Substance Use Disorders

This is a PDF version of the following document:
Section 2: Basic HIV Primary Care
Topic 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

Definitions and Terminology

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

Predictors of Substance Use Disorders

Risk factors for substance use disorders (SUD) are complex and likely include a combination of biologic and social factors. Studies indicated that a family history of substance use disorder is a strong risk factor for the development of SUD among individuals, influenced by both genetic and shared environmental factors.[3,4,5] Cooccurring mental health disorders have also been linked to higher incidence of SUD, in both adolescents and adults.[6,7] In addition, social structural factors, such as one’s social network and lived environment, have also been identified as risk factors for the development of SUD, and likely interact with genetic and other familial factors.[8,9]

Although different drugs produce different effects on an individual, dysregulation of brain reward pathways and an overactive brain stress system are important, common shared features that together reinforce use of the substance to achieve a pleasurable high, even if pursuing this high incurs great cost or negative consequences for the individual.[10] Research has demonstrated that neurobiological differences in self-control become evident in early childhood and may predispose some individuals to substance use disorders.[11] Although no specific neurological testing, imaging, or laboratory evaluation can accurately predict who will develop a substance use disorder, accurate identification of predictive markers remains an area of active investigation.

Data Sources for Substance Use in United States

The primary source of statistical information for substance use disorders in the general United States population originates from the National Survey on Drug Use and Health (NSDUH), which is an annual survey of the civilian, non-institutionalized population of the United States aged 12 years and older. The survey is sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA) within the Department of Health and Human Services, and was most recently conducted in 2018, with results published in August 2019.[12] Since its establishment in 1992, SAMHSA has led public health efforts to advance behavioral health, specifically tasked with making information, services, and research about substance use
and mental illness more accessible. Prevalence estimates for substance use disorders in persons with HIV are derived from several published studies, as there is no comparable annual survey for the population of individuals with HIV.

**DSM-5 Classification**

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

**Impaired Control**

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

**Social Impairment**

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

**Risk Use of the Substance**

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

**Pharmacologic Criteria**

- Tolerance as defined by either a need for markedly increased amounts to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount. (Does not apply for diminished effect when used appropriately under medical supervision)
- Withdrawal manifesting as either characteristic syndrome or the substance is used to avoid withdrawal (Does not apply when used appropriately under medical supervision)

**Screening Tools**

Although screening for alcohol abuse is often integrated in primary care settings, screening for abuse of other drugs is less standardized. The following summarizes available resources and direct links to screening tools that can be potentially used to evaluate for different types of substance use disorders:

- **University of Washington ADAI Library**: The University of Washington Alcohol and Drug Abuse Institute (ADAI) has compiled a [Substance Use Screening and Assessment Instruments Database](https://www.adai.org/instruments) that includes a search function for instruments used for substance use screening. This resource was created to help clinicians and researchers find instruments used for screening and assessment of substance use and substance use disorders.
- **DAST**: The Drug Abuse Screening Test (DAST), first developed in 1982, is available in 10-item, 20-item, and 28-item versions; all versions are self-administered and have moderate to high levels of
sensitivity, specificity, and validity.[13] Answers to this test are binary (yes/no), with different cutoff scores recommended with different versions and different populations.[13] The length of this test has proven to be a barrier to primary care screening, however, and subsequently other instruments have been trialed.

- **CAGE**: Conjoint screening tests that inquire simultaneously about alcohol and other drugs are available; the CAGE-AID, for example, consists of the same 4 CAGE questions for alcohol that have been expanded in scope to include drug use.[14]

- **AUDIT**: The Alcohol Use Disorders Identification Test (AUDIT) is a 10-item questionnaire that can be used to screen for hazardous alcohol consumption. Developed initially by the World Health Organization, the test has been shown to correctly identify 92% of persons with hazardous drinking and 94% of those without hazardous drinking.[15] A shorter 3-question version, known as the AUDIT-C, has also been validated and performs similarly to the AUDIT for detecting heavy drinking and/or active alcohol abuse or dependence.[16]

- **Opioid Risk Tool**: The Opioid Risk Tool (ORT) is an 11-item screening tool specifically for opioid addiction.[17]

- **TICS**: An even briefer, two-item conjoint screening, known as TICS, has a sensitivity and specificity of nearly 80% in detecting current substance abuse problems.[18] A single-question screen—“How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”—has been proven to have similar sensitivity and specificity for the detection of drug use and drug use disorders as the lengthier DAST, and is superior to conjoint screening in that it specifically identifies drug use.[19] More recently, the 4-item Substance Use Brief Screen (SUBS) has become available for screening primary care patients for tobacco, alcohol, and other drug use.[20] This is the only brief, self-administered, comprehensive screening instrument test that has been validated in the primary care setting and may facilitate screening of primary care populations.[20]

- **ASSIST**: The World Health Organization (WHO) has also developed the ASSIST (Alcohol, Smoking, and Substance Involvement Screening Test) to detect substance use and related problems in the primary care setting.[21] The ASSIST covers 12 items related to recent and lifetime use, dependence symptoms, substance-related problems, and intravenous use and addresses 10 categories of substances (tobacco, alcohol, cannabis, cocaine, stimulants, inhalants, sedatives/hypnotics, hallucinogens, opiates, and “other drugs”). A disadvantage to this tool is its length, but it has been effectively modified 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 (i.e. persons with HIV) compared with other primary care populations. New technologies allowing for patient-reported outcomes may allow for more such screening tools to be incorporated efficiently into busy HIV primary care clinics.[22,23,24]

**Overview**

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

Estimates of Substance Use Disorders in the United States

Data from the 2018 National Survey on Drug Use and Health (NSDUH) found that approximately 20.3 million people (7.4% of the population) aged 12 years and older in the United States had a substance use disorder in the past year, including 14.8 million with an alcohol use disorder and 8.1 million with an illicit drug use disorder (Figure 1).[12] In the same year, according to the NSDUH, 58.8 million people (21.5% of the population) were current tobacco users, including 47.0 million current cigarette smokers and 12.2 million current cigar smokers.[12] Smoking estimates were lower in the National Health Interview Survey (NHIS), another annual nationally representative survey, which reported that 13.7% of adults in the United States were current smokers in 2018.[25] This discrepancy is likely due to differences in the age range included in the surveys—NHIS collects data only for adults aged 18 years and older, whereas the NSDUH collects data for persons beginning at age 12.[12,25] Both of these surveys likely underestimate the prevalence of substance use disorders because they omit homeless and incarcerated populations that have higher rates of substance use disorders than the general population.

Estimates of Substance Use Disorders in Persons with HIV

Multiple studies and surveys have demonstrated high rates of substance use among persons with HIV in the United States.[26,27,28] For example, some data indicate that individuals with HIV smoke at more than twice the rate of those without HIV and the CDC estimated a smoking prevalence among persons with HIV of 34% for the year 2017.[29] In addition, use of alcohol and other substances are higher in persons with HIV infection compared to the general population. The Medical Monitoring Project (a CDC surveillance system that assesses behaviors and clinical characteristics of persons with HIV who have received outpatient medical care) estimated based on 2017 survey data that 30% of persons with HIV had used noninjection drugs in the prior 12 months for recreational purposes, 2% had used injection drugs in the prior 12 months, and 16% had engaged in binge drinking in the past 30 days.[29]
Impact of Substance Use Disorders on HIV Metrics

Substance Use Disorders and Impact on HIV Transmission

Recent studies have provided overwhelming evidence that persons with HIV who take antiretroviral therapy and consistently maintain undetectable plasma HIV RNA levels do not transmit HIV sexually to others, even with condomless sex.[30,31,32] Thus, any substance use disorder that interferes with antiretroviral medication adherence can impact transmission of HIV and have a significant public health consequence. Certain substance use disorders in persons with HIV have been consistently linked to decreased antiretroviral medication adherence and to activities that enhance the likelihood of HIV transmission to HIV negative sex and needle-sharing partners.[33,34,35,36]

