89]

### Topiramate

Topiramate is not currently approved for the treatment of alcohol use disorder, but multiple studies support its efficacy in improving abstinence rates and reducing alcohol craving, heavy drinking, and gamma-glutamyl transferase (GGT) levels (a biomarker of alcohol use).[90,91,92] In addition, topiramate has also been shown to reduce smoking in persons who smoke and have alcohol use disorder.[92] Topiramate is often limited by its central nervous system side effects, including excessive sedation.

## Treatment Considerations

Evidence suggests that a combination of psychosocial interventions and pharmacotherapy is the optimal approach for treating moderate to severe alcohol use disorders.[71,93,94] Clinical trials have shown a decrease in alcohol consumption among persons who receive pharmacotherapy, even among those who receive placebo, suggesting a potential psychological benefit from simply engaging with a medical provider.[95] For moderate to severe alcohol use disorder, more robust data favor the use of naltrexone and acamprosate.[71,96] In practice, many clinicians choose naltrexone as first-line therapy for two main reasons: (1) the easier once-daily dosing with naltrexone versus three times a day for acamprosate, and (2) the ability to start naltrexone while the individual is actively drinking as opposed to acamprosate, which should only be started after abstinence has been achieved. Among persons with HIV, more robust data exist for naltrexone.[97,98] To guide clinicians in the proper medication treatment of alcohol use disorders, the Substance Abuse and Mental Health Services Administration (SAMHSA) has published a Treatment Improvement Protocol.[70] Medication treatments for alcohol use disorder are the same for persons with HIV as for those without HIV. Despite data showing that medications for alcohol use disorder are beneficial, fewer than 10% of persons with alcohol use disorder are offered medication treatment.[99]

# Cannabis Use Disorder

## Prevalence of Cannabis Use Disorder in the United States

Cannabis (marijuana) is the most widely used psychoactive substance in the United States (Figure 7).[19] Based on the 2021 National Survey on Drug Use and Health, an estimated 52.5 million people, ages 12 and older, used cannabis in the last year in the United States, which equates to an estimated 18.7% of the population.[19] During 2021, the prevalence of cannabis use in the past year was highest among those 18 to 25 years of age (35.4%) (Figure 8).[19] The use of marijuana has steadily increased since 2002, and in the past 10 to 15 years there has been a steady increase in the number of states that have legalized marijuana.[19,20]

## Prevalence of Cannabis Use Disorder in Adults with HIV

Several multicenter cohorts in the United States have found marijuana prevalence rates among persons with HIV that ranged from 24 to 38%, though these data do not distinguish between cannabis use and cannabis use disorder.[41,48] The 2021 CDC Medical Monitoring Project reported that 39% of persons with HIV had smoked marijuana (including vaping marijuana) in the past 12 months.[35] Despite this high marijuana use, data from multiple studies have not shown a negative impact of cannabis on antiretroviral adherence across a range of studies; inadequate data exist for the use of synthetic cannabinoids on antiretroviral adherence.[84,100,101]

## Diagnostic Criteria

The DSM-5 defines cannabis use disorder by the presence of at least two symptoms (from a list of 11 symptoms) related to evidence of impaired control, social impairment, risky use, and pharmacological criteria.

## Treatment Considerations

No medications have been shown to be consistently effective for the treatment of cannabis use disorder. Buspirone was effective in reducing cannabis use in one clinical trial, but anxiolytics and antidepressants (selective serotonin reuptake inhibitors [SSRIs], mixed action, and atypical) have not been proven to lower rates of cannabis dependence; a recent systematic review found low-strength evidence that SSRIs do not reduce cannabis use and low-to-moderate strength evidence that buspirone does not reduce cannabis use.[102,103,104] Other medications, including N-acetylcysteine, topiramate, gabapentin, and varenicline, have been tried, but there is insufficient evidence to support their use. More favorable results have been observed with cognitive behavioral therapy, motivational interviewing, and motivational enhancement therapy in lowering cannabis use, severity of dependence, and overall cannabis problems.[105] Several programs have been established to help guide the treatment of cannabis use, including the brief marijuana dependency counseling (BMDC) program, which is a 12-week multidisciplinary intervention developed by the Center for Substance Abuse Treatment that involves motivational enhancement therapy, cognitive behavioral therapy, and case management.[106] Separate resources are available for treatment of youth with cannabis use disorders.

# Hallucinogen Use Disorder

## Prevalence among Adolescents and Adults in the United States

Hallucinogen use disorders are categorized by the type of hallucinogen used. For example, the DSM-5 divides hallucinogen use disorder into separate categories for those who use phencyclidine or a similar substance such as ketamine, and those who use other hallucinogens, such as mescaline, 3,4-methylenedioxy-methamphetamine (MDMA) and popularly known as “ecstasy or Molly”, and lysergic acid diethylamide (LSD).[3] Of note, MDMA is classified as a hallucinogen, though it is structurally similar to methamphetamine and has stimulant properties as well.[107] According to the 2021 National Survey on Drug Use and Health (NSDUH), an estimated 7.4 million people, ages 12 and older, used hallucinogens in the past year.[19] As with most other drugs, usage in the past year was highest for those 18 to 25 years of age, but the prevalence of usage remained stable over the time period of 2015 to 2018 for all age groups (Figure 9).[19]

## Prevalence among Adults with HIV in the United States

In the 2021 CDC Medical Monitoring Project, an estimated 5% of individuals with HIV who were enrolled in care reported in the past 12 months they had used club drugs (e.g., Ecstasy or X, ketamine or Special K, gamma-hydroxybutyrate [GHB] or Liquid Ecstasy).[35] Although detailed data on the use of “club drugs” or the prevalence of hallucinogen use disorders among persons with HIV are not available, evidence indicates that use of “club drugs” has been rising in the general population and especially among men who have sex with men (MSM).[107,108,109]

## Risk Factors

Risk factors for phencyclidine use disorder include low educational attainment, male sex, and living in the West or Northeast.[3] Use of other hallucinogens is linked to other substance use disorders (and early exposure to alcohol, tobacco, and cannabis), depression, drug use by peers, and high sensation-seeking behavior.[3] A recent population study that looked specifically at psychedelics (LSD, psilocybin, mescaline, peyote) found that psychedelic users were more likely to be younger, White, male, unmarried, with somewhat higher educational status, risk-takers, and more likely to have used other drugs; interestingly, this paper found no association between lifetime psychedelic use and increased likelihood of past year psychological distress, mental health treatment, depression, anxiety, or suicidality.[110]

## Diagnostic Criteria

The DSM-5 defines phencyclidine and hallucinogen use disorder by the presence of at least two symptoms (from a list of 11 symptoms) related to evidence of impaired control, social impairment, risky use, and pharmacological criteria.

## Treatment Considerations

Behavioral interventions, such as intensive counseling and contingency management, are the mainstay of treatment for persons with hallucinogen use disorders (or “club drug use” disorders).[109] No pharmacologic treatment is known to have any benefit. Clinicians should be aware of significant interactions that can occur between club drugs and antiretroviral medications, particularly the pharmacologic boosters ritonavir and cobicistat; there are several published case reports of fatal drug interactions.[108,109]

# Opioid Use Disorder

## Prevalence among Adolescents and Adults in United States

In 2021, an estimated 9.2million Americans over the age of 12, or 3.3% of the population, used opioids, the vast majority of whom misused prescription opiate medications.[19] These numbers likely underestimate the true prevalence of opioid misuse and opioid use disorder due to the large proportion of incarcerated persons who struggle with opiate use.[3] Even so, the reported rate of opiate misuse is staggering.

- **Heroin Use**: In 2021, an estimated 1.1 million persons in the United States reported they had used heroin in the past year.[19] In contrast to age use demographics for the use of other drugs, the highest use of heroin occurred in a relatively older age group (26 years of age and older) (Figure 10).[19] Between the time periods 2002 to 2004 and 2011 to 2013, heroin use (reported in the past year) increased by 114% among non-Hispanic White people.[111] In the past several years, however, there has been a shift away from heroin and towards fentanyl among many people who use opioids. This shift, beginning in 2018, has been associated with a steady decline in overdose deaths involving heroin (Figure 11).[112]
- **Fentanyl**: In the past two decades, there has been a marked increase in fentanyl-related harm, overdose, and death in the United States, with overdose deaths due to fentanyl far outnumbering those of other substances (Figure 12).[112,113] The CDC estimates that overdose deaths involving fentanyl and fentanyl analogs increased 56% from 2019 to 2020, and the number of overdose deaths involving fentanyl in 2020 was more than 18 times that of 2013.[21,112,114]
- **Misuse of Pain Reliever Medication**: During the past several decades, nonmedical use of opioid prescription pain medication has emerged as a particularly alarming problem in the United States, especially in recent years and particularly among young people. There was a 250% increase in prescription drug misuse (opioids are the most commonly misused prescription drug) over the past 20 years.[115,116] Between 2017 and 2019, the number of overdose deaths involving prescription opioids decreased slightly; however, the number of overdose deaths involving prescription opioids increased in 2020 and remained relatively stable in 2021 (Figure 13).[112]

## Prevalence among Adults with HIV

- **Injection Drug Use as Risk for HIV**: Persons who inject drugs remain disproportionately affected by the HIV epidemic in the United States, with several recent outbreaks of HIV occurring among networks of persons who inject drugs.[117,118] In 2021, persons who inject drugs accounted for approximately 1 in 10 new HIV infections in the United States.[119] Based on CDC prevalence estimates for 2021, an estimated 10.1% (121,900 of 1,212,400) of persons living with HIV in the United States had injection drug use as a reported transmission category plus an additional 5.2% (62,900 of 1,212,400) who reported injection drug use and male-male sexual contact as the transmission category.[119]
- **Injection Drug Use Among Persons with HIV:** Data from the 2021 CDC Medical Monitoring Project suggests that in the prior 12 months, 3% of persons with HIV used prescription opioids for nonmedical purposes, and 3% reported injection drug use.[35] The Medical Monitoring Project did not report specifically on use of synthetic opioids (e.g., fentanyl). Some data suggest that persons with HIV are more likely to have chronic pain and more likely to receive higher-dose opioid prescriptions, which can elevate the risk of opioid use disorder.[120] Injection opioid use has also been linked to HIV epidemics in rural populations historically at lower risk for HIV, illustrating the syndemic nature of this problem.[118,121]

## Risk Factors

Genetic and environmental factors appear to predispose individuals to substance use disorders and clearly correlate with the development of an opioid use disorder. Heroin use disorders have traditionally been associated with racial and ethnic minority populations in low-income settings, but over the past decade, have

become more common among White middle-class individuals (especially teenagers and women) as a consequence of nonmedical prescription-opioid use and increased illicit opioid availability.[3,122] Other risk factors for heroin use include co-occurring substance use within the previous year; in particular, abuse or dependency on opioid pain relievers is the strongest risk factor for developing a heroin use disorder.[111] Nonetheless, it is important to recognize that only a small percentage of individuals who use nonmedical prescription opioids initiate heroin use, and those who do often have “traditional” risk factors for addiction, including adverse childhood experiences.[122]

## Diagnostic Criteria

The DSM-5 defines opioid use disorder by the presence of at least two symptoms (from a list of 11 symptoms) related to evidence of impaired control, social impairment, risky use, and pharmacological criteria.

## Treatment Considerations

Opioid use disorder is a medical disorder, and medications for opioid use disorder (MOUD) are central to the treatment strategy; MOUD are highly effective and are associated with a 50% or greater reduction in all-cause and opioid-related mortality.[123] Behavioral interventions and/or detoxification, without medications for opioid use disorder, have poorer outcomes with high rates of relapse.[124,125] Pharmacologic therapies for opioid use disorder include three categories: opioid agonists, opioid partial agonists, and opioid antagonists.[126] Opioid agonists and partial agonists are used for maintenance therapy (also called opioid replacement therapy or opioid substitution therapy). For detailed information on this topic, SAMHSA has published a Treatment Improvement Protocol (TIP 63) for medication-assisted treatment for opioid use disorders.[127] For medication treatment of opioid use disorder, improved outcomes correlate with a lower treatment threshold, flexible-dose titration, and duration of therapy that is focused on harm reduction (i.e., retaining patients in care even in the setting of poor adherence and regardless of ongoing substance use) rather than on abstinence alone.[128] A brief overview of the key medication options is provided below, but medical providers interested in offering medications for opioid use disorder should consult the SAMHSA TIP as well as their local addiction specialists.[127]

### Access to Medications for Opioid Use Disorder

Despite the effectiveness of medications for opioid use disorder, access to and use of MOUD remains limited in the United States. In the past, physicians and advanced practice providers (APPs) were required to complete 8 to 24 hours of training prior to being eligible to obtain a buprenorphine prescribing waiver, also known as an X-waiver. As of January 2023, however, the X-waiver is no longer required, and practitioners with a current DEA license that includes schedule III authority can prescribe buprenorphine, subject to state requirements, for the treatment of opioid use disorder.[129] For more information on buprenorphine waiver, see the SAMHSA Waiver Elimination Act.

### Buprenorphine and Buprenorphine-Naloxone

Buprenorphine is a partial opioid agonist that can be prescribed in an outpatient office setting to reduce the craving and use of opioids, and it offers a better safety profile than methadone.[130] In 2004, the SAMHSA CSAT issued Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction that addresses key issues related to prescribing buprenorphine, with guidelines recently updated in 2021.[127]

- **Mechanism**: Buprenorphine is a partial agonist that has a high affinity for the mu-opioid receptor, but, when bound, produces a long-lasting, partial effect that has a ceiling. By binding to this receptor, buprenorphine competes with other opioids and thereby mitigates the impact of other opioids.
- **Preparations**: Buprenorphine is available in transmucosal (sublingual tablet, buccal film, and sublingual film) and depot (subcutaneous injectable and subdermal implant) preparations.[131,132,133] When depot formulations are given, the patient must first receive

induction buprenorphine with a transmucosal preparation of buprenorphine.

- **Dosing of Transmucosal Preparation**: The half-life of buprenorphine when given via the transmucosal route is 24 to 48 hours, with the sublingual formulation reaching maximum concentrations at 2.5 to 3 hours after administration. Transmucosal buprenorphine is typically prescribed for use on a daily or twice-daily basis, but can be given up to 3 times a day. If the buprenorphine dose is doubled or tripled, dosing can be extended to every other day or to three times weekly.[131] Typical maintenance doses of buprenorphine range from 4 to 24 mg daily, which is equivalent to approximately 60 mg of methadone.[131] A generic buprenorphine-naloxone fixed-dose formulation (8 mg/2 mg and 2 mg/0.5 mg) is also available, as well as several other brand-name formulations of buprenorphine and naloxone; the combination preparations are to decrease the risk of abuse, diversion, and overdose (since naloxone is an opioid antagonist that blocks the opioid activity of buprenorphine if it is injected).[126,134]
- **Dosing of Depot Preparations**: Extended-release injection buprenorphine is given as a subcutaneous injection in the abdominal region once a month, with a recommended standard dosing of 300 mg once monthly for 2 months, followed by a maintenance dose of 100 mg monthly.[133] Prior to the first dose of extended-release injection buprenorphine, the patient must have successfully initiated treatment with a transmucosal buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days.[133] Buprenorphine implant maintenance therapy consists of four 1-inch implants that are inserted in the same area under the skin in the upper arm; the implants should be removed or replaced by the end of the sixth month.[132,133] Prior to placing the buprenorphine implant, the patient must have achieved and sustained prolonged clinical stability of a low-to-moderate dose (e.g., a dose of no more than 8 mg per day) of a transmucosal buprenorphine-containing product.[132]
- **Adverse Effects**: Common side effects include drowsiness, constipation, headaches, and loss of appetite. Misuse of buprenorphine or buprenorphine-naloxone, such as taking doses higher than prescribed or injecting the medication, can result in life-threatening complications. Discontinuation of buprenorphine after long-term use can cause symptoms similar to heroin withdrawal; discontinuation should be supervised and achieved through gradual dose reductions.
- **Drug Interactions with Antiretroviral Medications**: Buprenorphine has the potential to have drug interactions with antiretroviral medications that are CYP enzyme inhibitors or inducers. Notably, the use of unboosted atazanavir with buprenorphine is contraindicated and caution with close monitoring is recommended with ritonavir, cobicistat, and all protease inhibitors. Efavirenz may lower buprenorphine levels. Significant interactions do not occur with integrase strand transfer inhibitors (INSTIs) or nucleoside reverse transcriptase inhibitors (NRTIs).

### Methadone Maintenance Therapy

Methadone maintenance therapy is the most established form of treatment for opioid use disorder and involves daily dosing of methadone through an Opioid Treatment Program (OTP). Methadone treatment is highly regulated, and methadone OTPs have limited clinical flexibility for dosing and dispensing methadone. Although daily dosing early in treatment is necessary for safety reasons, for some the rigid schedule can be a barrier. Methadone maintenance therapy is associated with significantly reduced heroin use and has been found to be superior to buprenorphine in retaining people in treatment.[135] Treatment is usually for 12 months or longer, with a longer duration of treatment associated with greater likelihood of abstinence.[136]

- **Mechanism**: Methadone is a synthetic long-acting opioid agonist, which has a half-life of 24 to 36 hours and is usually administered daily when used as opioid replacement therapy.[131] Methadone relieves drug cravings and withdrawal symptoms, dampens the euphoric and sedating effects of heroin, and, at stable dosages, does not cause euphoria or sedation.
- **Dosing**: Methadone is available in many formulations, but the liquid form is typically used in most methadone clinics in the United States. Standard initiation dosages of methadone are low and are titrated upward to achieve reduced symptoms of withdrawal without sedation. The goal for methadone dosing is to eliminate the craving for heroin, and this generally requires using doses in the range of 60 to 120 mg per day**.[**137**]**

- **Adverse Effects**: Methadone is a relatively safe drug, and when used during maintenance therapy, the most common adverse events are perspiration and constipation.[138] Additional possible complications of methadone maintenance therapy include cardiovascular effects (prolongation of QT interval and torsade de points, especially with higher doses), respiratory depression, decreased sexual function, and central nervous system effects.[131,139] Concomitant use of methadone with medications that prolong QTc should be avoided.
- **Drug Interactions with Antiretroviral Medications**: Methadone has multiple significant potential drug interactions when used with antiretroviral medications. Notably, efavirenz substantially lowers methadone levels; abacavir, rilpivirine, and ritonavir-boosted protease inhibitors can also lower methadone levels. The impact of cobicistat on methadone is not known, but caution should be used, and methadone should be titrated up from the lowest feasible dose. The INSTIs do not have significant drug interactions with methadone. Methadone can significantly increase zidovudine levels and potentially cause zidovudine-related toxicity.

