Review

Adverse Childhood Experiences and Prescription Stimulant Use in Adults: A Systematic Review

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Adverse Childhood Experiences and Prescription Stimulant Use in Adults: A Systematic Review

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Abstract: Nonmedical prescription stimulant use (NPSU) is an ongoing public health crisis in the United States. There exists, however, a dearth of research investigating specific childhood risk factors that may contribute to this illicit use. Adverse childhood experiences (ACEs) may be a significant risk factor to address in the prevention and treatment of NPSU, as research has provided evidence for increased substance use, potentially including prescription stimulant misuse, among individuals who have experienced trauma. A systematic review of the literature was conducted to gather and synthesize research articles specifically examining the relationship between nonmedical prescription stimulant use in adults and the experience of adverse childhood experiences (ACEs). Four studies met all inclusion criteria and were included in the review. The results demonstrated that nonmedical use of prescription stimulants in adults is significantly associated with ACEs, with a higher numerical count of ACEs associated with a greater likelihood of nonmedical prescription stimulant use. Gaps in the literature were identified, specifically noting a lack of information available regarding the relationship between ACEs and NPSU within gender- and racially-diverse populations. The findings have implications for informing interventions related to ACEs and the misuse of prescription stimulant medication in adults.

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Introduction

Nonmedical Prescription Stimulant Use

Prescription stimulant medications, such as dextroamphetamine (e.g., Adderall) and lisdexamfetamine dimesylate (e.g., Vyvanse), are a safe and effective treatment for children and adults with attention-deficit/hyperactivity disorder (ADHD) when used as prescribed There are common dose-dependent side effects associated with stimulant medications, such as decreased appetite, weight loss, dehydration, difficulty sleeping, and anxiety [1]–[3]. When prescription stimulant medications are misused (i.e., illicitly used without a valid prescription or for reasons other than prescribed), more severe side effects have been observed. These include risky sexual behaviors, psychosis, suicidal ideation, and reliance on medication [4], [5]. Prescription stimulants have a potential for psychological and physiological dependence and are classified by the Drug Enforcement Administration (DEA) as Schedule II medications [6]. Despite the potential health and legal consequences, nonmedical prescription stimulant use (NPSU) remains an ongoing public health concern in the United States [5], [7], [8]. Young adults between the ages of 18 to 25 appear especially vulnerable to nonmedical prescription stimulant use, with prevalence estimates indicating that approximately 7-10% of individuals within this age bracket reported NPSU in 2021 [6]. NPSU is also particularly problematic across college campuses, with reported prevalence rates ranging from 14% to 34% among college students in the United States [7], [9], [10]. This illicit use seems to persist post-graduation, as Holt and McCarthy (2020), among others, have found that over 50% of young adults continued to misuse prescription stimulants after graduating from college [11]

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Given the increasing rates of NPSU across the United States, as well as the harmful effects associated with its illicit use, it is crucial to identify potential risk factors that can inform the development of effective prevention and intervention methods. Research has increasingly focused on examining how childhood factors influence the trajectories of substance use in adulthood. However, there is limited research specifically exploring childhood risk factors that may contribute to NPSU. Adverse childhood experiences may be a significant risk factor to consider. Research has substantiated that they are linked to increased substance use, potentially including NPSU [12]–[14].