- Based on 2017 survey data, the Medical Monitoring Project reported that 24% of individuals with HIV reported using alcohol with sex, and 12% reported using noninjection drug use with sex; in this same survey, among the individuals with HIV who used injection drugs, 67% used them in the context of sex.[37]
- Additional 2017 data from the 2017 Medical Monitoring Project noted 4.9% of persons with HIV reported alcohol or drug use as the reason for missing their last dose of antiretroviral medications.[29]
- The Multicenter AIDS Cohort Study reported that methamphetamine use increased the number of condomless anal receptive sex partners, and several other studies, including a review of 61 studies, confirmed that men with HIV who have sex with men and use methamphetamine are more likely to report sex activities that place them at higher risk of acquiring HIV, such as condomless anal intercourse, or being high on alcohol or drugs at last sex act with a non-main partner.[38,39,40]

Substance Use Disorders and Impact on HIV Care

Substance use can create a barrier to care for individuals with HIV.[36,41,42] 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.[43,44,45] Antiretroviral medication adherence problems in individuals with a substance disorder use may have serious consequences, including suboptimal virologic control and potential emergence of virologic resistance. Studies have shown that persons with HIV can improve healthcare utilization and antiretroviral adherence patterns through treatment of substance use disorders, particularly with treatment of opiate use disorders; medications for opiate use disorder (MOUD) have been shown to increase rates of viral suppression, improved adherence to antiretrovirals, and lower overall mortality.[44,46,47]

Substance Use and HIV Disease Progression

Alcohol, tobacco smoking, and drug use can also impact HIV disease progression independent of antiretroviral adherence patterns. Tobacco smoking has been shown to increase immune activation and decrease T-cell function in persons with HIV.[48,49] 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.[50,51,52,53,54,55,56] Furthermore, methamphetamine has been shown to increase HIV replication in animal models.[57]
Alcohol Use Disorder

Prevalence of Alcohol Use Disorder in United States

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

Prevalence of Alcohol Use Disorder in Adults with HIV

As in the general population, hazardous drinking is common among persons with HIV.[58,59] In the HIV Cost and Services Utilization Study (HSCUS), which was the first representative study to provide estimates of alcohol use among persons receiving medical care for HIV, 53.4% of adults with HIV reported drinking alcohol in the past 4 weeks, an estimate that mirrors that of the general United States population.[59,60] In this HSCUS study, 8% of the survey respondents with HIV were classified as heavy drinkers, in comparison to recent estimates of heavy drinking in the general United States population of 6.1%.[12,59] More recent data from the 2017 Medical Monitoring Project indicate that 63% of persons with HIV consumed alcohol in the past year, and 15.6% engaged in binge drinking the past month.[29]

Risk Factors

Alcohol use disorder has a significant genetic component, with rates three to four times higher in individuals with a close relative with alcohol use disorder.[61] The risk for developing alcohol use disorder also depends on personal experiences with alcohol, peer influences, cultural attitudes toward drinking, and personal strategies for coping with stress.[2] Individuals with bipolar disorder, impulsivity, schizophrenia, personality disorders, anxiety, and depression are also at increased risk for developing an alcohol use disorder. For individuals with HIV, hazardous and heavy drinking has been associated with the use of other substances, such as heroin, cocaine, marijuana, and tobacco.[58,59,62] The rates of hazardous drinking are lower in persons with HIV who higher education levels, lower CD4 counts, and AIDS-defining illnesses.[59,62]

Screening Tools

Multiple screening instruments have been developed to identify patients with alcohol use disorders who present in primary care settings.[60,63]

- **AUDIT**: In comparison, the AUDIT (Alcohol Use Disorders Identification Test) is a 10-item questionnaire that was developed specifically to identify heavy drinking in addition to alcohol abuse and dependency. The AUDIT better identifies at-risk, harmful, or hazardous drinking patterns.[63]
- **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.[16,63]
- **CAGE**: The CAGE is a 4-question screening test that works well at detecting lifetime alcohol abuse and dependence, but is not sensitive for detecting heavy drinking and does not distinguish between past and present alcohol use.[16,63]
- **NIAAA Single Alcohol Screening Question**: The National Institute of Alcohol Abuse and Alcoholism (NIAAA) recommends a single prescreening question about binge drinking for individuals who drink any alcohol at all—“How many times in the past year have you had 5 (for men) or 4 (for women and all adults older than 65 years) or more drinks in a day? Any individual with one ore more days of
heavy drinking in the past year is considered an at-risk drinker.\[64\]

**Screening Recommendations**

The United States Preventive Services Task Force (USPSTF) recommends screening all patients aged 18 years and older for alcohol misuse in the primary care setting.\[60\] The USPSTF recommends using 1 to 3-item screening instruments, including the AUDIT-C or the NIAAA-recommended Single Alcohol Screening Question.\[60\] If a patient screens positive for alcohol misuse on a 1 to 3-item brief screening instrument, the USPSTF recommends follow-up with an in-depth risk assessment, such as the 10-question AUDIT.\[60\]

**Diagnostic Criteria**

The DSM-5 defines alcohol use disorder by the presence of at least two symptoms (from a list of 11 symptoms as defined in the DSM-5) related to evidence of impaired control, social impairment, risky use, and pharmacological criteria (Table 1).\[60\] Many more individuals will meet criteria for at-risk drinking, which includes drinking more than 4 drinks per day (or more than 14 in a week) for men and more than 3 drinks per day for women (or more than 7 per week).\[64\] The National Institute of Alcohol Abuse and Alcoholism (NIAAA) recommends that women of all ages and men older than 65 years consume no more than seven alcoholic drinks per week and no more than three per day (men age 65 years and younger should consume no more than 14 drinks per week and no more than 4 drinks per day); these limits reflect the fact that people who drink over recommended limits, even if they do not meet criteria for alcohol use disorder, are at significant risk for alcohol-related problems.\[65\]

**Behavioral Counseling**

The USPSTF recommends that persons who screen positive for alcohol misuse 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.\[60\] Another commonly employed method is the use of personalized normative feedback, where patients are given information on how their alcohol use compares to that of their peers. Other forms of behavioral counseling interventions include web-based, telephonic, or written counseling materials. The use of behavioral counseling interventions is informed by a robust systematic review demonstrating the efficacy of behavioral counseling interventions in improving behavioral outcomes, including reducing overall consumption as well as reducing heavy drinking days.\[66,67\]

**Data for Pharmacologic Therapy for Alcohol Use disorder**

Evidence suggests that a combination of psychosocial interventions and pharmacotherapy is the optimal approach for treating moderate to severe alcohol use disorders.\[68,69,70\] There are currently four U.S. FDA-approved medications for the treatment of alcohol use disorder: acamprosate, disulfiram, oral naltrexone, and extended-release naltrexone injection (Figure 4).\[71,72\] There have been several studies evaluating outcomes of persons treated for alcohol use disorder with naltrexone, acamprosate and disulfiram.

