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Wolters Kluwer

Substance use disorder in patients with HIV

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INTRODUCTION

Neuropsychiatric disorders are common in individuals infected with the human immunodeficiency virus (HIV), due to a several factors. These include direct effects of the virus, preexisting neuropsychiatric conditions and addictions, and the social isolation that is often associated with diagnosis of HIV. In addition, many patients with HIV have difficulty with treatment adherence, as well as neuropsychiatric disorders that are associated with HIV disease progression [1].

This topic reviews substance use disorder in patients with HIV. An overview of neuropsychiatric conditions associated with HIV infection, and reviews of specific neuropsychiatric conditions, are discussed separately. (See "[Overview of the neuropsychiatric aspects of HIV infection and AIDS](#)" and "[HIV-associated neurocognitive disorders: Epidemiology, clinical manifestations, and diagnosis](#)" and "[Depression, mania, and schizophrenia in patients with HIV](#)".)

DEFINITIONS

Although the word "addiction" has been repeatedly criticized in the literature, clinicians widely use the term to describe ongoing and disordered use of psychoactive substances. The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) uses the overarching term "substance-related and addictive disorders" to describe substance-related disorders, and classifies substance dependence as a subset of the more

general category of substance abuse, which occurs on a continuum from mild to severe [2]. We define addiction as a pattern of increasing drug use for intoxication despite the presence of increasing negative consequences of using that drug.

Dependence has two aspects: physical and psychological. Physical dependence refers to the physiological withdrawal symptoms that can occur in the absence of using the drug.

Psychological dependence describes the belief that it is necessary to continue using the substance to feel emotionally stable.

Disorders secondary to substance use disorders include substance-induced disorders, such as substance-induced psychotic disorder, substance-induced bipolar and related disorder, substance-induced depressive disorder, substance-induced anxiety disorder, substance-induced sleep disorder, substance-induced persisting dementia disorder, substance-induced amnestic disorder, and substance-induced sexual dysfunction. These secondary disorders typically resolve with cessation of the underlying substance use disorder.

SUBSTANCE USE DISORDER AND HIV TRANSMISSION

Substance use disorder is a vector for spreading HIV through several high-risk behaviors that occur when patients are disinhibited by intoxication, or when they obtain and use drugs:

- Sharing unclean needles
- Prostitution
- Risky sexual behavior (eg, not using condoms)
- Sexual contact within a high-risk population of patients with injection drug use

From 2008 to 2014, new HIV diagnoses attributable to patients with injection drug use steadily declined (48 percent, from 6604 to 3461), and appear to have stabilized thereafter [3]. This decline may be related to widespread use of both antiretrovirals and needle exchange programs [4]. Ongoing cases are attributed to [fentanyl](#) and methamphetamine-induced high-risk sexual behaviors, as well as the increasing perception that HIV is readily treatable [5].

The epidemic of opiate use and overdose deaths in the United States has also likely contributed to the spread of HIV. In response to the epidemic, clinicians are encouraged to stop prescribing opiates, leaving a large population of opiate-dependent patients without adequate treatment. This has fueled widespread injection of opiates, including heroin and illicit [fentanyl](#) [6], and caused a resurgence of injection-related infections of HIV in many communities [4], including rural and underserved areas [7]. Notably, new cases of HIV decreased with the initiation of a needle exchange program [4].

Substance use disorder also plays a major role in HIV transmission among noninjection drug users. For example, individuals who use crack cocaine are more likely to engage in prostitution to obtain money for drugs [8,9]. In addition, males who use crack cocaine are more likely to engage in unprotected anal sex with casual male contacts [10]. Lastly, alcohol intoxication precipitates risky sexual behaviors through cognitive impairment and disinhibition [11,12].

COMORBIDITIES

Extensive psychiatric, psychological, and medical comorbidities are associated with substance use disorder and addiction in HIV disease.