### Naltrexone

Naltrexone is an opioid receptor antagonist that is FDA-approved for relapse prevention of opioid use disorder. A large meta-analysis found that naltrexone was no more effective than placebo, even when combined with psychotherapy, but studies with the extended-release injectable formulation are more promising. Two randomized, controlled trials in Russia have demonstrated improved rates of retention in treatment and abstinence from opioid use with XR-naltrexone.[140,141] In addition, XR-naltrexone has also been associated with a lower rate of opioid relapse when compared to usual care among persons in the United States criminal justice system.[142] Nevertheless, large studies comparing XR-naltrexone to buprenorphine have shown that XR-naltrexone is inferior in preventing relapse and less cost-effective.[143,144]

- **Mechanism**: Naltrexone works by acting as an opioid receptor antagonist, which inhibits the euphoric response to opioids.[126]
- **Dosing**: Two formulations of naltrexone are available—naltrexone oral and extended-release naltrexone injection formulation. Naltrexone is well tolerated and does not carry a risk of abuse or overdose. A 50 mg dose of naltrexone attenuates or blocks opioid effects for 24 hours, and a 100 to 150 mg dose blocks opioid effects for up to 72 hours.[131]
- **Adverse Effects**: The most common adverse effect of naltrexone is nausea. There was a prior FDA black box warning regarding the potential for hepatotoxicity when naltrexone is given in excessive doses, but this warning was removed in 2013.[75] Because of its mechanism of action, which includes blocking opiate receptors, neither oral nor injectable naltrexone should be used when patients are actively using opioids or receiving treatment with methadone or buprenorphine. Naltrexone given to someone actively using opiates could precipitate sudden drug withdrawal. In addition, patients who discontinue naltrexone can subsequently have enhanced effects of opiates.
- **Drug Interactions with Antiretroviral Medications**: Naltrexone does not have any significant interactions with antiretroviral medications.

## Special Considerations for Persons with HIV

Efforts to integrate buprenorphine treatment into HIV care settings have produced mixed results, and challenges have been encountered, including a lack of clinical support staff, administrative obstacles, competing physician activities, and inadequate reimbursement.[145,146,147] Some models, however, found considerable success and have dramatically scaled up access to opioid substitution therapy in underserved communities at high risk for opioid addiction. The Massachusetts Model of Office-Based Opioid Treatment with Buprenorphine (OBOT-B), which has been implemented in community health centers, provides a particularly successful model that relies on collaboration between nursing case managers and prescribing physicians.[148] Among individuals with HIV who inject drugs, buprenorphine has been linked to improved engagement in care, and it is clear that mortality is lowest when antiretroviral therapy and opioid treatment are prescribed jointly.[149,150]

## Harm Reduction Approach

Medication therapy for opioid use disorder therapy is one of several practices that follow a harm reduction philosophy of “meeting patients where they are at” and engaging in helping them with their goals rather than prescribing rigid goals for them. Other such practices include syringe services, HIV prevention education, and overdose prevention strategies.

### Syringe Services

The consistent use of sterile needles and injection equipment is the most effective way for people who inject drugs to limit their risk of acquiring or transmitting HIV and other bloodborne pathogens. With only minor exceptions, federal funding for needle exchange programs in the United States was prohibited from the 1980s until late 2015. Nevertheless, multiple studies have concluded that providing sterile needles and injection equipment to people who inject drugs reduces injecting risk activities, reduces the risk of HIV infection, and facilitates entry into drug treatment.[151,152,153,154] Canada, Australia, several European countries, and the United States have sought to mitigate the risks of injection drug use by establishing supervised injection facilities, where people who inject drugs can obtain sterile equipment and inject pre-obtained drugs in the presence of health professionals, allowing for a response to overdoses and facilitating encounters that link clients with drug treatment services.[155] Data on the supervised injection site in Vancouver, Canada (InSite) show reduced overdose deaths in the city and surrounding areas, reduced HIV and hepatitis C virus (HCV) risk behaviors, reduced use of medical resources, and increased access to preventive, mental health, and primary care services.[155]

### HIV Prevention Education

Syringe service programs often provide a comprehensive set of services beyond basic needle exchange, including HIV counseling and testing screening for sexually transmitted infections, viral hepatitis, and tuberculosis vaccination services and referral to substance use treatment programs. It is extremely important to remember that persons who inject drugs can also acquire and transmit HIV via sexual contact and should be counseled about sexual risk reduction strategies. Many syringe services exchange sites can link interested persons who use drugs with formal education programs. A Cochrane review found that standard educational interventions, rather than multisession psychosocial interventions, are a cost-effective way to reduce injection and sexual risk behavior.[156]

### Opioid Overdose Prevention Strategies

Another harm reduction technique involves overdose education and distribution of naloxone to persons who use opioids, as well as to their friends, family, and other community members. The strategy of training potential bystanders to prevent, recognize, and respond to overdose situations was piloted in 19 Massachusetts communities through the OEND (opioid education and nasal naloxone distribution) program. Between 2002 and 2009, the adjusted rate ratios of death attributed to opioid overdose decreased in communities with both low and high enrollment compared with communities without OEND implementation.[157] This is especially pertinent as the availability of naloxone has greatly expanded and is being widely promoted nationally for both people who use recreational opioids and those prescribed higher doses of opioids for chronic pain conditions.[158] In the United States, most individual states have passed legislation improving layperson access to naloxone, while Good Samaritan laws, which encourage bystanders to summon emergency responders without concern for legal repercussions, continue to be expanded throughout the country.[159]

## Opioid Prescribing Practices

The epidemic of opioid use is intertwined with opioid prescribing practices in the United States. Due to increasing concern that pain was being undertreated, the number of opioid prescriptions quadrupled between

1999 and 2013, followed by an increase in opioid use disorders and overdose deaths.[160] The high prevalence of acute and chronic pain syndromes among persons with HIV means that clinicians caring for patients with HIV frequently have to balance pain management with the risk of creating iatrogenic opioid dependence.[161] There are numerous initiatives that have addressed reducing opioid prescriptions, providing daily dosing limits on opioids, and overall strategies for making prescribing safer (written contracts for patients, prescribing protocols, routine use of urine toxicology, electronic health records, prescription drug monitoring programs, and more training for primary care medical providers). Adherence with these initiatives, however, needs to be balanced with appropriate pain management prescribing for those patients who truly need it, with an emphasis on non-medication and non-opioid medication treatment approaches. Clearly, there is an ongoing need to educate clinicians and patients about the risks, benefits, and proper role for opioid pain medications.[162]

# Stimulant Use Disorder

## Prevalence of Stimulant Use Disorder in the United States

In 2021, the National Survey on Drug Use and Health estimated that 1.7% and 0.4% of the population had used cocaine and crack cocaine, respectively, in the past year, which corresponded to 4.8 million people using some form of cocaine in the prior year.[19] Cocaine use was by far the highest among those ages 18–25 years, with 2021 data estimating 3.5% use in this age group during the past year.[19] In 2021, an estimated 0.9% of the population over the age of 12, or 2.5 million people, had used methamphetamine in the past year, with the highest prevalence also among those 26 years of age and older.[19] Across all age groups, the rates of cocaine use were higher than with methamphetamine use (Figure 14).[19]

## Prevalence among Adults with HIV

The prevalence of stimulant use is much higher among persons with HIV than among the general population. The Adult and Adolescent ART Guidelines estimate a 5 to 15% prevalence of stimulant use among all persons with HIV in the United States.[84]

- The 2021 Medical Monitoring Project estimated that in the prior 12 months, 6% of persons with HIV used cocaine, 4.0% used crack cocaine, and 7% used methamphetamine.[35]
- In a longitudinal cohort of persons with HIV engaged in care at 8 clinical sites, 8.5% reported crack cocaine use, whereas other cohort studies, with inclusion criteria that favored higher numbers of people who use drugs, have found cocaine usage rates of up to 40 to 50%.[41,48,55]
- The CDC's National HIV Behavioral Surveillance survey demonstrated that HIV prevalence among MSM who primarily inject methamphetamine was nearly 50% higher than MSM who primarily inject other drugs, with the proportion of MSM who primarily inject methamphetamine being higher in western than eastern United States cities.[163] Data from the United States general population similarly show that methamphetamine use has historically been highest on the West Coast, but newer trends suggest more prevalent nationwide use, particularly among people who use other drugs.[164,165]

## Risk Factors

Risk factors for stimulant use disorder include psychiatric comorbidities (in particular, bipolar disorder, schizophrenia, and antisocial personality disorder), other substance use disorders, prenatal exposure to cocaine, experiencing community violence in childhood, and living in an unstable home.[3] Men who have sex with men also represent a discreet risk group for stimulant use disorder, particularly methamphetamine use and its associated sexual behavior.[166,167]

## Diagnostic Criteria

The DSM-5 category of stimulant use disorder includes problems associated with the use of one or more of the following substances: methamphetamine, amphetamines, or cocaine (but not caffeine or nicotine). The DSM-5 defines stimulant use disorder by the presence of at least two symptoms (from a list of 11 symptoms) related to evidence of impaired control, social impairment, risky use, and pharmacological criteria.

## Treatment Considerations

- **Behavioral Interventions**: Behavioral strategies, including cognitive behavioral therapy, motivational interviewing, and contingency management (a system of incentives for positive reinforcement, such as providing vouchers in exchange for abstinence) are the primary interventions for stimulant use disorders, though no single approach has been proven to be most effective.[168,169] In addition, SAMHSA has developed an intensive, outpatient cognitive-behavioral treatment approach called the Matrix Model, which has been effectively tailored to meet the needs of

different populations (men who have sex with men, for example).[170] Materials about the Matrix Model are available from SAMHSA but are geared toward counselors and substance users, rather than primary care providers.

- **Pharmacologic Therapies**: No pharmacologic treatment has been approved for the treatment of stimulant use disorder. Multiple medications have been investigated, including antipsychotics (risperidone, olanzapine, reserpine, aripiprazole), psychostimulants (dexamphetamine, bupropion, methylphenidate, modafinil), antidepressants (bupropion, mirtazapine), and others (baclofen and ondansetron).[171,172,173] In general, there remains a high rate of relapse among individuals who complete methamphetamine treatment programs.[109]
    - **Mirtazapine**: Some promising data have emerged for mirtazapine, in addition to behavioral counseling, as shown in a recent randomized, controlled trial of mirtazapine versus placebo for men who have sex with men; in this study, mirtazapine once daily (added to counseling) was shown to significantly reduce methamphetamine use and some HIV risk behaviors in comparison to placebo.[] A smaller study evaluated the effect of mirtazapine on methamphetamine use among men who have sex with men, and investigators reported that participants assigned to add mirtazapine therapy to substance use counseling had fewer methamphetamine-positive urine tests compared with participants taking placebo, despite low-to-moderate medication adherence.[175]
    - **Bupropion plus Injectable Naltrexone**: There is also evidence to support the use of bupropion and injectable naltrexone for methamphetamine use disorder. In a multisite, double-blind, placebo-controlled trial, the use of oral bupropion (450 mg per day) and injectable naltrexone (380 mg every 3 weeks) resulted in a higher response, defined as at least three methamphetamine-negative urine samples out of four samples obtained over a period of 4 weeks, when compared to placebo.[176]

# Tobacco Use Disorder

## Tobacco Use Prevalence in the United States

Tobacco use is a worldwide epidemic and is the leading preventable cause of death, disease, and disability in the United States. Results from the 2021 National Survey on Drug Use and Health found that approximately 22% of the population had used tobacco in the past month, and 15.6% had specifically used cigarettes in the past month.[19] Despite ongoing high rates of tobacco use, the proportion of the population who smoked cigarettes in the last month has declined approximately 10% over the past 2 decades (from 26% in 2002 to 16% in 2021).[19,20] Significant disparities in smoking prevalence persist, with the highest prevalence rates in Native Americans/Alaskan Natives, multiracial adults, persons living under the poverty line, and those with the lowest educational attainment.[177,178] Although cigarette smoking has declined, the prevalence of other tobacco use, such as cigars and pipe tobacco, has not changed significantly since 2002.[20]

## Tobacco Use Prevalence in Adults with HIV

Data from the 2021 CDC Medical Monitoring Project surveyed persons with HIV regarding tobacco use in the past 12 months and 29% reported there were current cigarette smokers and 23% reported daily smoking.[35] In addition, other data have noted that adults with HIV are less likely to quit smoking compared to persons without HIV.[179]

## Risk Factors

Individuals with psychiatric and/or other substance use disorders are at increased risk of smoking, and smoking rates have declined significantly less among persons with mental health conditions compared with those without mental health conditions.[180] In addition, tobacco use disorder has a strong degree of heritability, and differences in nicotine blood levels and nicotine metabolism vary among individuals, especially among certain ethnicities (i.e. African American males have higher blood nicotine levels for a given number of cigarettes).[3]

## Screening and Treatment Recommendations

Tobacco use is typically a chronic problem and often requires behavioral support, pharmacologic therapy, and multiple attempts to quit.[181,182,183] The U.S. Preventive Services Task Force (USPSTF) issued an updated recommendation statement in 2021 on Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women.[184] In 2018, the American College of Cardiology (ACC) published a decision pathway incorporating new evidence, for tobacco cessation treatment in adults; the following summarizes key points from the ACC recommendations.[185]

- Use the 5A’s: Ask about tobacco use at every visit; advise all tobacco users to quit; assess willingness to quit; assist the individual in quitting (medications, counseling); and arrange follow-up contact.
- Telephonic tobacco quitlines may be able to provide intensive tobacco cessation counseling (1-800-QUITNOW). Intensive counseling has been proven more effective than brief intervention. Pharmacologic interventions should be offered as a component of smoking cessation programs.
- Pharmacologic interventions should be offered as a component of smoking cessation programs. There are three main types of medications that have been shown to reliably increase long-term smoking abstinence rates and that are recommended for use in smoking cessation: varenicline, nicotine replacement products (gum, inhaler, lozenge, nasal spray, patch), and sustained-release bupropion ( Table 4).
    - First-line outpatient pharmacotherapy for smoking cessation consists of varenicline or combined nicotine replacement products.
    - Second-line outpatient pharmacotherapy for smoking cessation is sustained-release bupropion or a single nicotine replacement product.

    - Third-line outpatient pharmacotherapy for smoking cessation consists of nortriptyline.
- If a single agent is insufficient to achieve abstinence, the following combinations can be considered: varenicline plus a single nicotine replacement product, varenicline plus bupropion, and bupropion plus a single nicotine replacement product.

- Within 2 to 4 weeks of a quit attempt, follow-up contact with the individual attempting to quit is recommended, either in person or via telephone or electronic health record portal. This follow-up contact is important for monitoring tobacco cessation treatment, especially since the risk of smoking relapse is high in the immediate period after a quit attempt.
- Evidence regarding the use of electronic nicotine delivery systems (e-cigarettes, vaping) for tobacco cessation is insufficient to make recommendations.
- Evidence is also insufficient to assess the risks versus benefits of pharmacotherapy interventions for tobacco cessation in pregnant women.

Results from a randomized, controlled trial of electronic cigarette use versus nicotine replacement therapy for smoking cessation reported e-cigarettes were more effective than nicotine replacement therapy for smoking cessation, but nearly 40% of participants in the e-cigarette groups were still using electronic cigarettes at 52 weeks whereas only 4.3% of those in the nicotine replacement group were still using nicotine replacement therapy at 52 weeks.[186] After the release of the 2018 ACC guidelines, multiple reports have generated alarming concerns for the safety of vaping, and most experts would now advise extreme caution when considering electronic nicotine delivery systems.[187,188]

## Treatment Considerations for Persons with HIV

There are limited clinical trial data on pharmacotherapy for smoking cessation among persons with HIV. Available data suggest that varenicline is safe and effective in persons with HIV.[189,190] The Adult and Adolescent ART Guidelines support recommendations for smoking cessation as provided by the USPSTF and suggest that clinicians should consider evidence-based behavioral and pharmacotherapy strategies to promote smoking cessation and maximize survival among persons with HIV.[84,183] In general, pharmacotherapies used for smoking cessation have few drug interactions with HIV medications and can be used safely with most first-line antiretroviral regimens; the one major exception is that coadministration of bupropion with medications that are CYP2B6 inducers, such as efavirenz, lopinavir, and ritonavir, can reduce levels of bupropion.[84]

## Summary Points

- Substance use disorders are common among adults with HIV in the United States.
- Many substance use disorders in people with HIV are linked to decreased retention in care, reduced adherence to antiretroviral medications, and lower rates of virologic suppression.
- Combining psychosocial interventions with pharmacotherapy (acamprosate, disulfiram, oral naltrexone, or extended-release naltrexone injection) is the optimal approach for treating alcohol use disorder; all pharmacotherapies can be used to treat persons with HIV, keeping in mind that disulfiram has several clinically significant drug interactions with antiretroviral medications whereas acamprosate and naltrexone do not.
- There is a high rate of cannabis use among persons with HIV, and treatment for cannabis use disorders should focus on behavioral therapies.
- The use of methamphetamines and "club drugs" (e.g., hallucinogens and ecstasy) is significant among bisexual men and men who have sex with men, including those with HIV.
- Behavioral strategies are the primary intervention for stimulant and hallucinogen use disorders, although there is increasing evidence to support the use of mirtazapine or the combination of bupropion plus injectable naltrexone for persons with methamphetamine use disorder.
- The rise in opioid addiction has paralleled the rise in opioid prescribing habits over the past several decades; tackling the opioid epidemic will require educating clinicians and patients alike about the risks, benefits, and proper role of opioid pain medications.
- Medications for opioid use disorder are necessary and highly effective for the treatment of opioid use disorder, and options include opioid agonists (methadone), opioid partial agonists (buprenorphine), and, though less effective, opioid antagonists (naltrexone).
- Among persons with HIV who inject opioid drugs, both drug- and HIV-related mortality are lower when antiretroviral therapy and medications for opioid use disorder are prescribed jointly.
- Treatment strategies for substance use disorders should embrace a harm reduction philosophy in order to best serve those individuals at the highest risk for ongoing substance use.

