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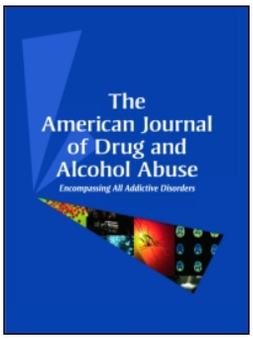

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ORIGINAL ARTICLE

Differential prevalence of Adverse Childhood Experiences (ACEs) by gender and substance used in individuals with cannabis, cocaine, opioid, and tobacco use disorders

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ABSTRACT

Background: Adverse childhood experiences (ACEs) show a graded association with the development of substance use disorders (SUDs) and engagement in risky substance use behaviors. Women are overrepresented among individuals with more severe childhood adversity (≥4 types of ACEs) and may be at particular risk for aberrant substance use.

Objectives: To assess the prevalence of ACEs among men and women with cannabis, opioid, cocaine, and tobacco use disorders.

Methods: Non-treatment-seeking individuals participating in clinical addiction research at a single site completed the ACE questionnaire and provided a detailed substance use history. Data were analyzed using proportional odds models and logistic regression.

Results: Most participants (424/565; 75%) reported at least one ACE, and more than one-quarter (156/565; 27%) reported severe childhood adversity. Relative to men ($n = 283$), women ($n = 282$) reported more ACEs (OR = 1.49; $p = .01$) and more experiences of emotional/physical abuse (OR = 1.52; $p = .02$), sexual abuse (OR = 4.08; $p = .04$), and neglect (OR = 2.30; $p < .01$). Participants in the cocaine (OR = 1.87; $n = .01$) and opioid (OR = 2.21; $p = .01$) use disorder, but not cannabis use disorder (OR = 1.46; $p = .08$), studies reported more severe adversity relative to the tobacco group. Relative to tobacco users, emotional/physical abuse (OR = 1.92; $p = .02$) and neglect (OR = 2.46; $p = .01$) scores were higher in cocaine users and household dysfunction scores were higher in opioid users (OR = 2.67; $p = .01$).

Conclusion: The prevalence of ACEs differs with respect to both participant gender and primary substance used. Novel SUD treatment strategies that incorporate ACEs may be uniquely beneficial in specific subpopulations of people with SUDs.

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Adverse childhood experiences; ACEs; substance use disorder; opioids; cocaine; cannabis

Introduction

Over half of adults in the United States (US) report having at least one adverse childhood experience (ACE) (1). ACEs constitute a broad array of experiences including parental divorce; problematic alcohol or drug use, mental illness, or suicide attempts in the home; family member incarceration; physical, sexual, or emotional abuse; and lack of emotional support or adequate food, clothing, or medical care (2). Beyond their acute negative impact in childhood, ACEs predispose individuals to physical and psychiatric diseases in adulthood, including the development of substance use disorders (SUDs) (2,3). These effects of ACEs are cumulative: exposure to multiple types of ACEs dose-dependently increases the odds of lifetime (4,5) or past-year (6) substance use, including cigarette smoking (4,7,8), and is positively correlated with odds of developing a SUD (9,10). The number of different types of ACEs a person has experienced also positively predicts the frequency of substance use (8) and likelihood of engaging in injection drug use (4,10,11). Critically, while the presence or absence of any ACE exposure does not predict outcomes in SUD treatment (12,13), evidence suggests that an individual's number of ACEs is associated with a greater risk of relapse following treatment for a SUD (14). As such, there may be a threshold number of ACEs past which there are greater clinical consequences.

Between 2015 and 2017, 16% of adults in 25 US states reported exposure to four or more types of ACEs, indicating "severe" childhood adversity, with women being

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overrepresented in this group (1,15). Women may therefore be at a greater relative risk for the development of SUDs and substance-associated consequences given the dose-dependent effects of ACEs. Supporting this hypothesis, Evans and colleagues (9) found that women were more likely than men to present with an SUD only if they had been exposed to at least three types of ACEs. Gender differences in the effects of ACEs have also been observed with respect to specific substance use behaviors. "Telescoping"—a shortened progression from substance use initiation to the development of a SUD, which is observed more commonly in women relative to men (16)—was found to be heightened in women with ACE exposure relative to women without ACE exposure and men with and without ACEs (17). In SUD treatment, two studies examining gender by ACE interactions found both lower likelihood of a successful tobacco quit attempt (18) and lower opioid treatment retention (13) in women that had been exposed to ACEs relative to women that had not, an effect not observed in men. Thus, the effects of ACEs both individually and cumulatively may be gender-specific.