Psychiatric comorbidity — The most significant psychiatric comorbidity with HIV and substance use disorder is major depression, which is associated with HIV and substance use disorder at a prevalence rate of 15 to 30 percent [13]. Depression is associated with worsening of addictions and resistance to treatment. While anhedonia in depression makes it difficult for patients to respond to and enjoy life's rewards, potential rewards may especially pale for patients with HIV and substance use disorder in comparison to the intense ephemeral charge of intoxicating drugs that stimulate the mesolimbic reward system of the brain. (See "[Depression, mania, and schizophrenia in patients with HIV](#)".)

Depressed patients also often find it more difficult to initiate and sustain treatment due to their anergy and negativism. Recognizing and treating depression early can maximize successful treatment outcomes for both substance use disorder and HIV disease. Because it can be difficult to distinguish transient depressive symptoms precipitated by drug withdrawal, demoralization, or grief reactions from persistent depressive symptoms, it may be necessary to observe the substance use disorder patient over a sustained period of abstinence to accurately diagnose depression.

Personality comorbidity — Personality factors may lead to greater risk taking and increased sensitivity to rewards. An increased tendency to take risks often precipitates a greater likelihood of engaging in high-risk behaviors, while greater sensitivity to rewards is associated with increased sensitivity to the reinforcing properties of drugs and decreased sensitivity to the negative consequences of drug use. On the other hand, consequence- and risk-avoidant personality features confer relative protection from addiction.

Maladaptive personality traits, generally found in antisocial, borderline, narcissistic, and histrionic personality disorders in the DSM-5, are present in as many as 49 percent of all

patients with substance use disorder [14]. Identifying personality vulnerabilities in these patients is important because they can affect treatment and prognosis.

Medical comorbidity — Patients with concurrent drug use disorders, another psychiatric disorder, and HIV are abundant in HIV treatment settings because of their symptom severity and chronicity. As an example, in the urban population of Baltimore, 44 percent of new entrants to the HIV medical clinic at Johns Hopkins had an active substance use disorder, and 24 percent of these patients had both a current substance use disorder and another nonsubstance-related Axis I diagnosis [15].

Accumulation of medical sequelae from chronic substance use disorder accelerates immunocompromise and amplifies accumulating burdens of HIV infection. Patients with injection drug use, for example, have a higher risk of developing pneumonia, sepsis, soft tissue infections, and infective endocarditis. Tuberculosis, sexually transmitted diseases, viral hepatitis, and coinfection with human T-lymphotropic virus types I and II also occur more commonly among patients with HIV and injection drug use.

Diagnosis and treatment of comorbid conditions is often difficult because there is substantial overlap between clinical manifestations of substance use disorder and sequelae of HIV infection. For example, both AIDS dementia and drug intoxication can present with apathy, disorientation, aggression, and altered consciousness, and both drug withdrawal and opportunistic infections of the central nervous system can present with seizures and neurovegetative symptoms. (See "[HIV-associated neurocognitive disorders: Epidemiology, clinical manifestations, and diagnosis](#)" and "[Approach to the patient with HIV and central nervous system lesions](#)".)

The duration of survival in patients with HIV and injection drug use has improved substantially since 1997 with the introduction of effective antiretroviral therapy, reaching rates similar to those in HIV-seronegative injection drug users [16]. However, clinicians must be especially mindful of interactions among antiretroviral agents, medicines that patients with HIV may take to prevent opportunistic infections, and substances that these patients may use. Opioid users, for example, are at particular risk for medication interactions. [Rifampin](#) increases the rate of elimination of [methadone](#) from the body and may result in rapid onset of withdrawal symptoms in patients on methadone maintenance therapy. Decreased plasma levels of methadone also occur with concurrent administration of [ritonavir](#), [nelfinavir](#), [efavirenz](#) and [nevirapine](#), which necessitates adjustments in methadone maintenance if withdrawal should occur [17].

Antiretroviral medications such as [didanosine](#) may also cause peripheral neuropathies that can be worsened by the neurotoxic effects of alcohol and malnutrition related to chronic substance

use disorder. Didanosine is no longer available in the United States though may still be available in other locations (eg, India). With the advent of newer antiretroviral agents with less mitochondrial toxicity, safer alternatives are now available.

