Substance Use Disorders

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

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https://www.hiv.uw.edu/go/basic-primary-care/substance-use-disorders/core-concept/all.

Background

Definitions and Terminology

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines substance use disorders as a constellation of recurrent pathological cognitive, behavioral, and physiological symptoms arising from the ongoing use of a substance.[1,2] In an effort to combat stigma, previously used terms of abuse and dependence are not recommended now when describing persons with substance use disorders.

Predictors of Substance Use Disorders

Risk factors for substance use disorders (SUD) are complex and likely include a combination of biologic and social factors.

- **Family History**: Studies indicated that a family history of substance use disorder is a strong risk factor for the development of SUD among individuals, influenced by both genetic and shared environmental factors.[3,4,5]
- **Mental Health Conditions**: Cooccurring mental health conditions have also been linked to higher incidence of SUD, in both adolescents and adults.[6,7]
- **Social Factors**: Multiple social structural factors, such as one's social network and lived environment, have also been identified as risk factors for the development of SUD, and likely interact with genetic and other familial factors.[8,9,10] A strong body of literature has linked adverse childhood experiences with substance use disorders, highlighting the way in which addiction can result as a consequence of harmful events incurred during one's formative years.[11] Other social factors such as lower socioeconomic status, lower education, and non-white race, while not impacting the prevalence of substance use disorders, are associated with increased consequences of addiction, especially criminal justice consequences.[12]
- **Neurobiologic Differences**: Although different drugs produce different effects on an individual, dysregulation of brain reward pathways in conjunction with an overactive brain stress system reinforce 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.[13] Neurobiological differences in self-control often become evident in early childhood and may correlate with the subsequent development of a substance use disorder.[14] Although no specific neurological testing, imaging, or laboratory evaluation can accurately predict who will develop a substance use disorder, accurate identification of predictive markers remains an area of active investigation.

Data Sources for Substance Use in the United States

The primary source of statistical information for substance use disorders 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 2018, with results published in August 2019.[15] A major limitation of the NSDUH is the fact that it does not sample from jails or prisons, and is therefore likely to underestimate the prevalence of substance use disorder in the United States. 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.

DSM-5 Classification

The DSM-5 has combined the DSM-IV categories of substance abuse and substance dependence under the single heading of substance use disorders.[1,2] 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.[1,2] The severity of the substance use disorder based on the number of symptom criteria (out of a total of 11) that are met: mild (2 to 3 criteria), moderate (4 to 5 criteria), and severe (more than 6 criteria).[1,2]

Impaired Control

- Taking the substance in larger amounts and for longer than intended
- Wanting to cut down or quit but not being able to do it
- Spending a lot of time obtaining, using, or recovering from use of the substance
- Craving or a strong desire to use the substance

Social Impairment

- Repeatedly unable to carry out major obligations at work, school, or home due to substance use
- Continued substance use despite persistent or recurring social or interpersonal problems caused or made worse by substance use
- Stopping or reducing important social, occupational, or recreational activities due to substance use

Risk Use of the Substance

- Recurrent use of the substance in physically hazardous situations
- Consistent use of the substance despite acknowledgment of persistent or recurrent physical or psychological difficulties from using the substance

Pharmacologic Criteria

- 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)
- Withdrawal manifesting as either characteristic syndrome or the substance is used to avoid withdrawal (does not apply when used appropriately under medical supervision)

Classes of Drugs Related to Substance Use Disorders

The DSM-V recognizes substance-related disorders resulting from the use of ten separate classes of drugs (listed in alphabetical order):

- Alcohol

- Caffeine
- Cannabis
- Hallucinogens
- Inhalants
- Opioids
- Sedative hypnotics, or anxiolytics
- Tobacco
- Other or unknown stimulant

Overview

The extensive body of literature informing the DSM-5 classification of substance use disorders will be applied throughout this lesson to substance use disorders among persons with HIV. This Core Concept will review the epidemiology of substance use in persons with HIV, examine the risk factors that predispose individuals to substance use disorders, and discuss current diagnostic and treatment paradigms for the most common substance use disorders in the United States.

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.[16] The USPSTF recommends using 1- to 3-item screening instruments, including the Alcohol Use Disorders Identification Test-Concise (AUDIT-C) or the National Institute on Alcohol Abuse and Alcoholism (NIAAA)-recommended Single Alcohol Screening Question.[16] If a patient screens positive for alcohol misuse on a 1- to 3-item brief screening instrument, the USPSTF recommends follow-up with an in-depth risk assessment, such as the 10-question AUDIT and for those with higher scores, an assessment for alcohol use disorder.[16]
- **Screening for Unhealthy Drug Use**: The USPSTF recently released an updated position statement on screening for unhealthy drug use in adults and adolescents.[17] In this statement, they recommended screening by asking questions about unhealthy drug use in adults age 18 years or older.[17] 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.[17] 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 also 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.[17,18] 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 identify heavy drinking in addition to alcohol abuse and dependency.[19] The AUDIT better identifies at-risk, harmful, or hazardous drinking patterns.[20] 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.[19] 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 abuse or dependence.[21]
- **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.[20,21]
- **CAGE**: The CAGE is a 4-question screening test that works well at detecting lifetime alcohol abuse and dependence, but is not sensitive for detecting heavy drinking and does not distinguish between past and present alcohol use.[[20,21]
- **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 an at-risk drinker.[22]

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.[23] The ASSIST covers 12 items related to recent and lifetime use, dependence symptoms, substance-related problems, and intravenous use and 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.[24,25,26]
- **DAST**: The Drug Abuse Screening Test (DAST), first developed in 1982, is available in 10-item, 20-item, and 28-item versions; all versions are self-administered and have moderate to high levels of sensitivity, specificity, and validity.[27] Answers to this test are binary (yes/no), with different cutoff scores recommended with different versions and different populations.[27] The length of this test has proven to be a barrier to primary care screening, however, and subsequently other instruments have been trialed.
- **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.[28] If a patient reports 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.[28]
- **NIDA-Modified ASSIST**: The NIDA-Modified ASSIST is an 8-item tool that asks about the frequency and type of drug use, the desire or urge to use drugs, consequences of drug use, failed attempts to cut down, and use of injection drugs.[28] It is modified from the WHO ASSIST tool, outlined below.[23,28]
- **Opioid Risk Tool**: The Opioid Risk Tool (ORT) is an 11-item screening tool specifically for opioid addiction.[29]
- **TICS**: An even briefer, two-item conjoint screening, known as TICS, has a sensitivity and specificity of nearly 80% in detecting current substance abuse problems.[30] 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 proven to have similar sensitivity and specificity for the detection of drug use and drug use disorders as the lengthier DAST, and is superior to conjoint screening in that it specifically identifies drug use.[31] More recently, the 4-item Substance Use Brief Screen (SUBS) has become available for screening primary care patients for tobacco, alcohol, and other drug use.[32] This is the only brief, self-administered, comprehensive screening instrument test that has been validated in the primary care setting and may facilitate screening of primary care populations.[32]

Epidemiology of Substance Use in United States

Estimates of Substance Use Disorders in the United States

Data from the 2018 National Survey on Drug Use and Health (NSDUH) found that approximately 20.3 million people aged 12 years and older in the United States had a substance use disorder in the past year, which represented approximately 7.4% of the United States population who were 12 years of age or older (Figure 1).[15] In the same year, according to the NSDUH, 58.8 million people (21.5% of the population) were current tobacco users, including 47.0 million current cigarette smokers and 12.2 million current cigar smokers.[15] Smoking estimates were lower in the National Health Interview Survey (NHIS), another annual nationally representative survey, which reported that 13.7% of adults in the United States were current smokers in 2018.[33] This discrepancy is likely due to differences in the age range included in the surveys—NHIS collects data only for adults aged 18 years and older, whereas the NSDUH collects data for persons beginning at age 12.[15,33] Both of these surveys likely underestimate the prevalence of substance use disorders because they omit homeless and incarcerated populations that have higher rates of substance use disorders than the general population.

Estimates of Substance Use Disorders in Persons with HIV

Multiple studies and surveys have demonstrated high rates of substance use among persons with HIV in the United States.[34,35,36] For example, some data indicate that individuals with HIV smoke at more than twice the rate of those without HIV and the Centers for Disease Control and Prevention (CDC) estimated a smoking prevalence among persons with HIV of 34% for the year 2017.[37] In addition, use of alcohol and other substances are higher in persons with HIV infection compared to the general population. 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 based on 2017 survey data that 30% of persons with HIV had used noninjection drugs in the prior 12 months for recreational purposes, 2% had used injection drugs in the prior 12 months, and 16% had engaged in binge drinking in the past 30 days.[37]

Impact of Substance Use Disorders on HIV Metrics

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.[38,39,40] Thus, any substance use disorder that interferes with antiretroviral medication adherence can impact transmission of HIV and have a significant public health consequence. 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 HIV negative sex and needle-sharing partners.[41,42,43,44]

- **Medical Monitoring Project**: Based on 2017 survey data, the Medical Monitoring Project reported that 24% of individuals with HIV reported using alcohol with sex, and 12% reported using noninjection drug use with sex; in this same survey, among the individuals with HIV who used injection drugs, 67% used them in the context of sex.[45] Additional 2017 data from this project noted 4.9% of persons with HIV reported alcohol or drug use as the reason for missing their last dose of antiretroviral medications.[37]
- **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.[46,47,48]

Substance Use Disorders and Impact on HIV Care

Substance use can create a barrier to care for individuals with HIV.[44,49,50] 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.[51,52,53] Antiretroviral medication adherence problems in individuals with a substance use disorder may have serious consequences, including suboptimal virologic control and potential emergence of virologic resistance. Studies have shown that persons with HIV can improve healthcare utilization and antiretroviral adherence patterns through treatment of substance use disorders, particularly with treatment of opiate use disorders; medications for opiate use disorder (MOUD) have been shown to increase rates of viral suppression, improved adherence to antiretrovirals, and lower overall mortality.[52,54,55]

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.[56,57] 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.[58,59,60,61,62,63,64] Furthermore, methamphetamine has been shown to increase HIV replication in animal models.[65]

Alcohol Use Disorder

Prevalence of Alcohol Use Disorder in the United States

In 2018, the National Survey on Drug Use and Health estimated that 139.8 million people had used alcohol in the past month, equating to approximately 51% of the population. Among those who consumed alcohol in the past month, 48% (67.1 million people) were current binge alcohol users, and 11.8% (16.6 million) were heavy alcohol users (Figure 2).[15] Similarly, in 2018, 5.4% of the United States population 12 years of age or older had an alcohol use disorder, which corresponds to an estimated 14.8 million people.[15] The prevalence of alcohol use disorder was highest for persons 18 to 25 years of age, among whom 10.1%, or 3.4 million people, were estimated to have alcohol use disorder.[15] Although the proportion of people, ages 18 to 25 years, with an alcohol use disorder fell from 17.7% in 2002 to 10.1% in 2018, the prevalence of AUD in the general population has seen less substantial declines (7.7% in 2002 and 5.4% in 2018) (Figure 3).[15] Despite modest declines in the prevalence of alcohol use disorder, several recent reports document that mortality from alcohol use has doubled over the past two decades, with the largest increases occurring among white women and persons in younger- and middle-aged groups.[66,67]

