Substance Use Disorders

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

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

Background

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

Definitions and Diagnostic Criteria

Definitions and Terminology

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

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

DSM-5 Diagnostic Criteria for Substance Use Disorder

The DSM-5 has combined the DSM-IV categories of substance abuse and substance dependence under the single heading of SUDs.[2,3] The diagnosis of substance use disorder is based on scoring from a total of 11 symptom criteria included in four major groups: Impaired Control, Social Impairment, Risk Use of a Substance, and Pharmacologic Criteria.[2,3] (Table 1)

Screening for Substance Use Disorders

USPSTF Recommendations for Substance Use Disorder Screening

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

Screening Resources for Unhealthy Alcohol and Drug Use

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

Specific Tools to Assess Alcohol Use

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

Screening Tools for Unhealthy Drug Use

- **ASSIST**: The WHO has also developed the Alcohol, Smoking, and Substance Involvement Screening

Test (ASSIST) to detect substance use and related problems in the primary care setting.[11] The ASSIST covers 12 items related to recent and lifetime use, dependence symptoms, substance-related problems, and intravenous use; it addresses 10 categories of substances: tobacco, alcohol, cannabis, cocaine, stimulants, inhalants, sedatives/hypnotics, hallucinogens, opiates, and other drugs. This tool is lengthy, but it has been effectively modified and condensed for use as a routine screening tool in some clinical settings, and it may be especially useful for screening patient populations with heavier polysubstance use, such as persons with HIV. New technologies that enable patient-reported outcomes may facilitate the incorporation of these screening tools into busy HIV primary care clinics.[12,13,14]

- **NIDA Quick Screen**: The National Institute on Drug Abuse (NIDA) Quick Screen is a 4-item screening tool that asks about the frequency of alcohol, tobacco, nonmedical prescription drugs, and illegal drug use in the past year.[15] If a patient reports the use of illegal drugs or prescription drugs for nonmedical reasons in the past year, this tool can be used in conjunction with the NIDA-Modified ASSIST for a more detailed assessment.[15]
- **TICS**: This brief, two-item conjoint screening, known as TICS, has a sensitivity and specificity of nearly 80% in detecting current substance use problems.[16] A single-question screen—“How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”— has been shown to accurately identify drug use.[17]
- **SUBS**: The 4-item Substance Use Brief Screen (SUBS) can be used with patients in a primary care setting for tobacco, alcohol, and other drug use.[18] This is the only brief, self-administered, comprehensive screening instrument validated in the primary care setting and may facilitate screening of primary care populations.[18]
- **TASP**: The Tobacco, Alcohol, Prescription Medication, and Other Substance Use (TASP) tool consists of a screening and brief assessment component. The tool begins with a 4-item screen, asking about the frequency of tobacco, alcohol, prescription drug, and other substance use in the past 12 months. For any positive screens, the assessment tool, consisting of brief substance-specific questions, is used to assess risk for substance use disorders.[19]

Epidemiology of Substance Use in the United States

Data Sources for Substance Use in the United States

The primary source of statistical information on SUDs in the general United States population originates from the National Survey on Drug Use and Health (NSDUH), which is an annual survey of the civilian, noninstitutionalized population 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 the most recent data are from 2024.[20] A major limitation of the NSDUH is that it does not sample persons living unhoused or those in jails or prisons, and is, therefore, likely to underestimate the prevalence of SUDs in the United States. Historically, data collection for the NSDUH was conducted in person, but starting in 2021, data collection occurred both in person and online.[20] Due to these differences in methodology, data from 2021 through 2024 are not comparable to prior years.[20] Prevalence estimates for substance use disorders in persons with HIV are derived from several published studies, as there is no comparable annual survey for the population of individuals with HIV.

Estimates of Substance Use Disorders in the United States

Data from the 2024 NSDUH found that in the United States, approximately 48.4 million people aged 12 years and older, or 16.8% of the population, had an SUD in the past year (Figure 1).[20] This included 27.9 million people with an alcohol use disorder and 28.2 million people with a drug use disorder.[20] In addition to alcohol and other drugs, the NSDUH reported that 63.7 million people, or 22.1% of the population 12 years of age and older, had used tobacco or nicotine in the past month.[20]

Predictors of Substance Use Disorders

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

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

Substance Use Disorders in People with HIV

Estimates of Substance Use Disorders in People with HIV

Multiple studies and surveys have demonstrated high rates of substance use among persons with HIV in the United States.[32,33,34] For example, the 2023 cycle of the Medical Monitoring Project (a CDC surveillance system that assesses behaviors and clinical characteristics of persons with HIV who have received outpatient medical care) estimated that 27% of people with HIV currently smoked, including an estimated 22% who smoked daily.[32] In addition, the use of alcohol and other substances is higher in persons with HIV compared to use in the general population. The 2023 Medical Monitoring Project estimated that 50% of persons with HIV had used one or more noninjection drugs in the prior 12 months for recreational purposes, 3% had used injection drugs in the prior 12 months, and 16% had engaged in binge drinking in the past 30 days.[32]

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.[35,36,37] Thus, any substance use disorder that interferes with antiretroviral medication adherence can impact the transmission of HIV and have significant public health consequences. Certain substance use disorders in persons with HIV have been consistently linked to decreased antiretroviral medication adherence and to activities that enhance the likelihood of HIV transmission to sex partners and needle-sharing partners who do not have HIV.[1,38,39,40]

- **Medical Monitoring Project**: The 2023 data from the Medical Monitoring Project noted that among people with HIV, 11% reported alcohol or drug use as the reason for missing their last dose of antiretroviral medications.[32]
- **Multicenter AIDS Cohort Study**: The Multicenter AIDS Cohort Study reported that methamphetamine use increased the number of condomless anal receptive sex partners.[41] In addition, several other studies, including a review of 61 studies, confirmed that men with HIV who have sex with men and use methamphetamine are more likely to report sex activities, such as condomless anal intercourse, that place them at higher risk of transmitting HIV to a sex partner.[42,43]

Substance Use Disorders and Impact on HIV Care

Substance use can create barriers to care for individuals with HIV.[40,44,45] 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.[46,47,48] Antiretroviral medication adherence problems in individuals with a substance use disorder may have serious consequences, including suboptimal virologic control and the potential emergence of virologic resistance.[49,50] Individuals with HIV can improve healthcare utilization, antiretroviral adherence, and rates of virologic suppression through the treatment of substance use disorders, particularly with treatment of opioid use disorders.[47,51,52,53,54]

Substance Use and HIV Disease Progression

Alcohol use, 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.[55,56] 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.[57,58,59,60,61,62,63] Furthermore, methamphetamine has been shown to increase HIV replication in animal models.[64]

Alcohol Use Disorder

Prevalence of Alcohol Use Disorder in Adults with HIV

Hazardous drinking is common among persons with HIV.[65] The 2023 Medical Monitoring Project found that 64% of people diagnosed with HIV had consumed alcohol in the past 12 months, with 6% reporting daily consumption of alcohol.[32] In this same survey, 16% of persons diagnosed with HIV were classified as having engaged in binge drinking in the past 30 days, which equates to greater than or equal to 5 alcoholic beverages in a single sitting for men and 4 or more for women.[32] In general, the approach to screening, diagnosis, counseling, and pharmacologic therapy for alcohol use disorder is the same for persons with HIV as for those without HIV.