# Citations


1. Hinkin CH, Hardy DJ, Mason KI, et al. Medication adherence in HIV-infected adults: effect of patient age, cognitive status, and substance abuse. AIDS. 2004;18 Suppl 1:S19-25.
[PubMed Abstract] -

2. Hasin DS, O'Brien CP, Auriacombe M, et al. DSM-5 criteria for substance use disorders: recommendations and rationale. Am J Psychiatry. 2013;170:834-51.
[PubMed Abstract] -

3. Substance Abuse and Mental Health Services Administration (SAMHSA). Substance Use Disorders.
[SAMHSA] -

4. US Preventive Services Task Force, Curry SJ, Krist AH, et al. Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2018;320:1899-1909.
[PubMed Abstract] -

5. Krist AH, Davidson KW, Mangione CM, et al. Screening for Unhealthy Drug Use: US Preventive Services Task Force Recommendation Statement. JAMA. 2020;323:2301-2309.
[PubMed Abstract] -

6. Patnode CD, Perdue LA, Rushkin M, O'Connor EA. Screening for Unhealthy Drug Use in Primary Care in Adolescents and Adults, Including Pregnant Persons: Updated Systematic Review for the U.S. Preventive Services Task Force [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2020 Jun. Report No.:19-05255-EF-1.
[PubMed Abstract] -

7. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction. 1993;88:791-804.
[PubMed Abstract] -

8. Fiellin DA, Reid MC, O'Connor PG. Screening for alcohol problems in primary care: a systematic review. Arch Intern Med. 2000;160:1977-89.
[PubMed Abstract] -

9. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. Arch Intern Med. 1998;158:1789-95.
[PubMed Abstract] -

10. National Institute on Alcohol Abuse and Alcoholism. Helping Patients Who Drink Too Much: A Clinician's Guide. NIH Publication No. 07–3769. Updated 2005 Edition.
[NIAAA] -

11. WHO ASSIST Working Group. The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST): development, reliability and feasibility. Addiction. 2002;97:1183-94.
[PubMed Abstract] -

12. Crane HM, Lober W, Webster E, et al. Routine collection of patient-reported outcomes in an HIV clinic setting: the first 100 patients. Curr HIV Res. 2007;5:109-18.

[PubMed Abstract] -

13. Fredericksen R, Crane PK, Tufano J, et al. Integrating a web-based, patient-administered assessment into primary care for HIV-infected adults. J AIDS HIV Res. 2012;4:47-55.
[PubMed Abstract] -

14. Fredericksen RJ, Edwards TC, Merlin JS, et al. Patient and provider priorities for self-reported domains of HIV clinical care. AIDS Care. 2015;27:1255-64.
[PubMed Abstract] -

15. National Institute on Drug Abuse (NIDA). NIDA Quick Screen and NIDA-Modified ASSIST
[NIDA] -

16. Brown RL, Leonard T, Saunders LA, Papasouliotis O. A two-item conjoint screen for alcohol and other drug problems. J Am Board Fam Pract. 2001;14:95-106.
[PubMed Abstract] -

17. Smith PC, Schmidt SM, Allensworth-Davies D, Saitz R. A single-question screening test for drug use in primary care. Arch Intern Med. 2010;170:1155-60.
[PubMed Abstract] -

18. McNeely J, Strauss SM, Saitz R, et al. A Brief Patient Self-administered Substance Use Screening Tool for Primary Care: Two-site Validation Study of the Substance Use Brief Screen (SUBS). Am J Med. 2015;128:784.e9-19.
[PubMed Abstract] -

19. Substance Abuse and Mental Health Services Administration. (2022). Key substance use and mental health indicators in the United States: Results from the 2021 National Survey on Drug Use and Health (HHS Publication No. PEP22-07-01-005, NSDUH Series H-57). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. December 2022.
[SAMHSA] -

20. Substance Abuse and Mental Health Services Administration (SAMHSA). (2019). Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.
[SAMHSA] -

21. Agrawal A, Lynskey MT. The genetic epidemiology of cannabis use, abuse and dependence. Addiction. 2006;101:801-12.
[PubMed Abstract] -

22. Tsuang MT, Bar JL, Harley RM, Lyons MJ. The Harvard Twin Study of Substance Abuse: what we have learned. Harv Rev Psychiatry. 2001;9:267-79.
[PubMed Abstract] -

23. Tsuang MT, Lyons MJ, Meyer JM, et al. Co-occurrence of abuse of different drugs in men: the role of drug-specific and shared vulnerabilities. Arch Gen Psychiatry. 1998;55:967-72.
[PubMed Abstract] -

24. Jones CM, Compton WM, Mustaquim D. Patterns and Characteristics of Methamphetamine Use Among Adults - United States, 2015-2018. MMWR Morb Mortal Wkly Rep. 2020;69:317-323.
[PubMed Abstract] -

25. Rao U, Ryan ND, Dahl RE, et al. Factors associated with the development of substance use disorder in depressed adolescents. J Am Acad Child Adolesc Psychiatry. 1999;38:1109-17.
[PubMed Abstract] -

26. Rowan ZR. Social Risk Factors of Black and White Adolescents' Substance Use: The Differential Role of Siblings and Best Friends. J Youth Adolesc. 2016;45:1482-96.
[PubMed Abstract] -

27. Knerich V, Jones AA, Seyedin S, et al. Social and structural factors associated with substance use within the support network of adults living in precarious housing in a socially marginalized neighborhood of Vancouver, Canada. PLoS One. 2019;14:e0222611.
[PubMed Abstract] -

28. Gage SH, Sumnall HR. Rat Park: How a rat paradise changed the narrative of addiction. Addiction. 2019;114:917-922.
[PubMed Abstract] -

29. Hughes K, Bellis MA, Hardcastle KA, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. Lancet Public Health. 2017;2:e356-e366.
[PubMed Abstract] -

30. Beatty LA, Jones DJ, Doctor L. Reducing HIV/AIDS and criminal justice involvement in African Americans as a consequence of drug abuse. J Health Care Poor Underserved. 2005;16:1-5.
[PubMed Abstract] -

31. Koob GF. The neurobiology of addiction: a neuroadaptational view relevant for diagnosis. Addiction. 2006;101 Suppl 1:23-30.
[PubMed Abstract] -

32. Moffitt TE, Arseneault L, Belsky D, et al. A gradient of childhood self-control predicts health, wealth, and public safety. Proc Natl Acad Sci U S A. 2011;108:2693-8.
[PubMed Abstract] -

33. Bing EG, Burnam MA, Longshore D, et al. Psychiatric disorders and drug use among human immunodeficiency virus-infected adults in the United States. Arch Gen Psychiatry. 2001;58:721-8.
[PubMed Abstract] -

34. Durvasula R, Miller TR. Substance abuse treatment in persons with HIV/AIDS: challenges in managing triple diagnosis. Behav Med. 2014;40:43-52.
[PubMed Abstract] -

35. Centers for Disease Control and Prevention. Behavioral and Clinical Characteristics of Persons with Diagnosed HIV Infection—Medical Monitoring Project, United States, 2021 Cycle (June 2021–May 2022). HIV Surveillance Special Report 32. Published August 2023.
[CDC] -

36. Bavinton BR, Pinto AN, Phanuphak N, et al. Viral suppression and HIV transmission in serodiscordant male couples: an international, prospective, observational, cohort study. Lancet HIV. 2018;5:e438-e447.
[PubMed Abstract] -

37. Rodger AJ, Cambiano V, Bruun T, et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. Lancet. 2019;393:2428-38.

[PubMed Abstract] -

38. Rodger AJ, Cambiano V, Bruun T, et al. Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy. JAMA. 2016;316:171-81.
[PubMed Abstract] -

39. Kalichman SC, Grebler T, Amaral CM, et al. Viral suppression and antiretroviral medication adherence among alcohol using HIV-positive adults. Int J Behav Med. 2014;21:811-20.
[PubMed Abstract] -

40. Mellins CA, Havens JF, McDonnell C, et al. Adherence to antiretroviral medications and medical care in HIV-infected adults diagnosed with mental and substance abuse disorders. AIDS Care. 2009;21:168-77.
[PubMed Abstract] -

41. Mimiaga MJ, Reisner SL, Grasso C, et al. Substance use among HIV-infected patients engaged in primary care in the United States: findings from the Centers for AIDS Research Network of Integrated Clinical Systems cohort. Am J Public Health. 2013;103:1457-67.
[PubMed Abstract] -

42. Forrest DW, Metsch LR, LaLota M, Cardenas G, Beck DW, Jeanty Y. Crystal methamphetamine use and sexual risk behaviors among HIV-positive and HIV-negative men who have sex with men in South Florida. J Urban Health. 2010;87:480-5.
[PubMed Abstract] -

43. Plankey MW, Ostrow DG, Stall R, et al. The relationship between methamphetamine and popper use and risk of HIV seroconversion in the multicenter AIDS cohort study. J Acquir Immune Defic Syndr. 2007;45:85-92.
[PubMed Abstract] -

44. Rajasingham R, Mimiaga MJ, White JM, Pinkston MM, Baden RP, Mitty JA. A systematic review of behavioral and treatment outcome studies among HIV-infected men who have sex with men who abuse crystal methamphetamine. AIDS Patient Care STDS. 2012;26:36-52.
[PubMed Abstract] -

45. Pence BW, Miller WC, Gaynes BN, Eron JJ Jr. Psychiatric illness and virologic response in patients initiating highly active antiretroviral therapy. J Acquir Immune Defic Syndr. 2007;44:159-66.
[PubMed Abstract] -

46. Remien RH, Bauman LJ, Mantell JE, et al. Barriers and facilitators to engagement of vulnerable populations in HIV primary care in New York City. J Acquir Immune Defic Syndr. 2015;69 Suppl 1:S16-24.
[PubMed Abstract] -

47. Celentano DD, Lucas G. Optimizing treatment outcomes in HIV-infected patients with substance abuse issues. Clin Infect Dis. 2007;45 Suppl 4:S318-23.
[PubMed Abstract] -

48. Sohler NL, Wong MD, Cunningham WE, Cabral H, Drainoni ML, Cunningham CO. Type and pattern of illicit drug use and access to health care services for HIV-infected people. AIDS Patient Care STDS. 2007;21 Suppl 1:S68-76.
[PubMed Abstract] -

49. Surratt HL, O'Grady CL, Levi-Minzi MA, Kurtz SP. Medication adherence challenges among HIV positive substance abusers: the role of food and housing insecurity. AIDS Care. 2015;27:307-14.
[PubMed Abstract] -

50. Roux P, Carrieri MP, Cohen J, et al. Retention in opioid substitution treatment: a major predictor of long-term virological success for HIV-infected injection drug users receiving antiretroviral treatment. Clin Infect Dis. 2009;49:1433-40.
[PubMed Abstract] -

51. Fanucchi L, Springer SA, Korthuis PT. Medications for Treatment of Opioid Use Disorder among Persons Living with HIV. Curr HIV/AIDS Rep. 2019;16:1-6.
[PubMed Abstract] -

52. Cropsey KL, Willig JH, Mugavero MJ, et al. Cigarette Smokers are Less Likely to Have Undetectable Viral Loads: Results From Four HIV Clinics. J Addict Med. 2016;10:13-9.
[PubMed Abstract] -

53. Valiathan R, Miguez MJ, Patel B, Arheart KL, Asthana D. Tobacco smoking increases immune activation and impairs T-cell function in HIV infected patients on antiretrovirals: a cross-sectional pilot study. PLoS One. 2014;9:e97698.
[PubMed Abstract] -

54. Agudelo M, Khatavkar P, Yndart A, et al. Alcohol abuse and HIV infection: role of DRD2. Curr HIV Res. 2014;12:234-42.
[PubMed Abstract] -

55. Baum MK, Rafie C, Lai S, Sales S, Page B, Campa A. Crack-cocaine use accelerates HIV disease progression in a cohort of HIV-positive drug users. J Acquir Immune Defic Syndr. 2009;50:93-9.
[PubMed Abstract] -

56. Baum MK, Rafie C, Lai S, Sales S, Page JB, Campa A. Alcohol use accelerates HIV disease progression. AIDS Res Hum Retroviruses. 2010;26:511-8.
[PubMed Abstract] -

57. Cook JA, Burke-Miller JK, Cohen MH, et al. Crack cocaine, disease progression, and mortality in a multicenter cohort of HIV-1 positive women. AIDS. 2008;22:1355-63.
[PubMed Abstract] -

58. Edelman EJ, Cheng DM, Krupitsky EM, et al. Heroin Use and HIV Disease Progression: Results from a Pilot Study of a Russian Cohort. AIDS Behav. 2015;19:1089-97.
[PubMed Abstract] -

59. Malbergier A, Amaral RA, Cardoso LD. Alcohol dependence and CD4 cell count: is there a relationship? AIDS Care. 2015;27:54-8.
[PubMed Abstract] -

60. Molina PE, Bagby GJ, Nelson S. Biomedical consequences of alcohol use disorders in the HIV-infected host. Curr HIV Res. 2014;12:265-75.
[PubMed Abstract] -

61. Passaro RC, Pandhare J, Qian HZ, Dash C. The Complex Interaction Between Methamphetamine Abuse and HIV-1 Pathogenesis. J Neuroimmune Pharmacol. 2015;10:477-86.
[PubMed Abstract] -

62. Crane HM, McCaul ME, Chander G, et al. Prevalence and Factors Associated with Hazardous Alcohol Use Among Persons Living with HIV Across the US in the Current Era of Antiretroviral Treatment. AIDS Behav. 2017;21:1914-25.
[PubMed Abstract] -

63. Schuckit MA. Genetics of the risk for alcoholism. Am J Addict. 2000 Spring;9:103-12.
[PubMed Abstract] -

64. Wilson SR, Knowles SB, Huang Q, Fink A. The prevalence of harmful and hazardous alcohol consumption in older U.S. adults: data from the 2005-2008 National Health and Nutrition Examination Survey (NHANES). J Gen Intern Med. 2014;29:312-9.
[PubMed Abstract] -

65. Moyer VA. Screening and behavioral counseling interventions in primary care to reduce alcohol misuse: U.S. preventive services task force recommendation statement. Ann Intern Med. 2013;159:210-8.
[PubMed Abstract] -

66. Jonas DE, Garbutt JC, Amick HR, et al. Behavioral counseling after screening for alcohol misuse in primary care: a systematic review and meta-analysis for the U.S. Preventive Services Task Force. Ann Intern Med. 2012;157:645-54.
[PubMed Abstract] -

67. Flanagan JC, Jones JL, Jarnecke AM, Back SE. Behavioral Treatments for Alcohol Use Disorder and Post-Traumatic Stress Disorder. Alcohol Res. 2018;39:181-92.
[PubMed Abstract] -

68. Witkiewitz K, Litten RZ, Leggio L. Advances in the science and treatment of alcohol use disorder. Sci Adv. 2019;5:eaax4043.
[PubMed Abstract] -

69. Friedmann PD. Clinical practice. Alcohol use in adults. N Engl J Med. 2013 Jan 24;368:365-73.
[PubMed Abstract] -

70. Substance Abuse and Mental Health Services Administration and National Institute on Alcohol Abuse and Alcoholism. Medication for the treatment of alcohol use disorder: a brief guide. HHS Publication No. (SMA) 15-4907. Rockville, MD: Substance Abuse and Mental Health Services Administration, October, 2015.
[SAMHSA] -

71. Jonas DE, Amick HR, Feltner C, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. JAMA. 2014;311:1889-900.
[PubMed Abstract] -

72. Rösner S, Leucht S, Lehert P, Soyka M. Acamprosate supports abstinence, naltrexone prevents excessive drinking: evidence from a meta-analysis with unreported outcomes. J Psychopharmacol. 2008;22:11-23.
[PubMed Abstract] -

73. Center for Substance Abuse Treatment. Incorporating Alcohol Pharmacotherapies into Medical Practice. Treatment Improvement Protocol (TIP) Series, No. 49. HHS Publication No. (SMA) 09-4380. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2009.
[SAMHSA] -

74. Anton RF. Naltrexone for the management of alcohol dependence. N Engl J Med. 2008;359:715-21. [PubMed Abstract] -

75. Stoddard J, Zummo J. Oral and long-acting injectable naltrexone: removal of boxed warning for hepatotoxicity. J Clin Psychiatry. 2015;76:1695. [PubMed Abstract] -

76. Maisel NC, Blodgett JC, Wilbourne PL, Humphreys K, Finney JW. Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful? Addiction. 2013;108:275-93. [PubMed Abstract] -

77. Garbutt JC, Kranzler HR, O'Malley SS, et al. Efficacy and tolerability of long-acting injectable naltrexone for alcohol dependence: a randomized controlled trial. JAMA. 2005;293:1617-25. [PubMed Abstract] -

78. Kranzler HR, Wesson DR, Billot L. Naltrexone depot for treatment of alcohol dependence: a multicenter, randomized, placebo-controlled clinical trial. Alcohol Clin Exp Res. 2004;28:1051-9. [PubMed Abstract] -

79. Lobmaier PP, Kunøe N, Gossop M, Waal H. Naltrexone depot formulations for opioid and alcohol dependence: a systematic review. CNS Neurosci Ther. 2011;17:629-36. [PubMed Abstract] -

80. Kenna GA, McGeary JE, Swift RM. Pharmacotherapy, pharmacogenomics, and the future of alcohol dependence treatment, part 1. Am J Health Syst Pharm. 2004;61:2272-9. [PubMed Abstract] -

81. Mason BJ, Heyser CJ. Acamprosate: a prototypic neuromodulator in the treatment of alcohol dependence. CNS Neurol Disord Drug Targets. 2010;9:23-32. [PubMed Abstract] -

82. Whitworth AB, Fischer F, Lesch OM, et al. Comparison of acamprosate and placebo in long-term treatment of alcohol dependence. Lancet. 1996;347:1438-42. [PubMed Abstract] -

83. Sass H, Soyka M, Mann K, Zieglgänsberger W. Relapse prevention by acamprosate. Results from a placebo-controlled study on alcohol dependence. Arch Gen Psychiatry. 1996;53:673-80. [PubMed Abstract] -

84. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Department of Health and Human Services. Considerations for antiretroviral use in special patient populations: substance use disorders and HIV. June 3, 2021. [HIV.gov] -

85. Skinner MD, Lahmek P, Pham H, Aubin HJ. Disulfiram efficacy in the treatment of alcohol dependence: a meta-analysis. PLoS One. 2014;9:e87366. [PubMed Abstract] -

86. Kranzler HR, Soyka M. Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. JAMA. 2018;320:815-24. [PubMed Abstract] -