Prevalence of Alcohol Use Disorder in Adults with HIV

As in the general population, hazardous drinking is common among persons with HIV.[68] In the HIV Cost and Services Utilization Study (HSCUS), which was the first representative study to provide estimates of alcohol use among persons receiving medical care for HIV, 53.4% of adults with HIV reported drinking alcohol in the past 4 weeks, an estimate that mirrors that of the general United States population.[16] In this HSCUS study, 8% of the survey respondents with HIV were classified as heavy drinkers, in comparison to recent estimates of heavy drinking in the general United States population of 6.1%.[15] More recent data from the 2017 Medical Monitoring Project indicate that 63% of persons with HIV consumed alcohol in the past year, and 15.6% engaged in binge-drinking the past month.[37]

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.[69] 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.[2] 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.[68] The rates of hazardous drinking are lower in persons with HIV who have lower CD4 counts and AIDS-defining illnesses.[70]

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.[16] The USPSTF recommends using 1- to 3-item screening instruments, including the AUDIT-C or the NIAAA-recommended Single Alcohol Screening Question.[16] If a patient screens positive for alcohol misuse on a 1- to 3-item brief screening instrument, the USPSTF recommends follow-up with an in-depth risk assessment, such as the 10-question AUDIT.[16]

Definition of Unhealthy Alcohol Use

Unhealthy alcohol use is defined as the consumption of risky amounts of alcohol—with or without associated alcohol problems—or having a current alcohol use disorder, as defined by DSM-5 criteria.[31,71] In this setting, risky alcohol consumption is defined as a weekly average alcohol intake of more than 14 drinks for men and 7 drinks for women, or exceeding more than 4 drinks per occasion for men and more than 3 drinks

per occasion for women in the past 30 days.[31,71]

Diagnostic Criteria

The DSM-5 defines alcohol use disorder by the presence of at least two symptoms (from a list of 11 symptoms as defined in the DSM-5) related to evidence of impaired control, social impairment, risky use, and pharmacological criteria (Table 1).[16] Many more individuals will meet criteria for unhealthy alcohol use, which includes drinking more than 4 drinks per day (or more than 14 in a week) for men and more than 3 drinks per day for women (or more than 7 per week).[22] 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 (men age 65 years and younger should consume no more than 14 drinks per week and no more than 4 drinks per day); these limits reflect the fact that people who drink over recommended limits, even if they do not meet criteria for alcohol use disorder, are at significant risk for alcohol-related problems.[72]

Behavioral Counseling

The USPSTF recommends that persons who screen positive for unhealthy alcohol use be assessed for alcohol use disorder (AUD). Those with unhealthy drinking, but without 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.[16] 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.[73,74]. Persons with 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.[75,76]

Pharmacologic Therapy for Alcohol Use Disorder

There are currently four United States Food and Drug Administration (FDA)-approved medications for the treatment of alcohol use disorder: acamprosate, disulfiram, oral naltrexone, and extended-release naltrexone injection (Figure 4).[77,78] 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.[79] 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.[80] The following summarizes available FDA-approved therapies for alcohol use disorder, as well as information on two medications (gabapentin and topiramate) that sometimes used to treat alcohol-use disorder, but do not have FDA-approval for this indication.

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 abuse potential.

- **Mechanism**: Naltrexone is an opioid antagonist that mediates the rewarding effects of alcohol and attenuates cravings (Figure 5).[81,82] 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.[78]
- **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).[81]
- **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.[83] 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.[84] 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 6).[85,86] 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.[85,86,87]
- **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 treatment initiation.[88,89]

- **Mechanism**: The mechanism of action of acamprosate is not well understood, but it is thought to decrease 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 with 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).[84] Trials in Europe have shown more benefit with acamprosate than those conducted in the United States, for unknown reasons (Figure 7).[90,91]
- **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 use of acamprosate and antiretroviral medications.[36]

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 8), which results in acetaldehyde levels rising within 10 to 30 minutes of alcohol ingestion, thereby triggering a

highly unpleasant "disulfiram-alcohol reaction".[81,92] 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).[77,78]
- **Treatment Data**: Findings from a meta-analysis supports 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).[92,93]
- **Side Effects**: Rare side effects with disulfiram include optic neuritis, peripheral neuropathy, polyneuritis, and hepatitis.[78]
- **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.[94] Disulfiram should not be used in patients taking ritonavir oral solution, as this formulation contains alcohol and may precipitate an alcohol-disulfiram reaction.[95]

Gabapentin

Gabapentin is not FDA-approved for treatment of alcohol use disorder but 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 (and reducing relapse-related symptoms including insomnia, dysphoria, and craving).[96]

Topiramate

Topiramate is not currently approved for treatment of alcohol use disorder, but multiple studies support its efficacy for improving abstinence rates and reducing alcohol craving, heavy drinking, and gamma-glutamyl transferase (GGT) levels (a biomarker of alcohol use).[97,98,99] In addition, topiramate has also been shown to reduce smoking in persons who smoke and have alcohol use disorder.[99] 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.[79,100,101] 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 by simply engaging with a medical provider.[102] For moderate to severe alcohol use disorder, more robust data favor the use of naltrexone and acamprosate.[79,81,103] In practice, many clinicians choose naltrexone as first line, given its easier dosing (once a day dosing with naltrexone versus three times a day for acamprosate) and the ability to start while the individual is actively drinking (acamprosate should be started only once abstinence has been achieved). Among persons with HIV, more robust data exist for naltrexone.[104,105] 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.[81] 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.[106]

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 9).[15] Based on the 2018 National Survey on Drug Use and Health, an estimated 43.5 million people, ages 12 and older, used cannabis in the last year in the United States, which equates to an estimated 15.9% of the population.[15] During 2018, the prevalence of cannabis use in the past year was highest among those 18 to 25 years of age (34.8%) (Figure 10).[15] The use of marijuana has steadily increased since 2002, and there has been a trend towards legalization in several states (Figure 11).[15]

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.[44,52] The 2017 CDC Medical Monitoring Project estimated that 26.4% of persons living with HIV, who were engaged in care, used cannabis in the past year.[37] 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 use of synthetic cannabinoids on antiretroviral adherence.[36,107,108]

Diagnostic Criteria

The DSM-5 defines cannabis use disorder by the presence of at least two symptoms (from a list of 11 symptoms as defined in the DSM-5) 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 (SSRIs, mixed action, and atypical) have not been proven to lower rates of cannabis dependence, and 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.[109,110,111] 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.[112] Several programs have been established to help guide treatment of cannabis users, 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.[113] 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).[2] Of note, MDMA is classified as a hallucinogen though it is structurally similar to methamphetamine and has stimulant properties as well.[114] According to the 2018 National Survey on Drug Use and Health (NSDUH) an estimated 5.6 million people, ages 12 and older, used hallucinogens in the past year.[15] As with 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 12).[15]

Prevalence among Adults with HIV in United States

In the 2017 CDC Medical Monitoring Project, an estimated 3% of individuals with HIV who were enrolled in care reported use of "club drugs" in the past year.[37] Although detailed data on the use of "club drugs" or the prevalence of hallucinogen use disorders among persons living with HIV are not available, evidence indicates that use of "club drugs", which typically refers to a group of substances that includes the hallucinogens ketamine, MDMA, and LSD, as well as gamma-hydroxybutyrate (GHB), methamphetamine, and flunitrazepam, has been rising in the general population and especially among men who have sex with men (MSM) who have HIV or are at risk for HIV acquisition.[114,115,116]

Risk Factors

Risk factors for phencyclidine use disorder include low educational attainment, male gender, and living in the West or Northeast.[2] 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.[2] 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.[117]

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 as defined in the DSM-5) 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).[116] No pharmacologic treatment is known to have any benefit. Clinicians should have awareness 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.[115,116]

Opioid Use Disorder

Prevalence among Adolescents and Adults in United States

In 2018, an estimated 10.3 million Americans over the age of 12, or 3.7% of the population, used opioids, the vast majority of whom misused prescription opiate medications.[15] 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.[2] Even so, the rate of opiate misuse is staggering.

- **Heroin Use**: Between the time periods 2002 to 2004 and 2011 to 2013, use of heroin (reported in the past year) increased by 114% among non-Hispanic whites.[118] The rate of heroin use has also increased sharply among persons 18 to 25 years of age, with the increases occurring faster among women than men.[118] Since 2013, the prevalence of heroin use has remained relatively stable and with consistently higher rates among persons 18 to 25 years of age (Figure 13).[15]
- **Fentanyl**: In the past two decades, there has been a marked increase in fentanyl-related harm, overdose, and death in the United States, with the age-adjusted rate of death involving synthetic opioids increasing by 80% between 2013 and 2014 (Figure 14).[119,120,121] Although confiscations of fentanyl by law enforcement have been seen throughout the United States, data from the National Forensic Laboratory Information System (NFLIS) indicated that the fentanyl use is most prevalent in the East and Midwest.[121]
- **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 and in 2013, 13% of 12th graders reported lifetime prescription opioid abuse.[122,123] From 2015 to 2018, the rate of misuse of prescription pain medications has declined slightly (Figure 15), likely due to aggressive public health messages warning providers and patients of the danger of the misuse of prescription opioid pain medications.[15]
- **Impact on Mortality**: The opioid epidemic is now having a significant impact on mortality statistics, with the highest rates of opioid-related deaths in males and in persons 25 to 44 years of age (Figure 16).[124] West Virginia continues to have the highest rate of opioid-involved death at 42.4 per 100,000.[124] According to the CDC, opioids were involved in 70% of the 67,367 drug-related deaths that occurred in the United States in 2018.[124] A marked increase in mortality among middle-aged white Americans, driven in large part by the opioid epidemic, has erased prior progress in overall mortality and appears to be a unique phenomenon in the United States, with no other high-income country seeing similar rises in middle-age mortality.[125]

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.[126,127] In 2018, among all persons newly diagnosed with HIV in the United States, 10.1% (3,783 of 37,289) had injection drug use as a reported transmission category.[128] Based on CDC prevalence estimates for 2016, an estimated 16.6% (189,500 of 1,140,400) of persons living with HIV in the United States had injection drug use as a reported transmission category.[129] Recent cycles of the National HIV Behavioral Surveillance System (NHBS) survey suggest that HIV prevalence among persons who inject drugs is more than 10-fold higher than the HIV prevalence in the general United States population.[129]
- **Injection Drug Use Among Persons with HIV:** Examining opioid use specifically among individuals with HIV, one multisite study reported a 14% prevalence of heroin use during the prior 12 months.[52] Another survey that examined overall drug use among individuals with HIV reported 3-month prevalence rates of 2% for opiate use, 10% for polydrug use (including heroin as one of the drugs), and 4% for injection drug use.[44] Interpretation of these data is complicated because injection drug

use was not always distinguished from opioid use, and the studies inconsistently accounted for polydrug use, which typically includes heroin. 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.[127,130]

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 ethnic minority populations in low-income settings, but are now becoming more common among white middle-class individuals (especially teenagers and women) as a consequence of nonmedical prescription-opioid use and increased heroin availability.[2,131] 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.[118] Nonetheless, it is important to recognize that only a small percentage of individuals who use nonmedical prescription opioids initiate heroin use, and those that do often have "traditional" risk factors for addiction, including adverse childhood experiences.[131]