- **Meta-Analyses of Multiple Medications**: 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.\[70\] In a similar meta-analysis of acamprosate and naltrexone, authors found that acamprosate was more effective in preventing a lapse in sobriety, whereas naltrexone was more effective in preventing relapse to heavy drinking following a lapse in sobriety.\[73\]
- **Naltrexone**: In a large, meta-analysis of randomized, placebo-controlled trials, oral naltrexone was found to have a small but significant effect in reducing craving and relapse.\[74\] Most of the studies in this meta-analysis were published prior to the U.S. FDA approval in 2006 of extended-release injectable naltrexone. Subsequently, two multi-center, double-blind, placebo-controlled trials in the United States confirmed that extended-release injectable naltrexone can reduce heavy drinking and
increase abstinence rates (Figure 5). In these trials, however, the secondary outcomes in each trial were not as promising: one trial showed no difference in the time study subjects returned to heavy drinking and the other trial showed no reduction in risky drinking.\[75,76,77\]

- **Disulfiram**: Data from a meta-analysis supports the efficacy of disulfiram, the clinical trial data showing a clear benefit are lacking.\[78,79\]
- **Acamprosate**: Although evidence with acamprosate has been mixed, a large meta-analysis of randomized, placebo-controlled trials found that acamprosate had a small but significant effect on promoting abstinence compared with placebo—calculating that approximately eight people would need to be treated to achieve one additional case of abstinence (NNT=7.5).\[74\] Trials in Europe have shown more benefit with acamprosate than those conducted in the United States, for unknown reasons (Figure 6).\[80,81\]

### Pharmacologic Treatment Considerations

Although there is no clear guidance on which pharmacotherapy to use for moderate to severe AUD, more robust data favors the use of naltrexone and acamprosate.\[70,82,83\] In practice, many clinicians choose naltrexone as first line, given its easy dosing (once a day dosing versus three times a day for acamprosate) and ability to start while the patient is actively drinking (acamprosate should be started only once abstinence has been achieved). Among persons with HIV, the most robust data exist for naltrexone.\[84,85\] In contrast, data on the use of acamprosate of disulfiram is lacking in persons with HIV. To guide clinicians in primary care and general medical settings in the proper medication treatment of alcohol use disorders, the Substance Abuse and Mental Health Services Administration (SAMHSA) has published a Treatment Improvement Protocol,\[82\] Medication treatments for alcohol use disorder are the same for persons with HIV infection as for those without HIV infection.

### 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 to promote sustained abstinence in patients who are abstinent from alcohol at treatment initiation.\[86,87\]

- **Mechanism**: The mechanism of action of acamprosate is not well understood, but it is thought to decrease activity of glutamate and increase the activity of the GABA-ergic system, thus restoring balance to GABA and glutamate systems that are disrupted in persons with alcohol use disorder.
- **Dosing**: The recommended dose of acamprosate is 666 mg three times daily (given as two 333 mg delayed-release tablets three times daily). Several advantages with acamprosate include good patient tolerance, ability to use in patients with liver disease, no tapering of doses required at the time of discontinuation, minimal overdose risk, and ability to use concomitantly with opioid therapy.
- **Drug Interactions**: No significant drug interactions occur with use of acamprosate and antiretroviral medications.\[28\]
- **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.

### Disulfiram

In 1951, disulfiram was the first FDA-approved medication for the treatment of alcohol use disorder. Disulfiram is taken as an oral medication once daily on a regular basis. The primary beneficial effect of disulfiram is as a deterrent to prevent relapse in persons with alcohol use disorder.
**Mechanism:** Disulfiram works by blocking the enzyme aldehyde dehydrogenase (Figure 7), which results in acetaldehyde levels rising within 10 to 30 minutes of alcohol ingestion, thereby triggering a highly unpleasant “disulfiram-alcohol reaction”.[79,82] 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 per once per day (range is 125 to 500 mg once daily).[71,72]

**Side Effects:** Rare side effects with disulfiram include optic neuritis, peripheral neuropathy, polyneuritis, and hepatitis.[72]

**Potential Drug Interactions:** There are multiple potential drug interactions that can occur with disulfiram, including medical contraindications to its use, so patients who are considering disulfiram should be carefully screened and counseled about the medication's risks and benefits. Certain antiretroviral medications can alter disulfiram levels—efavirenz has been shown to increase the activity of disulfiram on aldehyde dehydrogenase and atazanavir may decreases 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]

### Naltrexone Oral and Extended-Release Injectable Naltrexone

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

- **Mechanism:** Naltrexone is an opioid antagonist that mediates the rewarding effects of alcohol and attenuates cravings (Figure 8).[82,90,91] Although the exact mechanism of how naltrexone works to reduce alcohol consumption is not completely understood, the presumed major effect is via blockade of opiate receptors that play a role in the reward effects of alcohol.[72]
- **Dosing:** Naltrexone is currently available both as an oral tablet (50 mg once daily) and as an extended-release injectable naltrexone (380 mg IM every 4 weeks).[82]
- **Adverse Effects:** The most common adverse effect of naltrexone is nausea. There is an FDA black box warning regarding the potential for hepatotoxicity when naltrexone is given in excessive doses; based on this potentially serious reaction, naltrexone is contraindicated in persons with acute hepatitis or any form of liver failure. Liver toxicity is likely lower with injectable naltrexone, since in this form it avoids first-pass liver metabolism.[82] Because of its mechanism of action, which includes blocking opiate receptors, neither oral nor injectable naltrexone should be used in patients who use opioids or receive treatment with methadone or buprenorphine. Naltrexone given to someone actively using opiates could precipitate sudden drug withdrawal. In addition, patients who discontinue naltrexone can subsequently have enhanced effects of opiates.
- **Drug Interactions:** There are no clinically significant drug interactions between naltrexone and antiretroviral medications used for the treatment of HIV.

### Topiramate

Topiramate is not currently approved for treatment of alcohol use disorder, but multiple studies support its efficacy for improving abstinence rates and reducing alcohol craving, heavy drinking, and gamma-glutamyl transferase (GGT) levels (a biomarker of alcohol use).[92,93,94] In addition, topiramate has also been shown to reduce smoking in persons who smoke and have alcohol use disorder.[94]

### Gabapentin

Gabapentin is also not FDA approved for treatment of alcohol use disorder but may be another effective
treatment option. In a 12-week, double-blind, placebo-controlled trial involving 150 participants, gabapentin (900 mg to 1800 mg/day) was found to be safe and effective in treating alcohol dependence (and reducing relapse-related symptoms including insomnia, dysphoria, and craving).[95]
Cannabis Use Disorder

Prevalence of Cannabis Use Disorder in United States

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

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.[36,44] The 2017 CDC Medical Monitoring Project estimated that 26.4% of persons living with HIV, who were engaged in care, used cannabis in the past year.[29] Despite this high marijuana use, data from multiple studies have not shown a negative impact of cannabis on antiretroviral adherence across a range of studies; inadequate data exist for use of synthetic cannabinoids on antiretroviral adherence.[28,96,97]

Risk Factors

Risk factors for cannabis use disorder are varied and include being male, Native American, divorced or widowed, and having lower income.[98] In addition, mood disorders, anxiety disorders, and personality disorders are positively associated with cannabis use disorder, as are alcohol and other substance use disorders. Conduct disorder in childhood is a risk factor for the development of cannabis use disorder (as well as other substance use disorder), as is an unstable home environment and having a family member with cannabis use disorder.

Diagnostic Criteria

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

Treatment Considerations

No medications have been shown to be consistently effective for the treatment of cannabis use disorder. Buspirone was effective in reducing cannabis use in one clinical trial, but overall, anxiolytics and antidepressants (SSRIs, mixed action, and atypical) have not been proven to lower rates of cannabis dependence.[99,100] 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.[101] Several programs have been established to help guide treatment of cannabis users, including the brief marijuana dependency counseling (BMDC) program, which is a 12-week multidisciplinary intervention developed by the Center for Substance Abuse Treatment that involves motivational enhancement therapy, cognitive behavioral therapy, and case management.[102] SAMHSA has also developed Brief Counseling for Marijuana Dependence: A Manual for Treating Adults – 2005.[103] Separate resources are available for treatment of youth with cannabis use disorders.
Hallucinogen Use Disorder

Prevalence among Adolescents and Adults in United States

Hallucinogen use disorders are categorized by the type of hallucinogen used. For example, the DSM-5 divides hallucinogen use disorder into separate categories for those who use phencyclidine or a similar substance such as ketamine, and those who use other hallucinogens, such as mescaline, 3,4-methylenedioxy-methamphetamine (MDMA) and popularly known as “ecstasy or Molly”, and lysergic acid dethylamide (LSD).[2] Of note, MDMA is classified as a hallucinogen though it is structurally similar to methamphetamine and has stimulant properties as well.[104] According to the National Survey on Drug Use and Health (NSDUH), an estimated 5.6 million people, ages 12 and older, used hallucinogens in the past year.[12] As with other drugs, usage in the past year was highest for those 18 to 25 years of age, but the prevalence of usage remaining rather stable over the time period of 2015 to 2018 for all age groups (Figure 12).[12]