Of particular relevance to the population with HIV is coinfection with hepatitis C virus (HCV). Some clinics have reported that 50 percent of patients with HIV are also infected with HCV, and coinfection may be as high as 70 percent among patients with injection drug use. Underlying HIV infection also appears to facilitate HCV progression to cirrhosis and liver failure. (See ["Treatment of chronic hepatitis C virus infection in the patient with HIV".](#))

Although very little is known about specific psychiatric disturbances in patients with both HIV and HCV, neuropsychiatric complications of treatment with interferon (IFN)-alpha, a mainstay therapy for HCV, are well known. IFN-alpha has been associated with depressive syndromes, suicide, and mania. Patients with preexisting depression or bipolar disorder are more likely to develop affective symptoms while receiving IFN-alpha, but may not be more likely to stop treatment than patients developing these symptoms de novo [18]. Patients with both HIV and HCV should be screened for mental illness, and mental health monitoring should be performed during the period of treatment with IFN-alpha to achieve early recognition and treatment of affective symptoms.

TREATMENT OF SUBSTANCE USE DISORDERS IN HIV

A simplified series of steps for substance use disorder in patients with HIV includes:

- Acceptance of the role as a patient
- Detoxification
- Rehabilitation
- Treatment of comorbid conditions
- Maintenance treatment and relapse prevention

Acceptance of patient role — The most daunting task in treatment of drug addiction is often initial engagement and guiding the individual to accept the role of a patient to achieve longer-term health goals. Whereas individuals who are addicted to drugs tend to present to treatment settings for comfort or crisis relief, medical care providers are focused on long-range goals of improving health and overall functioning. It is the task of the health care provider to guide the patient's attitudes to coincide with those of the provider's treatment plan. Here, a number of stages that a patient goes through (transtheoretical stages of change) provide a framework for viewing the recovery process [19]:

- Precontemplation – Patient has no intention of altering addictive behavior
- Contemplation – Patient has considered change, often after recognizing negative consequences of their drug use, but remains ambivalent to change
- Preparation – The patient shows intent to change by making initial steps to seek treatment
- Action – Patients decide to modify behavior, environment, and circumstances to relinquish their addictive lifestyle
- Maintenance – The patient works to prevent relapse through consolidation of changed behavior and lifestyle

The most difficult transition in truly accepting the patient role is from contemplation to action. Using empathy and confrontation to amplify the discrepancy between current lifestyle and long-term life enhancing goals is essential. Motivational interviewing is a nonconfrontational intervention that can help transition patients along this process. (See ["Substance use disorders: Motivational interviewing"](#).)

Detoxification — It is virtually impossible for intoxicated patients to understand and process the cognitive steps needed for recovery without first undergoing detoxification. Slowly tapering either the drug of dependence or using a cross-dependent drug with similar pharmacologic mechanism best accomplishes this goal.

There is no evidence to support the notion that noxious withdrawal during detoxification improves outcome. Rather, some studies suggest that patients suffering through severe withdrawal develop conditioned withdrawal such that exposure to environments similar to the one experienced during severe withdrawal can bring back withdrawal symptoms months later. Effort should be directed to help patients remain comfortable during drug withdrawal. (See ["Management of moderate and severe alcohol withdrawal syndromes"](#) and ["Acute opioid intoxication in adults"](#).)

Sedative-hypnotic drugs that enhance gamma-aminobutyric acid transmission, such as benzodiazepines, barbiturates, and alcohol, cause a withdrawal that can be life threatening, and patients should be slowly tapered with long-acting benzodiazepines such as [diazepam](#), [chlordiazepoxide](#) or [oxazepam](#). Detoxification from opiates is accomplished through taper of long-acting opioid agonists, such as [methadone](#), slow-release [morphine](#), or slow-release [oxycodone](#). The use of [buprenorphine](#), a partial opioid agonist, can be problematic in higher dose users, as it can precipitate withdrawal in dependent patients. Most heroin users or those who are using modest opiate doses can be effectively tapered using buprenorphine, but for

patients on high doses of opiates (usually for chronic pain), an experienced clinician should be consulted before using a buprenorphine taper. The uncomfortable symptoms of sedative-hypnotic and opiate detoxification can be ameliorated with several adjunctive medications, including [clonidine](#), [carbamazepine](#), [gabapentin](#), [hydroxyzine](#), [methocarbamol](#), [pregabalin](#), and [valproic acid](#).