Diagnostic Criteria

The DSM-5 defines opioid use disorder by the presence of at least two symptoms (from a list of 11 symptoms as defined in the DSM-5) 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.[132] Behavioral interventions and/or detoxification, without medications for opioid use disorder, have poorer outcomes with high rates of relapse.[133,134] Pharmacologic therapies for opioid use disorder include three categories: opioid agonists, opioid partial agonists, and opioid antagonists.[135] Opioid agonists and partial agonists are used for maintenance therapy (also called opioid replacement therapy or opioid substitution therapy). In May 2020, SAMHSA published a Treatment Improvement Protocol (TIP 63) for medication-assisted treatment for opioid use disorders.[136] 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.[137] 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.[136]

Access to Medications for Opioid Use Disorder

Despite the effectiveness of medications for opioid use disorder, access to MOUD is limited in the United States. Data from the 2010–2015 Medicare Part D Prescription Drug Event Standard Analytic File suggests that in 2015, 60% of counties in the United States lacked access to a Medicare Part D buprenorphine prescriber, and more than 75% of counties lacked access to an oral naltrexone prescriber.[138] Similarly, studies of patients treated for opioid overdose in the emergency department or by emergency medical personnel indicate a high mortality in the year following these encounters.[139] Further, most emergency room physicians are not trained to provide MOUD.[140] In the past, physician 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. In April 2021, the Department of Health and Human Services relaxed requirements for buprenorphine prescribing in the wake of the ongoing opioid epidemic and a rising in overdose deaths.[141,142] Now physicians and APPs with an active state medical license and DEA

registration are able to submit a notice of intent to prescribe buprenorphine without completing any required training.[141,142] Under this exemption, physicians and APPs are issued an X-waiver and eligible to treat no more than 30 patients with buprenorphine at any one time.[141,142] Physicians and APPs who do not wish to be held to the 30-patient limit are eligible to qualify for a higher patient limit after completing the previously required 8 to 24 hours training.[141,142]

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.[143] 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 May 2020.[136]

- **Mechanism**: Buprenorphine is a partial agonist that has a high affinity for the mu-opioid receptor, but when bound, produces a long-lasting, but 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.[144,145,146] 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 can be prescribed for use on a daily or twice-daily basis. If the buprenorphine dose is doubled or tripled, dosing can be extended to every other day or to three-times weekly.[144] Typical doses of buprenorphine range from 8 to 16 mg daily, which is equivalent to approximately 60 mg of methadone.[144] 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).[135,147]
- **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.[146] 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.[146] The 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.[145,146] Prior to placing the buprenorphine implant, the patient must have achieved and sustained prolonged clinical stability of low-to-moderate dose (e.g. a dose no more than 8 mg per day) of a transmucosal buprenorphine-containing product. [145]
- **Adverse Effects**: Common side effects include drowsiness, constipation, headaches, and loss of appetite. Misuse of buprenorphine or buprenorphine-naloxone, such as with taking large doses 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, 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).
- **Physician Prescribing Requirements**: Physicians interested in providing buprenorphine or

buprenorphine-naloxone treatment in their practice settings need to submit a notice of intent to receive an X-waiver from the Center for Substance Abuse Treatment (CSAT).[141,142,148] Up until the spring of 2021, physicians without prior addiction certification needed to complete 8 hours of training on the treatment of opioid- addicted patients prior to being eligible for an X-waiver.[141,142] Physicians are now eligible to receive an X-waiver without completing prerequisite training. Physicians utilizing this exemption are eligible to treat up to 30 patients with buprenorphine at one time.[141,142] Physicians who wish to concurrently treat more than 30 patients with buprenorphine must complete the previously required training.[141,142]

- **Nurse Practitioners and Physician Assistants Prescribing Requirements**: In July 2016, section 303 of the Comprehensive Addiction and Recovery Act (CARA) was signed into law and this legislation provides nurse practitioners and physician assistants the ability to apply for a waiver to prescribe buprenorphine and/or buprenorphine-naloxone if they have completed the 24 hours of required training. This waiver process requires completion of the Waiver Notification Form and submission of copies of training certificates. As with physicians, APPs are now eligible to apply for an X-waiver without completing the prerequisite training.[141,142] This exemption allows APPs to concurrently treat up to 30 patients with buprenorphine, provided they are supervised by or working in collaboration with a DEA registered physician.[141,142] For detailed information regarding this process see (1) the SAMHSA information page Qualify for Nurse Practitioners and Physician Assistants Waiver and (2) the American Society of Addiction Medicine (ASAM) resource page Nurse Practitioners and Physician Assistants Prescribing Buprenorphine.
- **Buprenorphine Treatment Practitioner Locator**: The SAMHSA Buprenorphine website provides a state-by-state Buprenorphine Treatment Practitioner Locator for medical providers authorized to treat opioid addiction with buprenorphine; this site also provides links to buprenorphine training.[149]

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 with regard to dosing and dispensing of 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 (discussed below) in retaining people in treatment.[150] Treatment is usually for 12 months or longer, with longer duration of treatment associated with greater likelihood of abstinence.[151]

- **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.[144] Methadone relieves drug craving, 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, but 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 use of doses in the range of 60 to 120 mg per day.**[152]**
- **Adverse Effects**: Methadone is a relatively safe drug, and when used during maintenance therapy, the most common adverse events are perspiration and constipation.[153] 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.[144,154] Concomitant use of medications (with methadone) that prolong QTc should be avoided.
- **Drug Interactions with Antiretroviral Medications**: Methadone has significant multiple 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.[155,156] 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.[157] Nevertheless, large studies comparing XR-naltrexone to buprenorphine have shown that XR-naltrexone is inferior in preventing relapse and less cost-effective.[158,159]

- **Mechanism**: Naltrexone works by acting as an opioid receptor antagonist, which inhibits the euphoric response to opioids.[135]
- **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.[144]
- **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.[83] Because of its mechanism of action, which includes blocking opiate 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 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

Because HIV primary care providers can obtain certification to prescribe buprenorphine, persons with HIV and opioid use disorder can potentially receive comprehensive care for both their HIV and opioid use disorder at one setting.[160] Efforts to integrate buprenorphine treatment into HIV care settings, have produced mixed results and challenges have been encountered, including lack of clinical support staff, administrative obstacles, competing physician activities, and inadequate reimbursement stigma, and difficulties reaching marginalized patients.[161,162,163] 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 into community health centers, provides a particularly successful model that relies on collaboration between nursing case managers and prescribing physicians.[164] 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.[165,166]

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. Needle exchange (also called syringe services) remains a controversial topic. Opponents of syringe services argue that providing these programs condones and even encourages drug use, especially among youth. On the contrary, 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.[167,168,169,170] Canada, Australia, and several European countries 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.[171] 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.[171]

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 diseases, 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.[172]

Opioid Overdose Prevention Strategies

Another harm reduction technique involves overdose education and distribution of naloxone to persons who use injection drugs 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.[173] This is especially pertinent as the availability of naloxone has greatly expanded and is being widely promoted nationally for both people who use heroin and those prescribed higher doses of opioids for chronic pain conditions.[174] 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.[175]

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 under treated, the number of opioid prescriptions quadrupled between 1999 and 2013, followed by an increase in opioid use disorders and overdose deaths.[176] The high prevalence of acute and chronic pain syndromes among persons with HIV infection means that clinicians caring for patients with HIV/AIDS frequently have to balance pain management with the risk of iatrogenic opioid dependence and with underlying addiction.[177] 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.[178]

Stimulant Use Disorder

Prevalence of Stimulant Use Disorder in the United States

In 2018, the National Survey on Drug Use and Health estimated that 2.0% and 0.3% of the population had used cocaine and crack cocaine, respectively, in the past year.[15] Cocaine use was by far highest among those ages 18-25 years, with 2018 data estimating 5.8% use in this age group during the past year.[15] In 2018, an estimated 0.7% of the population over the age of 12, or 1.9 million people, had used methamphetamine, with the highest prevalence also among those 18-25 years of age.[15] For 2018, rates of past year methamphetamine use were lower in all age groups than past year cocaine use (Figure 17).[15] Older estimates of methamphetamine use, published in DSM-5 in 2013, reported amphetamine-type stimulant use disorder among adults 18 years of age and older was 0.2%, which was lower than cocaine use in all age groups age 12 years and older.[2]

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 ARV Guidelines estimate a 5 to 15% prevalence of stimulant use among all persons with HIV in the United States.[36]

- The 2017 Medical Monitoring Project estimated that only 0.5% of persons with HIV who were engaged in care injected cocaine, 1.8% injected methamphetamine, 6.1% used noninjection cocaine, 2.5% used crack cocaine, and 4.9% used noninjection methamphetamine.[37]
- 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%.[44,52,59]
- Other published estimates of methamphetamine use among adults with HIV have ranged from 10 to 23%, with even higher rates reported among men with HIV who have sex with men.[179]
- One study conducted among men who have sex with men in Los Angeles found a very strong association between methamphetamine use and HIV, with an HIV prevalence rate of 42% in men who have sex with men who used methamphetamine at least once per month for 6 months. The highest HIV prevalence rates were found among men who have sex with men seeking intensive outpatient treatment and residential treatment (61% and 85%, respectively).[180]
- More recent data from 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 injected other drugs, with the proportion of MSM who primarily inject methamphetamine being higher in western than eastern United States cities.[181] 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.[182,183] In particular, the use of heroin and methamphetamine together, often known as a goofball, has become increasingly prominent. There is some concern that the increasing use of methamphetamine among heroin users may contribute to sharing of injection equipment among persons with a higher HIV prevalence (MSM who inject methamphetamine), as well as with persons of lower HIV prevalence (heterosexual men and women who primarily inject opioids).[182,184,185,186]

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.[2] Men who have sex with men also represent a discreet risk group for stimulant use disorder, particularly methamphetamine use and its associated high-risk sexual behavior.[187,188,189]

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 as defined in the DSM-5) 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 providing incentives for positive reinforcement, such as delivery of vouchers in exchange for abstinence) are the primary interventions for stimulant use disorders, though no single approach has been proven to be most effective.[190,191] 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).[192] 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).[193,194,195] Some promising data have emerged for mirtazapine as shown in a recent randomized, controlled trial of mirtazapine versus placebo for men who have sex with men and transgender women who have sex with men; in this study, mirtazapine once daily was shown to significantly reduce methamphetamine use and some HIV risk behaviors in comparison to placebo.[196] 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 mirtazapine therapy had fewer methamphetamine-positive urine tests compared with participations taking placebo, despite low-to-moderate medication adherence.[197] In general, there is a high rate of relapse among individuals who complete methamphetamine treatment programs.[116]

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 2018 National Survey on Drug Use and Health found that approximately 21.5% of the population had used tobacco in the past month and 17.2% had specifically used cigarettes in the past month.[15] Despite ongoing high rates of tobacco use, the proportion of the population who smoked cigarettes in the last month has declined from approximately 1 in 4 people in 2002 to 1 in 6 people in 2018 (Figure 18).[15] Significant disparities in smoking prevalence persist, with highest prevalence rates in Native Americans/Alaskan Natives, multiracial adults, persons living under the poverty line, and those with lowest educational attainment.[198,199] Although cigarette smoking has declined, the prevalence of other tobacco use, such as cigars and pipe tobacco, has not changed significantly since 2002.[15]

Tobacco Use Prevalence in Adults with HIV

Data from the CDC Medical Monitoring Project has shown that among persons with HIV who engaged in medical care in the 2017-2018 time period, 34% were current smokers, 28% smoked daily, and 23% were former smokers.[37] In addition, other data have noted that adults with HIV are less likely to quit smoking compared to persons without HIV.[200]

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 illness compared with those without mental illness.[201] In addition, tobacco use disorder has a strong degree of heritability, and differences in nicotine blood levels and nicotine metabolism varies among individuals, especially among certain ethnicities (i.e. African American males have higher blood nicotine levels for a given number of cigarettes).[2]

Screening and Treatment Recommendations

Tobacco use is typically a chronic problem and often requires behavioral support, pharmacologic therapy, and multiple attempts to quit.[202,203,204] The U.S. Preventive Services Task Force (USPSTF) issued an updated recommendation statement in 2015 on Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women.[205] 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.[206]

- 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 2).
    - First-line outpatient pharmacotherapy for smoking cessation consists of varenicline or combination nicotine replacement products.
    - Second-line outpatient pharmacotherapy for smoking cessation is sustained release bupropion or a single nicotine replacement product.