Prevalence among Adults with HIV in United States

In the 2017 CDC Medical Monitoring Project, and estimated 3% of individuals with HIV who were enrolled in care reported use of “club drugs” in the past year.[29] Although detailed data on the use of “club drugs” or the prevalence of hallucinogen use disorders among persons living with HIV are not available, evidence indicates that use of “club drugs” (which typically refers to a group of substances that includes the hallucinogens ketamine, MDMA, and LSD, as well as GHB, methamphetamine, and flunitrazepam) has been rising in the general population and especially among bisexual men and men who have sex with men who have HIV or are at risk for HIV acquisition.[104,105,106]

Risk Factors

Risk factors for phencyclidine use disorder include low educational attainment, male gender, and living in the West or Northeast.[2] Use of other hallucinogens is linked to other substance use disorders (and early exposure to alcohol, tobacco, and cannabis), depression, drug use by peers, and high sensation-seeking behavior.[2] A recent population study that looked specifically at psychedelics (LSD, psilocybin, mescaline, peyote) found that psychedelic users were more likely to be younger, white, male, unmarried, with somewhat higher educational status, risk-takers, and more likely to have used other drugs; interestingly, this paper found no association between lifetime psychedelic use and increased likelihood of past year psychological distress, mental health treatment, depression, anxiety, or suicidality.[107]

Screening Tools

As noted earlier, a variety of screening instruments are available for detecting drug use and dependency. Instruments range from comprehensive inventories (DAST), to 4-item and 2-item conjoint screening tests for both alcohol and drug use (CAGE-AID, TICS), to single-question screening.[13,14,18,19] The 4-item Substance Use Brief Screen (SUBS) may offer the best option for brief yet comprehensive screening for drug use in primary care populations.[20]

Diagnostic Criteria

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

Treatment Considerations

Behavioral interventions, such as intensive counseling and contingency management, are the mainstay of
No pharmacologic treatment is known to have any benefit. Clinicians should have awareness of significant interactions that can occur between club drugs and antiretroviral medications, particularly the pharmacologic boosters ritonavir and cobicistat; there are several published case reports of fatal drug interactions.
Opioid Use Disorder

Prevalence among Adolescents and Adults in United States

In 2018, an estimated 10.3 million Americans over the age of 12, or 3.7% of the population, used opioids, the vast majority of whom misused prescription opiate medications.[12] These numbers likely underestimate the true prevalence of opioid misuse and opioid use disorder due to the large proportion of incarcerated persons who struggle with opiate use.[2] Even so, the rate of opiate misuse is staggering.

- **Heroin Use**: Between the time periods 2002 to 2004 period and the 2011 to 2013, use of heroin (in the past year) increased by 114% among non-Hispanic whites.[108] The rate of heroin use has also increased sharply in the 18 to 25 year-old age group it rose faster among women than men.[108] Since 2013, the prevalence of heroin use has remained relatively stable and with consistently higher rates among 18 to 25 year olds (Figure 13).[12]
- **Misuse of Pain Reliever Medication**: During the past several decades, non-medical use of opioid prescription pain medication has emerged as a particularly alarming problem in the United States in recent years, especially among young people. There was a 250% increase in prescription drug misuse (opioids are the most commonly misused prescription drug) over the past 20 years and in 2013, 13% of 12th graders reported lifetime prescription opioid abuse.[109,110] From 2015 to 2018, the rate of misuse of prescription pain medications has declined slightly (Figure 14), likely due to aggressive public health messages warning providers and patients of the danger of the misuse of prescription opioid pain medications.[12]
- **Impact on Mortality**: The opioid epidemic is now having a significant impact on mortality statistics, with the highest rates of opioid related deaths in males and in persons those ages 25–44 years of age (Figure 15).[111] West Virginia continues to have the highest rate of opioid-involved death at 42.4 per 100,000.[111] According to the CDC, opioids were involved in 70% of the 67,367 drug-related deaths that occurred in the United States in 2018.[111]

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. In 2018, among all persons newly diagnosed with HIV in the United States, 10.1% (3,783 of 37,289) had injection drug use as a reported transmission category.[112] Based on CDC prevalence estimates for 2016, an estimated 16.6% (n = 189,500 of 1,140,400) of persons living with HIV in the United States had injection drug use as a reported transmission category.[113] Recent cycles of the National HIV Behavioral Surveillance System (NHBS) survey suggest that HIV prevalence among persons who inject drugs is more than 10-fold higher than the HIV prevalence in the general United States population.[113] In 2018, among all persons newly diagnosed with HIV in the United States, 10.1% (3,783 of 37,289) were among people who inject drugs.[112]
- **Injection Drug Use Among Persons with HIV**: Examining opioid use specifically among individuals with HIV, one multisite study reported a 14% prevalence of heroin use during the prior 12 months.[44] Another survey that examined overall drug use among individuals with HIV reported 3-month prevalence rates of 2% for opiate use, 10% for polydrug use (including heroin as one of the drugs), and 4% for injection drug use.[36] Interpretation of these data is complicated because injection drug use was not always distinguished from opioid use, and the studies inconsistently accounted for polydrug use, which typically includes heroin. Opioid use has also been linked to HIV epidemics in rural populations historically at lower risk for HIV, illustrating the syndemic nature of this problem.[114,115]

Risk Factors

Genetic and environmental factors appear to predispose individuals to substance use disorders and clearly
correlate with the development of an opioid use disorder. Heroin use disorders have traditionally been associated with ethnic minority populations in low-income settings, but are now becoming more common among white middle-class individuals (especially teenagers and women) as a consequence of nonmedical prescription-opioid use and increased heroin availability.[2,116] Other risk factors for heroin use include co-occurring substance use within the previous year; in particular, abuse or dependency on opioid pain relievers is the strongest risk factor for developing a heroin use disorder.[108] Nonetheless, it is important to recognize that only a small percentage of individuals who use nonmedical prescription opioids initiate heroin use.[116]

Screening Tools

As noted earlier, a variety of screening instruments are available for detecting drug use and dependency. Screening instruments include the 10-item Drug Abuse Screening Test (DAST), the 11-item Opioid Risk Tool (ORT), the 4-item and 2-item conjoint screening tests for both alcohol and drug use (CAGE-AID and TICS), and the single-question screening.[13,14,18,19] The 4-item Substance Use Brief Screen (SUSB) may offer the best option for brief yet comprehensive screening for past-year unhealthy drug use in primary care populations.[20]

Diagnostic Criteria

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

Treatment Considerations

Opioid use disorder is a medical disorder, and medications for opioid use disorder are central to the treatment strategy. 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). The Substance Abuse and Mental Health Services Administration (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] A brief overview of the key medication options is provided below, but providers interested in offering medications for opioid use disorder should consult the TIP and also their local addiction specialists.

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.[122] In 2004, the SAMHSA CSAT issued Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction that addresses key issues related to prescribing buprenorphine; this publication has not been updated since 2004.

- **Mechanism**: Buprenorphine is a partial agonist that has a high affinity for the Mu opioid receptor, but when bound, produces a long-lasting, but partial effect. By binding to this receptor, buprenorphine competes with other opioids and thereby mitigates the impact of other opioids.

- **Dosing**: The half-life of buprenorphine is 4 to 6 hours and it can be prescribed for use on a daily or twice daily basis. If the buprenorphine dose is doubled or tripled, dosing can be extended to every other day or to three-times weekly.[123] Typical doses of buprenorphine range from 8 to 16 mg daily, which is equivalent to approximately 60 mg of methadone.[123] A buprenorphine-naloxone fixed dose
formulation (8 mg/2 mg and 2 mg/0.5 mg) is also available 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).[119,124]

• **Adverse Effects:** Common side effects include drowsiness, constipation, headaches, and loss of appetite. Misuse of buprenorphine or buprenorphine-naloxone, such as with taking large doses or injecting the medication, can result in life-threatening complications. Discontinuation of buprenorphine after long-term use can cause symptoms similar to heroin withdrawal; discontinuation should be supervised and achieved through gradual dose reductions.