Gender effects on the relationship between ACEs and substance use are deeply intertwined with the differential contribution of each unique type of ACE on outcomes. While childhood physical abuse is reported at a roughly equal rate across genders, childhood sexual abuse is more commonly reported by women relative to men (9,19–23). Concurrently, childhood sexual abuse shows a stronger relationship with problematic substance use relative to other kinds of abuse or neglect (23–25), in part due to its strong association with experiencing additional ACEs (19). Further evidence suggests that the association between different types of ACEs and substance use outcomes may be modified by gender: women have been shown to drive the relationship between childhood sexual abuse and SUDs overall (26,27) as well as tobacco use specifically (22,28). Epidemiological research also supports a gender-mediated relationship between exposure to abuse or neglect and the class of substance used by an individual (29,30) though gender effects have not been shown with ACEs related to household dysfunctions, such as parental suicide attempt (31). This gender-mediated association between ACE exposure and different forms of SUDs may in turn explain the relationship between ACEs and drug-related arrests or injection drug use. For example, Afifi and colleagues (29) reported increased odds of having a heroin use disorder in women, but not men, following physical abuse, and men, but not women, following sexual abuse when considering relevant sociodemographic characteristics and the potential contribution of comorbid psychiatric disorders.

Taken together, ACE exposure has a strong, graded impact on substance use behavior and its associated problems, including development of SUDs and incidence of drug-related arrests. While many studies have examined the individual contributions of cumulative ACE exposure, type of ACE experienced by an individual, and gender on SUDs, very few have examined these factors in combination or examined their prevalence across different addictive substances simultaneously. Furthermore, while large epidemiological studies are useful in describing populations of individuals with ACEs or SUDs generally, it is important to differentiate individuals who are specifically willing to engage with treatment and/or research to better tailor effective interventions for SUDs. The present study sought to examine the prevalence of ACEs among men and women presenting for clinical research in cannabis, opioid, cocaine, and tobacco use disorders, with the goal of informing future ACE- and gender-informed treatment approaches to SUDs.

Materials and methods

Study participants

Five hundred and sixty-five non-treatment-seeking adults with SUDs were recruited via media advertisement for four clinical studies, one per substance, at the Medical University of South Carolina. Results for two studies (tobacco: NCT01576874 and cocaine: NCT01573273) have been published previously (32–35), and two studies (cannabis: NCT03729869 and opioids: NCT03718065) are actively recruiting participants. Studies primarily sought to examine gender differences in SUDs, with additional aims focused on gender differences in response to pharmacological agents being evaluated for their impact on substance use. All studies assessed gender via self-report and biological sex (i.e., hormones, karyotype, etc.) was not assessed; all participants self-identified as men or women. Three of the four studies targeted an equal number of men and women for enrollment, while the tobacco study over-recruited women to assess the effects of menstrual cycle phase. Inclusion/exclusion criteria across studies were similar, but not identical. Participants were required to be at least 18 years old, report regular use of the primary substance of interest for a given study and/or meet DSM-IV or DSM-V criteria for disordered use (substance dependence or SUD, respectively), and report limited use of other substances other than caffeine or tobacco. Major medical illnesses, psychotic disorders, and bipolar I diagnoses were exclusionary in all studies. Women who were pregnant,

nursing, or were not using an effective means of birth control were excluded from all studies; three out of four studies also excluded women using hormonal birth control.

Procedures

Individuals interested in participating in any of the studies first completed a phone screening to preliminarily assess study-specific inclusion/exclusion criteria. If an individual was preliminarily eligible based on phone screening, an in-person screening visit was scheduled to determine study eligibility. During the in-person screening visit, following informed consent procedures, potential participants completed the ACE questionnaire (2). Items included in the questionnaire are listed in the supplementary material (Supplementary S1), as are the groups of items composing each ACE subtype (described below). Endorsement of each unique item on the questionnaire was associated with a 1-point increase in ACE score. Potential participants also provided a brief overview of their history with substance use (e.g., age of first use), and substance use for at least 2 months prior to screening was assessed using the Time Line Follow-Back (36). Individuals were compensated up to $100 for completing the screening visit. All study procedures were approved by the Medical University of South Carolina Institutional Review Board and were in accordance with the Declaration of Helsinki.

Statistical analyses

The study population characteristics are summarized using sample means, standard deviations (SDs), and percentages. Because ACE scores were highly skewed, scores were collapsed to form a three-level ordinal variable (no ACEs, 1–3 ACEs, ≥4 ACEs) with higher levels indicating more severe trauma. Four or more ACEs have been used as a cutoff for "severe" childhood adversity in other work examining health outcomes, including SUDs (1,15). A proportional odds model was used to examine adjusted associations between the ordinal ACE outcome, substance use, and gender. The model included substance as a four-category variable, with tobacco serving as the reference group. The model additionally controlled for three potential confounders: age, race (White, Black, other), and completed education (less than high school, high school, some college, four-year degree, or more). The proportional odds assumption was assessed using a score test (37). To examine effect modification between substance and gender, the model initially included an interaction between substance and gender; however, this was found to be non-significant and was excluded from the final model. Next, four adjusted logistic regression models were fit to assess associations between substance, gender, and any experience of four ACE subtypes: emotional/physical abuse, household dysfunction, sexual abuse, and neglect. These subtypes were derived from a three-factor model proposed by Ford and colleagues (38), modified to include additional ACE items pertaining to neglect. Supplemental descriptive analyses were used to examine differences in the endorsement of individual ACE items within each subtype by substance used and gender. Results from all models are reported in terms of adjusted odds ratios, 95% confidence intervals (CIs), and p-values. Hypothesis tests were conducted at the 0.05 significance level. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