87. McCance-Katz EF, Gruber VA, Beatty G, et al. Interaction of disulfiram with antiretroviral medications:

efavirenz increases while atazanavir decreases disulfiram effect on enzymes of alcohol metabolism. Am J Addict. 2014;23:137-44.
[PubMed Abstract] -

88. Cvetkovic RS, Goa KL. Lopinavir/ritonavir: a review of its use in the management of HIV infection. Drugs. 2003;63:769-802.
[PubMed Abstract] -

89. Mason BJ, Quello S, Goodell V, Shadan F, Kyle M, Begovic A. Gabapentin treatment for alcohol dependence: a randomized clinical trial. JAMA Intern Med. 2014;174:70-7.
[PubMed Abstract] -

90. Blodgett JC, Del Re AC, Maisel NC, Finney JW. A meta-analysis of topiramate's effects for individuals with alcohol use disorders. Alcohol Clin Exp Res. 2014;38:1481-8.
[PubMed Abstract] -

91. Guglielmo R, Martinotti G, Quatrale M, et al. Topiramate in Alcohol Use Disorders: Review and Update. CNS Drugs. 2015;29:383-95.
[PubMed Abstract] -

92. Shinn AK, Greenfield SF. Topiramate in the treatment of substance-related disorders: a critical review of the literature. J Clin Psychiatry. 2010;71:634-48.
[PubMed Abstract] -

93. Anton RF, Moak DH, Latham P, et al. Naltrexone combined with either cognitive behavioral or motivational enhancement therapy for alcohol dependence. J Clin Psychopharmacol. 2005;25:349-57.
[PubMed Abstract] -

94. Anton RF, O'Malley SS, Ciraulo DA, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. JAMA. 2006;295:2003-17.
[PubMed Abstract] -

95. Litten RZ, Castle IJ, Falk D, et al. The placebo effect in clinical trials for alcohol dependence: an exploratory analysis of 51 naltrexone and acamprosate studies. Alcohol Clin Exp Res. 2013;37:2128-37.
[PubMed Abstract] -

96. Rösner S, Hackl-Herrwerth A, Leucht S, Lehert P, Vecchi S, Soyka M. Acamprosate for alcohol dependence. Cochrane Database Syst Rev. 2010;:CD004332.
[PubMed Abstract] -

97. Edelman EJ, Moore BA, Holt SR, et al. Efficacy of Extended-Release Naltrexone on HIV-Related and Drinking Outcomes Among HIV-Positive Patients: A Randomized-Controlled Trial. AIDS Behav. 2019;23:211-221.
[PubMed Abstract] -

98. Springer SA, Di Paola A, Azar MM, et al. Extended-Release Naltrexone Improves Viral Suppression Among Incarcerated Persons Living With HIV With Opioid Use Disorders Transitioning to the Community: Results of a Double-Blind, Placebo-Controlled Randomized Trial. J Acquir Immune Defic Syndr. 2018;78:43-53.
[PubMed Abstract] -

99. Kranzler HR, Soyka M. Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. JAMA. 2018;320:815-824.

[PubMed Abstract] -

100. Lake S, Kerr T, Capler R, Shoveller J, Montaner J, Milloy MJ. High-intensity cannabis use and HIV clinical outcomes among HIV-positive people who use illicit drugs in Vancouver, Canada. Int J Drug Policy. 2017;42:63-70.
[PubMed Abstract] -

101. Lorenz DR, Dutta A, Mukerji SS, Holman A, Uno H, Gabuzda D. Marijuana Use Impacts Midlife Cardiovascular Events in HIV-Infected Men. Clin Infect Dis. 2017;65:626-35.
[PubMed Abstract] -

102. Weinstein AM, Gorelick DA. Pharmacological treatment of cannabis dependence. Curr Pharm Des. 2011;17:1351-8.
[PubMed Abstract] -

103. Marshall K, Gowing L, Ali R, Le Foll B. Pharmacotherapies for cannabis dependence. Cochrane Database Syst Rev. 2014;12:CD008940.
[PubMed Abstract] -

104. Kondo KK, Morasco BJ, Nugent SM, et al. Pharmacotherapy for the Treatment of Cannabis Use Disorder: A Systematic Review. Ann Intern Med. 2020;172:398-412.
[PubMed Abstract] -

105. Cooper K, Chatters R, Kaltenthaler E, Wong R. Psychological and psychosocial interventions for cannabis cessation in adults: a systematic review short report. Health Technol Assess. 2015;19:1-130.
[PubMed Abstract] -

106. Substance Abuse and Mental Health Services Administration (SAMHSA). National Registry of Evidence-Based Programs and Practices (NREPP). Brief Marijuana Dependence Counseling (BMDC).
[SAMHSA] -

107. Romanelli F, Smith KM, Pomeroy C. Use of club drugs by HIV-seropositive and HIV-seronegative gay and bisexual men. Top HIV Med. 2003;11:25-32.
[PubMed Abstract] -

108. Bracchi M, Stuart D, Castles R, Khoo S, Back D, Boffito M. Increasing use of 'party drugs' in people living with HIV on antiretrovirals: a concern for patient safety. AIDS. 2015;29:1585-92.
[PubMed Abstract] -

109. Colfax G, Guzman R. Club drugs and HIV infection: a review. Clin Infect Dis. 2006;42:1463-9.
[PubMed Abstract] -

110. Krebs TS, Johansen PØ. Psychedelics and mental health: a population study. PLoS One. 2013;8:e63972.
[PubMed Abstract] -

111. Jones CM, Logan J, Gladden RM, Bohm MK. Vital Signs: Demographic and Substance Use Trends Among Heroin Users - United States, 2002-2013. MMWR Morb Mortal Wkly Rep. 2015;64:719-25.
[PubMed Abstract] -

112. National Institute on Drug Abuse (NIDA). Drug Overdose Death Rates
[NIDA] -

113. Jannetto PJ, Helander A, Garg U, Janis GC, Goldberger B, Ketha H. The Fentanyl Epidemic and Evolution

of Fentanyl Analogs in the United States and the European Union. Clin Chem. 2019;65:242-253. [PubMed Abstract] -

114. Hedegaard H, Miniño AM, Spencer MR, Warner M. Drug overdose deaths in the United States, 1999–2020. NCHS Data Brief, no 428. Hyattsville, MD: National Center for Health Statistics. 2021. [NCHS] -

115. McCabe SE, West BT, Teter CJ, Boyd CJ. Medical and nonmedical use of prescription opioids among high school seniors in the United States. Arch Pediatr Adolesc Med. 2012;166:797-802. [PubMed Abstract] -

116. McHugh RK, Nielsen S, Weiss RD. Prescription drug abuse: from epidemiology to public policy. J Subst Abuse Treat. 2015;48:1-7. [PubMed Abstract] -

117. Golden MR, Lechtenberg R, Glick SN, et al. Outbreak of Human Immunodeficiency Virus Infection Among Heterosexual Persons Who Are Living Homeless and Inject Drugs - Seattle, Washington, 2018. MMWR Morb Mortal Wkly Rep. 2019;68:344-9. [PubMed Abstract] -

118. Peters PJ, Pontones P, Hoover KW, et al. HIV Infection Linked to Injection Use of Oxymorphone in Indiana, 2014-2015. N Engl J Med. 2016;375:229-39. [PubMed Abstract] -

119. Centers for Disease Control and Prevention. Estimated HIV Incidence and Prevalence in the United States, 2017–2021. HIV Surveillance Supplemental Report. 2023;28(3). Published May 2023. [CDC] -

120. Cunningham CO. Opioids and HIV Infection: From Pain Management to Addiction Treatment. Top Antivir Med. 2018;25:143-6. [PubMed Abstract] -

121. Conrad C, Bradley HM, Broz D, et al. Community Outbreak of HIV Infection Linked to Injection Drug Use of Oxymorphone--Indiana, 2015. MMWR Morb Mortal Wkly Rep. 2015;64:443-4. [PubMed Abstract] -

122. Compton WM, Jones CM, Baldwin GT. Relationship between nonmedical prescription-opioid use and heroin use. N Engl J Med. 2016;374:154-63. [PubMed Abstract] -

123. Larochelle MR, Bernson D, Land T, et al. Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality: A Cohort Study. Ann Intern Med. 2018;169:137-145. [PubMed Abstract] -

124. Bart G. Maintenance medication for opiate addiction: the foundation of recovery. J Addict Dis. 2012;31:207-25. [PubMed Abstract] -

125. Bailey GL, Herman DS, Stein MD. Perceived relapse risk and desire for medication assisted treatment among persons seeking inpatient opiate detoxification. J Subst Abuse Treat. 2013;45:302-5. [PubMed Abstract] -

126. Nguyen TA, Hahn JH, Strakowski SM. Pharmacotherapies for treating opioid use disorder. CNS Spectr. 2013;18:289-95.

[PubMed Abstract] -

127. Substance Abuse and Mental Health Services Administration (SAMHSA). Medications for Opioid Use Disorder. Treatment Improvement Protocol (TIP) Series, No. 63. HHS Publication No. (SMA) 09-4380. Rockville, MD: Substance Abuse and Mental Health Services Administration, Updated 2021. [SAMHSA] -

128. Kourounis G, Richards BD, Kyprianou E, Symeonidou E, Malliori MM, Samartzis L. Opioid substitution therapy: Lowering the treatment thresholds. Drug Alcohol Depend. 2016;161:1-8. [PubMed Abstract] -

129. Department of Health and Human Services. Practice Guidelines for the Administration of Buprenorphine for Treating Opioid Use Disorder. April 28, 2021. [Department of Health and Human Services.] -

130. Fudala PJ, Bridge TP, Herbert S, et al. Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. N Engl J Med. 2003;349:949-58. [PubMed Abstract] -

131. Center for Substance Abuse Treatment. Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) Series, No. 43. HHS Publication No. (SMA) 12-4214. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2005. [SAMHSA] -

132. Itzoe M, Guarnieri M. New developments in managing opioid addiction: impact of a subdermal buprenorphine implant. Drug Des Devel Ther. 2017;11:1429-37. [PubMed Abstract] -

133. Rosenthal RN, Goradia VV. Advances in the delivery of buprenorphine for opioid dependence. Drug Des Devel Ther. 2017;11:2493-2505. [PubMed Abstract] -

134. Khalsa J, Vocci F, Altice F, Fiellin D, Miller V. Buprenorphine and HIV primary care: new opportunities for integrated treatment. Clin Infect Dis. 2006;43 Suppl 4:S169-72. [PubMed Abstract] -

135. Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev. 2014;2:CD002207. [PubMed Abstract] -

136. Hser YI, Evans E, Grella C, Ling W, Anglin D. Long-term course of opioid addiction. Harv Rev Psychiatry. 2015;23:76-89. [PubMed Abstract] -

137. Fareed A, Casarella J, Amar R, Vayalapalli S, Drexler K. Methadone maintenance dosing guideline for opioid dependence, a literature review. J Addict Dis. 2010;29:1-14. [PubMed Abstract] -

138. Center for Behavioral Health Statistics and Quality. (2015). Behavioral health trends in the United States: Results from the 2014 National Survey on Drug Use and Health (HHS Publication No. SMA 15-4927, NSDUH Series H-50). [SAMHSA] -

139. Stringer J, Welsh C, Tommasello A. Methadone-associated Q-T interval prolongation and torsades de

pointes. Am J Health Syst Pharm. 2009;66:825-33.
[PubMed Abstract] -

140. Minozzi S, Amato L, Vecchi S, Davoli M, Kirchmayer U, Verster A. Oral naltrexone maintenance treatment for opioid dependence. Cochrane Database Syst Rev. 2011;:CD001333.
[PubMed Abstract] -

141. Krupitsky E, Nunes EV, Ling W, Illeperuma A, Gastfriend DR, Silverman BL. Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial. Lancet. 2011;377:1506-13.
[PubMed Abstract] -

142. Lee JD, Friedmann PD, Kinlock TW, et al. Extended-Release Naltrexone to Prevent Opioid Relapse in Criminal Justice Offenders. N Engl J Med. 2016;374:1232-42.
[PubMed Abstract] -

143. Lee JD, Nunes EV Jr, Novo P, et al. Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial. Lancet. 2018;391:309-318.
[PubMed Abstract] -

144. Murphy SM, McCollister KE, Leff JA, et al. Cost-Effectiveness of Buprenorphine-Naloxone Versus Extended-Release Naltrexone to Prevent Opioid Relapse. Ann Intern Med. 2019;170:90-98.
[PubMed Abstract] -

145. Weiss L, Egan JE, Botsko M, Netherland J, Fiellin DA, Finkelstein R. The BHIVES collaborative: organization and evaluation of a multisite demonstration of integrated buprenorphine/naloxone and HIV treatment. J Acquir Immune Defic Syndr. 2011;56 Suppl 1:S7-13.
[PubMed Abstract] -

146. Weiss L, Netherland J, Egan JE, et al. Integration of buprenorphine/naloxone treatment into HIV clinical care: lessons from the BHIVES collaborative. J Acquir Immune Defic Syndr. 2011;56 Suppl 1:S68-75.
[PubMed Abstract] -

147. Finkelstein R, Netherland J, Sylla L, Gourevitch MN, Cajina A, Cheever L. Policy implications of integrating buprenorphine/naloxone treatment and HIV care. J Acquir Immune Defic Syndr. 2011;56 Suppl 1:S98-S104.
[PubMed Abstract] -

148. LaBelle CT, Han SC, Bergeron A, Samet JH. Office-Based Opioid Treatment with Buprenorphine (OBOT-B): Statewide Implementation of the Massachusetts Collaborative Care Model in Community Health Centers. J Subst Abuse Treat. 2016;60:6-13.
[PubMed Abstract] -

149. Nosyk B, Min JE, Evans E, et al. The Effects of Opioid Substitution Treatment and Highly Active Antiretroviral Therapy on the Cause-Specific Risk of Mortality Among HIV-Positive People Who Inject Drugs. Clin Infect Dis. 2015;61:1157-65.
[PubMed Abstract] -

150. Walley AY, Palmisano J, Sorensen-Alawad A, et al. Engagement and Substance Dependence in a Primary Care-Based Addiction Treatment Program for People Infected with HIV and People at High-Risk for HIV Infection. J Subst Abuse Treat. 2015;59:59-66.
[PubMed Abstract] -

151. Abdul-Quader AS, Feelemyer J, Modi S, et al. Effectiveness of structural-level needle/syringe programs to reduce HCV and HIV infection among people who inject drugs: a systematic review. AIDS Behav. 2013;17:2878-92.
[PubMed Abstract] -

152. Des Jarlais DC. Structural interventions to reduce HIV transmission among injecting drug users. AIDS. 2000;14 Suppl 1:S41-6.
[PubMed Abstract] -

153. Marrazzo JM, del Rio C, Holtgrave DR, et al. HIV prevention in clinical care settings: 2014 recommendations of the International Antiviral Society-USA Panel. JAMA. 2014;312:390-409.
[PubMed Abstract] -

154. Palmateer N, Kimber J, Hickman M, Hutchinson S, Rhodes T, Goldberg D. Evidence for the effectiveness of sterile injecting equipment provision in preventing hepatitis C and human immunodeficiency virus transmission among injecting drug users: a review of reviews. Addiction. 2010;105:844-59.
[PubMed Abstract] -

155. Vancouver Coastal Health/Insite - Supervised Injection Site
[Insite] -

156. Meader N, Li R, Des Jarlais DC, Pilling S. Psychosocial interventions for reducing injection and sexual risk behaviour for preventing HIV in drug users. Cochrane Database Syst Rev. 2010;:CD007192.
[PubMed Abstract] -

157. Walley AY, Xuan Z, Hackman HH, et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. BMJ. 2013;346:f174.
[PubMed Abstract] -

158. Bachhuber MA, McGinty EE, Kennedy-Hendricks A, Niederdeppe J, Barry CL. Messaging to Increase Public Support for Naloxone Distribution Policies in the United States: Results from a Randomized Survey Experiment. PLoS One. 2015;10:e0130050.
[PubMed Abstract] -

159. The Network for Public Health Law. Legal interventions to reduce overdose mortality: naloxone access and overdose Good Samaritan laws.
[Network for Public Health Law] -

160. Wright AP, Becker WC, Schiff GD. Strategies for Flipping the Script on Opioid Overprescribing. JAMA Intern Med. 2016;176:7-8.
[PubMed Abstract] -

161. Lum PJ, Little S, Botsko M, et al. Opioid-prescribing practices and provider confidence recognizing opioid analgesic abuse in HIV primary care settings. J Acquir Immune Defic Syndr. 2011;56 Suppl 1:S91-7.
[PubMed Abstract] -

162. Jamison RN, Sheehan KA, Scanlan E, Matthews M, Ross EL. Beliefs and attitudes about opioid prescribing and chronic pain management: survey of primary care providers. J Opioid Manag. 2014;10:375-82.
[PubMed Abstract] -

163. Nerlander LMC, Hoots BE, Bradley H, Broz D, Thorson A, Paz-Bailey G. HIV infection among MSM who inject methamphetamine in 8 US cities. Drug Alcohol Depend. 2018;190:216-223.
[PubMed Abstract] -

164. Daniulaityte R, Silverstein SM, Crawford TN, et al. Methamphetamine Use and Its Correlates among Individuals with Opioid Use Disorder in a Midwestern U.S. City. Subst Use Misuse. 2020;:1-9.
[PubMed Abstract] -

165. Palamar JJ, Han BH, Keyes KM. Trends in characteristics of individuals who use methamphetamine in the United States, 2015-2018. Drug Alcohol Depend. 2020;213:108089.
[PubMed Abstract] -

166. Hoenigl M, Chaillon A, Moore DJ, Morris SR, Smith DM, Little SJ. Clear Links Between Starting Methamphetamine and Increasing Sexual Risk Behavior: A Cohort Study Among Men Who Have Sex With Men. J Acquir Immune Defic Syndr. 2016;71:551-7.
[PubMed Abstract] -

167. Koblin BA, Murrill C, Camacho M, et al. Amphetamine use and sexual risk among men who have sex with men: results from the National HIV Behavioral Surveillance study--New York City. Subst Use Misuse. 2007;42:1613-28.
[PubMed Abstract] -

168. Knapp WP, Soares BG, Farrel M, Lima MS. Psychosocial interventions for cocaine and psychostimulant amphetamines related disorders. Cochrane Database Syst Rev. 2007;:CD003023.
[PubMed Abstract] -