Treatment of comorbid psychiatric conditions — Comorbid psychiatric conditions should always be treated to maximize compliance and abstinence. Conditions such as major depression, bipolar disorder, and schizophrenia are best managed with the pharmacologic strategies routinely employed for other patients with these disorders. Medications should be started at low doses and titrated slowly to minimize adverse side effects and delirium. (See ["Depression, mania, and schizophrenia in patients with HIV"](#).)

Personality disorders may manifest as staff splitting, doctor shopping, general noncompliance, and manipulative behavior. These symptoms are magnified by the discomforts of withdrawal and the discomforts of facing the consequences of addictive behaviors during the early periods of sobriety. These individuals are best managed through psychotherapy with firm limit setting and consistency on the part of all their health care providers. There should be a documented treatment plan with clear goals agreed upon by all treatment staff. This treatment plan should be reviewed with patients at the initiation of treatment so that they clearly understand what is expected of them and what they can expect from the treatment providers if they are adherent to the stated goals.

Maintenance treatment and relapse prevention — Because patients with HIV and substance use disorder are complicated and vulnerable to recidivism, an integrated approach to long-term treatment should include a treatment team of medical providers, psychiatrists, social workers, housing counselors, daycare workers, and substance use disorder counselors. Group therapy is also important because more experienced members of the group can provide both confrontation and support for newly initiated members and a positive view of the benefits of recovery.

Commitment to a community of recovery fosters protection from the influences of the drug community and provides new bonds that help maintain a sense of purposefulness and hopefulness. Specific HIV-positive recovery groups are also available. Although these groups specifically address HIV-related issues, they are not necessary for recovery from substance use disorder.

Individual and family therapies can enhance the treatment, but they should not replace group therapy. Successful therapy generally focuses on identifying and then avoiding triggers of

substance use, minimizing exposure to substances, and defining a clear plan of action if relapse occurs. Relapse is often the rule rather than the exception, and prophylactic plans should be made for early intervention. Monitoring measures such as urine and serum toxicologies and Breathalyzer tests can help enforce compliance, and contingency management using positive and negative reinforcers linked to urine toxicology results are highly effective in helping patients maintain sobriety.

Adjunctive pharmacotherapy — Pharmacologic approaches to maintenance and relapse prevention can be divided into aversive therapy (eg, [disulfiram](#) for alcohol use disorder), blockade of reinforcement (eg, [naltrexone](#) for opioid use disorder), drive suppression (eg, [bupropion](#) or [naltrexone](#) for tobacco use disorder, [buprenorphine](#) for cocaine use disorder) and substituted agonist therapy (eg, [methadone](#) or [buprenorphine](#) for opioid use disorder). Because relapse can occur impulsively in a single moment, many patients benefit from these strategies.

[Disulfiram](#) inhibits acetaldehyde dehydrogenase, causing accumulation of acetaldehyde after alcohol ingestion, which results in nausea, flushing, headaches, and hypotension. Due to the risk of hepatotoxicity, liver enzymes should be monitored during disulfiram treatment. It has rarely been successful as a monotherapy for alcohol, but may be useful in preventing relapse in a situation known to have triggers (such as attending an event where alcohol will be served). (See "[Alcohol use disorder: Treatment overview](#)".)

In treating opiate use disorder with agonist therapy, [methadone](#) is the opioid agonist most traditionally used for opiate maintenance treatment, and it has the highest retention of the drugs used for opiate use disorder. Doses range from 40 to 140 mg daily. Methadone is administered under daily supervision until the patient achieves sustained abstinence, at which point take-home doses are allowed. Although methadone can help patients remain in treatment and reduce opioid use, it is also a specialized treatment that can be difficult to access. (See "[Opioid use disorder: Pharmacologic management](#)".)