• **Drug Interactions with Antiretroviral Medications:** Buprenorphine has the potential to have drug interactions with antiretroviral medications that are CYP enzyme inhibitors or inducers. Notably, use of unboosted atazanavir with buprenorphine is contraindicated and caution with close monitoring is recommended with ritonavir, cobicistat, and all protease inhibitors. Efavirenz may lower buprenorphine levels. Significant interactions do not occur with INSTIs or nucleoside reverse transcriptase inhibitors (NRTIs).

• **Physician Prescribing Requirements:** Physicians interested in providing buprenorphine or buprenorphine-naloxone treatment in their practice settings need to receive a waiver from the Center for Substance Abuse Treatment (CSAT). Most physicians without prior addiction certification will need to complete 8 hours of training on the treatment of opioid-addicted patients and these trainings are now offered online or at all-day conferences.

• **Nurse Practitioners and Physician Assistants Prescribing Requirements:** In July 2016, section 303 of the Comprehensive Addiction and Recovery Act (CARA) was signed into law and this legislation provides nurse practitioners and physician assistants the ability to apply for a waiver to prescribe buprenorphine and/or buprenorphine-naloxone if they have completed the 24 hours of required training. This waiver process requires completion of the Waiver Notification Form and submission of copies of training certificates. For detailed information regarding this process see (1) the SAMSA information page [Qualify for Nurse Practitioners and Physician Assistants Waiver](http://www.samhsa.gov/qualify-for-nurse-practitioners-and-physician-assistants-waiver) and (2) the American Society of Addiction Medicine (ASAM) resource page [Nurse Practitioners and Physician Assistants Prescribing Buprenorphine](http://www.asam.org/clinical-guidelines/nurse-practitioners-and-physician-assistants-prescribing-buprenorphine).

• **Buprenorphine Treatment Practitioner Locator:** The SAMHSA Buprenorphine website provides a state-by-state [Buprenorphine Treatment Practitioner Locator](http://www.samhsa.gov/treatment/find-treatment) for medical providers authorized to treat opioid addiction with buprenorphine; this site it also provides links to buprenorphine training.

**Methadone Maintenance Therapy**

Methadone maintenance therapy is the most established form of treatment for opioid dependency and involves daily dosing of methadone through a methadone clinic; treatment is usually for 12 months or longer, with longer duration of treatment associated with greater likelihood of abstinence.[125] Methadone maintenance therapy is associated with significantly reduced heroin use and has been found to be superior to buprenorphine (discussed below) in retaining people in treatment.[126]

• **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.[123] Methadone relieves drug-craving, withdrawal symptoms, dampens the euphoric and sedating effects of heroin, and, at stable dosages, does not cause euphoria or sedation.

• **Dosing:** Methadone is available in many formulations but the liquid form is typically used in most methadone clinics in the United States. Standard initiation dosages of methadone are low, but are titrated upward to achieve reduced symptoms of withdrawal without sedation. The goal for methadone dosing is to eliminate the craving for heroin and this generally requires use of doses in the 60 to 120 mg per day range.[127]

• **Adverse Effects:** Methadone is a relatively safe drug, and when used during maintenance therapy, the most common adverse events are perspiration and constipation.[98] Additional possible complications of methadone maintenance therapy include cardiovascular effects (prolongation of QT interval and torsade de points, especially with higher doses), respiratory depression, decreased sexual function, and central nervous system effects.[123,128] Concomitant use of medications (with
methadone) that prolong QTc should be avoided.

- **Drug Interactions with Antiretroviral Medications:** Methadone has significant multiple potential drug interactions when used with antiretroviral medications. Notably, efavirenz substantially lowers methadone levels; abacavir, rilpivirine, and ritonavir-boosted protease inhibitors can also lower methadone levels. The impact of cobicistat on methadone is not known but caution should be used and methadone should be titrated up from the lowest feasible dose. The integrase strand transfer inhibitors (INSTIs) do not have significant drug interactions with methadone. Methadone can significantly increase zidovudine levels and potentially cause zidovudine-related toxicity.

**Naltrexone**

Naltrexone is an opioid receptor antagonist that is FDA-approved for relapse prevention of opioid use disorder. A large meta-analysis found that naltrexone was no more effective than placebo, even when combined with psychotherapy, but studies with the extended-release injectable formulation are more promising. Two randomized controlled trials in Russia have demonstrated improved rates of retention in treatment and abstinence from opioid use with naltrexone-SR.[129, 130]

- **Mechanism:** Naltrexone works by acting as an opioid receptor antagonist inhibiting 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.[123]
- **Adverse Effects:** The most common adverse effect of naltrexone is nausea. There is an FDA black box warning regarding the potential for hepatotoxicity when naltrexone is given in excessive doses; based on this potentially serious reaction, naltrexone is contraindicated in persons with acute hepatitis or any form of liver failure. Liver toxicity is likely lower with injectable naltrexone, since in this form it avoids first-pass liver metabolism.[82] Because of its mechanism of action, which includes blocking opiate receptors, neither oral nor injectable naltrexone should be used in patients who use opioids or receive treatment with methadone or buprenorphine. Naltrexone given to someone actively using opiates could precipitate sudden drug withdrawal. In addition, patients who discontinue naltrexone can subsequently have enhanced effects of opiates.
- **Drug Interactions with Antiretroviral Medications:** Naltrexone does not have any significant interactions with antiretroviral medications.

**Special Considerations for Persons with HIV**

Because HIV primary care providers can obtain certification to prescribe buprenorphine, persons with HIV and opioid use disorder can potentially receive comprehensive care for both their HIV and opioid use disorder at one setting.[131] Efforts to integrate buprenorphine treatment into HIV care settings, have produced mixed results and challenges have been encountered, including lack of clinical support staff, administrative obstacles, competing physician activities, and inadequate reimbursement stigma, and difficulties reaching marginalized patients.[132, 133, 134] Some models, however, have found considerable success and have dramatically scaled up access to opioid substitution therapy in underserved communities at high risk for opioid addiction. The Massachusetts Model of Office-Based Opioid Treatment with Buprenorphine (OBOT-B), which has been implemented into community health centers, provides a particularly successful model that relies on collaboration between nursing case managers and prescribing physicians.[135] 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.[136, 137]

**Harm Reduction Approach**

Medication therapy for opioid use disorder therapy is one of several practices that follow a harm reduction
philosophy. Other such practices include syringe services, HIV prevention education, and overdose prevention strategies.