- - Third-line out-patient pharmacotherapy for smoking cessation consists of nortriptyline.
  - If a single agent was 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.[207] 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.[208,209]

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.[210,211] The Adult and Adolescent ARV 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.[36,204] 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.[36]

Summary Points

- Substance use disorders are common among adults with HIV in the United States.
- Risk factors for substance use disorders are complex and likely include a combination of biologic and social factors.
- Many substance use disorders are linked to decreased adherence to antiretroviral medications, risk-taking behaviors, and HIV disease progression (independent of medication nonadherence).
- 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 for persons with methamphetamine use disorder.
- The rise in opioid addiction has paralleled the rise in opioid prescribing habits over the past 15 years, and tackling the opioid epidemic will require educating clinicians and patients alike about the risks, benefits, and proper role of opioid pain medications.
- Medications for opiate 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 opiate use disorder are prescribed jointly.
- Individuals with HIV who are able to remain abstinent from drug use have excellent health utilization and antiretroviral adherence patterns, thereby emphasizing the importance of securing access to substance use treatment programs.
- Treatment strategies for substance use disorders should embrace a harm reduction philosophy in order to best serve those individuals at highest risk for ongoing substance use and associated HIV risk behavior.

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  [PubMed Abstract] -

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  [PubMed Abstract] -

Figures

Figure 1 Number of Persons Age 12 and Older with a Past Year Substance Disorder, United States, 2018

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.
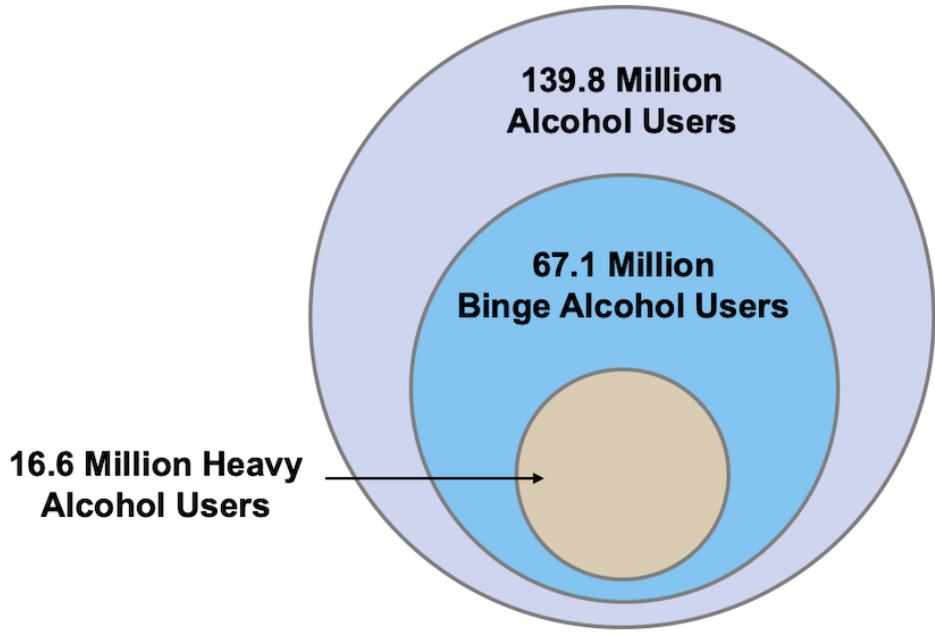
Source: Substance Abuse and Mental Health Services Administration. (2019). Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.
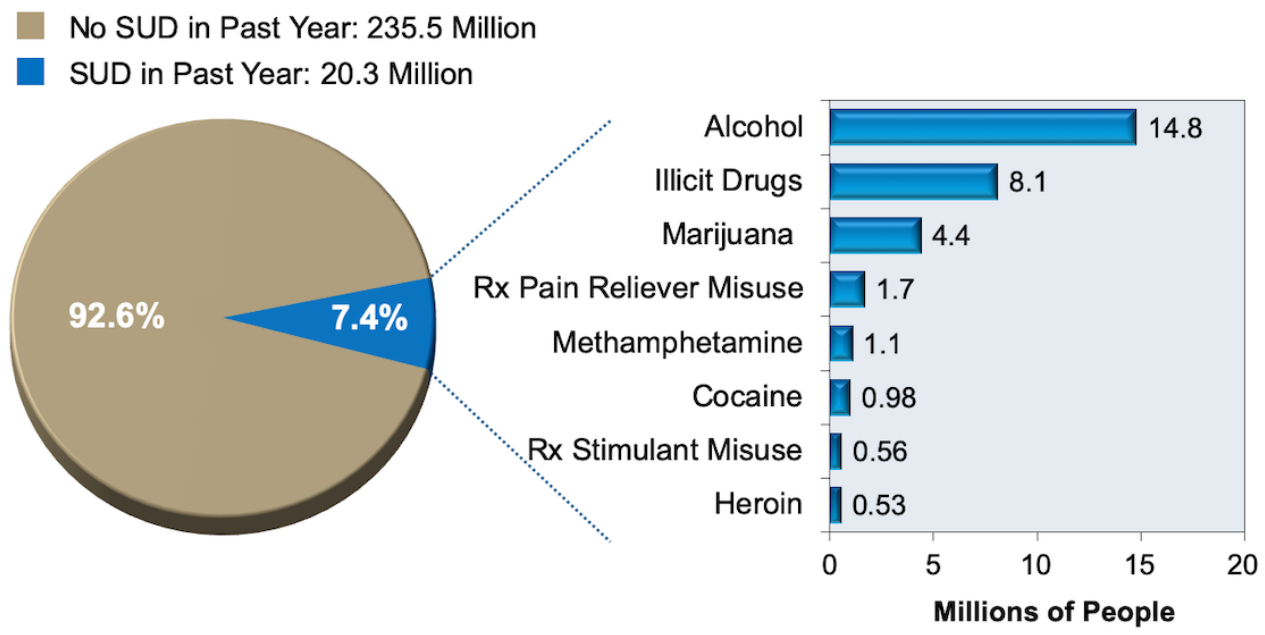
Figure 2 Current, Binge, and Heavy Alcohol Use Among People Age 12 Years or Older, United States, 2018

The 67.1 million binge drinkers represent 48% of all alcohol users. The 16.6 million heavy alcohol users represent 24.7% of binge alcohol users and 11.8% of all alcohol users.

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 3 Past Year Alcohol Use Disorder 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.
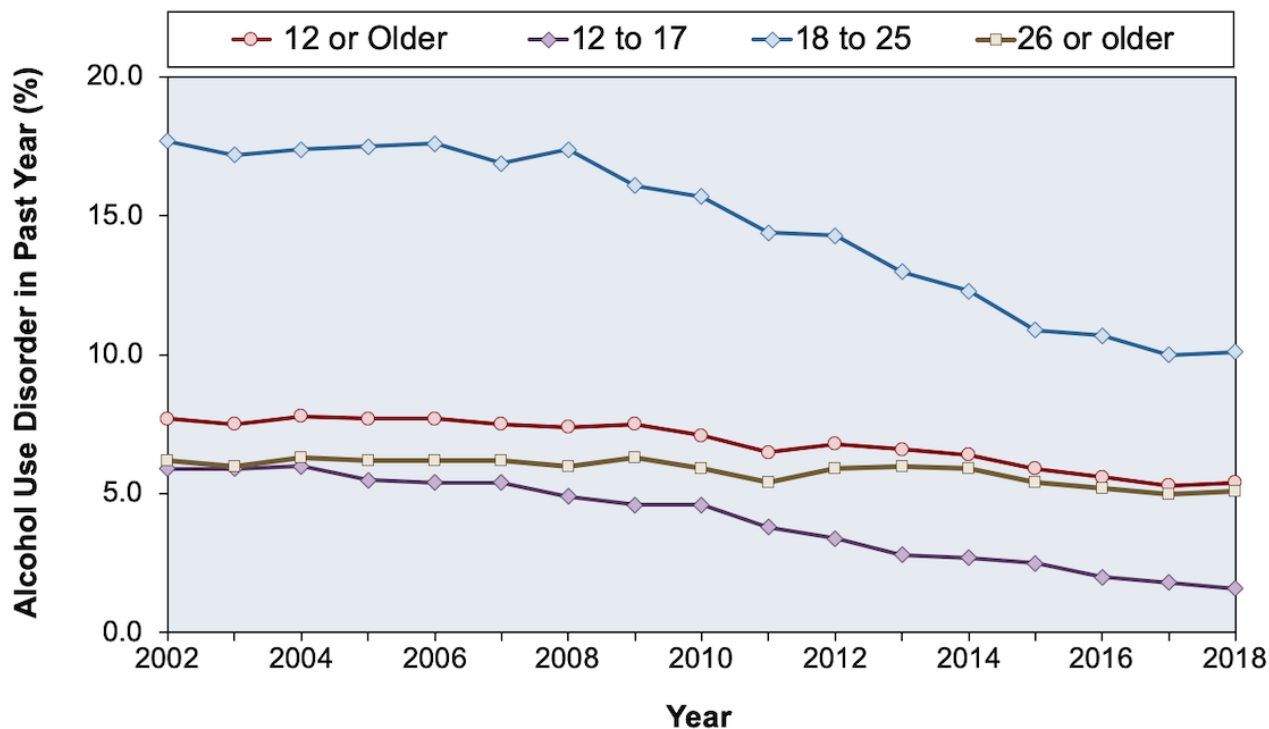
Figure 4 U.S. FDA-Approved Medications to Treat Alcohol Use Disorder

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, 2015.

U.S. FDA-Approved Medications for Treating Alcohol Use Disorder

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

Figure 5 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 of associated with alcohol ingestion.