The partial agonist [buprenorphine](#) is a widely used alternative to [methadone](#) and has the advantage that it can be administered by primary care clinicians to opiate-dependent individuals, thereby removing the stigma associated with daily visits to drug treatment centers, which can interfere with medication adherence. Patients should be tapered from active opiates so the antagonist action of the buprenorphine does not precipitate opiate withdrawal, a process that requires some expertise. Buprenorphine is best used as part of a treatment program and not simply a medication solution to addiction. Newer formulations include injectable long-acting versions and implantable drug-eluting inserts. The most widely used formulation is compounded with [naloxone](#) to discourage injection (the naloxone prevents the effect of the drug when injected but not when taken sublingually), and is given daily in divided doses.

In opiate use disorder, an alternative to agonist therapy is antagonist (or opiate blocker) therapy. Daily [naltrexone](#) or extended-release naltrexone will “block the high” from opiates. Multiple successful approaches have been described, but without a programmatic approach, retention tends to be less successful than full or partial agonist therapy.

Using medication-assisted treatment within HIV clinics, as well as providing HIV care in substance treatment settings, may reduce injection-related risk behaviors and increase viral suppression, compared with disconnected programs [20,21]. The best results combine psychiatric care, substance use disorder treatment, and medical care in a coordinated manner.

SUMMARY AND RECOMMENDATIONS

- Substance use disorder is defined as a maladaptive pattern of substance use that has become socially, legally, or occupationally problematic for the individual. Substance dependence refers to the physical need for a substance. Tolerance is the need to use increasing amounts of a substance in to achieve the desired effect. (See '[Definitions](#)' above.)
- Substance use disorder is a primary vector for the spread of HIV through high-risk behaviors, either when intoxicated or to obtain drugs. Such behaviors include sharing unclean needles, prostitution, and sexual contact within a high-risk population of injection drug users. (See '[Substance use disorder and HIV transmission](#)' above.)
- Substance use disorders in HIV disease are frequently comorbid with major depression, personality disorders and maladaptive personality traits, pneumonia, sepsis, soft tissue infections, endocarditis, tuberculosis, sexually transmitted diseases, viral hepatitis, and coinfection with human T-lymphotropic virus types I and II. (See '[Comorbidities](#)' above.)
- Treatment of substance use disorder in patients with HIV includes the patient accepting the role of the patient, detoxification, treatment of comorbid conditions, maintenance treatment, and relapse prevention. (See '[Treatment of substance use disorders in HIV](#)' above.)
- Accepting the patient role involves several stages, including precontemplation, contemplation, preparation, action, and maintenance. (See '[Acceptance of patient role](#)' above.)
- Detoxification is best accomplished by slowly tapering the drug of dependence or using a cross-dependent, longer-acting drug with a similar pharmacologic mechanism.

Benzodiazepine, barbiturate, and alcohol withdrawal can be life threatening, and patients should be slowly tapered with a long-acting benzodiazepine such as [chlordiazepoxide](#). Detoxification from opiates is often accomplished with [clonidine](#). There are no specific guidelines for detoxification from psychomotor stimulants such as cocaine or amphetamines, although some clinicians promote the use of antidepressants. (See '[Detoxification](#)' above.)

- Comorbid major depression, bipolar disorder, or schizophrenia are best managed with pharmacotherapy that is routinely employed for other patients with these disorders. Personality disorders are best managed through psychotherapy with firm limit setting and consistency on the part of all their health care providers. (See '[Treatment of comorbid psychiatric conditions](#)' above.)
- Group therapy is typically used for rehabilitation, maintenance treatment, and relapse prevention of substance use disorders in HIV disease. Other treatments include aversive therapy, blockade of reinforcement, drive suppression, and substituted addiction. (See '[Maintenance treatment and relapse prevention](#)' above.)

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