**Syringe Services**

The consistent use of sterile needles and injection equipment is the most effective way for people who inject drugs to limit their risk of acquiring or transmitting HIV and other bloodborne pathogens. With only minor exceptions, federal funding for needle exchange programs in the United States was prohibited from the 1980s until late 2015. Needle exchange (also called syringe services) remains a controversial topic. Opponents of syringe services argue that providing these programs condones and even encourages drug use, especially among youth. On the contrary, multiple studies have concluded that providing sterile needles and injection equipment to people who inject drugs reduces injecting risk activities, reduces the risk of HIV infection, and facilitates entry into drug treatment.[138,139,140,141] Canada, Australia and several European countries have sought to mitigate the risks of injection drug use by establishing supervised injection facilities, where people who inject drugs can obtain sterile equipment and inject pre-obtained drugs in the presence of health professionals, allowing for a response to overdoses and facilitating encounters that link clients with drug treatment services.[142] Data on the supervised injection site in Vancouver Canada (InSite) show reduced overdose deaths in the city and surrounding areas, reduced HIV and HCV risk behaviors, reduced use of medical resources, and has increased access to preventive, mental health, and primary care services.[142]

**HIV Prevention Education**

Syringe service programs often provide a comprehensive set of services beyond basic needle exchange, including HIV counseling and testing; screening for sexually transmitted diseases, viral hepatitis, and tuberculosis; vaccination services; and referral to substance use treatment programs. It is extremely important to remember that persons who inject drugs can also acquire and transmit HIV via sexual contact and should be counseled about sexual risk reduction strategies. Many syringe services exchange sites can link interested persons who use drugs to formal education programs. A Cochrane review found that standard educational interventions, rather than multi-session psychosocial interventions, are a cost-effective way to reduce injection and sexual risk behavior.[143]

**Opioid Overdose Prevention Strategies**

Another harm reduction technique involves overdose education and distribution of naloxone to persons who use injection drugs as well as to their friends, family, and other community members. The strategy of training potential bystanders to prevent, recognize, and respond to overdose situations was piloted in 19 Massachusetts communities through the OEND (opioid education and nasal naloxone distribution) program. Between 2002 and 2009, the adjusted rate ratios of death attributed to opioid overdose decreased in communities with both low and high enrollment compared with communities without OEND implementation.[144] This is especially pertinent as the availability of naloxone has greatly expanded and is being widely promoted nationally for both people who use heroin users and those prescribed higher doses of opioids for chronic pain conditions.[145] In the United States, most states have passed legislation improving layperson access to naloxone, while Good Samaritan laws, which encourage bystanders to summon emergency responders without concern for legal repercussions, continue to be expanded throughout the country.[146]

**Opioid Prescribing Practices**

The epidemic of opioid use is intertwined with opioid prescribing practices in the United States. Due to increasing concern that pain was being undertreated, the number of opioid prescriptions quadrupled between 1999 and 2013, followed by an increase in opioid use disorders and overdose deaths.[147] The high prevalence of acute and chronic pain syndromes among persons with HIV infection means that clinicians caring for patients with HIV/AIDS frequently have to balance pain management with the risk of iatrogenic opioid dependence and with underlying addiction.[148] There are numerous initiatives that have addressed
reducing opiate prescriptions, providing daily dosing limits on opiates, and overall strategies for making prescribing safer (written contracts for patients, prescribing protocols, routine use of urine toxicology, electronic health records, prescription drug monitoring programs, and more training for primary care medical providers). Adherence with these initiatives, however, needs to be balanced with appropriate pain management prescribing for those patients who truly need it. Clearly, there is an ongoing need to educate clinicians and patients about the risks, benefits, and proper role for opioid pain medications.[149]
Stimulant Use Disorder

Prevalence of Stimulant Use Disorder in United States

In 2018, the National Survey on Drug Use and Health estimated that 2.0% and 0.3% of the population had used cocaine and crack cocaine, respectively, in the past year.[12] Cocaine use was by far highest among those ages 18-25 years, with 2018 data estimating 5.8% use in this age group during the past year.[12] In 2018, an estimated 0.7% of the population over the age of 12, or 1.9 million people, had used methamphetamine, with the highest prevalence also among those 18-25 years of age.[12] For 2018, rates of past year methamphetamine were lower in all age groups than past year cocaine use (Figure 16).[12] Older estimates of methamphetamine use, published in DSM-5 in 2013, reported amphetamine-type stimulant use disorder among adults 18 years of age and older was 0.2%, which was lower than cocaine use in all age groups age 12 years and older.[2]

Prevalence among Adults with HIV

The prevalence of stimulant use is much higher among persons with HIV than among the general population. The 2017 Medical Monitoring Project estimated that only 0.5% of persons with HIV who were engaged in care injected cocaine, 1.8% injected methamphetamine, 6.1% used non-injection cocaine, 2.5% used crack, and 4.9% used non-injection methamphetamine.[29] The Adult and Adolescent ARV Guidelines estimates a prevalence of stimulant use among all persons living with HIV is estimated in the 5-15% range.[28] In a longitudinal cohort of persons with HIV engaged in care at 8 clinical sites, 8.5% reported crack-cocaine use, whereas other cohort studies, with inclusion criteria that favored higher numbers of people who use drugs, have found cocaine usage rates of up to 40 to 50%. Other published estimates of methamphetamine use among adults with HIV have ranged from 10 to 23%, with even higher rates reported among men with HIV who have sex with men.[150] One study conducted among men who have sex with men in Los Angeles found a very strong associations between methamphetamine use and HIV, with an HIV prevalence rate of 42% in men who have sex with men who used methamphetamine at least once per month for 6 months. The highest HIV prevalence rates were found among men who have sex with men seeking intensive outpatient treatment and residential treatment (61% and 85%, respectively).[151]

Risk Factors

Risk factors for stimulant use disorder include psychiatric comorbidities (in particular, bipolar disorder, schizophrenia, and antisocial personality disorder), other substance use disorders, prenatal exposure to cocaine, experiencing community violence in childhood, and living in an unstable home.[2] Men who have sex with men also represent a discreet risk group for stimulant use disorder, particularly methamphetamine use and its associated high-risk sexual behavior.[152,153,154]

Screening Tools

As noted earlier, a variety of screening instruments are available for detecting drug use and dependency. Instruments range from comprehensive inventories (DAST), to 4-item and 2-item conjoint screening tests for both alcohol and drug use (CAGE-AID, TICS), to single-question screening.[13,14,18,19] The 4-item Substance Use Brief Screen (SUBS) may offer the best option for brief yet comprehensive screening for past-year unhealthy stimulant use in primary care populations.[20]

Diagnostic Criteria

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

**Treatment Considerations**

- **Behavioral Interventions**: Behavioral strategies, including cognitive behavioral therapy, motivational interviewing, and contingency management (a system of providing incentives for positive reinforcement, such as delivery of vouchers in exchange for abstinence) are the primary intervention for stimulant use disorders, though no single approach has been proven to be most effective.\[155,156\] The Substance Abuse and Mental Health Services Administration (SAMHSA) 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).\[157,158\] Materials about the Matrix Model are available from SAMHSA but are geared toward counselors and substance users, rather than primary care providers.

- **Pharmacologic Therapies**: No pharmacologic treatment has been approved for the treatment of stimulant use disorder. Multiple medications have been investigated, including antipsychotics (risperidone, olanzapine, reserpine, aripiprazole), psychostimulants (dexamphetamine, bupropion, methylphenidate, modafinil), antidepressants (bupropion, mirtazapine), and others (baclofen and ondansetron).\[159,160,161\] Some promising data have emerged for mirtazapine as shown in a recent randomized controlled trial of mirtazapine versus placebo for men who have sex with men and transgender women who have sex with men; in this study, mirtazapine once daily was shown to significantly reduce methamphetamine use and some HIV risk behaviors in comparison to placebo. A smaller study evaluated the effect of mirtazapine on methamphetamine use among men who have sex with men and investigatory reported participants assigned to mirtazapine therapy had fewer methamphetamine-positive urine tests compared with participants taking placebo, despite low-to-moderate medication adherence.\[162\] In general, there is a high rate of relapse among individuals who complete methamphetamine treatment programs.\[106\]
Tobacco Use Disorder

Tobacco Use Prevalence in United States

Tobacco use is a worldwide epidemic and is the leading preventable cause of death, disease, and disability in the United States. Results from the 2018 National Survey on Drug Use and Health found that approximately 21.5% of the population had used tobacco in the past month and 17.2% had specifically used cigarettes in the past month.\(^{[12]}\) Despite ongoing high rates of tobacco use, the proportion of the population who smoked cigarettes in the last month has declined from approximately 1 in 4 people in 2002 to 1 in 6 people in 2018 (Figure 17).\(^{[12]}\) Significant disparities in smoking prevalence persist, with highest prevalence rates in Native Americans/Alaskan Natives, multiracial adults, persons living under the poverty line, and those with lowest educational attainment.\(^{[163,164]}\) Although cigarette smoking has declined, the prevalence of other tobacco use, such as cigars and pipe tobacco, has not changed significantly since 2002.\(^{[12]}\)