Source: Anton RF. Naltrexone for the management of alcohol dependence. N Engl J Med. 2008;359:715-21. © 2017 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.
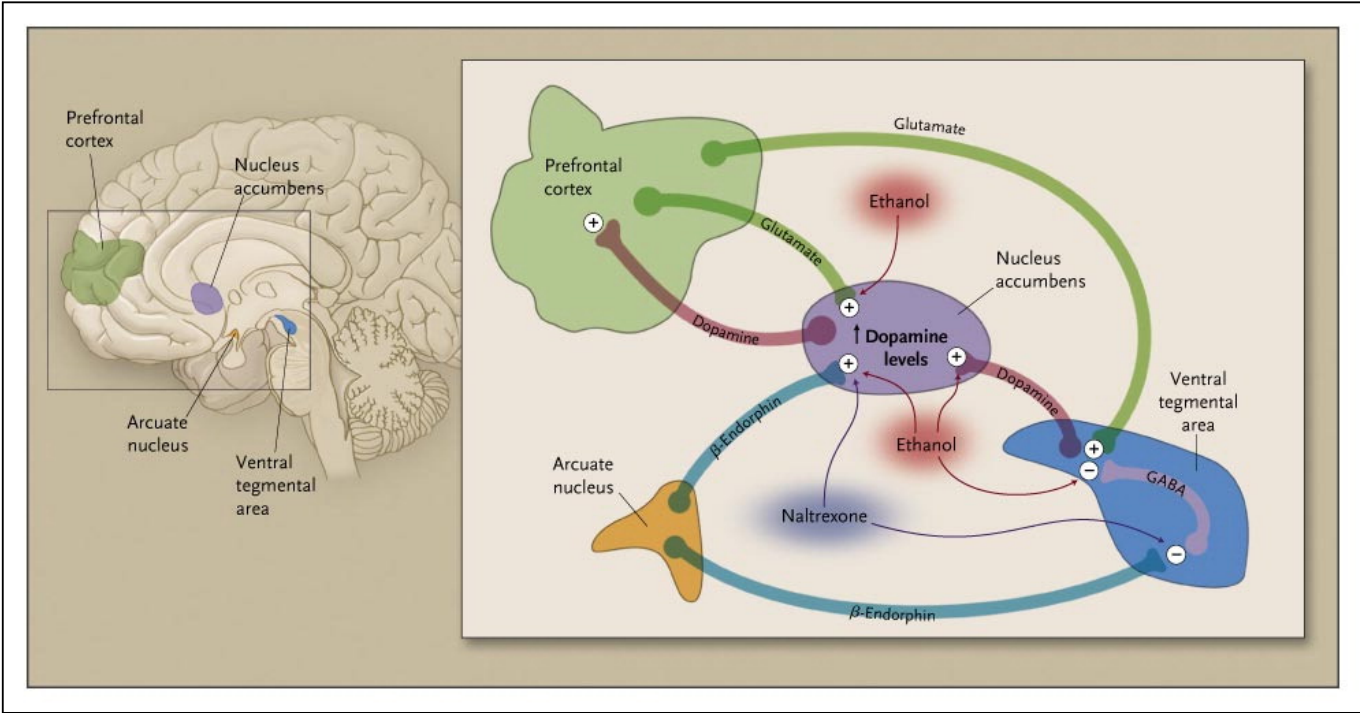
Figure 6 Impact of Long-Acting Naltrexone on Median Heavy Drinking Days per Month

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.
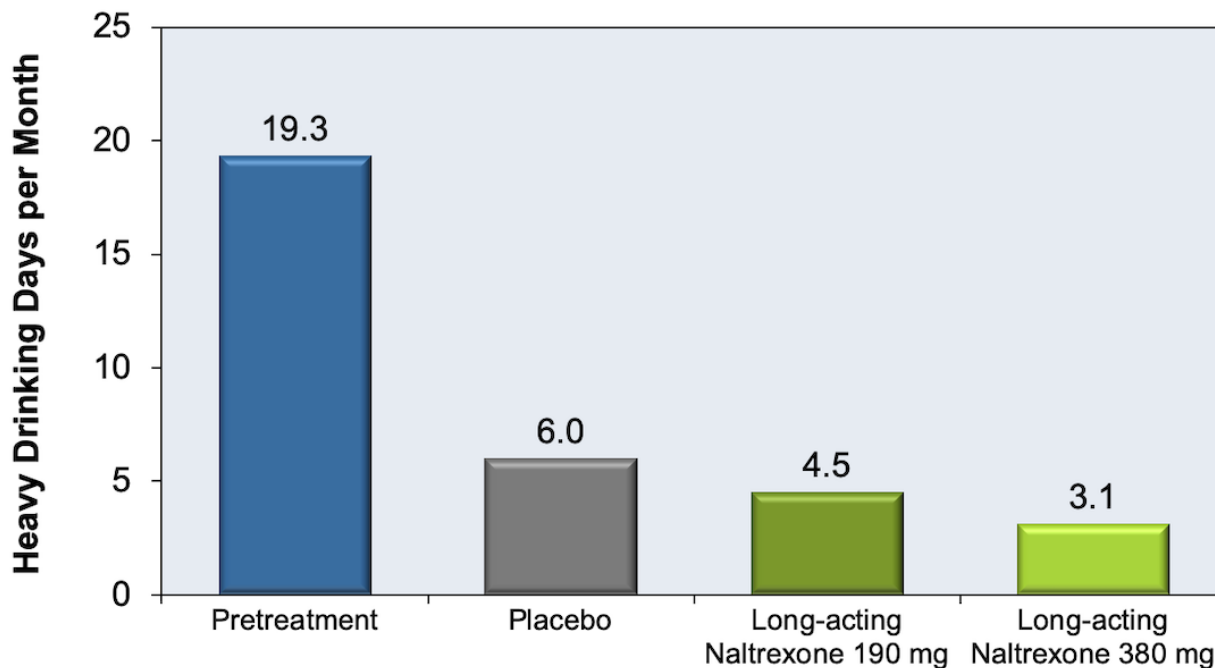
Figure 7 Acamprosate in Persons with Alcohol Dependence

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 post treatment).

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.
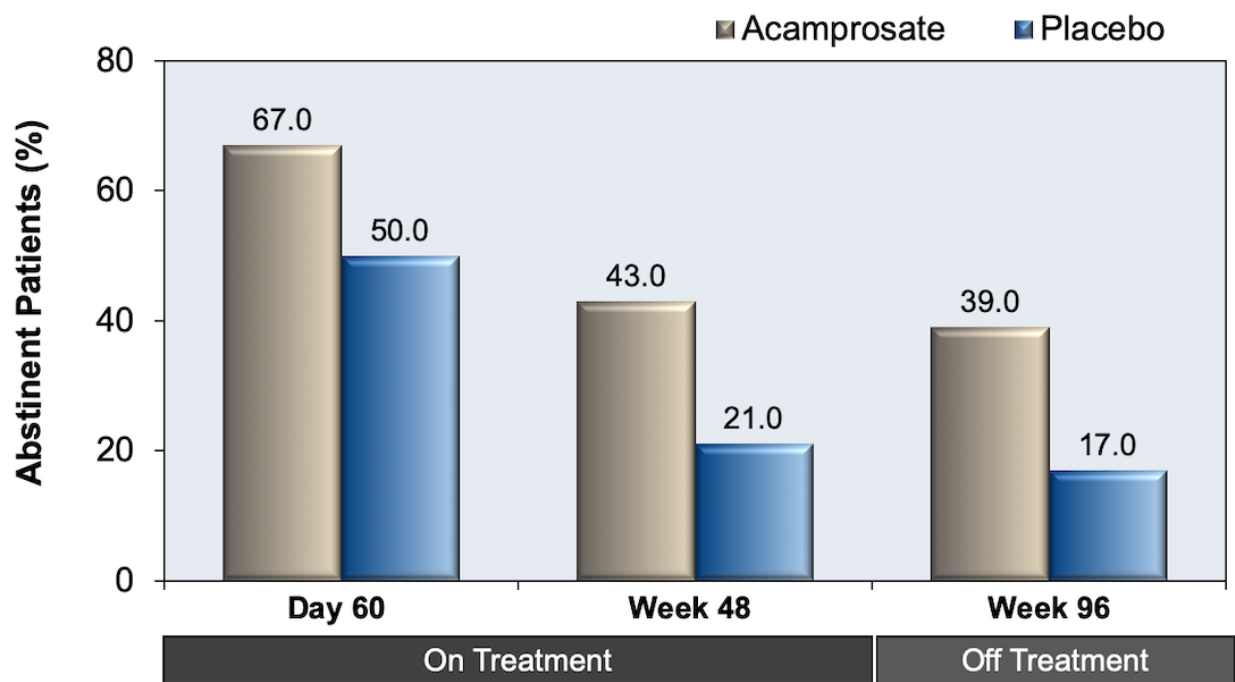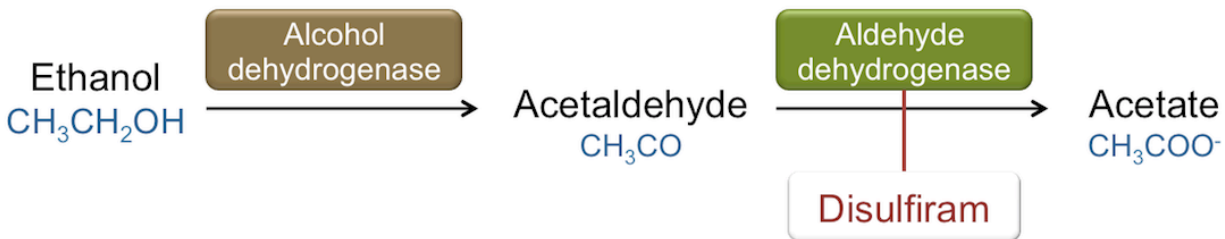
Figure 8 Inhibition of Alcohol Metabolism by Disulfiram

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.