169. Lee NK, Rawson RA. A systematic review of cognitive and behavioural therapies for methamphetamine dependence. Drug Alcohol Rev. 2008;27:309-17.
[PubMed Abstract] -

170. Carrico AW, Flentje A, Gruber VA, et al. Community-based harm reduction substance abuse treatment with methamphetamine-using men who have sex with men. J Urban Health. 2014;91:555-67.
[PubMed Abstract] -

171. Kishi T, Matsuda Y, Iwata N, Correll CU. Antipsychotics for cocaine or psychostimulant dependence: systematic review and meta-analysis of randomized, placebo-controlled trials. J Clin Psychiatry. 2013;74:e1169-80.
[PubMed Abstract] -

172. Pérez-Mañá C, Castells X, Torrens M, Capellà D, Farre M. Efficacy of psychostimulant drugs for amphetamine abuse or dependence. Cochrane Database Syst Rev. 2013;:CD009695.
[PubMed Abstract] -

173. Brackins T, Brahm NC, Kissack JC. Treatments for methamphetamine abuse: a literature review for the clinician. J Pharm Pract. 2011;24:541-50.
[PubMed Abstract] -

174. Colfax GN, Santos GM, Das M, et al. Mirtazapine to reduce methamphetamine use: a randomized controlled trial. Arch Gen Psychiatry. 2011;68:1168-75.
[PubMed Abstract] -

175. Trivedi MH, Walker R, Ling W, et al. Bupropion and Naltrexone in Methamphetamine Use Disorder. N Engl J Med. 2021;384:140-53.
[PubMed Abstract] -

176. Jamal A, Agaku IT, O'Connor E, King BA, Kenemer JB, Neff L. Current cigarette smoking among adults--United States, 2005-2013. MMWR Morb Mortal Wkly Rep. 2014;63:1108-12.
[MMWR] -

177. Jamal A, Homa DM, O'Connor E, et al. Current Cigarette Smoking Among Adults - United States, 2005-2014. MMWR Morb Mortal Wkly Rep. 2015;64:1233-40.
[PubMed Abstract] -

178. Mdodo R, Frazier EL, Dube SR, et al. Cigarette smoking prevalence among adults with HIV compared with the general adult population in the United States: cross-sectional surveys. Ann Intern Med. 2015;162:335-44.
[PubMed Abstract] -

179. Cook BL, Wayne GF, Kafali EN, Liu Z, Shu C, Flores M. Trends in smoking among adults with mental illness and association between mental health treatment and smoking cessation. JAMA. 2014;311:172-82.
[PubMed Abstract] -

180. Borup G, Mikkelsen KL, Tønnesen P, Christrup LL. Exploratory survey study of long-term users of nicotine replacement therapy in Danish consumers. Harm Reduct J. 2015;12:2.
[PubMed Abstract] -

181. Le Houezec J, Aubin HJ. Pharmacotherapies and harm-reduction options for the treatment of tobacco dependence. Expert Opin Pharmacother. 2013;14:1959-67.
[PubMed Abstract] -

182. U.S. Public Health Service. A clinical practice guideline for treating tobacco use and dependence: 2008 update. A U.S. Public Health Service report. Am J Prev Med. 2008;35:158-76.
[PubMed Abstract] -

183. Krist AH, Davidson KW, Mangione CM, et al. Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Persons: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;325:265-79.
[PubMed Abstract] -

184. Barua RS, Rigotti NA, Benowitz NL, et al. 2018 ACC Expert Consensus Decision Pathway on Tobacco Cessation Treatment: A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol. 2018;72:3332-65.
[PubMed Abstract] -

185. Hajek P, Phillips-Waller A, Przulj D, et al. A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy. N Engl J Med. 2019;380:629-37.
[PubMed Abstract] -

186. Butt YM, Smith ML, Tazelaar HD, et al. Pathology of Vaping-Associated Lung Injury. N Engl J Med. 2019;381:1780-1.
[PubMed Abstract] -

187. Layden JE, Ghinai I, Pray I, et al. Pulmonary Illness Related to E-Cigarette Use in Illinois and Wisconsin - Final Report. N Engl J Med. 2020;382:903-16.
[PubMed Abstract] -

188. Ashare RL, Thompson M, Serrano K, et al. Placebo-controlled randomized clinical trial testing the

efficacy and safety of varenicline for smokers with HIV. Drug Alcohol Depend. 2019;200:26-33.
[PubMed Abstract] -

189. Mercié P, Arsandaux J, Katlama C, et al. Efficacy and safety of varenicline for smoking cessation in people living with HIV in France (ANRS 144 Inter-ACTIV): a randomised controlled phase 3 clinical trial. Lancet HIV. 2018;5:e126-e135.
[PubMed Abstract] -

## References

- Department of Health and Human Services. Practice Guidelines for the Administration of Buprenorphine for Treating Opioid Use Disorder. Federal Register / Vol. 86, No. 80 / Wednesday, April 28, 2021
[DHHS] -

- Metsch LR, Feaster DJ, Gooden L, et al. Effect of Patient Navigation With or Without Financial Incentives on Viral Suppression Among Hospitalized Patients With HIV Infection and Substance Use: A Randomized Clinical Trial. JAMA. 2016;316:156-70.
[PubMed Abstract] -

- Spillane S, Shiels MS, Best AF, et al. Trends in Alcohol-Induced Deaths in the United States, 2000-2016. JAMA Netw Open. 2020;3:e1921451.
[PubMed Abstract] -

- Spivak AM, Andrade A, Eisele E, et al. A pilot study assessing the safety and latency-reversing activity of disulfiram in HIV-1-infected adults on antiretroviral therapy. Clin Infect Dis. 2014;58:883-90.
[PubMed Abstract] -

- Sterling LH, Windle SB, Filion KB, Touma L, Eisenberg MJ. Varenicline and Adverse Cardiovascular Events: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc. 2016;5(2).
[PubMed Abstract] -

- Substance Abuse and Mental Health Services Administration (SAMHSA). Buprenorphine treatment physician locator.
[SAMHSA] -

- Substance Abuse and Mental Health Services Administration (SAMHSA). Buprenorphine.
[SAMHSA] -

- Tetrault JM, Tate JP, McGinnis KA, et al. Hepatic safety and antiretroviral effectiveness in HIV-infected patients receiving naltrexone. Alcohol Clin Exp Res. 2012;36:318-24.
[PubMed Abstract] -

- Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. Pain Med. 2005 Nov-Dec;6(6):432-42.
[PubMed Abstract] -

- Weiner SG , MD, MPH, Baker O , PhD, Bernson D , MPH, Schuur JD , MD, MS. One year mortality of patients treated with naloxone for opioid overdose by emergency medical services. Subst Abus. 2020:1-5.
[PubMed Abstract] -

- White AM, Castle IP, Hingson RW, Powell PA. Using Death Certificates to Explore Changes in Alcohol-Related Mortality in the United States, 1999 to 2017. Alcohol Clin Exp Res. 2020;44:178-187. [PubMed Abstract] -

- Wilson N, Kariisa M, Seth P, Smith H 4th, Davis NL. Drug and Opioid-Involved Overdose Deaths —United States, 2017-2018. MMWR Morb Mortal Wkly Rep. 2020;69:290-7. [PubMed Abstract] -

# Figures

**Figure 1 Number of Persons Age 12 and Older with a Past Year Substance Disorder, United States, 2021**

Abbreviations: SUD = substance use disorder; Rx denotes medical prescription
Note: SUD refers to dependence or abuse in the past year related to the use of alcohol or illicit drugs in that same period.

Source: Substance Abuse and Mental Health Services Administration. (2022). Key substance use and mental health indicators in the United States: Results from the 2021 National Survey on Drug Use and Health (HHS Publication No. PEP22-07-01-005, NSDUH Series H-57). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. December 2022.

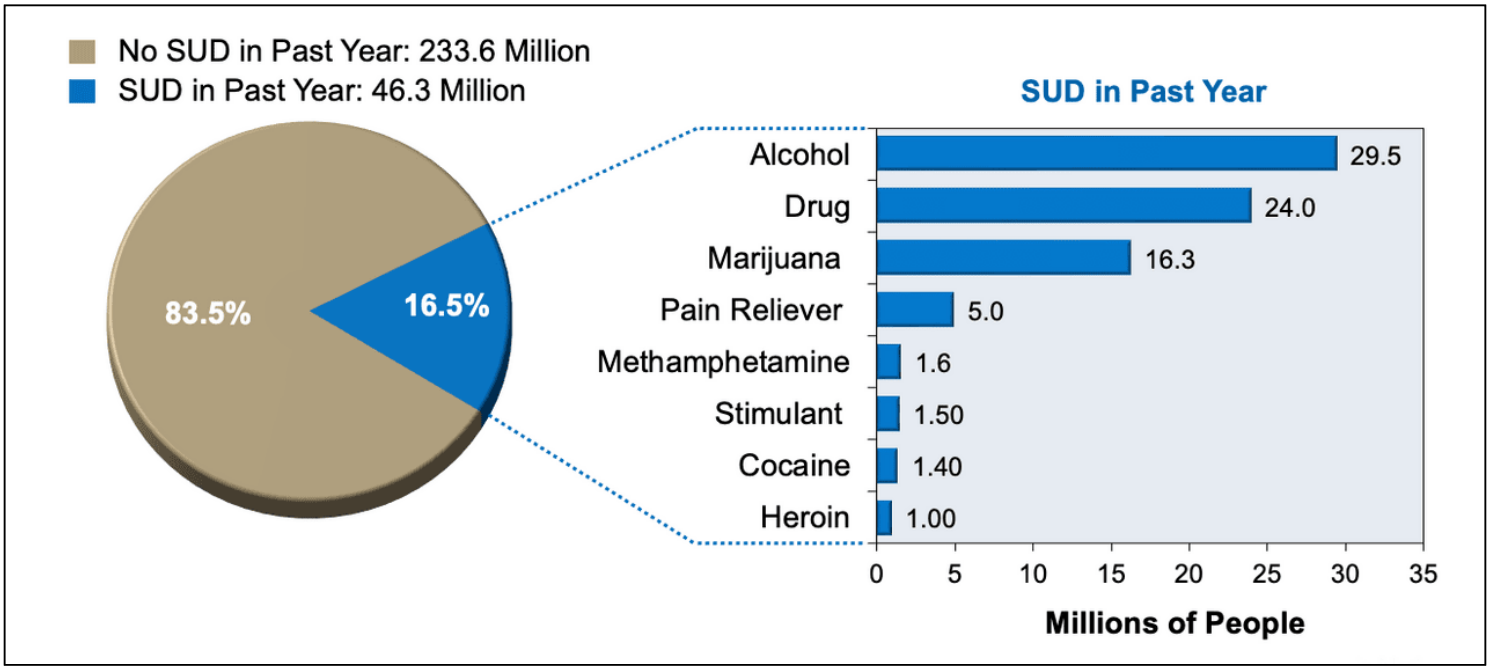

**Figure 2 Current, Binge, and Heavy Alcohol Use Among People Age 12 Years or Older, United States, 2021**

Note: Binge Alcohol Use is defined as drinking ≥5 drinks (for males) or ≥4 drinks (for females) on the same occasion on ≥1 day in the past 30 days. Heavy Alcohol Use is defined as binge drinking on the same occasion on ≥5 days in the past 30 days; all heavy alcohol users are also binge alcohol users.

Source: Substance Abuse and Mental Health Services Administration. (2022). Key substance use and mental health indicators in the United States: Results from the 2021 National Survey on Drug Use and Health (HHS Publication No. PEP22-07-01-005, NSDUH Series H-57). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. December 2022.

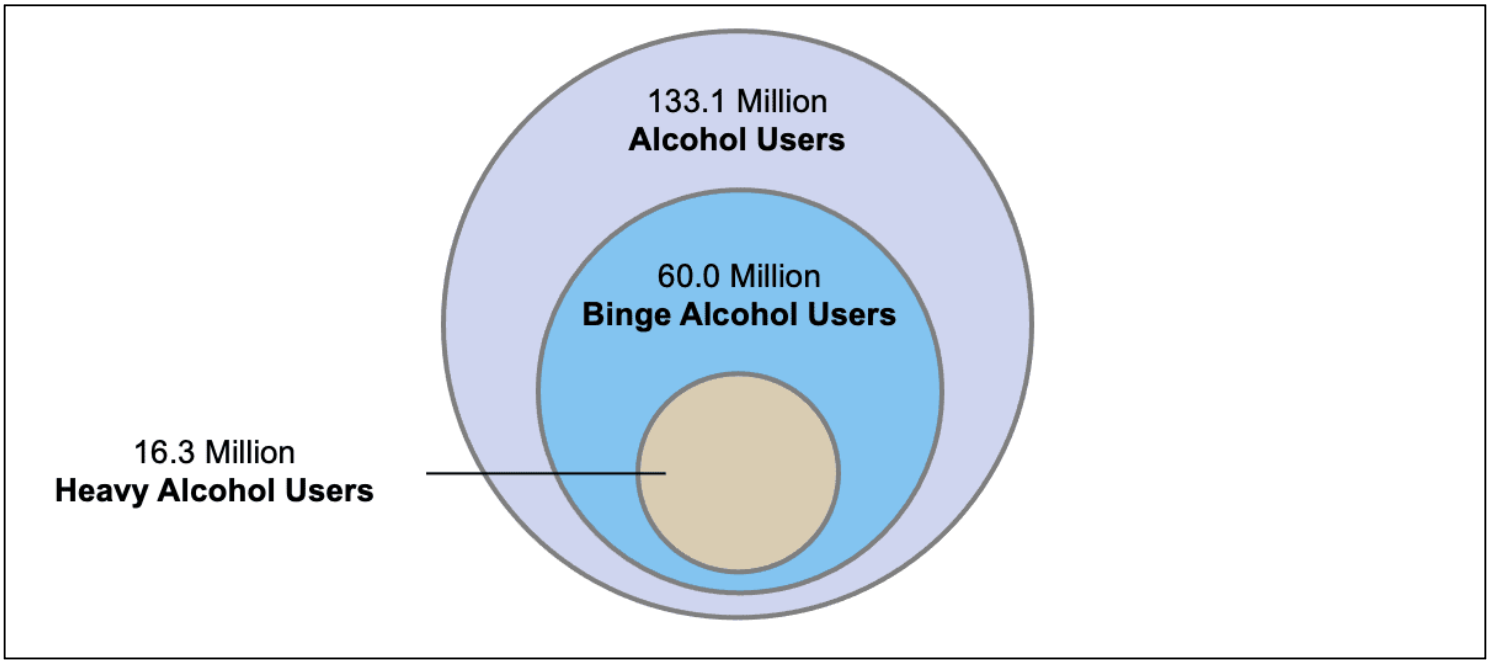

**Figure 3 Neurochemical Circuits Involved in Alcohol Dependence and Craving**

This figure shows ethanol leading to increased dopamine levels in nucleus accumbens. Naltrexone works by blocking opioid receptors and causes a reduction in dopamine levels in the nucleus accumbens, which reduces the reward or pleasure associated with alcohol ingestion.

Source: Anton RF. Naltrexone for the management of alcohol dependence. N Engl J Med. 2008;359:715-21.


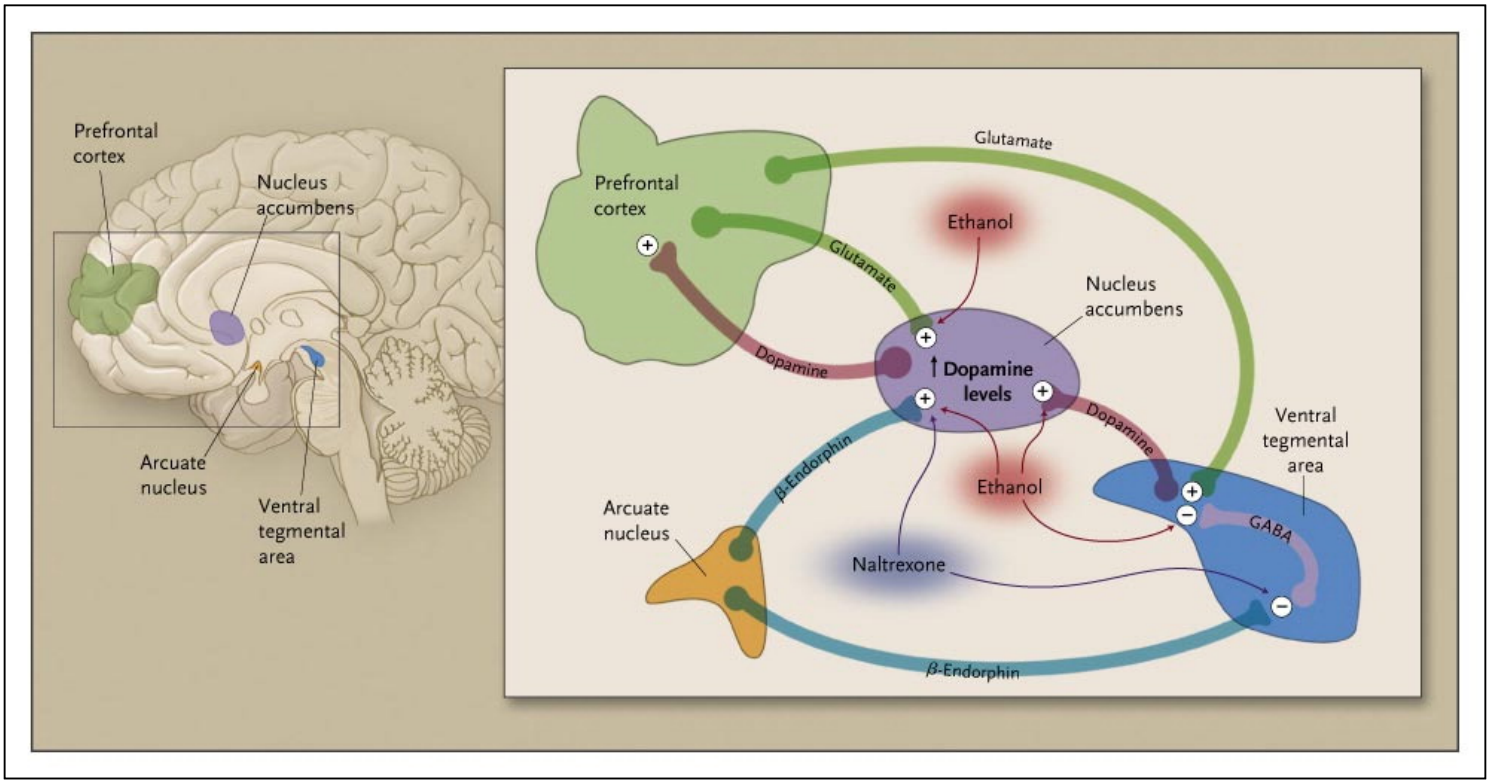

**Figure 4 Impact of Long-Acting Naltrexone on Median Heavy Drinking Days per Month**

This graphic shows results from a 6-month, placebo-controlled study that randomized 624 alcohol-dependent adults to receive either placebo or one of two doses of extended release injectable naltrexone (190 mg per month or 380 mg every 4 weeks).