Adverse Childhood Experiences

Adverse childhood experiences (ACEs) refer to potentially traumatic events that occur before the age of 18 that can have detrimental effects on an individual's health and well-being across the lifespan [12], [15]–[17]. Felitti and colleagues (1998) first operationalized ACEs as exposure to abuse (e.g., sexual, physical, emotional) and household dysfunction (e.g., substance use by a household member, household member with a mental illness, witnessing domestic violence, and familial incarceration). Other studies have also included additional ACEs, such as neglect (e.g., emotional and physical), parental separation, loss of family members and/or friends, longstanding financial hardship, and community violence [12], [15]–[17]. ACEs affect a large proportion of the adult population, with approximately 62% of adults reporting an experience of at least one ACE [6], [18]. It is well substantiated in the literature that ACEs are associated with detrimental health outcomes and adverse health risk behaviors [12], [15]–[17]. Physiological research has substantiated that exposure to ACEs can lead to toxic stress and persistent activation of the stress response system. This stress response can alter the nervous, endocrine, and immune systems, which adversely affects an individual's executive functioning, decision-making abilities, impulse control, brain reward systems, and emotion regulation throughout the lifespan [3], [12], [13]. Similarly, previous work has found that ACEs are significantly associated with emotion regulation difficulties in adulthood ((i.e., an individual's ability to effectively manage distressing emotions). In line with the self-medication hypothesis, adults with a history of ACEs may turn to illicit substances such as nonmedical prescription stimulants, to stimulate their mood and cope with their emotions (e.g., [19], [20]).

Extant literature has demonstrated a strong relationship between ACEs and illicit substance use [12], [15]–[17]. In fact, ACEs are among the most robust predictors of substance use in adulthood, and research has consistently found that ACEs are significantly associated with the initiation of illicit substance use at an early age [12], [15]–[17]. Additionally, recent studies have also shown a cumulative effect between ACEs and substance use. Specifically, as the number of ACE exposures increases, the risk of developing a substance use disorder also increases [17], [21]. Greater instances of ACEs were also found to be associated with an increased risk for more severe substance use, including earlier initiation of more dangerous illicit substances (e.g., injection of drugs) and increased rates of overdoses [13], [16], [22]. Despite the well-established associations between ACEs and substance use in adulthood, critical questions about the relationship between ACEs and the misuse of prescription stimulants in adults still exist.

The purpose of the present paper is to systematically review and summarize the literature within the past ten years regarding the association between nonmedical prescription stimulant use and ACEs among adult populations. The present review aims to (a) determine the percentage of studies on nonmedical prescription stimulant use that included an investigation of adverse childhood experiences (ACEs) and/or traumatic childhood events, (b) explore the specific association between ACEs and nonmedical prescription stimulant use among adults populations, (c) identify trends of ACEs experienced by adults who misuse prescription stimulant medications, (d) differentiate between specific prescription stimulant medications commonly misused by adults with a history of ACE(s), and (e) determine the prevalence of demographic factors such as age, sex, gender, and race/ethnicity that may be linked to ACEs and prescription stimulant use in adults.

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Methods

Search and Retrieval

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a systematic review of the literature was conducted to examine the association between nonmedical prescription stimulant misuse and ACEs among adults [23]. PRISMA is an evidence-based framework and is designed to facilitate a comprehensive search of databases using specific keywords and search terms, screening articles following review of the title, abstract, and full-text [23]. Consistent with previous research, nonmedical prescription stimulant use (NPSU) was operationalized as the use of prescription stimulants without a valid prescription or for reasons other than prescribed (e.g., more frequent use, using higher doses, combining with other illicit substances, and/or for nonmedical purposes. Furthermore, Adverse Childhood Experiences (ACEs) were operationalized as any traumatic event that occurred before the age of 18, encompassing abuse (e.g., sexual, physical, emotional), neglect (e.g., physical, emotional), and/or household dysfunction (e.g., a household member with mental illness, witnessing domestic violence, divorce, familial incarceration) [21]).

All researchers were trained in the systematic review study protocol before article and data retrieval. A combination of the following keywords were searched within the bibliographic databases PubMed and PsycINFO: *nonmedical prescription stimulant use* AND *Adverse Childhood Experiences (ACEs); nonmedical prescription stimulant use* AND *early trauma; prescription stimulant use* AND *Adverse Childhood Experiences (ACEs); nonmedical prescription stimulant use* AND *Adverse Childhood Experiences (ACEs)* AND *trauma* AND *Methylphenidate* OR *Amphetamines/Dextroamphetamine* OR *Lisdexamfetamine* OR *Vyvanse* OR *Adderall.* The search included articles that were published between January 1, 2013, and May 1, 2023.

Eligibility criteria

Inclusion Criteria

1. The study investigated the relationship between nonmedical prescription stimulant use and ACEs.
2. The study included only adult participants.
3. The sample size of the study was n > 1.
4. The study was published in the last 10 years.
5. The study was originally published in English.
6. The study used an original or secondary dataset.
7. The study was published in a peer-reviewed journal.

Exclusion Criteria

1. The study did not explicitly identify nonmedical prescription stimulant misuse.
2. The study did not explicitly examine the relationship between ACEs and nonmedical prescription stimulant use.
3. The study did not include ACEs and prescription stimulants use, or misuse was investigated in non-adult samples (i.e., child and adolescent samples).
4. Meta-analyses, systematic reviews, protocols for future research, and case studies were excluded.
5. Studies were not published in English.
6. Studies were not published in a peer-reviewed journal.

Data Extraction

The studies included in the review were reviewed and information relevant to study goals was extracted and compiled into one table (i.e., see Table 1). The following information was extracted

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from each article: sample size and description, specific ACEs and prescription stimulant medications studied, and sample demographics (i.e., age, gender, and race/ethnicity).

Table 1.
Summary of Included Articles

Article	Sample	ACEs	Stimulant	Age (M)	Gender	Race/ethnicity
Fairman et al., 2021	N = 3,418 college students	Parental mental health & substance use; Sexual, physical, & emotional abuse; Maltreatment	Adderall, Vyvanse, Ritalin, Concerta	20.72	54.8% Female	White: 82% Nonwhite: 18% **Partial**
Forster et al., 2018	N = 2953 college students	Household substance use; Domestic violence; Verbal, physical, & sexual abuse	Ritalin & Adderall	21.34	73% Female	Hispanic: 37% White: 33%; Black: 4% Asian Pacific Islander:15% Multiracial 7% Other: 4% **Full**
Pakdaman et al., 2022	N = 3,899 college students	Parental substance use & mental health; Verbal, physical, & sexual abuse; Homelessness	Adderall	24.55	69.9% Female	Hispanic: 55% White 27.9% Asian & Pacific Islander:16% **Full**
Tang et al., 2020	N = 36,309 adults	Household: substance use, mental illness, incarceration, domestic violence, parental separation or divorce; Verbal, physical, emotional, & sexual abuse	Stimulant	N/A	N/A	N/A

Results

Study Selection

A total of 398 articles were identified via the bibliographic databases PubMed and PsycINFO. After systematic reviews, meta-analyses, and articles not published in English were excluded, the remaining (N = 165) articles were screened based on title and abstract review. Remaining articles (N = 36) then underwent a full-text review. The full-text review resulted in four final studies that met eligibility criteria and were included in the systematic review. See Figure 1 for more detail.

Summary of Included Articles

Review of NPSU and ACEs

Regarding the first research aim of identifying the percentage of studies on nonmedical prescription stimulant use that also examined ACEs, findings revealed that only four studies in the last 10 years specifically investigated the relationship between nonmedical prescription stimulant use in adulthood and ACEs, representing approximately 1.01% of all studies yielded by the search criteria. The sample sizes of the four studies ranged from 219 to 36,309. Combined, the studies yielded 46,579 total participants.

Adverse Childhood Experiences

Regarding the aim to explore the specific associations between ACEs and nonmedical prescription stimulant use among adults, findings revealed that all four studies demonstrated a significant, positive relationship between ACEs and nonmedical prescription stimulant use in adulthood. Regarding the specific aim of exploring how ACEs were operationalized in each study and the identification of any trends and/or patterns regarding specific ACEs and nonmedical prescription stimulant use, results revealed that ACEs were similarly defined in all four of the included studies. Each study included sexual, physical, and emotional abuse in their operationalization of ACEs. There were common trends observed across some of the studies. For example, Pakdaman et al. (2022) and Fairman et al. (2021) included parental substance use and

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parental mental health in their operationalization of ACEs, while Tang et al. (2020) and Forster et al. (2018) extended this definition to include household substance use and mental illness, as well as witnessing and/or experiencing domestic violence. Tang et al. (2020) also included household incarceration and parental separation or divorce. Finally, Pakdaman et al. (2022) was the only study that specifically included housing insecurity as an ACE. Regarding specific trends and/or patterns regarding specific ACEs and nonmedical prescription stimulant use, findings from each study similarly revealed that each form of abuse (e.g., sexual, physical, and emotional), as well as each cluster of adverse events (e.g., household dysfunction), was significantly associated with NPSU. Across the four studies, childhood emotional abuse, divorce, and parental substance use were the most common ACEs associated with nonmedical prescription stimulant use.

Prescription stimulant medications and ACEs

Further, regarding the third research aim which aimed to differentiate between specific prescription stimulant medications commonly misused by adults with a history of ACEs, findings revealed that none of the included studies delineated between different prescription stimulant medications and ACEs. From the narrowest perspective, Pakdaman and colleagues (2022) investigated the relationship specifically between only Adderall and ACEs, with no other prescription stimulant medications included in analyses. Forester et al (2018), on the other hand, studied the relationship between nonmedical use of Ritalin and/or Adderall with ACEs. No distinction was made between the two medications and other stimulant medications were not included for analysis. Similarly, Fairman et al (2021) combined the misuse of Adderall, Vyvanse, Ritalin, and Concerta into one prescription stimulant variable, and studied the relationship between the misuse of any of these medications with ACEs. Even more broadly, Tang et al (2020) did not specifically delineate the independent associations of prescription stimulant medications and ACEs, instead comparing the misuse of any prescription stimulant medication with no history of misuse.

Summary of Demographic Findings: Age, Gender, Race, Specific Populations

The final aim of the review sought to describe the incorporation and reporting of demographic factors (e.g., age, sex, gender, ethnicity) across each study. Regarding age, differences were seen across studies, however it was generally found that age was limited to young adulthood. Three studies investigated the relationship between nonmedical prescription stimulant use and ACEs among college student populations. Tang and colleagues (2018), however, investigated NPSU and ACEs among a nationally representative sample of the non-institutionalized adult population 18 years old or older in the United States. While Tang and colleagues (2021) omitted age apart from specifying that participants were all over the age of 18, the average participant age of the remaining three studies was approximately 22 years old. Furthermore, concerning gender, a majority of the studies (n = 3) reported having a predominantly female sample [17], [22], [24]. All three of these studies reported gender according to a biological binary, with no inclusion of other gender identities. The fourth study did not include any data on the distribution of genders within the sample [21]

In line with recent literature, only studies reporting the distribution of *at least* three different racial groups were considered to have fully reported racial demographics, and studies that only reported one or two races were considered to have partially reported racial demographics. Two studies fully reported racial demographics [17], [22], [24] (e.g., Forster et al., 2018 & Pakdaman et al., 2021). Specifically, Pakdaman et al. (2021) noted that 55% of their sample identified as Hispanic, 27.9% as White, and 17% as Asian Pacific Islander. Additionally, Forster et al. (2018) reported that 37% of their sample identified as Hispanic, 33% as White, 15% as Asian Pacific Islander, 7% as Biracial, 4% as Black, and 4% as Other. Partial reporting of demographic information was evident by Fairman et al. (2021). Race was dichotomized as Non-Hispanic White (82%) and Nonwhite (18%; Fairman et al., 2021). Lastly, Tang et al. (2021) omitted reporting on racial demographics.

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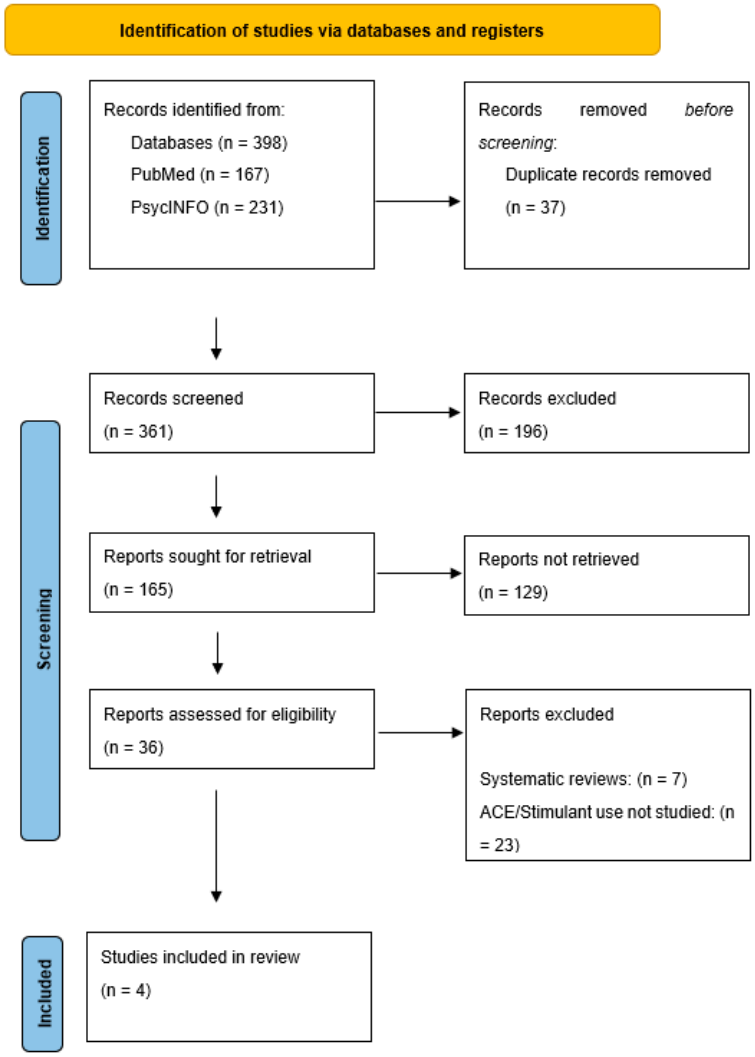

Figure 1. Flow diagram according to the PRISMA guidelines. *Note.* This flow diagram has been modeled after Page, M. J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi 10.1136/bmj.n7

Discussion

The purpose of the current paper was to systematically review and summarize the literature within the past ten years that investigated the relationship between NPSU and ACEs among adult populations. Specifically, the present review sought to (a) determine the percentage of studies on nonmedical prescription stimulant use that included an investigation of adverse childhood experiences (ACEs) and/or traumatic childhood events, (b) explore the specific association between ACEs and nonmedical prescription stimulant use among adults populations, (c) identify trends of ACEs experienced by adults who misuse prescription stimulant medications, (d) differentiate between specific prescription stimulant medications commonly misused by adults with a history of ACE(s), and (e) determine the prevalence of demographic factors such as age, sex, gender, and race/ethnicity that may be associated with increased risk of nonmedical prescription stimulant use.

Results revealed that, of the 398 articles centering on nonmedical prescription stimulant use conducted within the past decade (2013–2023), only 1.01% (N = 4) specifically investigated ACEs as a risk factor for NPSU. This finding underscores the need for future research to explore the complex association of NPSU and ACE, especially given that the studies reviewed indicated a significant relationship between ACEs and NPSU. All studies demonstrated that greater ACEs were associated with increased stimulant use and initiation of use at a younger age [17], [21], [22], [24]. These findings

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suggest the importance of prioritizing ACEs in health initiatives and interventions that are aimed at mitigating prescription stimulant misuse.