Diagnostic Criteria

The National Institute of Alcohol Abuse and Alcoholism (NIAAA) recommends that women of all ages and men older than 65 years limit alcohol consumption to no more than seven alcoholic drinks per week and no more than three per day.[10] Recommendations for men 65 years of age and younger are to limit alcohol consumption to no more than 14 drinks per week and no more than 4 drinks per day.[10] These guidelines underscore that people who drink over recommended limits, even if they do not meet the criteria for alcohol use disorder, are at significant risk for alcohol-related problems.[10,66] The DSM-5 defines alcohol use disorder by the presence of at least two symptoms (from a list of 11 symptoms) related to evidence of impaired control, social impairment, risky use, and pharmacological criteria.[2] (Table 2)

Behavioral Counseling

The USPSTF recommends that persons who screen positive for unhealthy alcohol use be assessed for alcohol use disorder. Those with unhealthy drinking, but without an alcohol use disorder, should receive brief behavioral counseling, which may include giving general feedback to patients regarding their drinking, how it relates to recommended limits, and how to cut back on drinking.[4] The use of behavioral counseling has been shown to improve behavioral outcomes, including reducing overall consumption as well as reducing heavy drinking days.[67,68] Persons with an alcohol use disorder should be considered for pharmacologic treatment and 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.[69,70]

Pharmacologic Therapy for Alcohol Use Disorder

There are currently three United States Food and Drug Administration (FDA)-approved medications for the treatment of alcohol use disorder: naltrexone (oral and extended-release injectable formulations), acamprosate, and disulfiram.[71,72,73] In a 2023 systematic review and meta-analysis, which included data from 118 studies, investigators found the strongest evidence for treatment of alcohol use disorder with oral acamprosate and oral naltrexone (50 mg/day).[74] Data were limited on higher-dose oral naltrexone (100 mg/day) and injectable naltrexone.[74] Similarly, 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.[75] The following summarizes available FDA-approved therapies for alcohol use disorder, as well as information on two medications (gabapentin and topiramate) that are sometimes used to treat alcohol use disorder but do not have FDA approval for this indication.(Table 3)

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), low potential for misuse, and

convenient dosing, including once daily oral and once monthly injectable options.

- **Mechanism**: Naltrexone is an opioid antagonist that mediates the rewarding effects of alcohol and attenuates cravings (Figure 2).[76,77] 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.[71]
- **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).[76]
- **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.[78] 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 withdrawal. In addition, persons who discontinue naltrexone can subsequently have enhanced effects of opioids.
- **Treatment Data**: In large meta-analyses, oral naltrexone has been shown to reduce alcohol cravings and relapse.[74,79] In multicenter, double-blind, placebo-controlled trials, extended-release injectable naltrexone has also been shown to reduce heavy drinking and increase abstinence rates (Figure 3).[80,81] In these trials, however, the secondary outcomes in each trial were not as promising; one of the trials showed no difference in the time study subjects returned to heavy drinking, and the other trial showed no reduction in risky drinking.[80,81,82]
- **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.[83,84]

- **Mechanism**: The mechanism of action of acamprosate is not well understood, but it is thought to decrease the activity of glutamate and increase the activity of the GABAergic system, thus restoring balance to GABA and glutamate systems that are disrupted in persons with alcohol use disorder.[73]
- **Dosing**: The recommended dose of acamprosate is 666 mg three times daily (given as two 333 mg delayed-release tablets three times daily). Several advantages of acamprosate include good patient tolerance, ability to use in patients with liver disease, no tapering of doses required at the time of discontinuation, minimal overdose risk, and ability to use concomitantly with opioid therapy.
- **Treatment Data**: Although evidence with acamprosate has been mixed, a large meta-analysis of randomized, placebo-controlled trials found that acamprosate had a small but significant effect on promoting abstinence compared with placebo.[79] Another meta-analysis showed acamprosate, when compared with placebo, reduced return to any drinking or drinking days, but it was not associated with a reduction in return to heavy drinking.[74]
- **Side Effects**: The most common side effect is diarrhea. A baseline evaluation of renal function should be performed prior to prescribing acamprosate, as severe renal impairment (creatinine clearance less than or equal to 30 mL/min) is a contraindication for the use of acamprosate. For individuals with moderate renal impairment (creatinine clearance 30–50 mL/min), the dose of acamprosate should be reduced to 333 mg three times daily. There are no identified drug interactions between acamprosate and antiretroviral therapies used to treat HIV.
- **Potential Drug Interactions**: No significant drug interactions occur with the use of acamprosate and antiretroviral medications.[85]

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 benefit of disulfiram is to serve as a deterrent for relapse in persons with alcohol use disorder.

- **Mechanism**: Disulfiram works by blocking the enzyme aldehyde dehydrogenase (Figure 4), which results in acetaldehyde levels rising within 10 to 30 minutes of alcohol ingestion, thereby triggering a highly unpleasant disulfiram-alcohol reaction.[76,86] 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).[71,72]
- **Treatment Data**: Findings from a meta-analysis support the efficacy of disulfiram, but clinical trial data showing a clear benefit are lacking (in trials where adherence was assured, a positive effect was observed).[86,87]
- **Side Effects**: Rare side effects with disulfiram include optic neuritis, peripheral neuropathy, polyneuritis, and hepatitis.[71]
- **Potential Drug Interactions**: 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.[88] Disulfiram should not be used in patients taking ritonavir oral solution, as this formulation contains alcohol and may precipitate an alcohol-disulfiram reaction.[89]

Gabapentin

Although gabapentin is not FDA-approved for the treatment of alcohol use disorder, it may be another effective treatment option. In a 12-week, double-blind, placebo-controlled trial involving 150 participants, gabapentin (900 mg to 1800 mg/day) was found to be safe and effective in treating alcohol dependence, as well as in reducing relapse-related symptoms, including insomnia, dysphoria, and craving.[90]

Topiramate

Topiramate is not currently approved for the treatment of alcohol use disorder, but multiple studies support its efficacy in improving abstinence rates and reducing alcohol craving, heavy drinking, and gamma-glutamyl transferase (GGT) levels (a biomarker of alcohol use).[91,92,93] In addition, topiramate has also been shown to reduce smoking in people who smoke and have alcohol use disorder.[93] 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.[75,94,95] Clinical trials have shown a decrease in alcohol consumption among persons who receive pharmacotherapy, even among those who receive a placebo, suggesting a potential psychological benefit from simply engaging with a medical provider.[96] For moderate to severe alcohol use disorder, more robust data favor the use of naltrexone and acamprosate.[75,97] In practice, many clinicians choose naltrexone as first-line therapy for two main reasons: (1) easier once-daily (oral) or once monthly (injectable) dosing schedule with naltrexone versus three times a day dosing with oral acamprosate, and (2) the ability to start naltrexone while the individual is actively drinking as opposed to acamprosate, which should only be started after abstinence has been achieved. Among persons with HIV, more robust data exist for naltrexone.[98,99]

Cannabis Use Disorder

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.[12,40,47] The 2023 CDC Medical Monitoring Project reported that 40.5% of persons with HIV had smoked marijuana (including vaping marijuana) in the past 12 months.[32] Despite this high marijuana use, data from multiple studies have not shown a negative impact of cannabis on antiretroviral adherence across a range of studies; inadequate data exist for the use of synthetic cannabinoids on antiretroviral adherence.[85,100,101,102]

Diagnostic Criteria

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

Treatment Considerations

No medications have been shown to be consistently effective for the treatment of cannabis use disorder. 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.[103,104,105] Several programs have been established to help guide the treatment of cannabis use, including the brief marijuana dependency counseling (BMDC) program, which is a 12-week multidisciplinary intervention developed by the Center for Substance Abuse Treatment that involves motivational enhancement therapy, cognitive behavioral therapy, and case management.[106]

Hallucinogen Use Disorder

Prevalence among Adults with HIV in the United States

In the 2023 CDC Medical Monitoring Project, an estimated 5.7% of individuals with HIV who were enrolled in care reported in the past 12 months that they had used club drugs (e.g., Ecstasy or X, ketamine or Special K, gamma-hydroxybutyrate [GHB] or Liquid Ecstasy).[32] Although detailed data on the use of “club drugs” or the prevalence of hallucinogen use disorders among persons with HIV are not available, evidence indicates that use of “club drugs” has been rising in the general population and especially among men who have sex with men (MSM).[107,108,109]