Source: Garbutt JC, Kranzler HR, O'Malley SS, et al. Efficacy and tolerability of long-acting injectable naltrexone for alcohol dependence: a randomized controlled trial. JAMA. 2005;293:1617-25.

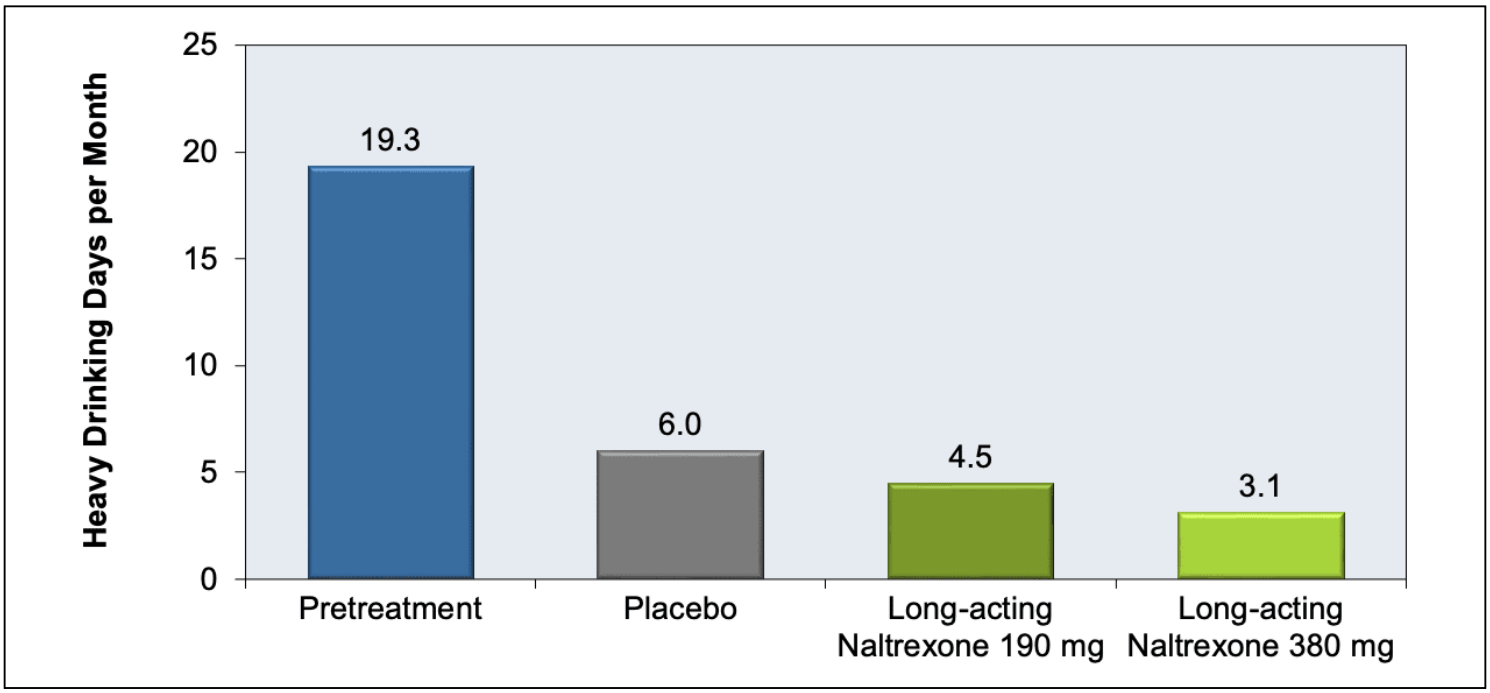

**Figure 5 Acamprosate in Persons with Alcohol Dependence**

This graph shows results of acamprosate versus placebo in 272 persons with alcohol dependence. Results are shown for day 60 during treatment, at week 48 (end-of-treatment), and week 96 (48 weeks posttreatment).

Source: Sass H, Soyka M, Mann K, Zieglgänsberger W. Relapse prevention by acamprosate. Results from a placebo-controlled study on alcohol dependence. Arch Gen Psychiatry. 1996;53:673-80.

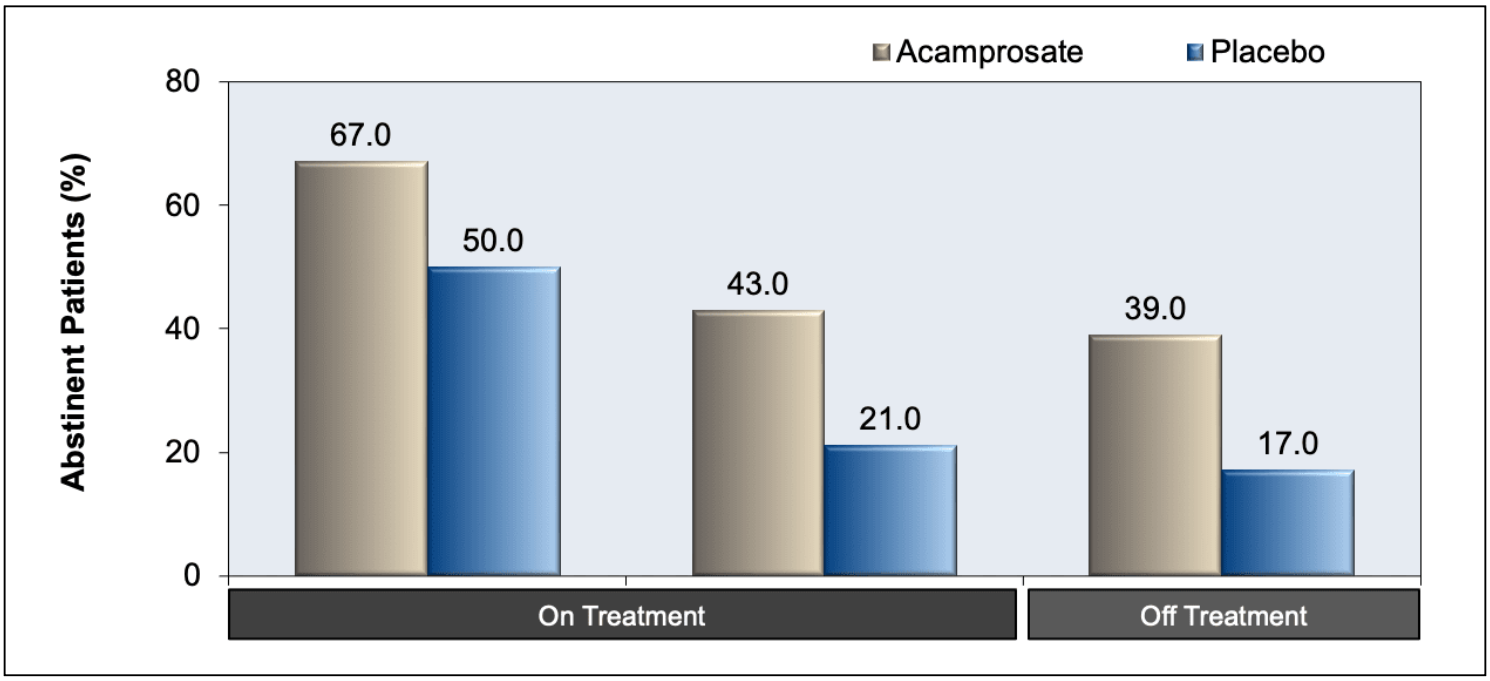

**Figure 6 Inhibition of Alcohol Metabolism by Disulfiram**

Normal ethanol (alcohol) metabolism is shown in top figure, with conversion of ethanol to acetate. Disulfiram inhibits the enzyme aldehyde dehydrogenase, leading to accumulation of acetaldehyde, which is associated with adverse effects.

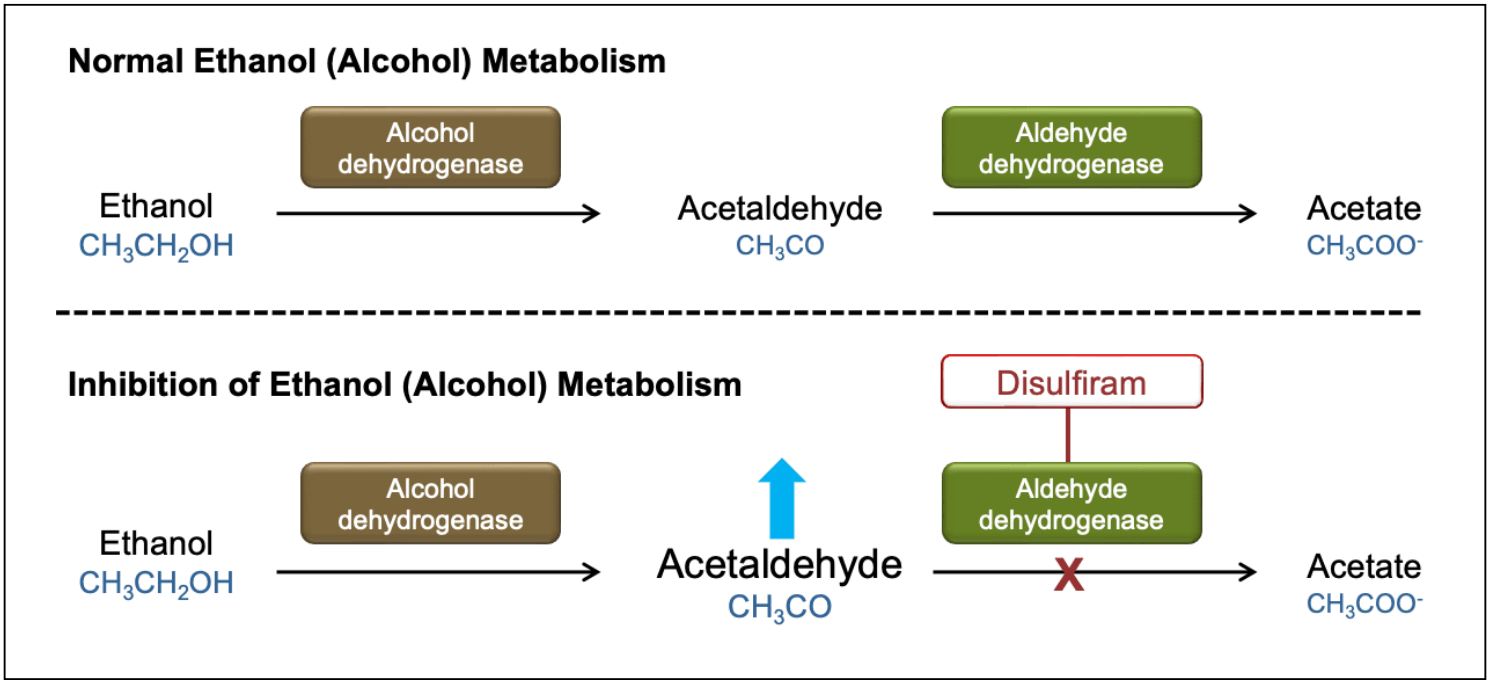

**Figure 7 Past Year Illicit Drug Use among Persons 12 Years of Age and Older, United States, 2021**

Source: Substance Abuse and Mental Health Services Administration. (2022). Key substance use and mental health indicators in the United States: Results from the 2021 National Survey on Drug Use and Health (HHS Publication No. PEP22-07-01-005, NSDUH Series H-57). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. December 2022.

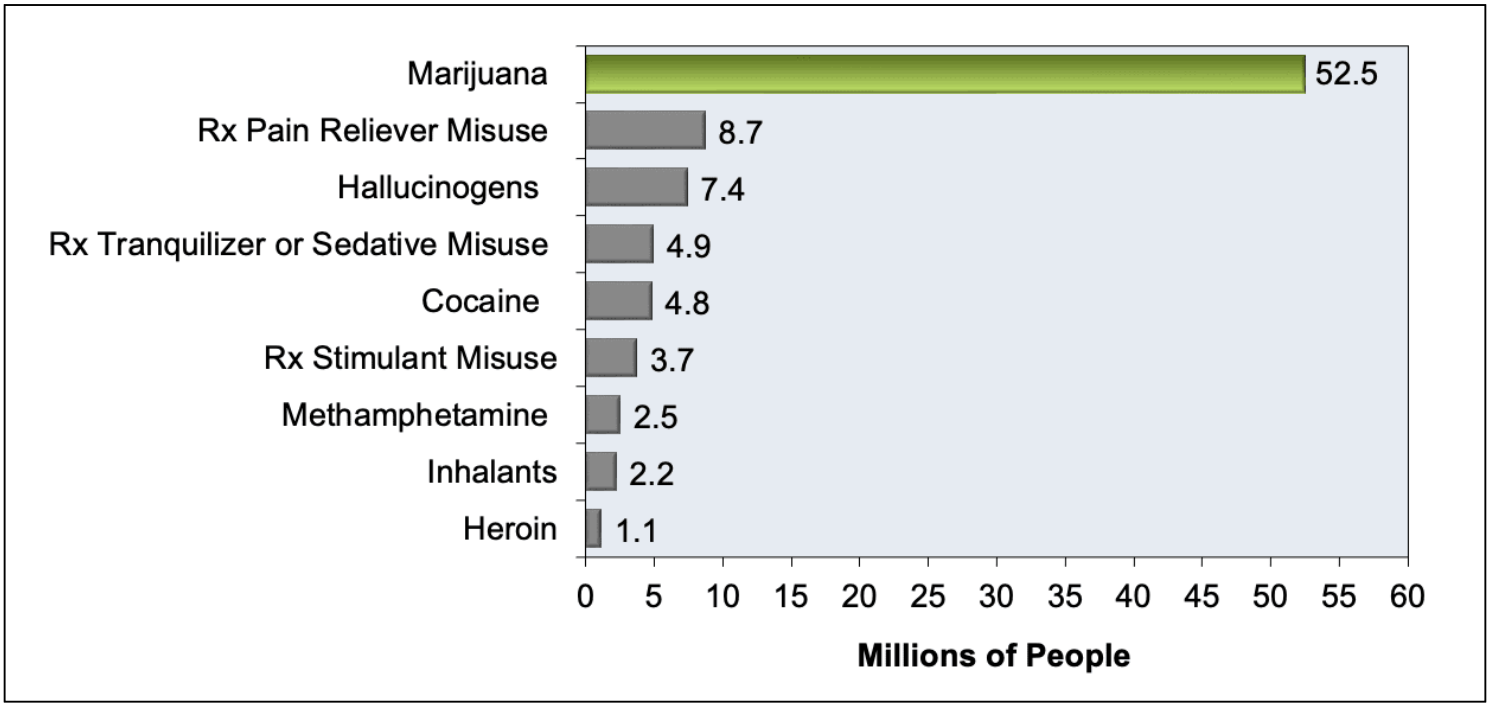

**Figure 8 Past Year Marijuana Use, by Age Group, United States, 2021**

Source: Substance Abuse and Mental Health Services Administration. (2022). Key substance use and mental health indicators in the United States: Results from the 2021 National Survey on Drug Use and Health (HHS Publication No. PEP22-07-01-005, NSDUH Series H-57). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. December 2022.

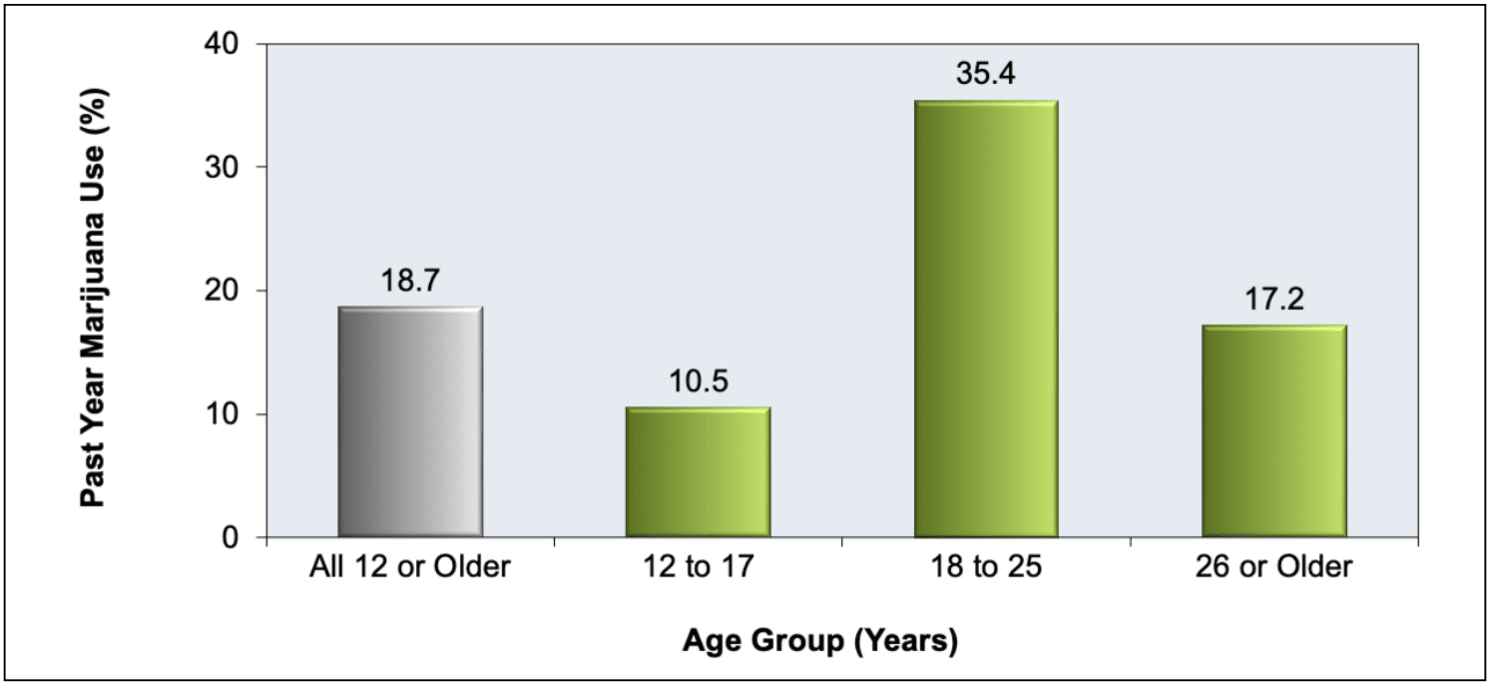

**Figure 9 Past Year Hallucinogen Use among People Aged 12 Years or Older, United States, 2021**

Source: Substance Abuse and Mental Health Services Administration. (2022). Key substance use and mental health indicators in the United States: Results from the 2021 National Survey on Drug Use and Health (HHS Publication No. PEP22-07-01-005, NSDUH Series H-57). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. December 2022.