Normal Ethanol (Alcohol) Metabolism

Ethanol CH_3CH_2OH → [Alcohol dehydrogenase] → Acetaldehyde CH_3CO → [Aldehyde dehydrogenase] → Acetate CH_3COO^-

Inhibition of Ethanol (Alcohol) Metabolism

Ethanol CH_3CH_2OH → [Alcohol dehydrogenase] → Acetaldehyde CH_3CO → [Aldehyde dehydrogenase] → Acetate CH_3COO^-
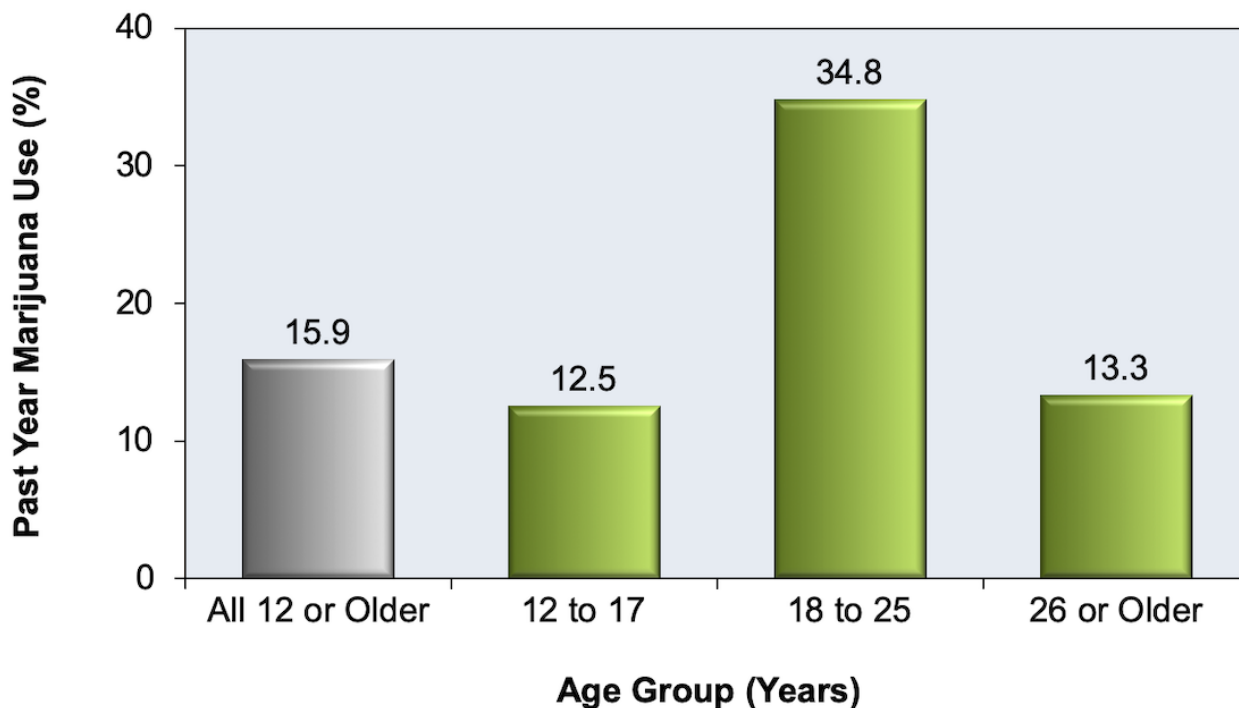
Disulfiram

Figure 9 Past Year Illicit Drug Use among Persons 12 Years of Age and Older, United States, 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.
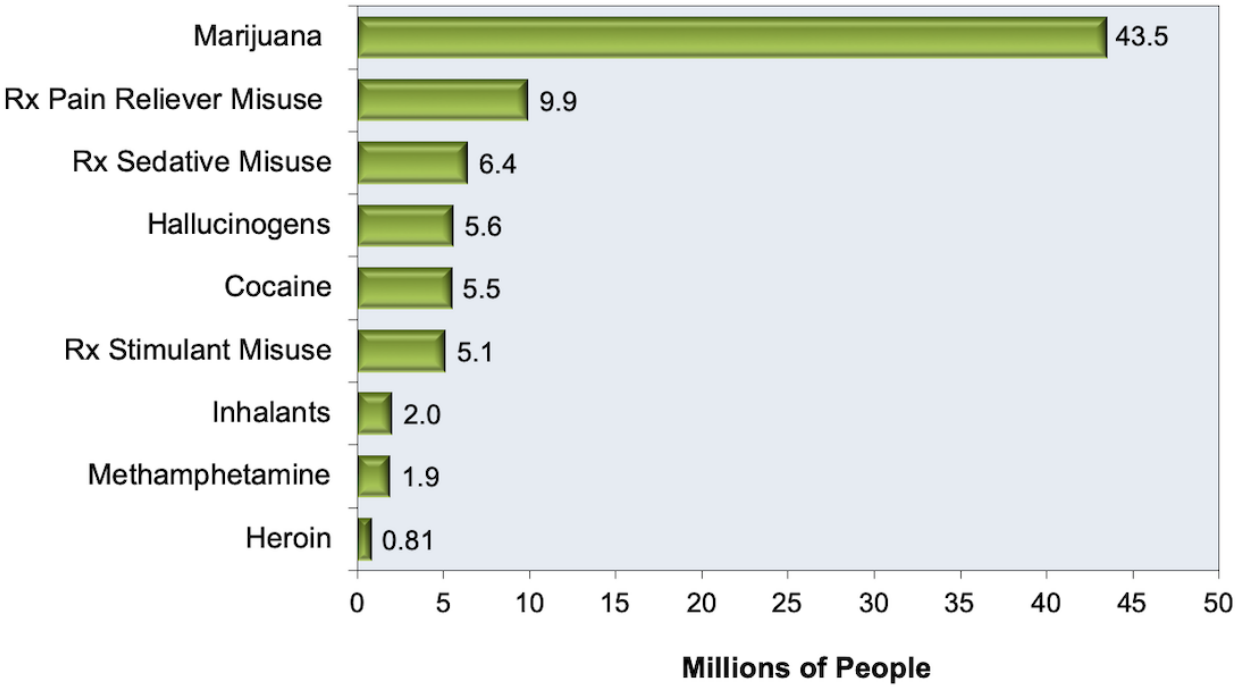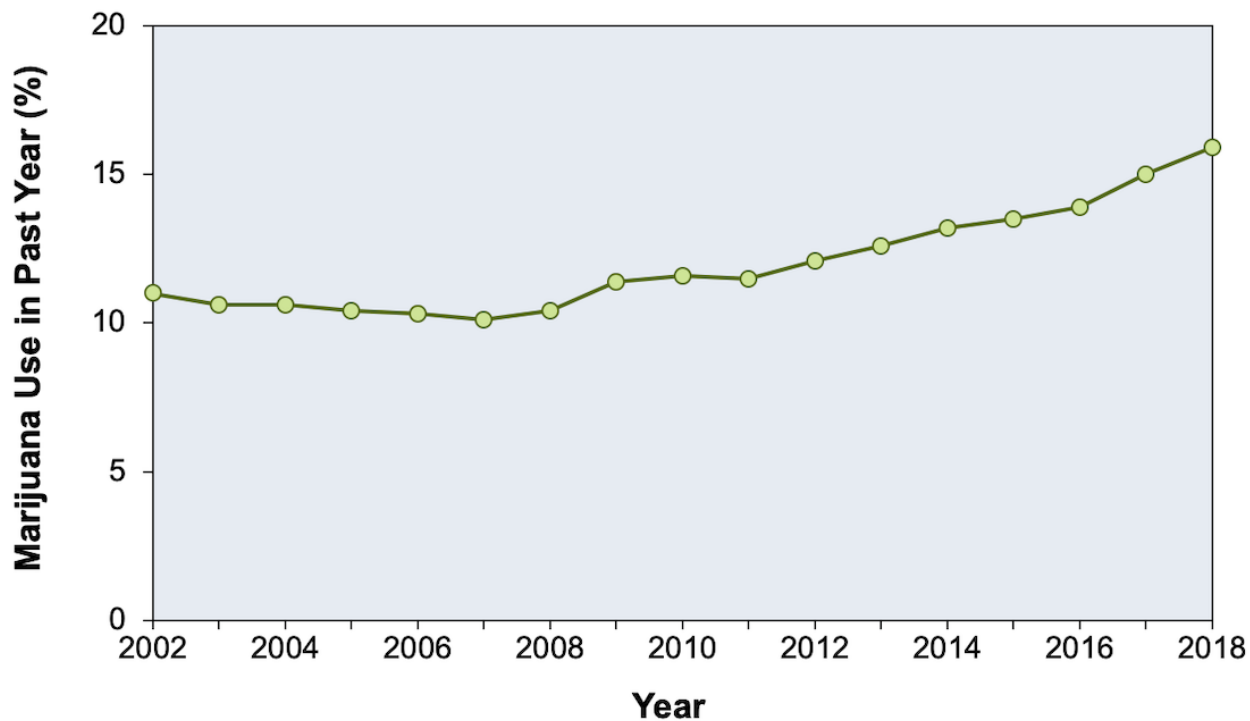
Figure 10 Past Year Marijuana Use, by Age Group, United States, 2018

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 Past Year Marijuana Use among People Aged 12 Years or Older, United States, 2002-2018
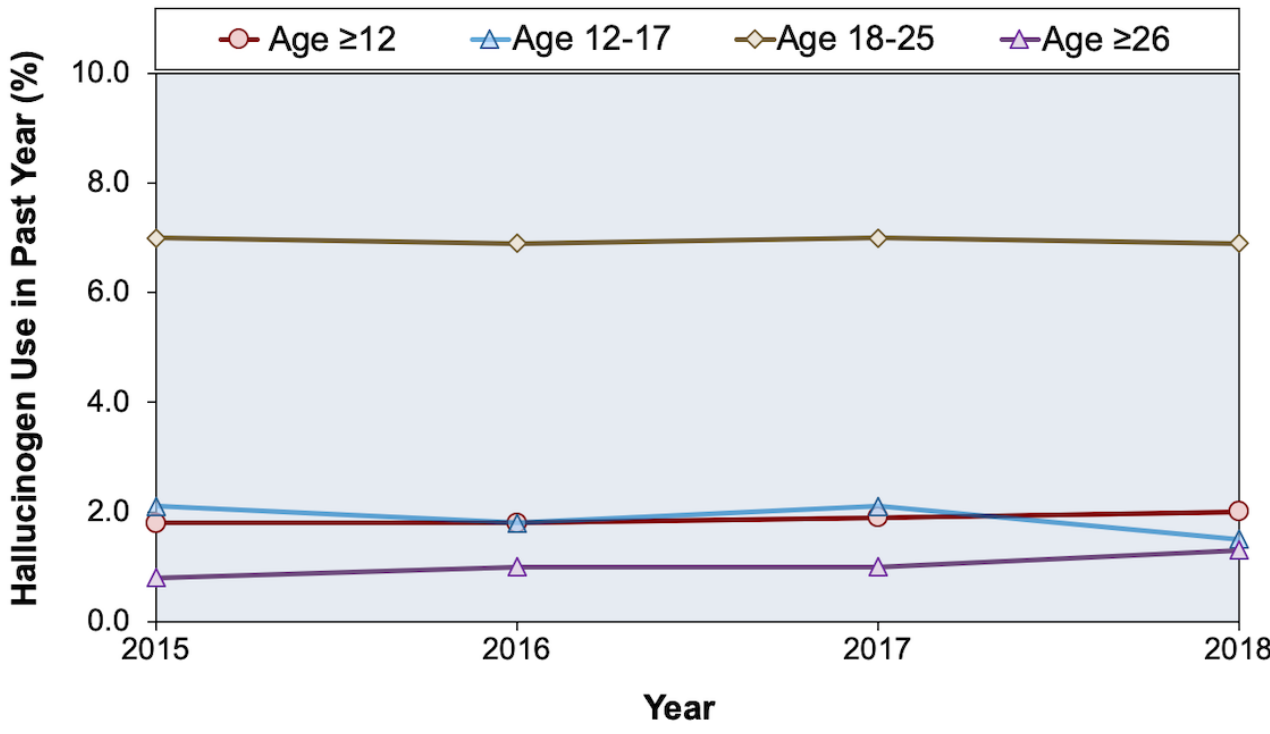
Source: Substance Abuse and Mental Health Services Administration. (2019). Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.
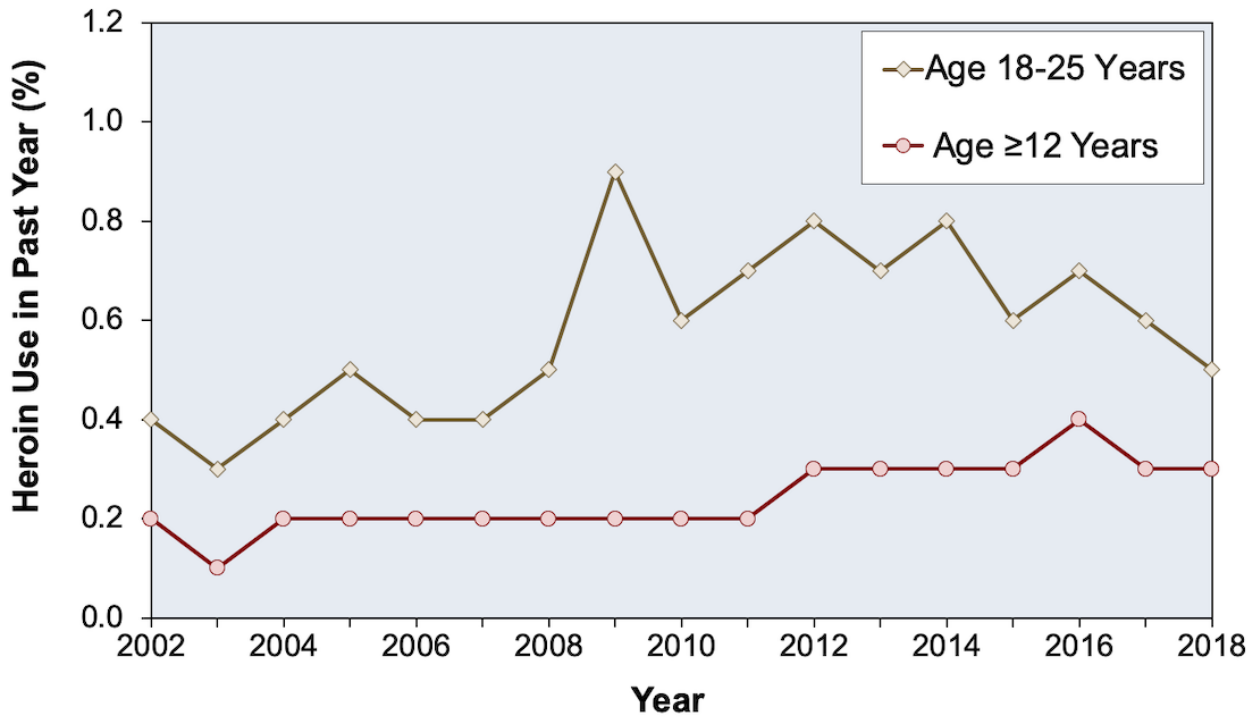
Figure 12 Past Year Hallucinogen Use among People Aged 12 Years or Older, United States, 2015-2018