Tobacco Use Prevalence in Adults with HIV

Data from the CDC Medical Monitoring Project has shown that among persons with HIV who engaged in medical care in the 2017-2018 time period, 34% were current smokers, 28% smoked daily, and 23% were former smokers.\(^{[29]}\) In addition, other data have noted that adults with HIV are less likely to quit smoking compared to persons without HIV.\(^{[165]}\)

Risk Factors

Individuals with psychiatric and/or other substance use disorders are at increased risk of smoking, and smoking rates have declined significantly less among persons with mental illness compared with those without mental illness.\(^{[166]}\) In addition, tobacco use disorder has a strong degree of heritability, and differences in nicotine blood levels and nicotine metabolism varies among individuals, especially among certain ethnicities (i.e. African American males have higher blood nicotine levels for a given number of cigarettes).\(^{[2]}\)

Screening and Treatment Recommendations

Tobacco use is typically a chronic problem and often requires behavioral support, pharmacologic therapy, and multiple attempts to quit.\(^{[167,168,169]}\) The U.S. Preventive Services Task Force (USPSTF) issued an updated recommendation statement in 2015 on Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women.\(^{[170]}\) The key points in this recommendation are summarized as follows:

- The 5A’s: \textbf{Ask} about tobacco use at every visit, \textbf{Advise} all tobacco users to quit, \textbf{Assess} willingness to quit, \textbf{Assist} the patient in quitting (medications, counseling), and \textbf{Arrange} follow-up contact.
- Physician and nurse counseling, as well as telephonic tobacco counseling, have been effective as a component of smoking cessation programs.
- Nicotine replacement therapy, sustained-release bupropion, and varenicline all reliably increase long-term smoking abstinence rates when compared with placebo.
- Data indicate that smoking abstinence can increase from 10% in control groups to 17% in persons using any form of nicotine replacement therapy, from 11% in control groups to 19% in those using sustained release bupropion, and from 12% in control groups to 28% in those using varenicline.
- Combining two types of nicotine replacement therapy increases abstinence rates more than use of a single nicotine replacement therapy.
- Abstinence rates for individuals using nicotine replacement therapy versus bupropion SR or varenicline do not differ significantly.
- Four studies have found lower abstinence rates with bupropion SR compared with varenicline, but the results did not reach statistical significance in all studies.
The combination of behavioral interventions and pharmacotherapy appears to be more effective than either approach alone.

There are no high-quality studies that evaluate the efficacy of using e-cigarettes (also referred to as electronic nicotine delivery systems, or ENDS) for smoking cessation; the two available studies, which were conducted outside the United States, had conflicting results on abstinence rates.

For pregnant women who smoke, the USPSTF recommends behavioral interventions but found insufficient safety and efficacy data to recommend the use of any pharmacologic treatments.

For smokers who are not yet ready to quit using tobacco products, harm reduction strategies are gaining increasing research support, including long-term use of nicotine replacement products or smoke-free products, which are a safer alternative to tobacco smoking.

Behavioral intervention strategies include in-person counseling and support, telephone counseling, provision of self-help materials, and motivational interviewing. Intensive counseling has been found to be more effective than brief counseling, and several studies of internet-based and mobile phone-based interventions have shown positive results.[171,172]

The 2008 USPSTF clinical practice guideline for treating tobacco use and dependence provide specific suggestions for the clinical use of pharmacotherapies for smoking cessation (Table 2).[169] In addition, the American Academy of Family Physicians has published a Pharmacologic Product Guide of FDA-approved medication for Smoking Cessation.

After publication of the 2015 USPSTF recommendations, results from a randomized, controlled trial of electronic cigarette use versus nicotine replacement therapy for smoking cessation were published, reporting 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.[173]

**Treatment Considerations for Persons with HIV Infection**

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.[174,175] 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.[28,169] 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.[28]
Summary Points

- More than 25% of persons living with HIV in the United States meet criteria for one or more substance use disorders.
- Substance use disorders are linked to decreased adherence to antiretroviral medications, risk-taking behaviors, and HIV disease progression (independent of non-adherence behaviors).
- Combining psychosocial interventions with pharmacotherapy (acamprosate, disulfiram, oral naltrexone, or extended-release naltrexone injection) is the optimal approach for treating alcohol use disorders; all pharmacotherapies can be used to treat persons with HIV, keeping in mind that disulfiram has several clinically significant drug interactions with antiretroviral medications whereas acamprosate and naltrexone do not.
- There is a high rate of cannabis use among persons with HIV and treatment for cannabis use disorders should focus on behavioral therapies.
- The use of club drugs, which includes methamphetamine as well as hallucinogens such as LSD and MDMA (“ecstasy”), is a significant problem among bisexual men and men who have sex with men who are HIV-infected or at risk for HIV acquisition.
- Behavioral strategies are the primary intervention for stimulant and hallucinogen use disorders, though no single approach has been proven to be most effective and there is a high rate of relapse.
- The rise in opioid addiction has paralleled the rise in opioid prescribing habits over the past 15 years, and tackling the opioid epidemic will require educating clinicians and patients alike about the risks, benefits, and proper role of opioid pain medications.
- Medication-assisted treatment is a necessary and highly effective treatment for opioid use disorder, and includes three categories: opioid agonists (methadone), opioid partial agonists (buprenorphine), and though less effective, opioid antagonists (naltrexone).
- Among persons with HIV who inject drugs, both drug- and HIV-related mortality are lowest when antiretroviral therapy and medication-assisted treatment of opioid use disorder are prescribed jointly.
- Individuals with HIV who stop using illicit substances have excellent health utilization and antiretroviral adherence patterns, thereby emphasizing the importance of securing access to substance use treatment programs.
- Treatment strategies for substance use disorders should embrace a harm reduction philosophy in order to better retain in care those patients at highest risk for ongoing substance use and associated HIV risk behavior.
Citations


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


[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]


44. 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] -


64. National Institute on Alcohol Abuse and Alcoholism. Helping Patients Who Drink Too Much: A Clinician's Guide. [NIAAA] -


74. 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] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[SAMHSA] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[SAMHSA] -


137. 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
[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

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

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

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

[PubMed Abstract] -

[PubMed Abstract] -


158. Substance Abuse and Mental Health Services Administration (SAMHSA). Buprenorphine training for physicians. [SAMHSA]


[PubMed Abstract] -


[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

References

[PubMed Abstract] -

[AAFP] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[SAMHSA] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -
  [PubMed Abstract] -

  [PubMed Abstract] -

  [PubMed Abstract] -

• Jozaghi E, Andresen MM. Should North America's first and only supervised injection facility (InSite) be expanded in British Columbia, Canada? Harm Reduct J. 2013;10:1.
  [PubMed Abstract] -

  [PubMed Abstract] -

  [PubMed Abstract] -

  [PubMed Abstract] -

  [PubMed Abstract] -

  [PubMed Abstract] -

  [PubMed Abstract] -

  [PubMed Abstract] -

  [PubMed Abstract] -

• Stinson FS, Ruan WJ, Pickering R, Grant BF. Cannabis use disorders in the USA: prevalence, correlates and co-morbidity. Psychol Med. 2006;36:1447-60.
  [PubMed Abstract] -

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


Figures

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

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

Figure 2 Current, Binge, and Heavy Alcohol Use Among People Age 12 Years or Older, United States, 2018

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

Figure 3 Past Year Alcohol Use Disorder among People Aged 12 Year or Older, United States, 2002-2018