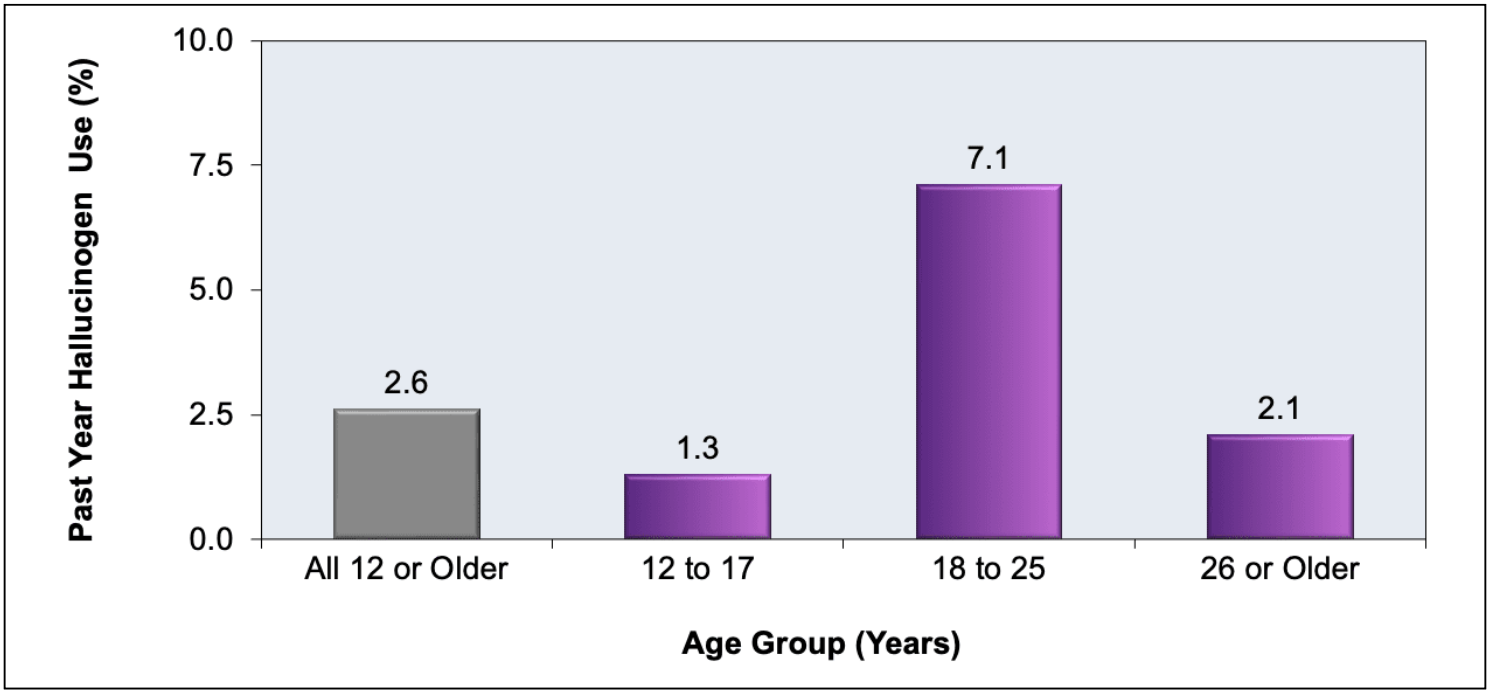

**Figure 10 Past Year Heroin Use among People Aged 12 Years or Older, United States, 2002-2018**

Source: Substance Abuse and Mental Health Services Administration. (2019). Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.

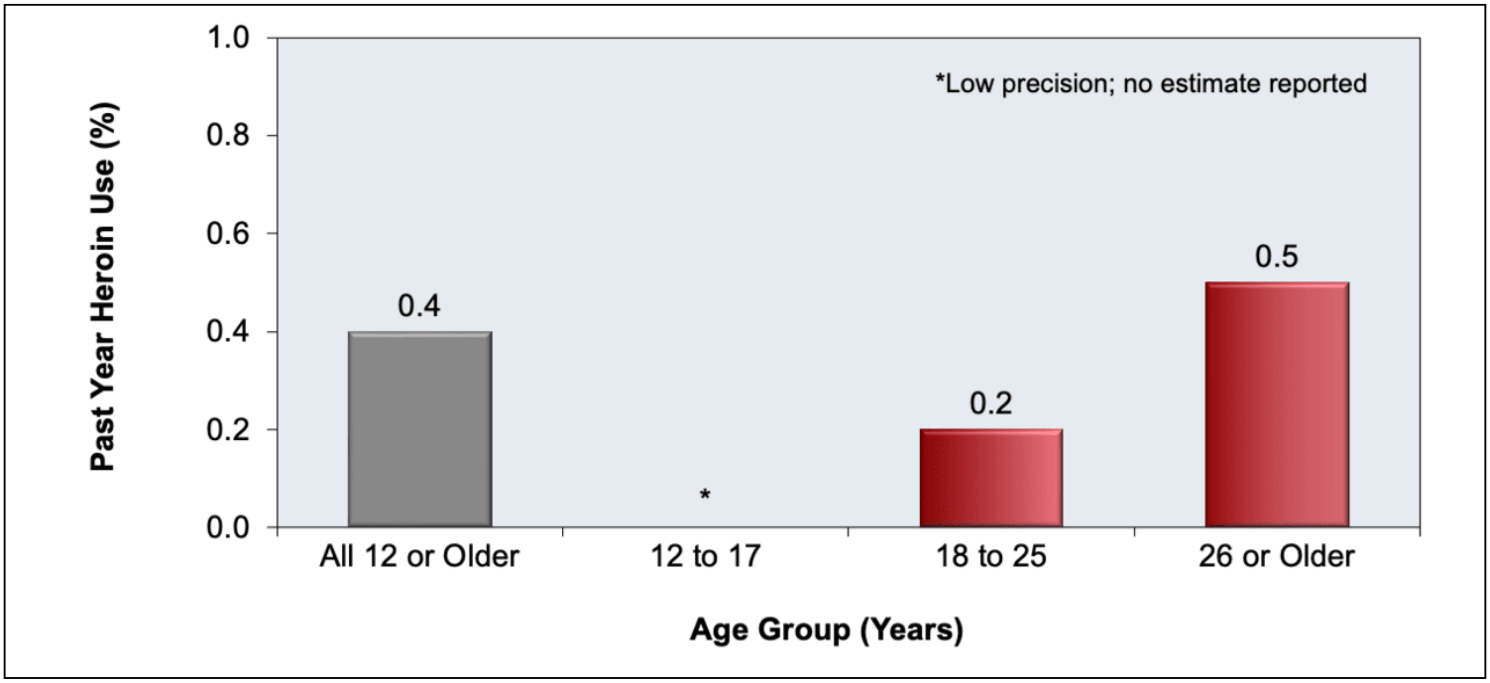

**Figure 11 National Overdose Deaths* Involving Heroin, 1999-2021**

*Among deaths with drug overdose as the underlying cause, the heroin category was determined by the T40.1 ICD-10 multiple cause-of-death code. Data from: CDC, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

Source: National Institute on Drug Abuse (NIDA). Drug Overdose Death Rates

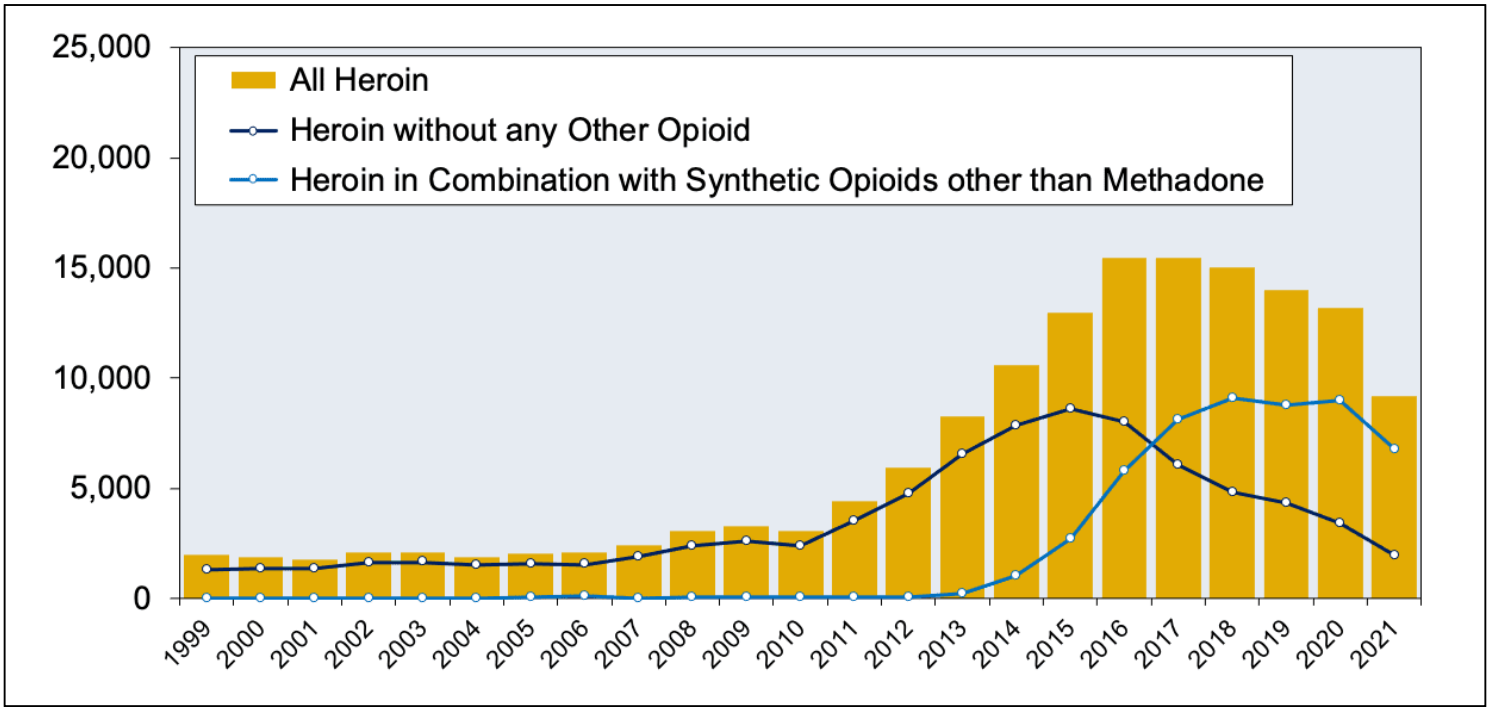

**Figure 12 National Drug-Involved Overdose Deaths*, 1999-2021**

*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Data from: CDC, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

Source: National Institute on Drug Abuse (NIDA). Drug Overdose Death Rates

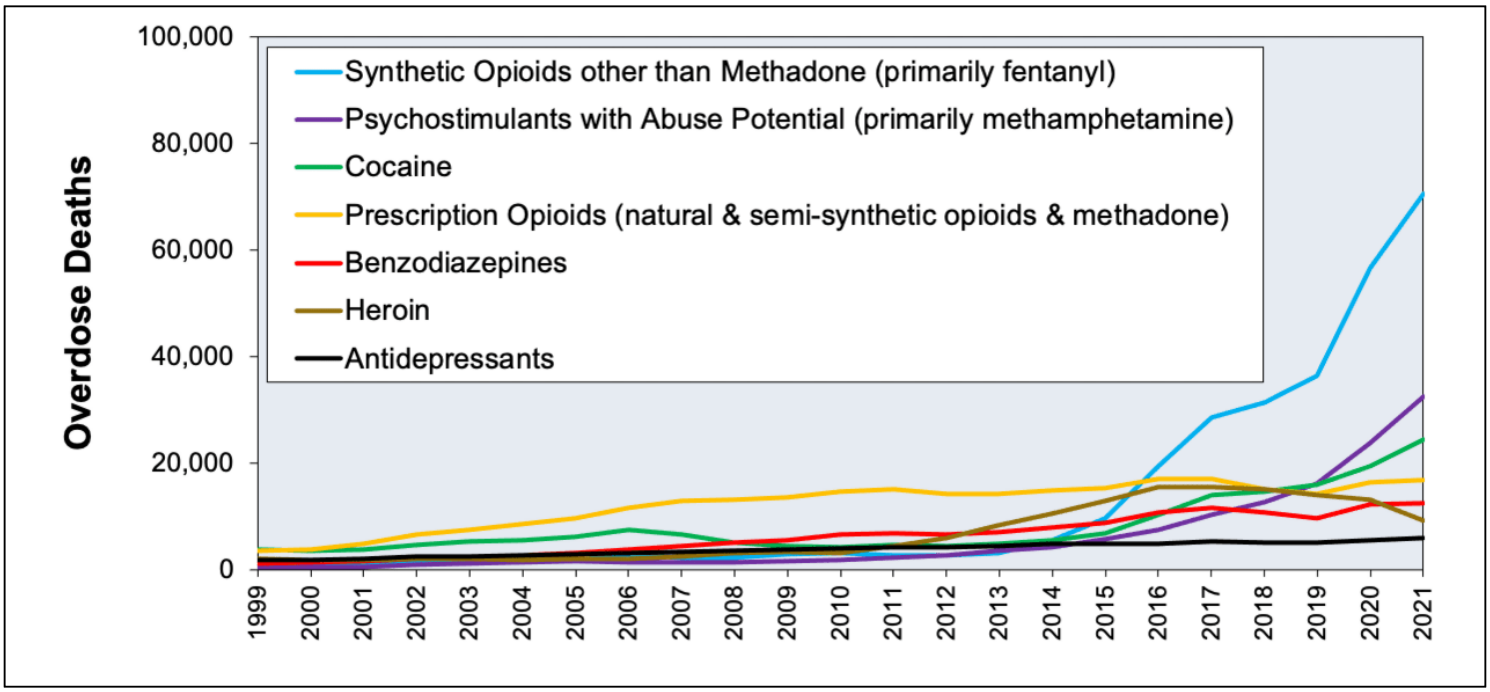

**Figure 13 National Overdose Deaths* Involving Prescription Opioids, 1999-2021**

*Among deaths with drug overdose as the underlying cause, the prescription opioid subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2) or methadone (T40.3). Data from: CDC, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

Source: National Institute on Drug Abuse (NIDA). Drug Overdose Death Rates

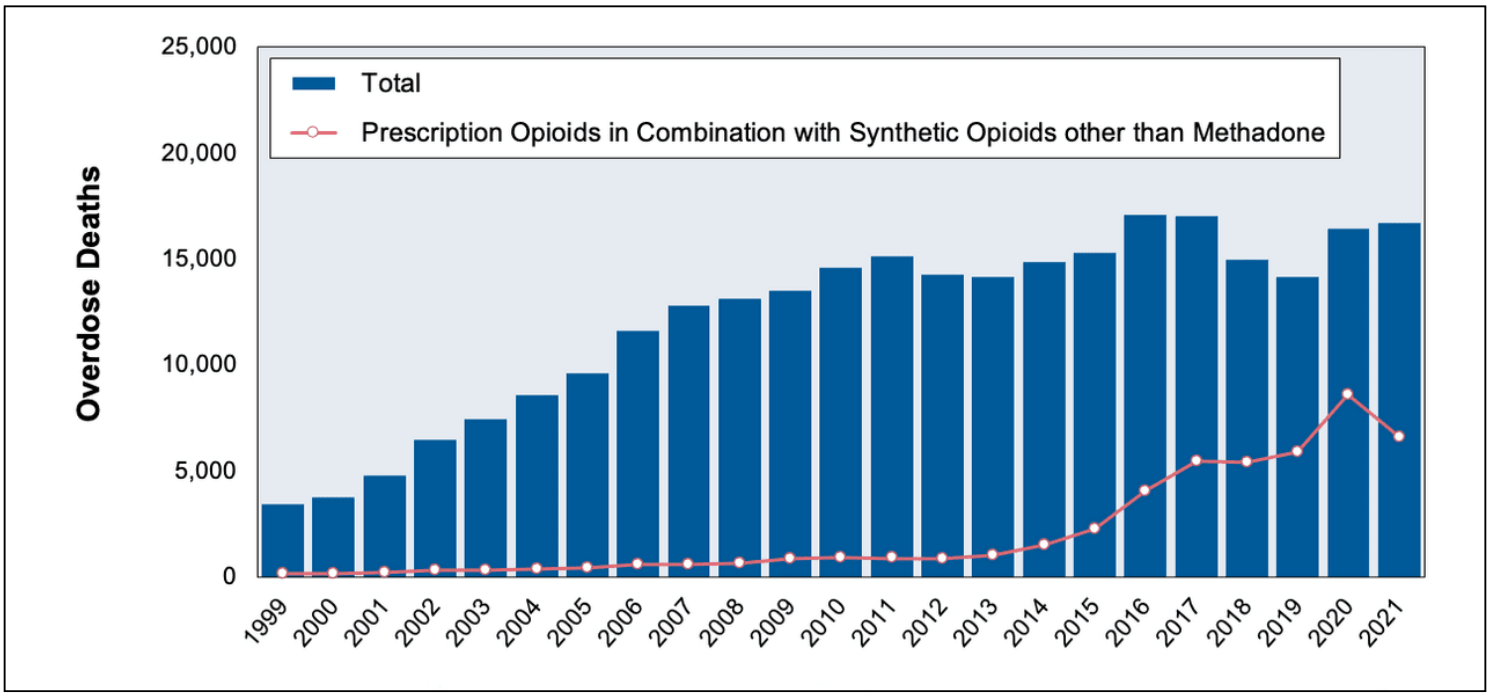

**Figure 14 Past Year Stimulant Use, by Age Group, United States, 2021**

Source: Substance Abuse and Mental Health Services Administration. (2022). Key substance use and mental health indicators in the United States: Results from the 2021 National Survey on Drug Use and Health (HHS Publication No. PEP22-07-01-005, NSDUH Series H-57). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. December 2022.