Diagnostic Criteria

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

Treatment Considerations

Behavioral interventions, such as intensive counseling and contingency management, are the mainstay of treatment for persons with hallucinogen use disorders (or “club drug use” disorders).[108] No pharmacologic treatment is known to have any benefit. Clinicians should be aware of significant interactions that can occur between club drugs and antiretroviral medications, particularly the pharmacologic boosters ritonavir and cobicistat; there are several published case reports of fatal drug interactions.[107,108]

Opioid Use Disorder

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.[110,111,112] In 2022, people who inject drugs accounted for approximately 7.2% (2,300 of 31,800) of new HIV infections in the United States.[113] In addition, there were 3.5% (1,100 of 31,800) of persons with new HIV infection who reported injection drug use and male-male sexual contact as the transmission category.[113] Based on CDC prevalence estimates for 2022, an estimated 9.8% (121,200 of 1,238,000) of persons living with HIV in the United States had injection drug use as a reported transmission category, plus an additional 5.1% (63,000 of 1,238,000) who reported injection drug use and male-male sexual contact as the transmission category.[113]
- **Injection Drug Use Among People with HIV:** Data from the 2023 CDC Medical Monitoring Project suggest that in the prior 12 months, 3% of persons with HIV used prescription opioids for nonmedical purposes, and 3% reported injection drug use.[32] The Medical Monitoring Project did not report specifically on the use of synthetic opioids (e.g., fentanyl). Some data suggest that persons with HIV are more likely to have chronic pain and more likely to receive higher-dose opioid prescriptions, which can elevate the risk of opioid use disorder.[114] Injection opioid use has also been linked to HIV epidemics in rural populations historically at lower risk for HIV, illustrating the syndemic nature of this problem.[111,115]

Diagnostic Criteria

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

Treatment Considerations

Opioid use disorder is a medical disorder, and medications for opioid use disorder (MOUD) are central to the treatment strategy; MOUD are highly effective and are associated with a 50% or greater reduction in all-cause and opioid-related mortality.[116] Behavioral interventions and/or detoxification, without medications for opioid use disorder, have poorer outcomes with high rates of relapse.[117,118] Pharmacologic therapies for opioid use disorder include three categories: opioid agonists, opioid partial agonists, and opioid antagonists.[119] Opioid agonists and partial agonists are used for maintenance therapy (also called opioid replacement therapy or opioid substitution therapy). For detailed information on this topic, SAMHSA has published a Treatment Improvement Protocol (TIP 63) for medication-assisted treatment for opioid use disorders.[120] 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.[121]

Access to Medications for Opioid Use Disorder

Despite the effectiveness of medications for opioid use disorder, access to and use of MOUD remains limited in the United States. In the past, physicians and advanced practice providers (APPs) were required to complete 8 to 24 hours of training prior to being eligible to obtain a buprenorphine prescribing waiver, also known as an X-waiver. As of January 2023, however, the X-waiver is no longer required, and practitioners with a current DEA license that includes schedule III authority can prescribe buprenorphine, subject to state requirements, for the treatment of opioid use disorder.[122] For more information on the buprenorphine waiver, see the SAMHSA Waiver Elimination Act.

Buprenorphine and Buprenorphine-Naloxone

Buprenorphine is a partial opioid agonist that can be prescribed in an outpatient office setting to reduce the craving and use of opioids, and it offers a better safety profile than methadone.[123] In 2004, the SAMHSA CSAT issued Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction that address key issues related to prescribing buprenorphine, with guidelines recently updated in 2021.[120]

- **Mechanism**: Buprenorphine is a partial agonist that has a high affinity for the mu-opioid receptor, but, when bound, produces a long-lasting, partial effect that has a ceiling. By binding to this receptor, buprenorphine competes with other opioids and thereby mitigates the impact of other opioids.
- **Preparations**: Buprenorphine is available in transmucosal (sublingual tablet, buccal film, and sublingual film) and depot (subcutaneous injectable and subdermal implant) preparations.[124,125,126]
- **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.[127] Transmucosal buprenorphine is typically prescribed for use 1 to 4 times a day. Although maintenance doses of buprenorphine typically range from 4 to 24 mg daily, patients who are using fentanyl may require higher maintenance dosing.[127] Buprenorphine is usually coformulated with naloxone; this combination is used 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).[119,128]
- **Dosing of Depot Preparations**: Extended-release injection buprenorphine is given as a subcutaneous injection in the abdominal region once a month. The recommended starting dose is 300 mg for the first two injections, followed by a maintenance dose of 100 mg to 300 mg monthly.[126,129]
- **Adverse Effects**: The main adverse effect experienced when starting buprenorphine is precipitated opioid withdrawal due to its high affinity for the opioid receptor and ability to displace stronger full opioid agonists. Because buprenorphine is a partial opioid agonist, misuse of buprenorphine or buprenorphine-naloxone does occur, such as taking doses higher than prescribed or injecting the medication, can result in life-threatening complications. Discontinuation of buprenorphine after long-term use can cause symptoms similar to heroin withdrawal; discontinuation should be supervised and achieved through gradual dose reductions.
- **Drug Interactions with Antiretroviral Medications**: Buprenorphine has the potential to have drug interactions with antiretroviral medications that are CYP enzyme inhibitors or inducers. Notably, the use of unboosted atazanavir with buprenorphine is contraindicated, and caution with close monitoring is recommended with ritonavir, cobicistat, and all protease inhibitors. Efavirenz may lower buprenorphine levels. Significant interactions do not occur with integrase strand transfer inhibitors (INSTIs) or nucleoside reverse transcriptase inhibitors (NRTIs).

Methadone Maintenance Therapy

Methadone maintenance therapy is the most established form of treatment for opioid use disorder and involves daily dosing of methadone through an Opioid Treatment Program (OTP). Methadone treatment is highly regulated, and methadone OTPs have limited clinical flexibility for dosing and dispensing methadone. Although daily dosing early in treatment is necessary for safety reasons, the rigid schedule can be a barrier for some. Methadone maintenance therapy is associated with significantly reduced heroin use and has been found to be superior to buprenorphine in retaining people in treatment.[130] Treatment is usually for more than 12 months, with a longer treatment duration associated with a greater likelihood of abstinence.[131]

- **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.[124] Methadone relieves drug cravings and withdrawal symptoms, dampens the euphoric and sedating effects of non-prescription opioids, and, at stable dosages, does not cause euphoria or sedation.
- **Dosing**: Methadone is available in many formulations, but the liquid form is typically used in most

methadone clinics in the United States. Standard initiation dosages of methadone are low and are titrated upward to achieve reduced symptoms of withdrawal without sedation. The goal for methadone dosing is to eliminate the craving for heroin, and this generally requires using doses in the range of 60 to 120 mg per day**.[**132**]**

- **Adverse Effects**: Methadone is a relatively safe drug, given the strict monitoring requirements, and when used during maintenance therapy, the most common adverse events are perspiration and constipation.[133] Additional possible complications of methadone maintenance therapy include cardiovascular effects (prolongation of the QTc interval and torsade de points, especially with higher doses), respiratory depression, decreased sexual function, and central nervous system effects.[124,134] Concomitant use of methadone with medications that prolong QTc should be avoided.
- **Drug Interactions with Antiretroviral Medications**: Methadone has multiple significant potential drug interactions when used with antiretroviral medications. Notably, efavirenz substantially lowers methadone levels; abacavir, rilpivirine, and ritonavir-boosted protease inhibitors can also lower methadone levels. The impact of cobicistat on methadone is not known, but caution should be used, and methadone should be titrated up from the lowest feasible dose. The INSTIs do not have significant drug interactions with methadone. Methadone can significantly increase zidovudine levels and potentially cause zidovudine-related toxicity.

Naltrexone

Naltrexone is an opioid receptor antagonist that is FDA-approved for relapse prevention of opioid use disorder. A large meta-analysis found that naltrexone was no more effective than placebo, even when combined with psychotherapy, but studies with the extended-release (XR) injectable formulation are more promising. In a 2025 Cochrane review that included data from 22 studies, XR-naltrexone was found to reduce illicit opioid use when compared to treatment as usual, but XR-naltrexone was associated with higher in-treatment illicit opioid use when compared to opioid agonist treatment.[135] Similarly, large studies comparing XR-naltrexone to buprenorphine have shown that XR-naltrexone is inferior in preventing relapse and less cost-effective.[136,137]

- **Mechanism**: Naltrexone works by acting as an opioid receptor antagonist, which inhibits the euphoric response to opioids.[119]
- **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.[124] To initiate naltrexone without precipitating withdrawal, it is recommended that individuals abstain from opioid use for 7–10 days prior to starting.
- **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.[78] Because of its mechanism of action, which includes blocking opiate receptors, neither oral nor injectable naltrexone should be used when patients are actively using opioids or receiving treatment with methadone or buprenorphine. Naltrexone given to someone actively using opiates could precipitate sudden drug withdrawal. In addition, patients who discontinue naltrexone can subsequently have enhanced effects of opiates.
- **Drug Interactions with Antiretroviral Medications**: Naltrexone does not have any significant interactions with antiretroviral medications.

Special Considerations for Persons with HIV

Efforts to integrate buprenorphine treatment into HIV care settings have produced mixed results, and challenges have been encountered, including a lack of clinical support staff, administrative obstacles, competing physician activities, and inadequate reimbursement.[138,139,140] Some models, however, have found considerable success and have dramatically scaled up access to opioid substitution therapy in communities at high risk for opioid use disorder. The Massachusetts Model of Office-Based Opioid Treatment

with Buprenorphine (OBOT-B), which has been implemented in community health centers, provides a particularly successful model that relies on collaboration between nursing case managers and prescribing physicians.[141] 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.[142,143]

Harm Reduction Approach

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

HIV Prevention 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. Multiple studies have concluded that providing sterile needles and injection equipment to people who inject drugs reduces the risk of HIV infection and facilitates entry into drug treatment.[144,145,146,147] Syringe service programs often provide a comprehensive set of services that include HIV counseling and testing, screening for sexually transmitted infections, screening for viral hepatitis, screening for tuberculosis, providing immunizations, 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. A Cochrane review found that standard educational interventions, rather than multisession psychosocial interventions, are a cost-effective way to reduce injection and sexual risk activities.[148]

Opioid Overdose Prevention Strategies

Another harm reduction technique involves overdose education and distribution of naloxone to persons who use opioids, as well as to their friends, family, and other community members. The availability of naloxone has greatly expanded in the wake of the opioid epidemic, with broad promotion nationally for both people who use recreational opioids and those prescribed higher doses of opioids for chronic pain conditions.[149] In the United States, most individual states have passed legislation improving the layperson’s 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.[150]

Opioid Prescribing Practices

The epidemic of opioid use is intertwined with opioid prescribing practices in the United States. The high prevalence of acute and chronic pain syndromes among persons with HIV means that clinicians caring for patients with HIV frequently have to balance pain management with the risk of creating iatrogenic opioid dependence.[151] Numerous initiatives have addressed opioid prescribing practices, including reducing the number of opioid prescriptions, implementing daily dosing limits, and strategies to make 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 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 of opioid pain medications.[152]

Stimulant Use Disorder

Prevalence among Adults with HIV

The prevalence of stimulant use is much higher among persons with HIV than among the general population, with an estimated 5 to 15% prevalence of stimulant use among all persons with HIV in the United States.[40,153,154]

- The 2023 Medical Monitoring Project estimated that in the prior 12 months, 6.0% of persons with HIV used cocaine, 3.2% used crack cocaine, and 7.7% used methamphetamine.[32]
- The CDC's National HIV Behavioral Surveillance survey demonstrated that HIV prevalence among MSM who primarily inject methamphetamine was nearly 50% higher than MSM who primarily inject other drugs, with the proportion of MSM who primarily inject methamphetamine being higher in western than eastern United States cities.[155]

Diagnostic Criteria

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

Treatment Considerations

- **Behavioral Interventions**: Behavioral strategies, including cognitive behavioral therapy, motivational interviewing, and contingency management (a system of incentives for positive reinforcement, such as providing vouchers in exchange for abstinence), are the primary interventions for stimulant use disorders.[156,157] 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).[158,159] Materials about the Matrix Model are available from SAMHSA but are geared toward counselors and substance users, rather than primary care providers.
- **Pharmacologic Therapies**: There are no FDA-approved pharmacologic treatments for stimulant use disorder. There are, however, multiple medications that have been investigated, including antipsychotics (risperidone, olanzapine, reserpine, aripiprazole), psychostimulants (dexamphetamine, bupropion, methylphenidate, modafinil), antidepressants (bupropion, mirtazapine), and others (baclofen and ondansetron).[160,161,162] In general, there remains a high rate of relapse among individuals who complete methamphetamine treatment programs.[108]
    - **Mirtazapine**: Some promising data have emerged for mirtazapine, in addition to behavioral counseling, as shown in a randomized, controlled trial of mirtazapine versus placebo for men who have sex with men.[163] In this study, mirtazapine once daily (added to counseling) was shown to significantly reduce methamphetamine use and some HIV risk behaviors in comparison to placebo.[163] A smaller study evaluated the effect of mirtazapine on methamphetamine use among men who have sex with men, and investigators reported that participants assigned to add mirtazapine therapy to substance use counseling had fewer methamphetamine-positive urine tests compared with participants taking placebo, despite low-to-moderate medication adherence.[164]
    - **Bupropion plus Injectable Naltrexone**: There is also evidence to support the use of bupropion and injectable naltrexone for methamphetamine use disorder. In a multisite, double-blind, placebo-controlled trial, the use of oral bupropion (450 mg per day) and injectable naltrexone (380 mg every 3 weeks) resulted in a higher response, defined as at least three methamphetamine-negative urine samples out of four samples obtained over a period of 4 weeks, when compared to placebo.[165]

Tobacco Use Disorder

Tobacco Use in Adults with HIV

Data from the 2023 CDC Medical Monitoring Project surveyed persons with HIV regarding tobacco use in the past 12 months and 27.3% reported they were current cigarette smokers, and 22.2% reported daily smoking.[32] Individuals with HIV smoke at approximately twice the rate of those without HIV.[166,167,168] Among persons with HIV in the United States, there was no significant difference in the prevalence of smoking among women versus men.[166] Smoking is linked to multiple medical problems among individuals with HIV, including major cardiovascular disease, bacterial pneumonia, and non-AIDS-defining cancers, including lung cancer.[169] Indeed, several studies have shown that people with HIV who receive suppressive antiretroviral therapy and who smoke are substantially more likely to die from lung cancer than from AIDS-related causes.[170,171,172]

Screening and Treatment Recommendations

Tobacco use is typically a chronic problem and often requires behavioral support, pharmacologic therapy, and multiple attempts to quit.[173,174,175] The U.S. Preventive Services Task Force (USPSTF) issued an updated recommendation statement in 2021 on Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women.[176] 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.[177]

- 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 to be 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. 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. Note that nicotine patches, gum, and lozenges are available as over-the-counter treatments.

Table 4. 2018 ACC Expert Consensus Decision Pathway Summary of Medications for Smoking Cessation

FDA-Approved Smoking Cessation Medications: First-Line Medications for Tobacco Cessation Treatment*					
Drug (doses)	Dosing Instructions	Administration	Common Side Effects:	Advantages	Disadvantage
Nicotine patch 21 mg 14 mg 7 mg	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.	Apply a new patch each morning to dry skin. Rotate application site to avoid skin irritation. May start patch before or on quit date.	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	User cannot alt dose if cravings occur during th day.

FDA-Approved Smoking Cessation Medications: First-Line Medications for Tobacco Cessation Treatment*					
Drug (doses)	Dosing Instructions	Administration	Common Side Effects:	Advantages	Disadvantage
	Use ≥3 months. After 6 weeks, continue original dose or taper to lower doses (either option acceptable).	Keep using even if a slip occurs. If insomnia or disturbing dreams, remove patch at bedtime.		cover situational cravings.	
Nicotine lozenge 4 mg 2 mg	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 drin 15 minutes pric to use and duri use.
Nicotine gum 4 mg 2 mg	If first cigarette is ≤30 minutes of waking: 4 mg. If first cigarette is >30 minutes of waking: 2 mg. Use ≥3 months.	Chew briefly until mouth tingles, then '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).	Mouth irritation Jaw soreness Heartburn Hiccups Nausea	User controls nicotine dose. Oral substitute for cigarettes. May be added to patch to cover situational cravings.	Not chewed in same way as regular gum; requires carefu instruction. Can damage dental work an be difficult to u with dentures. No food or drin 15 minutes pric to use and duri use.
Nicotine inhaler 10-mg cartridge	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.	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	Frequent puffin required.

FDA-Approved Smoking Cessation Medications: First-Line Medications for Tobacco Cessation Treatment*					
Drug (doses)	Dosing Instructions	Administration	Common Side Effects:	Advantages	Disadvantage
		Use 1 cartridge every 1-2 hours (Max: 16/day).		cravings.	
Nicotine nasal spray 10 mg/mL (10 mL bottle)	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 s effects of all NR products. Some users cannot tolerate local irritation t nasal mucosa.
Varenicline (tablet) 0.5 mg 1.0 mg	Days 1–3: 0.5 mg/day. Days 4–7: 0.5 mg twice a day. Day 8+: 1 mg twice a day. Use 3-6 months.	Start 1–4 weeks before quit date. Take with food and a tall glass of water to minimize nausea.	Nausea Insomnia Vivid dreams Headache	Quit date can be flexible, from 1 week to 3 months after starting drug. Dual action: relieves nicotine withdrawal and blocks reward of smoking. Oral agent (pill).	Because of previous FDA warning (now removed), man patients fear psychiatric adverse events even though th are no more common than v other cessation medications.
Bupropion sustained release (SR) (tablet) 150 mg	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 seizu risk: not for use seizure disorde 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. Patch dosing differs slightly from FDA labeling.

Abbreviations: FDA = U.S. Food and Drug Administration; NRT = nicotine replacement therapy; OTC = over t 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]

- First-line outpatient pharmacotherapy for smoking cessation consists of varenicline or combined nicotine replacement products. Second-line outpatient pharmacotherapy for smoking cessation is sustained-release bupropion or a single nicotine replacement product.
- If a single agent is insufficient to achieve abstinence, the following combinations can be considered: varenicline plus a single nicotine replacement product, varenicline plus bupropion, and bupropion plus a single nicotine replacement product. Prior guidelines have concluded that certain pharmacotherapies are more effective than others, certain combinations are more effective than others, and the combination of counseling and medication is more effective than either alone (Figure 5).[175]
- 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.

Results from a randomized, controlled trial of electronic cigarette use versus nicotine replacement therapy for smoking cessation reported that 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.[178] 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.[179,180]

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.[181,182] 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.[85,175] 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.[85]

Summary Points

- Substance use disorders are common among adults with HIV in the United States and they are linked to decreased retention in care, reduced adherence to antiretroviral medications, and lower rates of virologic suppression.
- Combining psychosocial interventions with pharmacotherapy (acamprosate, disulfiram, oral naltrexone, or extended-release naltrexone injection) is the optimal approach for treating alcohol use disorder.
- 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 evidence to support the use of mirtazapine or the combination of bupropion plus injectable naltrexone for persons with methamphetamine use disorder.
- Medications for opioid use disorder are highly effective; options include opioid agonists (methadone), opioid partial agonists (buprenorphine), and, though less effective, opioid antagonists (naltrexone).
- Among persons with HIV who inject opioid drugs, both drug- and HIV-related mortality are lower when antiretroviral therapy and medications for opioid use disorder are prescribed jointly.
- Tobacco use is common among persons with HIV; management should include counseling and pharmacologic therapy.

Citations

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

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

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

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

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

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

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

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

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

10. National Institute on Alcohol Abuse and Alcoholism. Core Resource on Alcohol. The Basics: Defining How Much Alcohol is Too Much
[NIAAA] -

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

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

[PubMed Abstract] -

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

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

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

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

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

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

19. McNeely J, Wu LT, Subramaniam G, et al. Performance of the Tobacco, Alcohol, Prescription Medication, and Other Substance Use (TAPS) Tool for Substance Use Screening in Primary Care Patients. Ann Intern Med. 2016;165:690-9.
[PubMed Abstract] -

20. Substance Abuse and Mental Health Services Administration. (2025). Key substance use and mental health indicators in the United States: Results from the 2024 National Survey on Drug Use and Health (HHS Publication No. PEP25-07-007, NSDUH Series H-60). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.
[SAMHSA] -

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

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

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

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

25. Rao U, Ryan ND, Dahl RE, et al. Factors associated with the development of substance use disorder in

depressed adolescents. J Am Acad Child Adolesc Psychiatry. 1999;38:1109-17.
[PubMed Abstract] -

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

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

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

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

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

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

32. Centers for Disease Control and Prevention. Behavioral and Clinical Characteristics of Persons with Diagnosed HIV Infection—Medical Monitoring Project, United States, 2023 Cycle (June 2023–May 2024). Published March 16, 2026.
[CDC] -

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

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

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

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

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

[PubMed Abstract] -

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

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

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

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

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

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

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

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

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

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

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

49. Ma J, Luu B, Ruderman SA, et al. Alcohol and drug use severity are independently associated with

antiretroviral adherence in the current treatment era. AIDS Care. 2024;36:618-630.
[PubMed Abstract] -

50. Xu L, Youngson E, Lin M, Dwivedi R, Fujiwara E. Hospital-Based Health Care Service Utilization in Persons With HIV With or Without Mental Health and Substance Use Comorbidities. J Acquir Immune Defic Syndr. 2025;100:97-104.
[PubMed Abstract] -

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

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

53. Kim J, Lesko CR, Fojo AT, et al. The Effect of Buprenorphine on Human Immunodeficiency Virus Viral Suppression. Clin Infect Dis. 2021;73:1951-6.
[PubMed Abstract] -

54. Low AJ, Mburu G, Welton NJ, et al. Impact of Opioid Substitution Therapy on Antiretroviral Therapy Outcomes: A Systematic Review and Meta-Analysis. Clin Infect Dis. 2016;63:1094-1104.
[PubMed Abstract] -

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

73. Haber PS. Identification and Treatment of Alcohol Use Disorder. N Engl J Med. 2025 ;392:258-66.
[PubMed Abstract] -

74. McPheeters M, O'Connor EA, Riley S, et al. Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis. JAMA. 2023;330:1653-65.

[PubMed Abstract] -

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

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

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

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

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

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

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

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

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

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

85. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Department of Health and Human Services. Considerations for antiretroviral use in special patient populations: substance use disorders and HIV. September 12, 2024.
[HIV.gov] -

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

87. Kranzler HR, Soyka M. Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. JAMA.

2018;320:815-24.
[PubMed Abstract] -

88. McCance-Katz EF, Gruber VA, Beatty G, et al. Interaction of disulfiram with antiretroviral medications: efavirenz increases while atazanavir decreases disulfiram effect on enzymes of alcohol metabolism. Am J Addict. 2014;23:137-44.
[PubMed Abstract] -

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

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

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

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

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

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

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

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

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

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

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

[PubMed Abstract] -

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

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

102. Crane HM, Nance RM, Whitney BM, et al. Drug and alcohol use among people living with HIV in care in the United States by geographic region. AIDS Care. 2021;33:1569-76.
[PubMed Abstract] -

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

104. Gates PJ, Sabioni P, Copeland J, Le Foll B, Gowing L. Psychosocial interventions for cannabis use disorder. Cochrane Database Syst Rev. 2016;2016:CD005336.
[PubMed Abstract] -