Figure 4 U.S. FDA Approved Medications to Treat Alcohol Use Disorder


<table>
<thead>
<tr>
<th>Medication</th>
<th>Typical Dose</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acamprosate</td>
<td>666 mg three times daily</td>
<td>Dose reduction required with renal impairment</td>
</tr>
<tr>
<td>Disulfiram</td>
<td>500 mg once daily for 1-2 weeks, then decrease to maintenance dose (range 125-500 once daily)</td>
<td>Not for use in persons actively drinking alcohol; avoid alcohol in other products</td>
</tr>
<tr>
<td>Oral Naltrexone</td>
<td>50 mg once daily</td>
<td>Cannot be given to patients taking opioids</td>
</tr>
<tr>
<td>Extended-Release Naltrexone</td>
<td>380 mg IM every 4 weeks; administer in gluteal area with 1.5 inch 20-gauge needle</td>
<td>Cannot be given to patients taking opioids</td>
</tr>
</tbody>
</table>
**Figure 5 Impact of Long-Acting Naltrexone on Median Heavy Drinking Days per Month**

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

Figure 6 Acamprosate in Persons with Alcohol Dependence

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

Figure 7 Inhibition of Alcohol Metabolism by Disulfiram

Normal ethanol (alcohol) metabolism is shown in top figure, with conversion of ethanol to acetate. Disulfiram inhibits the enzyme aldehyde dehydrogenase, leading to accumulation of acetaldehyde, which is associated with adverse effects.
Figure 8 Neurochemical Circuits Involved in Alcohol Dependence and Craving

This figure shows ethanol leading to increased dopamine levels in nucleus accumbens. Naltexone 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.

Figure 9 Past Year Illicit Drug Use Among Persons 12 Years of Age and Older, United States, 2018

Figure 10 Past Year Marijuana Use, by Age Group, United States, 2018

Figure 11 Past Year Marijuana Use among People Aged 12 Year or Older, United States, 2002-2018

Figure 12 Past Year Hallucinogen Use among People Aged 12 Year or Older, United States, 2015-2018

Figure 13 Past Year Heroin Use among People Aged 12 Year or Older, United States, 2002-2018

Figure 14 Past Year Prescription Pain Reliever Misuse among People Aged 12 Year or Older, United States, 2015-2018

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

Figure 16 Past Year Stimulant Use, by Age Group, United States, 2018

Figure 17 Past Month Cigarette Use in Persons 12 Years of Age and Older: National Health Interview Survey, United States, 2002-2018

### 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-mo period:

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Having times when the patient drank more, or longer, than intended</td>
</tr>
<tr>
<td>2. More than once wanted to cut down or stop, tried it, but could not</td>
</tr>
<tr>
<td>3. Spending a lot of time drinking or being sick/getting over the aftereffects of drinking</td>
</tr>
<tr>
<td>4. Wanting to drink so badly that they could not think of anything else</td>
</tr>
<tr>
<td>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</td>
</tr>
<tr>
<td>6. Continuing to drink even though it was causing trouble with family and friends</td>
</tr>
<tr>
<td>7. Given up or cut back on activities that were important or interesting in order to drink</td>
</tr>
<tr>
<td>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)</td>
</tr>
<tr>
<td>9. Continued to drink even though it was causing depression or anxiety, other health problems, or causing memory blackouts</td>
</tr>
<tr>
<td>10. Having 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</td>
</tr>
<tr>
<td>11. Experiencing the symptoms of withdrawal after the effects of alcohol were wearing off, such as trouble sleeping, shakiness, restlessness, nausea, sweating, racing heart, or seizure</td>
</tr>
</tbody>
</table>

Severity is determined based on the number of symptoms present:

- **Mild**: 2 to 3 criteria
- **Moderate**: 4 to 5 criteria
- **Severe**: more than 6 criteria

Source:

Table 2.
Suggestions for the Clinical Use of Pharmacotherapies for Smoking Cessation*

<table>
<thead>
<tr>
<th>Pharmacotherapy</th>
<th>Precautions, contraindications</th>
<th>Adverse effects</th>
<th>Dosage</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustained release bupropion hydrochloride</td>
<td>History of seizure</td>
<td>Insomnia</td>
<td>150 mg every morning for 3 days, then 150 mg twice daily (begin treatment 1-2 weeks pre-quit)</td>
<td>7 - 12 weeks Maintenance up to 6 months</td>
</tr>
<tr>
<td></td>
<td>History of eating disorders</td>
<td>Dry Mouth</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Seizures</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotine gum</td>
<td>Mouth soreness</td>
<td></td>
<td>1-24 cigarettes/day: 2mg gum (up to 24 pieces/day)</td>
<td>Up to 12 weeks</td>
</tr>
<tr>
<td></td>
<td>Dyspepsia</td>
<td></td>
<td>≥ 25 cigarettes/day: 4 mg gum (up to 24 pieces/day)</td>
<td></td>
</tr>
<tr>
<td>Nicotine inhaler</td>
<td>Local irritation of mouth and throat</td>
<td></td>
<td>6-16 cartridges/day</td>
<td>Up to 6 months</td>
</tr>
<tr>
<td>Nicotine lozenge</td>
<td>Nausea</td>
<td>Heartburn</td>
<td>First cigarette smoked ≥30 minutes after awakening: initiate with 2 mg lozenge</td>
<td>Up to 12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>First cigarette smoked &lt;30 min after awakening: initiate with 4 mg lozenge</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Weeks 1-6: 1 lozenge every 1-2 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Weeks 7-9: 1 lozenge every 2-4 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Weeks 10-12: 1 lozenge every 4-8 hours</td>
<td></td>
</tr>
<tr>
<td>Nicotine nasal spray</td>
<td>Nasal irritation</td>
<td></td>
<td>8-40 doses/day</td>
<td>3-6 months</td>
</tr>
<tr>
<td>Nicotine 24-hour patch</td>
<td>Local skin reaction</td>
<td></td>
<td>If smokes ≥10 cigarettes per day</td>
<td>8 weeks</td>
</tr>
<tr>
<td></td>
<td>Insomnia</td>
<td></td>
<td>• Weeks 1-4: 21 mg/24</td>
<td></td>
</tr>
</tbody>
</table>

*Table 2: Suggestions for the Clinical Use of Pharmacotherapies for Smoking Cessation*

**Pharmacotherapy**
- Sustained release bupropion hydrochloride
- Nicotine gum
- Nicotine inhaler
- Nicotine lozenge
- Nicotine nasal spray
- Nicotine 24-hour patch
<table>
<thead>
<tr>
<th>Pharmacotherapy</th>
<th>Precautions, contraindications</th>
<th>Adverse effects</th>
<th>Dosage</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine 16-hour patch</td>
<td></td>
<td>Local skin reaction</td>
<td>If smokes ≥15 cigarettes per day</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Weeks 1-8: 25 mg/16 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Weeks 9 and 10: 15 mg/16 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Weeks 11 and 12: 10 mg/16 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>If smokes &lt;15 cigarettes per day</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Weeks 1 to 8: 8.15 mg/16 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Weeks 9-12: 10 mg/16 hours</td>
<td></td>
</tr>
<tr>
<td>Varenicline</td>
<td>Significant kidney disease</td>
<td>Nausea, trouble sleeping</td>
<td>Begin treatment 1 week pre-quit</td>
<td>3-6 months</td>
</tr>
<tr>
<td></td>
<td>Patients on dialysis</td>
<td>Abnormal or vivid/ strange dreams</td>
<td>• 0.5 mg/day for 3 days, then</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Depressed mood and other psychiatric symptoms</td>
<td>• 0.5 mg twice/day for 4 days, then</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 1 mg twice/day</td>
<td></td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>Precautions, contraindications</td>
<td>Adverse effects</td>
<td>Dosage</td>
<td>Duration</td>
</tr>
<tr>
<td>-----------------</td>
<td>--------------------------------</td>
<td>----------------</td>
<td>--------</td>
<td>----------</td>
</tr>
</tbody>
</table>

* The information contained in this table is not comprehensive; see package inserts for additional safety information. Much of the content in this table is based on information in the 2008 U.S. Public Health Service Clinic Practice Guideline for Treating Tobacco Use and Dependence.

Source:
