

Substance Use Disorders in Adults: A Narrative Review

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ABSTRACT

Research on substance use disorders published in 2024 has included smoking, cannabis, alcohol disorder, stimulant-related and opioid-related disorders. Prevalence rates for substance use disorders in U.S. adults have varied from 9-18% over the last year depending on the type of substance use disorder. The negative effects have included limited exercise capacity, lung and respiratory muscle function, violence and suicidality. Predictors/risk factors have been disparate including male gender, childhood maltreatment, early onset use, narcissism, reward sensitivity, anger, cancer and being an elite athlete. Comorbidities include loneliness, pain and depression. The most common treatments have been cognitive behavior therapy and ketamine. Potential underlying biological mechanisms have included low heart rate variability, aberrant EEG patterns and gene variants related to the brain's reward system. Methodological limitations of this literature include the greater frequency of reviews and meta-analyses than empirical studies, the inclusion of adults with different types of substance use disorders in both the empirical studies and the meta-analyses and the rare multi-variable studies to determine the relative importance of different risk factors as well as the efficacy of different therapies.

According to the National Survey on Drug Use and Health (NSDUH, 2024), as many as 9-18 % of U.S. adults were diagnosed with substance use disorders in 2024 [1]. These are problematic given that the same survey revealed that only 13% are receiving treatment for substance use disorders. These disorders are further complicated by the comorbid conditions of affective, anxiety and personality disorders and the negative drug use effects on violence and suicidality [2-4]. These data highlight the importance of research on substance use disorders.

In this narrative review on research published in 2024, 29 empirical research and review papers on substance use disorders in adults are summarized. The papers were derived from a search on PubMed and PsycINFO entering the terms substance use disorders in adults and the year 2024. Exclusion criteria for this review included proposed protocols, case studies and non-English language papers. The publications can be categorized as different types of substance use disorders, negative effects of substance use disorders, predictors/risk factors, comorbidities, interventions and potential underlying biological mechanisms for substance use disorders. Accordingly, this review is divided into sections that correspond to those categories. Although some

papers can be grouped in more than one category, 1 paper is focused on different types of substance use disorders, 3 papers are focused on the negative effects, 7 papers on comorbidities, 7 papers on predictors/risk factors for substance use disorders, 6 papers on interventions and 3 papers on potential underlying biological mechanisms. A discussion of methodological limitations of this literature follows those sections.

Types of Substance Use Disorders

Only one study in the current literature focused on the different types of substance use disorders. This study sampled patients who were socially isolated (N =2050, mean age = 48) [5]. This research group reported a prevalence of 17% substance use disorders in this sample. This disorder occurred more frequently in young age males. The prevalence of smoking was 49%, opioid-related disorder 17%, stimulant-related disorders 16%, cannabis 15%, and alcohol disorder 14%.

Negative Effects of Substance Use Disorders

The negative effects have been primarily physical and life-threatening. These have included limited exercise capacity, lung and respiratory muscle function, violence and suicidality (see table 1).

Table 1: Negative effects of substance use disorders (and first authors).

Negative Effects	First Authors
Lower lung function, muscle strength and exercise capacity	Mustafaoglu
Violence	Prince
Suicidality (suicidal thoughts and attempts)	Leza

In a paper entitled “Exercise capacity, lung and respiratory muscle function in substance use disorders”, 86% of the sample (N= 183) were diagnosed with substance use disorders [6]. The participants experienced the negative effects of shortness of breath, wheezing, **lower lung function parameters, lower muscle strength and exercise capacity.**

Violence has also been more prevalent in those with substance use disorders. In the National Survey of Drug Use and Health sample (N = 10,551), those who used alcohol were 2.2 times more likely to be violent, opioid users 3.45 times more likely, opioid plus alcohol users were 4.28 more likely to be violent and cocaine plus alcohol users were 5.85 more likely to be violent [3]. Surprisingly, other research on the association between substance use disorders and violence was not found in this literature despite the prevalence of incarcerations for violence in those with substance use disorders.

Suicidality has also been associated with substance use disorders. In a paper entitled “Substance use disorders and lifetime suicidal behavior”, 30 studies were reviewed [4]. The prevalence of suicidal ideation ranged from 20 to 62% and the range for suicide attempts was 16 to 52%. However, only three studies evaluated suicidal behaviors with a specific instrument, limiting the validity of these findings.

Predictors/Risk Factors for Substance Use Disorders

Several disparate predictors/risk factors for substance use disorders have appeared in this literature. These include male gender, early onset of substance use, childhood maltreatment, narcissism, reward sensitivity, anger, cancer and being an elite athlete (see table 2).

Table 2: Predictors/Risk factors for substance use disorders (and first authors).

Predictors/Risk Factors	First Authors
Male gender	McHugh
Childhood maltreatment	Erga, Guadtaferro, Azagba, Mongan
Early onset substance use	Yuksel
Impulsivity and narcissism	Hildebrandt
Reward sensitivity	Liu
Anger	Miloslavich
Cancer survivors	Jones
Elite athletes	Nkyi

Male gender was a notable risk factor for substance use disorders in the National Survey of Drug use and Health database [7]. In this sample (N=282,768), the prevalence of substance use

disorders was greater for males than for females on every drug, although the smallest gender difference was noted for the use of prescription medication.

Childhood maltreatment was reported as a risk factor for substance use disorders in at least four studies. In a relatively small sample of adults with substance use disorders (N =111), 92% reported at least one childhood maltreatment incident [8]. As many as 36% reported several instances of childhood maltreatment.

Childhood maltreatment was also a risk factor in a larger sample of adults (N=5194) [9]. In this research, those adults who had experienced childhood maltreatment were three times more likely to have substance use disorders.

In still another study on associations between childhood maltreatment and substance use disorders (N=4,729), two adverse child experiences (ACEs) were related to a two-fold increase in substance use disorders [10]. Three ACEs contributed to a three-fold increase in the odds of developing a substance use disorder.

In a paper entitled “Examining the pathways from adverse child experiences to substance use (N=30,978), 71% had experienced at least one ACE [11]. In this sample the association between ACEs and substance use disorders was mediated by depression disorder. Depression in this case was called a mediator, as the research group had a theory that depression was a mediator and therefore conducted a mediation analysis. Other research groups have referred to depression as a comorbidity of substance use disorders.

Early onset substance use was another risk factor for substance use disorders in a sample from Turkey (N= 100 adults with substance use disorders) [12]. Early onset of substance use (at less than 18 years) was associated with more traumatic experiences, an increased risk of developing PTSD, more depressive symptoms and substance use disorders.

In a paper entitled “Impulsivity mediates the association between narcissism and substance - related problems”, poly substance users were sampled (N=139) [13]. **Impulsivity** explained as much as one-third of the association between narcissism and poly substance use disorders.

Reward sensitivity was still another risk factor for substance use disorders [14]. In this study, reward sensitivity was notably greater during adolescence and early adulthood with reward sensitivity being a risk factor for later substance use disorders. The early reward sensitivity could precede the early onset of drug use. The reward sensitivity, in turn, would likely be enhanced by the dopamine release following drug use.

Anger was the most significant risk factor for substance use disorders in a large sample of adults (N=28,753) [15]. However, anger was most strongly associated specifically with alcohol use disorder in this study.

Being an adult **cancer survivor** was another risk factor in a U.S. sample (N=6101) [16]. In this sample, 3.8% had substance use

disorders with alcoholism being the most common disorder (9%). This substance use disorder was most prevalent in survivors of head and neck cancer, including cancer of the mouth, tongue, lips, throat, and pharynx. Alcohol use and anger may have contributed to the development of these cancers. As noted in the previous study, anger was more strongly associated with alcohol use than other substance use disorders [15].

In a paper entitled “Substance misuse in **elite athletes**”, the most encountered substances were alcohol (binge drinking), cannabis (marijuana) and tobacco (nicotine vaping) [17]. This substance misuse in athletes, especially elite athletes, is surprising given the physical demands of their sports and the earlier report that shortness of breath, wheezing, lower lung function, muscle strength and exercise capacity resulted from substance use disorders [6].

Comorbidities of Substance Use Disorders

Other risk factors that have been referred to as comorbidities in this literature include affective disorders, anxiety disorders, personality disorders, depression and pain (see table 3). In a paper entitled “Co-occurrence of substance use disorders and other mental disorders”, 69% of a sample in Spain (N=1783) were experiencing comorbid disorders [2]. Those using cocaine were also experiencing comorbid **affective disorders**. Those using cannabis were also experiencing **anxiety disorders**. Those with any type of substance use disorder were also experiencing **personality disorders**.

Table 3: Comorbidities of substance use disorders (and first authors).

Comorbidities	First Authors
Affective disorders, anxiety disorders, personality disorders	Fernandez-Miranda
Depression	Nkyi, Onaemo
Loneliness	Nkyi
Pain	Lysandrou

At least two other studies have noted **depression** to be comorbid with substance use disorders. In a sample of patients with substance use disorders from Ghana (N= 378), depression was comorbid with substance use disorders [17]. Both depression and substance use disorders, in turn, were comorbid with **loneliness**. The authors reported that no gender differences were noted in their sample which was surprising given that depression and loneliness are typically more prevalent in women.

In another study, substance use disorders and major depression were comorbid (N= 25,113 Canadians) [18]. In this sample, those with comorbid substance use disorders and major depression were 4 to 9 times more likely to experience disability. Given that this was a cross-sectional study, causal inferences could not be made.

Co-occurring **pain** and addiction have been noted in healthcare professionals with substance use disorders (N = 663) [19]. This sample of healthcare professionals had lower average pain intensity, but they were more vulnerable to pain-related disruptions in craving and abstinence self-efficacy. As these

authors noted, chronic pain is both an important antecedent and consequence of substance use disorders.

As for all these comorbidities with substance use disorders, directionality cannot be determined. Cross-sectional studies have the problem of not determining direction of effects. The pain may have led to the addiction and/ or the addiction could have led to the pain.

Potential Underlying Biological Mechanisms for Substance Use Disorders

Only a few papers on potential underlying biological mechanisms appeared in this literature on substance use disorders. They included one on low heart rate variability, one on aberrant EEG patterns and one on gene variants (see table 4).

Table 4: Potential underlying biological mechanisms for substance use disorders (first authors).

Mechanisms	First Authors
Low heart rate variability	Moon
Aberrant EEG patterns	Cavicchioli
Gene variants	Contella

Heart rate variability, otherwise known as vagal activity, is controlled by the vagus nerve, the largest nerve in the brain that has branches to the heart, the lungs and the digestive tract. In a review of 14 studies entitled “Heart rate variability in adults with substance use disorders”, heart rate variability was low [20]. The authors associated this with stress and craving experienced by those with substance use disorders.

Aberrant EEG patterns have been noted in individuals with substance use disorders [21]. These include augmented resting-state beta waves and reduced resting- state alpha and theta waves, which together suggest an aroused nervous system. The author referred to these patterns as aberrant neural activity mediated by complex genetic interactions.

Gene variants or permanent changes in the DNA sequence of a gene have also been noted in adults with substance use disorders [22]. These variants were identified as IDO-1, IDO-2, TDO and KMO, all known to be associated with tryptophan and the dopamine reward system that is stimulated by substance use. In this study, the cocaine using cohort had the most variants (13), followed by cannabis (11), opioids (3), and alcohol had the least number of variants (1).

Interventions for Substance Use Disorders

Only seven papers on interventions for substance use disorder appeared in this 2024 literature. They included two empirical studies, one review of different therapies, one review on ketamine and 3 papers on the gap in treatment and predictors of failures and successes in treatment (see table 5).

In an empirical study on dialectical behavior therapy, participants who were receiving methadone maintenance therapy (N=50) were randomly assigned to a group that continued to receive methadone maintenance alone (called the control group) and a group that received both **methadone maintenance and dialectical behavior therapy** [23]. The dialectical behavioral

therapy was comprised of twelve 90-minute sessions. The group that received both methadone maintenance and dialectical behavior therapy showed less risky decision making and better cognitive and executive function, as well as better attention, cognitive flexibility, problem solving and planning.

Table 5: Interventions for substance use disorders (and first authors).

Interventions	First Authors
Dialectical behavior therapy	Khezrian
Internet dialectical behavior therapy	Dharos
Ketamine	Tran
CBT, group, phone/internet, mindfulness, acceptance & commitment	Mendez
Gap in substance use disorder treatment	Sahker
Pain predicts dropout from treatment	Farrior
Sex differences in variables affecting short-term success	Desei

The second empirical study was entitled “Feasibility, acceptability and potential efficacy of a self-guided **Internet-delivered dialectical behavior therapy** intervention for substance use disorders” [24]. In this sample (N= 72 adults with substance use disorders), 94% started the internet dialectical behavior therapy but only 50% were still active 4 weeks later. At four weeks there was less substance use and at 12 weeks there was less depression, anxiety, suicidal behavior, emotional dysregulation and functional disability. Given the apparent efficacy of dialectical behavior therapy at least in these small samples, it’s surprising that it didn’t meet the criteria for the following review.

In a review of 37 psychotherapy trials for substance use disorders, **cognitive behavioral therapy** appeared in the majority of the trials (11) [25]. The other therapies included **group therapy** (9 trials), **phone/internet** (6), **mindfulness** (5), **primary care** (4) and **acceptance and commitment** (2). Several novel therapies were also included, suggesting that multiple therapies are still being assessed for their efficacy in treating substance use disorders. The many different types of substance use disorders (at least 10 plus others not yet researched) and poly use highlights the need for different types of interventions.

Ketamine has also been effective for substance use disorders, as it has been for depressive disorders. In a review of the literature on substance use disorders published between 2018 and 2023, two systematic reviews were found and one randomized controlled trial on the use of ketamine for the treatment of patients with alcohol use disorder, cocaine use disorder and opioid use disorder [26]. Evidence from the two systematic reviews suggested that a combination of ketamine plus psychotherapy may be effective in reducing consumption of alcohol and cocaine use. Mixed effects were noted for the effects of ketamine on withdrawal and craving. Only mild and transient adverse side effects were noted including dissociative effects (e.g. distorted perceptions).

Despite the efficacy of these therapies, the National Survey on Drug Use and Health (N = 12,111) revealed that only 13% of those with substance use disorders were receiving treatment,

suggesting a **treatment gap in the U.S.** [1]. According to this survey, Asian Americans were less likely to be receiving treatment and those attending general mental health services were more likely to be receiving treatment.

These data also raised questions about **reasons for attrition**. In a study entitled “Pain predicts dropout from substance use treatment” (N= 1095 adults in residential treatment), **greater pain intensity** was the most significant predictor of dropout [27]. In another study entitled “**Sex differences in variables affecting short-term success of treatment** for substance use disorder (N = 1039 patients), longer length of stay led to treatment failure for both females and males [28]. However, gender differences were noted on other predictor variables. For females, goal-directed thinking predicted success while taking unnecessary risks, having detailed suicide plans and constricted thinking led to failure. For males, prior arrest for driving under the influence, presence of phobias, paranoid ideas and delusions led to failure. Surprisingly, no predictors for success were noted for males.

Methodological Limitations of this Literature

Methodological limitations can be noted for this 2024 literature on substance use disorders. This literature primarily included systematic reviews and meta-analyses as very few empirical studies were published at this time. This could have resulted from significant research having already been conducted on substance use disorders that was now being reviewed. Although research, for example, on ketamine as a potential therapy for substance use disorders has been rare and still is rare. In several of the meta-analyses, different types of substance use disorders were included even though several of the empirical studies reviewed here noted different effects and different risks for the different types of substance use disorders. This would suggest that combining the different disorders may have resulted in the low effect sizes and inconclusive data reported for some of the meta-analyses.

In the case of the empirical studies reviewed here, most were cross-sectional as opposed to being longitudinal, so that inferences could not be made about directionality or causality. Some variables have been referred to as risk factors, negative effects, mediators or comorbidities by different researchers, suggesting that they may be bi-directional, for example depression and substance use disorders.

Most of the studies were focused on single variables rather than multiple variables, making it difficult to determine the relative significance of the risk factors or the severity of the negative effects. In the few multi-variable studies that appeared in this literature, for example on risk factors, the risk factors were not entered into regressions or structural equation modeling to determine their relative contributions to the substance use disorders. The severity of the different disorders and the degree to which they contributed to the negative effects were also not determined.

Comorbidities, for example depression, that are often comorbid with substance use disorders were rarely considered. The rarity of potential underlying mechanism and intervention studies papers was also a limitation of this literature. The rarity of this research may relate to the low treatment prevalence (13%) and therefore the limited availability of research participants.

In those studies that involved comparison groups, the samples were often unequal sizes which is a statistical problem that limits the power of the data analyses. The absence of active control groups in the therapy studies is problematic as having passive control groups leads to inconclusive findings. Typically, any intervention is more effective than no intervention. Surprisingly, waitlist control groups were not used. And, surprisingly, only one of the reviews on intervention studies focused on medications, e.g. ketamine, even though medications are reputedly being increasingly used for treating adults with substance use disorders. Some of the intervention researchers reported positive effects on emotions and cognition but little or no change in substance use.

Despite these methodological limitations, this current research on substance use disorders has been informative. The serious negative effects of substance use disorders on physical health, suicidality and violence highlight the need for more empirical studies on risk factors to identify those who need therapy.

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