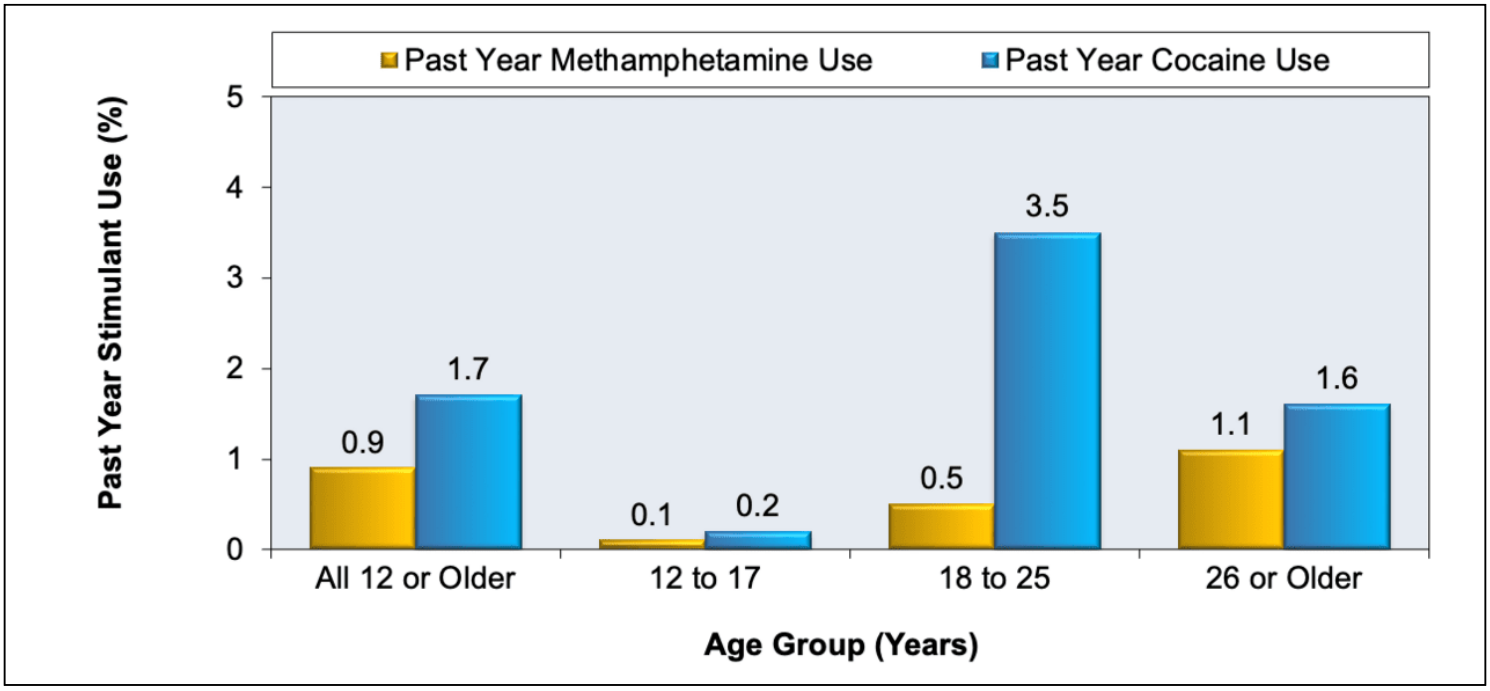

**Figure 15 Past Month Cigarette Use in Persons 12 Years of Age and Older: National Health Interview Survey, United States, 2002-2018**

Source: Substance Abuse and Mental Health Services Administration. (2019). Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.

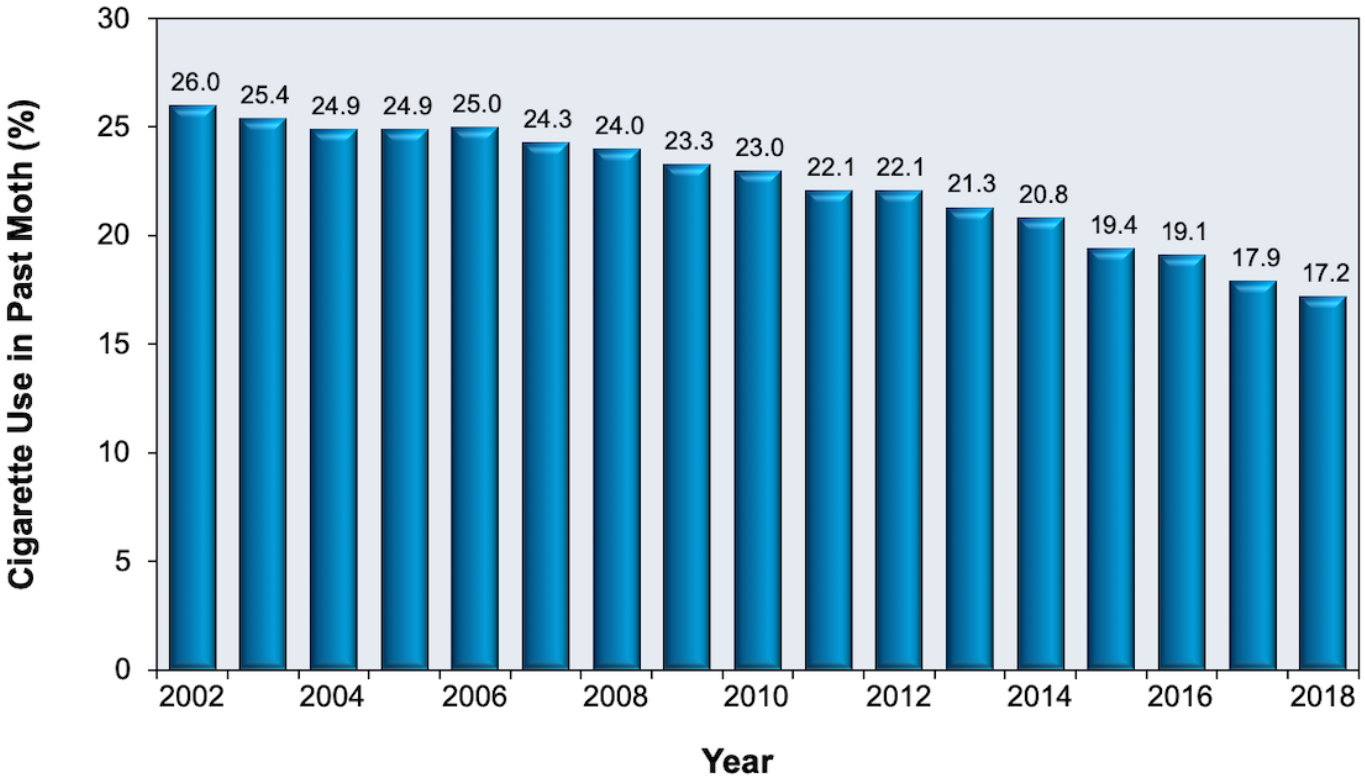

Table 1.

**DSM-5 Diagnostic Criteria for Substance Use Disorders**

| |
|---|
| **Scoring System**: The diagnosis of substance use disorder is based on scoring from a total of 11 symptom criteria (listed below). The severity of the substance use disorder is based on the number of symptom criteria that are met:<br><br>• Mild Substance Use Disorder: 2 to 3 criteria met<br>• Moderate Substance Use Disorder: 4 to 5 criteria met<br>• Severe Substance Use Disorder: more than 6 criteria met |
| **A. Impaired Control**<br><br>(1) Taking the substance in larger amounts and for longer than intended<br><br>(2) Wanting to cut down or quit but not being able to do it<br><br>(3) Spending a lot of time obtaining, using, or recovering from use of the substance<br><br>(4) Craving or a strong desire to use the substance |
| **B. Social Impairment**<br><br>(5) Repeatedly unable to carry out major obligations at work, school, or home due to substance use<br><br>(6) Continued substance use despite persistent or recurring social or interpersonal problems caused or made worse by substance use<br><br>(7) Stopping or reducing important social, occupational, or recreational activities due to substance use |
| **C. Risk Use of the Substance**<br><br>(8) Recurrent use of the substance in physically hazardous situations<br><br>(9) Consistent use of the substance despite acknowledgment of persistent or recurrent physical or psychological difficulties from using the substance |
| **D. Pharmacologic Criteria**<br><br>(10) Tolerance as defined by either a need for markedly increased amounts to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount (does not apply for diminished effect when used appropriately under medical supervision)<br><br>(11) Withdrawal manifesting as either characteristic syndrome or the substance is used to avoid withdrawal (does not apply when used appropriately under medical supervision) |

Source:


- Hasin DS, O'Brien CP, Auriacombe M, et al. DSM-5 criteria for substance use disorders: recommendations and rationale. Am J Psychiatry. 2013;170:834-51. [PubMed Abstract]

Table 2.

**DSM-5 Diagnostic Criteria for Alcohol Use Disorder**

| **A maladaptive pattern of alcohol use leading to clinically significant impairment or distress, as manifested by 2 (or more) of the following, occurring within a 12-month period:** |
|---|
| 1. Had times when the patient drank more, or longer, than intended |
| 2. More than once wanted to cut down or stop, tried it, but could not |
| 3. Spent a lot of time drinking or being sick/getting over the aftereffects of drinking |
| 4. Wanted to drink so badly that they could not think of anything else |
| 5. Found that drinking (or being sick from drinking) often interfered with taking care of home or family responsibilities, caused problems at work, or caused problems at school |
| 6. Continued to drink even though it was causing trouble with family and friends |
| 7. Given up or cut back on activities that were important, interesting, or pleasurable in order to drink |
| 8. More than once gotten into situations while or after drinking that increased the chances of getting hurt (e.g., driving, swimming, unsafe sexual behavior) |
| 9. Continued to drink even though it was causing depression or anxiety, other health problems, or causing memory blackouts |
| 10. Had to drink much more than previously in order to get the desired effect, or finding that the usual number of drinks had much less effect than previously |
| 11. Experienced symptoms of withdrawal after the effects of alcohol were wearing off, such as trouble sleeping, shakiness, restlessness, nausea, sweating, racing heart, or seizure Severity is determined based on the number of symptoms present:<br>• Mild: 2 to 3 symptoms<br>• Moderate: 4 to 5 symptoms<br>• Severe: more than 6 symptoms |

Source:


- US Preventive Services Task Force, Curry SJ, Krist AH, et al. Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2018;320:1899-1909. [PubMed Abstract]

Table 3.

| Medication | Typical Dose | Comment |
|---|---|---|
| Acamprosate | 666 mg three times daily | Dose reduction required with renal impairment |
| Disulfiram | 500 mg once daily for 1-2 weeks, then decrease to maintenance dose (range 125-500 once daily) | Not for use in persons actively drinking alcohol; avoid alcohol in other products |
| Oral Naltrexone | 50 mg once daily | Cannot be given to patients taking opioids |
| Extended-Release Naltrexone | 380 mg IM every 4 weeks; administer in gluteal area with 1.5 inch 20-gauge needle | Cannot be given to patients taking opioids |

Source:

- Substance Abuse and Mental Health Services Administration and National Institute on Alcohol Abuse and Alcoholism. Medication for the treatment of alcohol use disorder: a brief guide. HHS Publication No. (SMA) 15-4907. Rockville, MD: Substance Abuse and Mental Health Services Administration, October, 2015. [SAMHSA]

Table 4. **2018 ACC Expert Consensus Decision Pathway on Tobacco Cessation Treatment.**

**FDA-Approved Recommended Medications for Tobacco Cessation Treatment***

| Drug (doses) | How Sold (U.S.) | Dosing Instructions | Administration | Common Side Effects | Advantages | Disadvantages |
|---|---|---|---|---|---|---|
| Nicotine patch<br><br>21 mg<br><br>14 mg<br><br>7 mg | OTC or Rx | Starting dose:<br><br>21 mg for ≥10 cigarettes per day.<br><br>14 mg for <10 cigarettes per day.<br><br>After 6 weeks, option to taper to lower doses for 2-6 weeks.<br><br>Use ≥3 months.<br><br>After 6 weeks, continue original dose or taper to lower doses (either option acceptable). | Apply a new patch each morning to dry skin.<br><br>Rotate application site to avoid skin irritation.<br><br>May start patch before or on quit date.<br><br>Keep using even if a slip occurs.<br><br>If insomnia or disturbing dreams, remove patch at bedtime. | Skin irritation<br><br>Trouble sleeping<br><br>Vivid dreams (patch can be removed at bedtime to manage insomnia or vivid dreams) | The easiest nicotine product to use.<br><br>Provides a steady nicotine level.<br><br>Combination NRT therapy: as needed, can add gum, lozenge, inhaler, or nasal spray to patch to cover situational cravings. | User cannot alter dose if cravings occur during the day. |
| Nicotine lozenge<br><br>4 mg<br><br>2 mg | OTC or Rx | If first cigarette is ≤30 minutes of waking: 4 mg.<br><br>If first cigarette is >30 minutes of waking: 2 mg.<br><br>Use ≥3 months. | Place between gum and cheek, let it melt slowly. Use 1 piece every 1-2 hours (Max: 20/day). | Mouth irritation<br><br>Hiccups<br><br>Heartburn<br><br>Nausea | User controls nicotine dose.<br><br>Oral substitute for cigarettes.<br><br>May be added to patch to cover situational cravings.<br><br>Easier to use than gum for those with dental work or dentures. | No food or drink 15 minutes prior to use and during use. |
| Nicotine gum<br><br>4 mg | OTC or Rx | If first cigarette is ≤30 minutes of waking: 4 | Chew briefly until mouth tingles, then | Mouth irritation<br><br>Jaw soreness | User controls nicotine dose.<br><br>Oral substitute | Not chewed in same way as<br><br>regular gum; |

| Drug (doses) | How Sold (U.S.) | Dosing Instructions | Administration | Common Side Effects | Advantages | Disadvantages |
|---|---|---|---|---|---|---|
| 2 mg | | mg.<br><br>If first cigarette is >30 minutes of waking: 2 mg.<br><br>Use ≥3 months. | 'park' gum inside cheek until tingle fades. Repeat chew-and-park each time tingle fades. Discard gum after 30 minutes of use.<br><br>Use ~ 1 piece per hour (Max: 24/day). | Heartburn<br><br>Hiccups<br><br>Nausea | for cigarettes.<br><br>May be added to patch to cover situational cravings. | requires careful instruction.<br><br>Can damage dental work and be difficult to use with dentures.<br><br>No food or drink 15 minutes prior to use and during use. |
| Nicotine inhaler<br><br>10-mg cartridge | Rx only | 10 mg/cartridge.<br><br>Each cartridge has ~80 puffs.<br><br>Use ≥3 months. | Puff into mouth/throat until cravings subside. Do not inhale into lungs.<br><br>Change cartridge when nicotine taste disappears.<br><br>Use 1 cartridge every 1-2 hours (Max: 16/day). | Mouth and throat irritation<br><br>Coughing if inhaled too deeply | User controls nicotine dose.<br><br>Mimics hand-to-mouth ritual of smoking cigarettes.<br>May be added to patch to cover situational cravings. | Frequent puffing required. |
| Nicotine nasal spray<br><br>10 mg/mL<br><br>(10 mL bottle) | Rx only | 10 mg/mL.<br><br>0.5 mg per spray.<br><br>Each bottle has ~200 sprays.<br><br>Use ≥3 months. | Use 1 spray to each nostril.<br><br>Use spray every 1-2 hours (Max: 80/day). | Nasal and throat irritation<br><br>Rhinitis<br><br>Sneezing<br><br>Coughing<br><br>Tearing | User controls nicotine dose.<br><br>Most rapid delivery of nicotine among all NRT products.<br><br>May be added to patch to cover situational cravings. | Has the most side effects of all NRT products.<br><br>Some users cannot tolerate local irritation to nasal mucosa. |
| Varenicline (tablet)<br><br>0.5 mg<br><br>1.0 mg | Rx only | Days 1-3: 0.5 mg/day.<br><br>Days 4-7: 0.5 mg twice a day. | Start 1-4 weeks before quit date.<br><br>Take with food and a tall glass | Nausea<br><br>Insomnia<br><br>Vivid dreams | Quit date can be flexible, from 1 week to 3 months after starting drug. | Because of previous FDA warning (now removed), many patients fear |

| Drug (doses) | How Sold (U.S.) | Dosing Instructions | Administration | Common Side Effects | Advantages | Disadvantages |
|---|---|---|---|---|---|---|
| | | Day 8+: 1 mg twice a day.<br><br>Use 3-6 months. | of water to minimize nausea. | Headache | Dual action:<br><br>relieves nicotine withdrawal and blocks reward of smoking.<br><br>Oral agent (pill). | psychiatric adverse events, even though they are no more common than with other cessation medications. |
| Bupropion sustained release (SR) (tablet)<br><br>150 mg | Rx only | 150 mg/day for 3 days, then 150 mg twice a day.<br><br>Use 3-6 months. | Start 1-2 weeks before quit date. | Insomnia<br><br>Agitation<br><br>Dry mouth<br><br>Headache | May lessen post-cessation weight gain while drug is being taken.<br><br>Oral agent (pill). | Increases seizure risk: not for use if seizure disorder or binge drinking. |

* All are FDA-approved as smoking cessation aids and listed as a first-line medication by U.S. Clinical Practice Guidelines (Fiore, 2008)

+ Recommended duration of use for medications is at least 3 months but extending dose to 6 months is frequently done to prevent relapse to tobacco use. Patching dosing differs slightly from FDA labeling.

Abbreviations: FDA = U.S. Food and Drug Administration; NRT = nicotine replacement therapy; OTC = over the counter (no prescription required); Rx = prescription required.

Source:


- Barua RS, Rigotti NA, Benowitz NL, et al. 2018 ACC Expert Consensus Decision Pathway on Tobacco Cessation Treatment: A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol. 2018;72:3332-65. [PubMed Abstract]