105. Gorelick DA. Cannabis-Related Disorders and Toxic Effects. N Engl J Med. 2023;389:2267-75.
[PubMed Abstract] -

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

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

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

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

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

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

112. Des Jarlais DC, Sypsa V, Feelemyer J, et al. HIV outbreaks among people who inject drugs in Europe, North America, and Israel. Lancet HIV. 2020;7:e434-e442.
[PubMed Abstract] -

113. Centers for Disease Control and Prevention. Estimated HIV Incidence and Prevalence in the United States, 2018–2022. HIV Surveillance Supplemental Report. 2024;29(No. 1):1-131. Published May 2024 (revised February 7, 2025).
[CDC] -

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

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

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

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

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

119. Nguyen TA, Hahn JH, Strakowski SM. Pharmacotherapies for treating opioid use disorder. CNS Spectr. 2013;18:289-95.
[PubMed Abstract] -

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

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

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

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

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

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

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

127. Harris MTH, Weinstein ZM, Walley AY. Medications for Opioid Use Disorder, Opioid Withdrawal, and Opioid Overdose: A Review. JAMA. 2026;335:986-98.
[PubMed Abstract] -

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

129. Sublocade—buprenorphine solution. Daily Med.
[Daily Med] -

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

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

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

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

134. Stringer J, Welsh C, Tommasello A. Methadone-associated Q-T interval prolongation and torsades de pointes. Am J Health Syst Pharm. 2009;66:825-33.
[PubMed Abstract] -

135. Kornør H, Lobmaier PPK, Kunøe N. Sustained-release naltrexone for opioid dependence. Cochrane Database Syst Rev. 2025;5:CD006140.
[PubMed Abstract] -

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

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

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

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

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

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

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

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

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

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

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

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

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

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

150. The Network for Public Health Law. Legal interventions to reduce overdose mortality: naloxone access

and overdose Good Samaritan laws.
[Network for Public Health Law] -

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

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

153. Rosen MI, Black AC, Arnsten JH, et al. Association between use of specific drugs and antiretroviral adherence: findings from MACH 14. AIDS Behav. 2013;17:142-7.
[PubMed Abstract] -

154. Hartzler B, Dombrowski JC, Crane HM, et al. Prevalence and Predictors of Substance Use Disorders Among HIV Care Enrollees in the United States. AIDS Behav. 2017;21:1138-1148.
[PubMed Abstract] -

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

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

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

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

159. Leyde S, Tilhou AS, Tsui JI. Methamphetamine Use Disorder. JAMA. 2025;334:1192-3.
[PubMed Abstract] -

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

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

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

163. Coffin PO, Santos GM, Hern J, et al. Effects of Mirtazapine for Methamphetamine Use Disorder Among

Cisgender Men and Transgender Women Who Have Sex With Men: A Placebo-Controlled Randomized Clinical Trial. JAMA Psychiatry. 2019:77:246-55.
[PubMed Abstract] -

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

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

166. Weinberger AH, Smith PH, Funk AP, Rabin S, Shuter J. Sex Differences in Tobacco Use Among Persons Living With HIV/AIDS: A Systematic Review and Meta-Analysis. J Acquir Immune Defic Syndr. 2017;74:439-453.
[PubMed Abstract] -

167. Frazier EL, Sutton MY, Brooks JT, Shouse RL, Weiser J. Trends in cigarette smoking among adults with HIV compared with the general adult population, United States - 2009-2014. Prev Med. 2018;111:231-4.
[PubMed Abstract] -

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

169. Lifson AR, Neuhaus J, Arribas JR, van den Berg-Wolf M, Labriola AM, Read TR. Smoking-related health risks among persons with HIV in the Strategies for Management of Antiretroviral Therapy clinical trial. Am J Public Health. 2010;100:1896-903.
[PubMed Abstract] -

170. Helleberg M, Afzal S, Kronborg G, et al. Mortality attributable to smoking among HIV-1-infected individuals: a nationwide, population-based cohort study. Clin Infect Dis. 2012;56:727-34.
[PubMed Abstract] -

171. Reddy KP, Kong CY, Hyle EP, et al. Lung Cancer Mortality Associated With Smoking and Smoking Cessation Among People Living With HIV in the United States. JAMA Intern Med. 2017;177:1613-1621.
[PubMed Abstract] -

172. Helleberg M, May MT, Ingle SM, et al. Smoking and life expectancy among HIV-infected individuals on antiretroviral therapy in Europe and North America. AIDS. 2015;29:221-9.
[PubMed Abstract] -

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

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

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

[PubMed Abstract] -

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

177. 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] -

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

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

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

181. Ashare RL, Thompson M, Serrano K, et al. Placebo-controlled randomized clinical trial testing the efficacy and safety of varenicline for smokers with HIV. Drug Alcohol Depend. 2019;200:26-33.
[PubMed Abstract] -

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

References

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

- Elf JL, Variava E, Chon S, et al. Prevalence and Correlates of Smoking Among People Living With HIV in South Africa. Nicotine Tob Res. 2018;20:1124-31.
[PubMed Abstract] -

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

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

- Lee JD, Friedmann PD, Kinlock TW, et al. Extended-Release Naltrexone to Prevent Opioid Relapse in

Criminal Justice Offenders. N Engl J Med. 2016;374:1232-42.
[PubMed Abstract] -

- Mdege ND, Shah S, Ayo-Yusuf OA, Hakim J, Siddiqi K. Tobacco use among people living with HIV: analysis of data from Demographic and Health Surveys from 28 low-income and middle-income countries. Lancet Glob Health. 2017;5:e578-e592.
[PubMed Abstract] -

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

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

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

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

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

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

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

Figures

Figure 1 Number of Persons Age 12 and Older with a Past Year Substance Use Disorder, United States, 2024

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. (2025). Key substance use and mental health indicators in the United States: Results from the 2024 National Survey on Drug Use and Health (HHS Publication No. PEP25-07-007, NSDUH Series H-60). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.