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 13 Past Year Heroin Use among People Aged 12 Years or Older, United States, 2002-2018
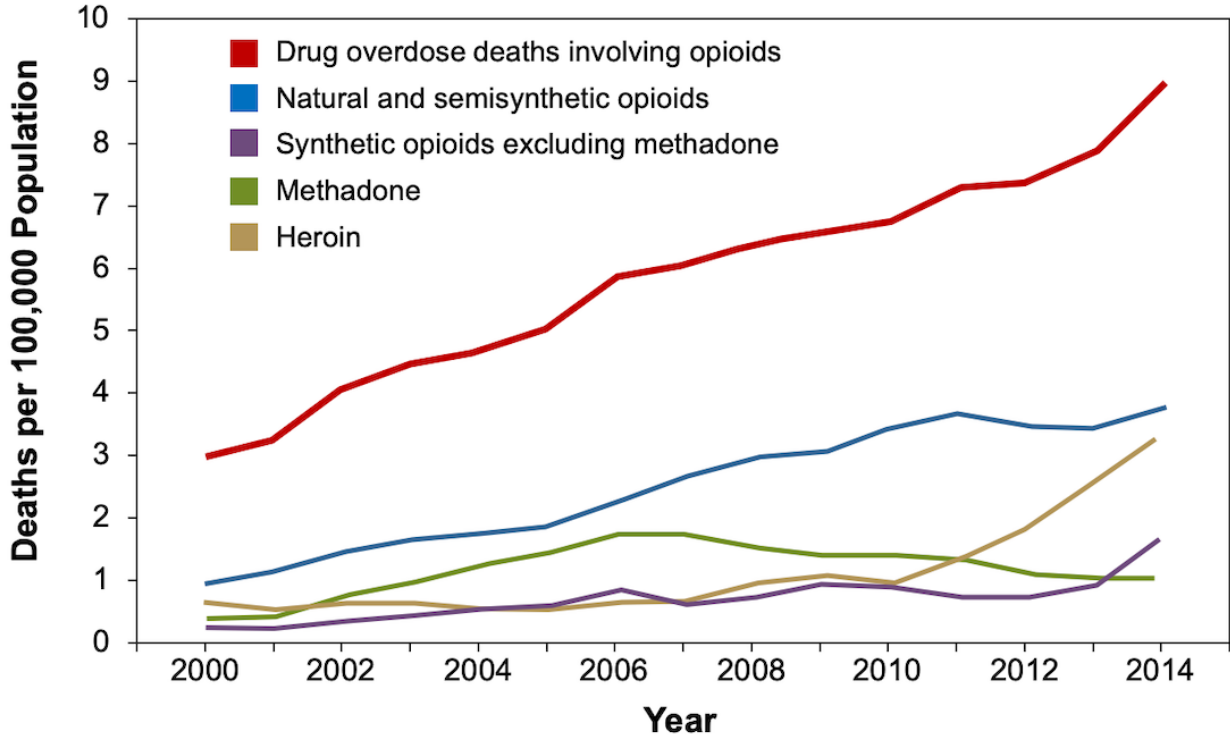
Source: Substance Abuse and Mental Health Services Administration. (2019). Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.

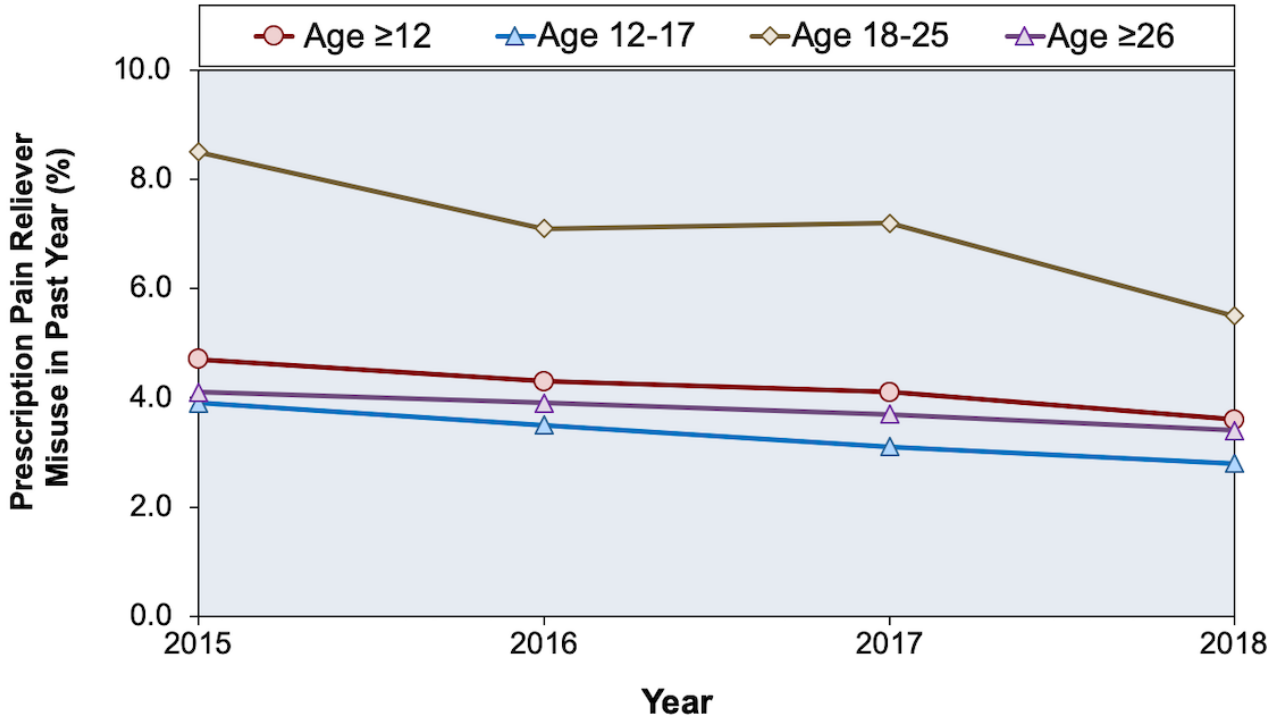**Figure 14 Drug Overdose Deaths Involving Opioids, by Type of Opioid United States, 2000–2014**

Age-adjusted death rates were calculated by applying age-specific death rates to the 2000 U.S. standard population age distribution.Opioids include drugs such as morphine, oxycodone, hydrocodone, heroin, methadone, fentanyl, and tramadol.

Source: Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in Drug and Opioid Overdose Deaths--United States, 2000-2014. MMWR Morb Mortal Wkly Rep. 2016;64:1378-82.

Figure 15 Past Year Prescription Pain Reliever Misuse among People Aged 12 Years or Older, United States, 2015-2018

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 16 Drug Overdose Deaths Involving all Opioids and Prescription Opioids, by Age Group and Sex, United States, 2018

In 2018, the number of overdose deaths was 3-fold higher in males than in females. The 25-44 year old age group had by far the highest number of overdose deaths.

Source: 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.