Furthermore, a majority of the studies did not explore the relationship between individual ACEs with the illicit use of different prescription stimulant medications. Most of the studies combined various stimulant medications into one prescription stimulant variable, while one study only investigated ACEs with the nonmedical use of one specific stimulant (e.g., Adderall). This approach limits the generalizability of results, given that prior literature has demonstrated both dose and medication-dependent effects of different stimulant medications. To adequately inform intervention and prevention programs, future research should investigate whether certain stimulants are more commonly misused among adults with ACEs, as well as to identify if ACEs have idiosyncratic effects with specific prescription stimulant medications.

Demographic differences (e.g., gender, race, age) were also an important consideration in the current study. The majority of the sample across articles was comprised by women [17], [21], [22], [24]. The inclusion of a primarily female sample is concerning given the robust evidence in the literature suggesting that men are more likely to misuse prescription stimulant medication compared to women [25]. Another concern that arose among the studies included in the systematic review was how gender was investigated and reported on. Of the 3 studies that reported gender demographics (e.g., [17], [22], [24]) each operationalized gender as a binary distribution of male and female participants. This is a critical oversight, as it excludes non-binary and genderqueer individuals from the investigation of ACEs and nonmedical prescription stimulant use. The exclusion of greater gender diversity is particularly concerning given the recent literature demonstrating that gender minority populations experience higher levels of ACEs and discrimination compared to their cisgender peers, as well as increased rates of comorbid substance and psychiatric disorders [26]. As such, future studies would greatly benefit from inclusion of gender-minority populations in the investigation of ACEs and nonmedical prescription stimulant use.

Overall, half of the included studies (n = 2) reported on 3 or more races (e.g., Forster et al., 2018; Pakdaman et al., 2021), while Fairman et al. (2021) investigated ACEs and stimulant use among a predominately white population. Given the disproportional rates of ACEs experienced by people of color, it is critical to include diverse populations when investigating the association of ACEs and nonmedical prescription stimulant use. For example, Pakdaman and colleagues (2018), who reported full racial demographic data, found that Asian Pacific Islanders (API) and Hispanics who experienced ACEs were significantly more likely to misuse prescription stimulants compared to White and Black participants with ACEs. This finding highlights the ongoing need for future research to include racially and culturally diverse populations in their investigation of ACEs and nonmedical prescription stimulant use. Concerningly, race was not included in any capacity in one of the four articles examining the relationship between NPSU and ACEs in the last decade [21].

Regarding age, three of the four included studies investigated ACEs and prescription stimulant use in college populations. Although these designs are reflective of the increased use of stimulants among younger adults, research has also shown that the use of illicit prescription medications in older adults is gradually increasing. Specifically, illicit prescription medication use is more prevalent in older Americans than in adults in any other country [27]. Thus, future studies should aim to recruit and include older adults (i.e., above aged 44) in their participant samples.

Conclusions

The nonmedical use of prescription stimulant medications is an ongoing public health concern across the United States. Despite the detrimental effects associated with illicit prescription stimulant use, there is a dearth of research that has investigated the risk factors that perpetuate this use. The current systematic review demonstrated that ACEs are significantly associated with nonmedical prescription stimulant misuse in a variety of adult populations and that greater ACEs were associated with increased stimulant use and initiation of use at an earlier age. These findings provide strong support for the integration of ACEs in intervention and prevention efforts aimed at decreasing illicit prescription stimulant use. These findings also underscore the importance of appropriate ACE

screening in psychiatric clinics, as well as the need for college students to have access to trauma-informed programs and resources on campus. Advancing comprehensive strategies to prevent ACEs and treating underlying trauma among those using stimulants holds great promise to reduce stimulant use and its health and social consequences in the United States.

Supplementary Materials: Table 1 (*Summary of Included Articles*) can be found following the presented manuscript, depicting a description of the sample of each study, as well as its definition of ACEs and stimulant medication. Figure 1 (*Flow diagram according to PRISMA guidelines*) can be found following the presented manuscript, depicting the flow of the synthesis of articles for use in the systematic review

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