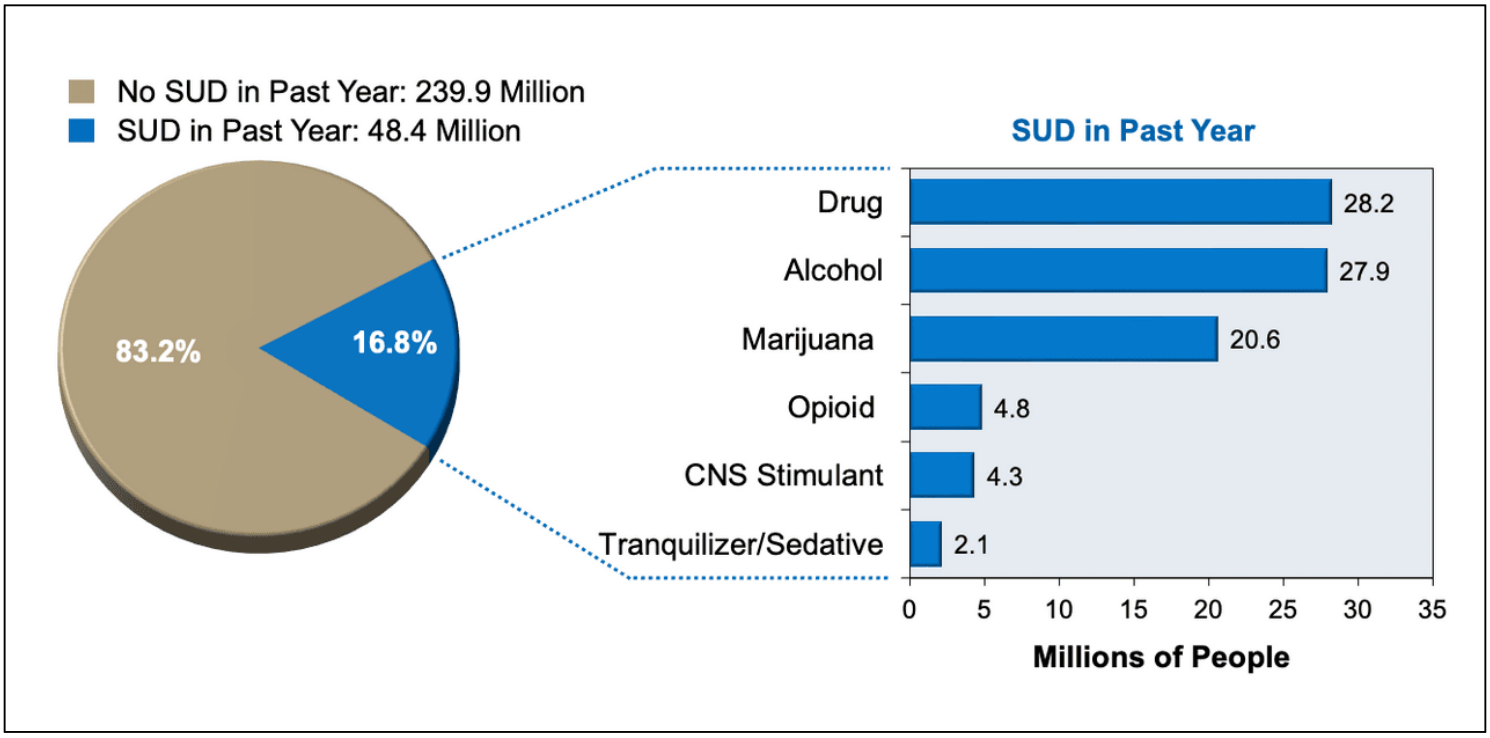


Figure 2 Neurochemical Circuits Involved in Alcohol Dependence and Craving

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

Source: Anton RF. Naltrexone for the management of alcohol dependence. N Engl J Med. 2008;359:715-21.
© 2017 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

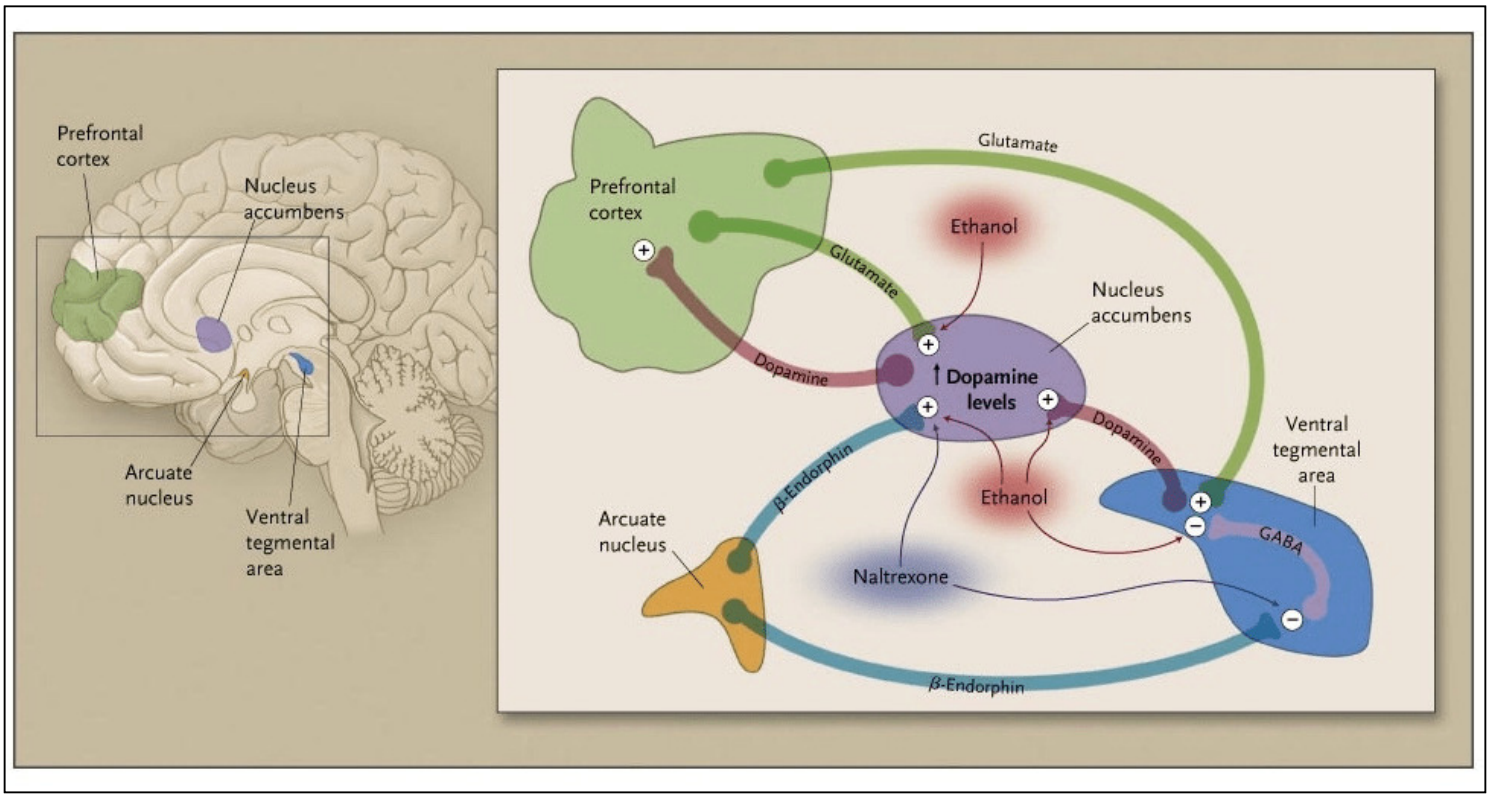


Figure 3 Impact of Long-Acting Naltrexone on Median Heavy Drinking Days per Month

This graphic shows results from a 6-month, placebo-controlled study that randomized 624 alcohol-dependent adults to 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.