Figure 17 Past Year Stimulant Use, by Age Group, United States, 2018
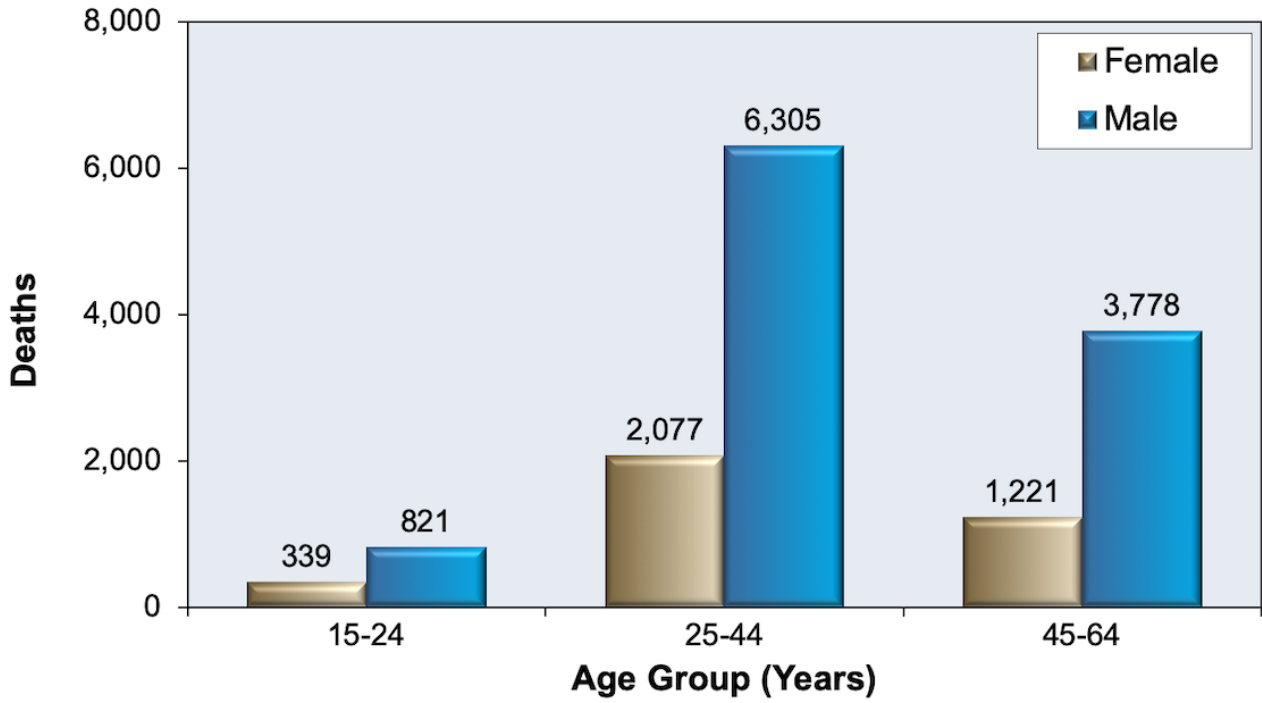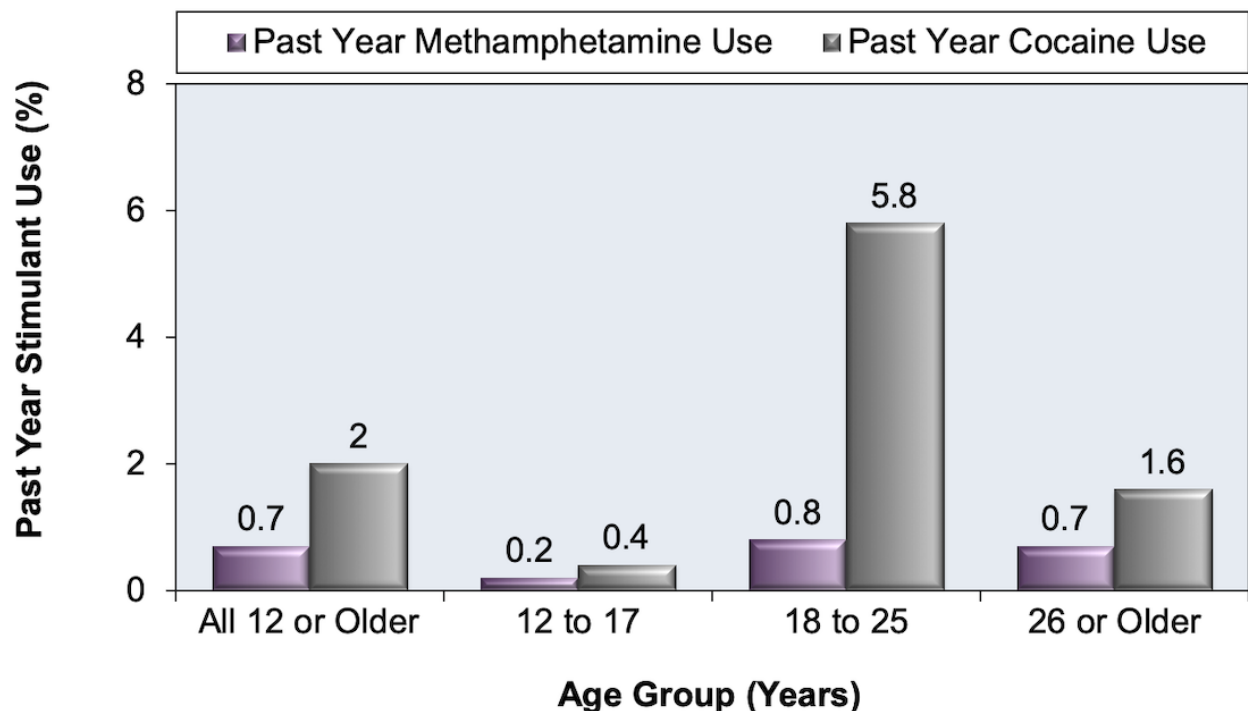
Source: Substance Abuse and Mental Health Services Administration. (2019). Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.

Figure 18 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.
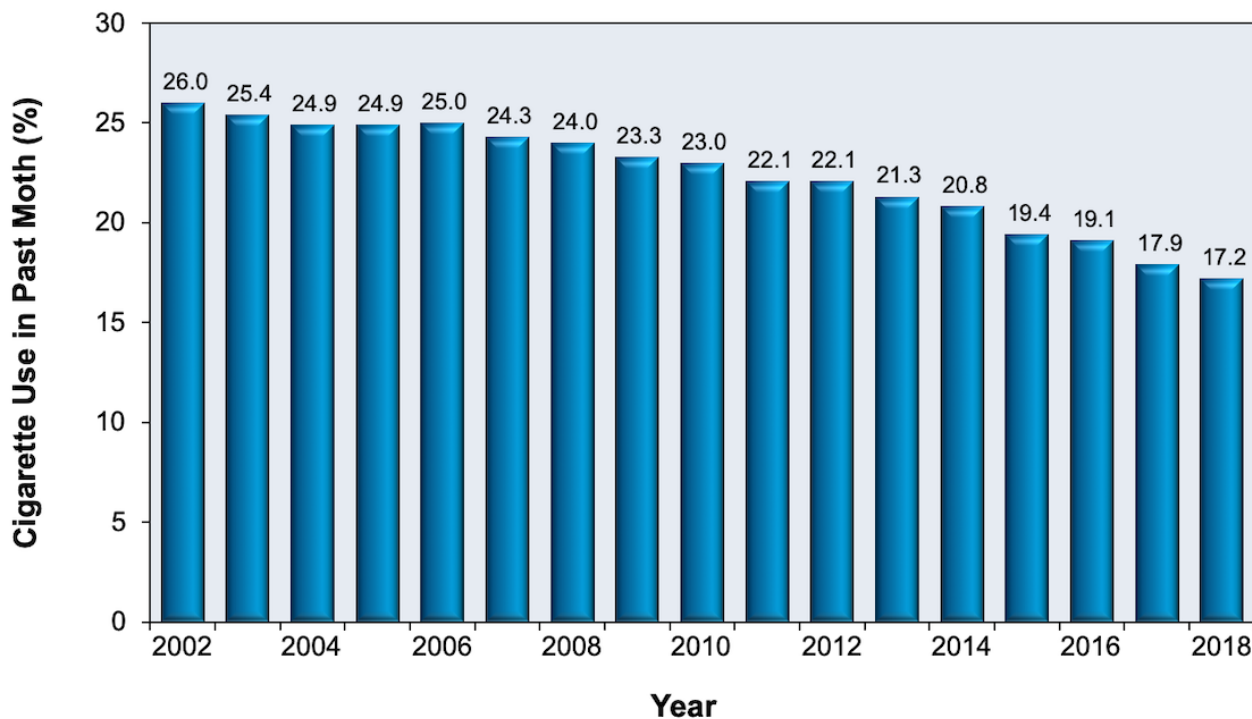
Table 1.
DSM-5 Diagnostic Criteria for Alcohol Use Disorder
A maladaptive pattern of alcohol use leading to clinically significant impairment or distress, as manifested by 2 (or more) of the following, occurring within a 12-month period:
1. Had times when the patient drank more, or longer, than intended
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 (eg, 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: • Mild: 2 to 3 symptoms • Moderate: 4 to 5 symptoms • 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 2. **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 21 mg 14 mg 7 mg	OTC or Rx	Starting dose: 21 mg for ≥10 cigarettes per day. 14 mg for <10 cigarettes per day. After 6 weeks, option to taper to lower doses for 2-6 weeks. Use ≥3 months. After 6 weeks, continue original dose or taper to lower doses (either option acceptable).	Apply a new patch each morning to dry skin. Rotate application site to avoid skin irritation. May start patch before or on quit date. Keep using even if a slip occurs. If insomnia or disturbing dreams, remove patch at bedtime.	Skin irritation Trouble sleeping Vivid dreams (patch can be removed at bedtime to manage insomnia or vivid dreams)	The easiest nicotine product to use. Provides a steady nicotine level. 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 4 mg 2 mg	OTC or Rx	If first cigarette is ≤30 minutes of waking: 4 mg. If first cigarette is >30 minutes of waking: 2 mg. Use ≥3 months.	Place between gum and cheek, let it melt slowly. Use 1 piece every 1-2 hours (Max: 20/day).	Mouth irritation Hiccups Heartburn Nausea	User controls nicotine dose. Oral substitute for cigarettes. May be added to patch to cover situational cravings. 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 4 mg	OTC or Rx	If first cigarette is ≤30 minutes of waking: 4	Chew briefly until mouth tingles, then	Mouth irritation Jaw soreness	User controls nicotine dose. Oral substitute	Not chewed in same way as regular gum;

Drug (doses)	How Sold (U.S.)	Dosing Instructions	Administration	Common Side Effects	Advantages	Disadvantages
2 mg		mg. If first cigarette is >30 minutes of waking: 2 mg. 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. Use ~ 1 piece per hour (Max: 24/day).	Heartburn Hiccups Nausea	for cigarettes. May be added to patch to cover situational cravings.	requires careful instruction. Can damage dental work and be difficult to use with dentures. No food or drink 15 minutes prior to use and during use.
Nicotine inhaler 10-mg cartridge	Rx only	10 mg/cartridge. Each cartridge has ~80 puffs. Use ≥3 months.	Puff into mouth/throat until cravings subside. Do not inhale into lungs. Change cartridge when nicotine taste disappears. Use 1 cartridge every 1-2 hours (Max: 16/day).	Mouth and throat irritation Coughing if inhaled too deeply	User controls nicotine dose. Mimics hand-to-mouth ritual of smoking cigarettes. May be added to patch to cover situational cravings.	Frequent puffing required.
Nicotine nasal spray 10 mg/mL (10 mL bottle)	Rx only	10 mg/mL. 0.5 mg per spray. Each bottle has ~200 sprays. Use ≥3 months.	Use 1 spray to each nostril. Use spray every 1-2 hours (Max: 80/day).	Nasal and throat irritation Rhinitis Sneezing Coughing Tearing	User controls nicotine dose. Most rapid delivery of nicotine among all NRT products. May be added to patch to cover situational cravings.	Has the most side effects of all NRT products. Some users cannot tolerate local irritation to nasal mucosa.
Varenicline (tablet) 0.5 mg 1.0 mg	Rx only	Days 1-3: 0.5 mg/day. Days 4-7: 0.5 mg twice a day.	Start 1-4 weeks before quit date. Take with food and a tall glass	Nausea Insomnia 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. Use 3-6 months.	of water to minimize nausea.	Headache	Dual action: relieves nicotine withdrawal and blocks reward of smoking. Oral agent (pill).	psychiatric adverse events, even though they are no more common than with other cessation medications.
Bupropion sustained release (SR) (tablet) 150 mg	Rx only	150 mg/day for 3 days, then 150 mg twice a day. Use 3-6 months.	Start 1-2 weeks before quit date.	Insomnia Agitation Dry mouth Headache	May lessen post-cessation weight gain while drug is being taken. 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]