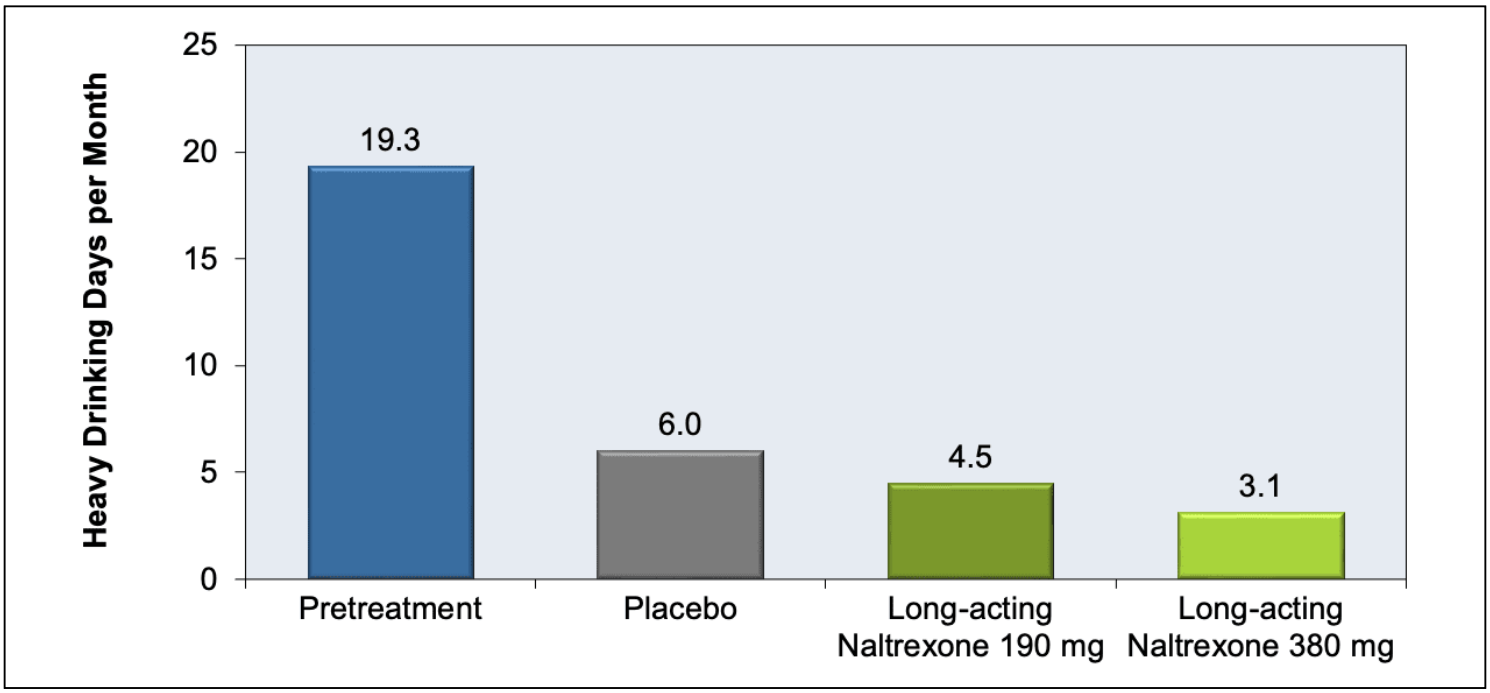


Figure 4 Inhibition of Alcohol Metabolism by Disulfiram

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

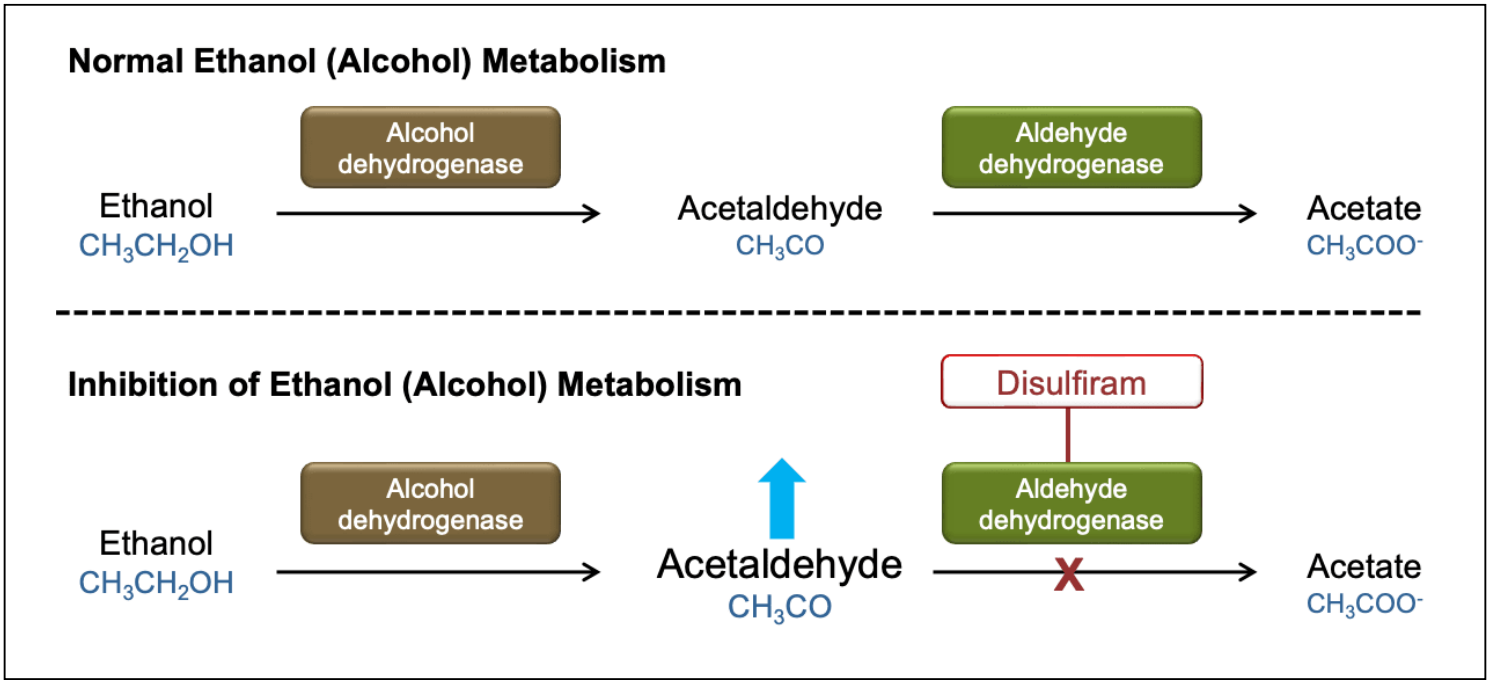


Figure 5 Effectiveness and Abstinence Rates for Various Medications at 6 Months after Quitting

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

Medication	Estimated Abstinence Rate* (95% CI)
Placebo	13.8
Monotherapy	
Varenicline 2 mg/day	33.2
Bupropion SR	24.2
Nicotine spray	26.7
Nicotine gum (> 14 weeks)	26.1
Nicotine inhaler	25.4
Nicotine patch (> 14 weeks)	23.7
Combination Therapy	
Patch + nicotine gum or spray	36.5
Patch + bupropion SR	28.9
*Abstinence rate 6 months post quit	

Table 1. DSM-5 Diagnostic Criteria for Substance Use Disorders

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

Source:

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

Table 2. DSM-5 Diagnostic Criteria for Alcohol Use Disorder

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

Source:

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

Table 4. 2018 ACC Expert Consensus Decision Pathway Summary of Medications for Smoking Cessation

FDA-Approved Smoking Cessation Medications: First-Line Medications for Tobacco Cessation Treatment*					
Drug (doses)	Dosing Instructions	Administration	Common Side Effects:	Advantages	Disadvantages
Nicotine patch 21 mg 14 mg 7 mg	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	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 2 mg	If first cigarette is ≤30 minutes of waking: 4 mg. If first cigarette is >30 minutes of waking: 2 mg. Use ≥3 months.	Chew briefly until mouth tingles, then ‘park’ gum inside cheek until tingle fades. Repeat chew-and-park each time tingle fades. Discard gum after 30	Mouth irritation Jaw soreness Heartburn Hiccups Nausea	User controls nicotine dose. Oral substitute for cigarettes. May be added to patch to cover situational cravings.	Not chewed in same way as regular gum; requires careful instruction. Can damage dental work and be difficult to use with dentures.

FDA-Approved Smoking Cessation Medications: First-Line Medications for Tobacco Cessation Treatment*					
Drug (doses)	Dosing Instructions	Administration	Common Side Effects:	Advantages	Disadvantages
		minutes of use. Use ~ 1 piece per hour (Max: 24/day).			No food or drink 15 minutes prior to use and during use.
Nicotine inhaler 10-mg cartridge	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)	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	Days 1–3: 0.5 mg/day. Days 4–7: 0.5 mg twice a day. Day 8+: 1 mg twice a day. Use 3-6 months.	Start 1–4 weeks before quit date. Take with food and a tall glass of water to minimize nausea.	Nausea Insomnia Vivid dreams Headache	Quit date can be flexible, from 1 week to 3 months after starting drug. Dual action: relieves nicotine withdrawal and blocks reward of smoking. Oral agent (pill).	Because of previous FDA warning (now removed), many patients fear psychiatric adverse events, even though they are no more common than with other cessation medications.
Bupropion sustained release (SR) (tablet)	150 mg/day for 3 days, then 150 mg twice a day.	Start 1-2 weeks before quit date.	Insomnia Agitation	May lessen post-cessation weight gain while drug is being taken.	Increases seizure risk: not for use if seizure disorder or binge drinking.

FDA-Approved Smoking Cessation Medications: First-Line Medications for Tobacco Cessation Treatment*					
Drug (doses)	Dosing Instructions	Administration	Common Side Effects:	Advantages	Disadvantages
150 mg	Use 3-6 months.		Dry mouth Headache	Oral agent (pill).	
*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. Patch 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]