The study characteristics are presented in Table 1. Of the 565 participants, most were White (59.3%) or Black (37.5%), never married (64.9%), employed full time (35.7%), and had at least a high-school education (87.7%). The mean age was 33.4 (SD = 10.0) years. Most participants were enrolled in the tobacco study (33.1%), followed by the cannabis (29.9%), cocaine (23.2%), and opioid (13.8%) studies. Participants in the tobacco study made up the greatest proportion of women (43.6% of total), whereas participants in the cannabis study made up the greatest proportion of men (35.3% of total). The average age when a participant first used the primary substance for a given study was 18.6 (SD = 5.7) years and participants used the primary substance 25.2 (SD = 7.2) days per month on average. Modest demographic differences were noted between substance use studies: specifically, participants in the tobacco and cannabis studies were, on average, younger than those in the cocaine and opioid studies (27.6 (SD = 7.5) vs. 40.8 (SD = 9.5) years), reported greater monthly substance use days (27.0 (SD = 3.4) vs. 19.8 (SD = 8.8) days), and reported less total years of use (9.3 (SD = 7.2) vs. 14.9 (SD = 8.8) years). Cannabis study participants were also more likely to be White, college educated, and employed full-time relative to opioid and cocaine study participants. Mean ACE scores by gender were 1.98 (SD = 1.88) for men and 2.59 (SD = 2.45) for women. Average ACE scores by substance were 1.98 (SD = 2.20) for tobacco, 2.33 (SD = 2.24) for cannabis, 2.39 (SD = 2.17) for cocaine, and 2.72 (SD = 2.14) for opioids.

Table 2 presents adjusted odds ratios (ORs) from the proportional odds model examining associations between the ordinal ACE variable, substance, and

Table 1. Study characteristics.

	Total sample (*n*=565)	Men (*n*=283)	Women (*n*=282)
Demographics			
Age (years), mean (SD)	33.42 (10.07)	34.01 (11.19)	32.82 (8.80)
Race, *n* (%)			
Black/African-American	211 (37.48)	110 (39.15)	101 (35.82)
White	334 (59.33)	161 (57.30)	173 (61.35)
Other	18 (3.20)	10 (3.56)	8 (2.84)
Ethnicity, *n* (%)			
Hispanic or Latino	22 (3.92)	11 (3.91)	11 (3.93)
Marital status, *n* (%)			
Married or living as married	88 (15.66)	40 (14.29)	48 (17.02)
Formerly married or separated	109 (19.40)	51 (18.21)	58 (20.57)
Never married	365 (64.95)	189 (67.50)	176 (62.41)
Education, *n* (%)			
Less than high school	69 (12.26)	34 (12.10)	35 (12.41)
High school	161 (28.60)	85 (30.25)	76 (26.95)
Some college or 2-year degree	236 (41.92)	116 (41.28)	120 (42.55)
4-year degree or more	97 (17.23)	46 (16.37)	51 (18.09)
Employment, *n* (%)			
Full-time	201 (35.70)	109 (38.79)	92 (32.62)
Part-time	79 (14.03)	42 (14.95)	37 (13.12)
Unemployed	193 (34.28)	93 (33.10)	100 (35.46)
Retired	61 (10.83)	20 (7.12)	41 (14.54)
Student	29 (5.15)	17 (6.05)	12 (4.26)
Substance use			
Primary substance used, *n* (%)			
Tobacco	187 (33.10)	64 (22.61)	123 (43.62)
Cannabis	169 (29.91)	100 (35.34)	69 (24.47)
Cocaine	131 (23.19)	75 (26.50)	56 (19.86)
Opioids	78 (13.81)	44 (15.55)	34 (12.06)
Age of first use (years), mean (SD)	18.57 (5.71)	18.76 (6.39)	18.38 (4.93)
Total years of use, mean (SD)	12.70 (8.24)	12.64 (8.62)	12.77 (7.84)
Use days/month, mean (SD)	25.21 (7.23)	24.35 (7.49)	26.08 (6.87)
Tobacco use, n (%)	379 (67.32)	171 (60.85)	208 (73.76)
Adverse childhood experiences (ACEs)			
Total score, mean (SD)	2.28 (2.20)	1.98 (1.88)	2.59 (2.45)
Number of adverse experiences, *n* (%)			
0	141 (24.96)	73 (25.80)	68 (24.11)
1–3	268 (47.43)	146 (51.59)	122 (43.26)
≥4	156 (27.61)	64 (22.61)	92 (32.62)
Type of adverse experience			
Emotional/physical	212 (37.59)	97 (34.28)	115 (40.93)
Household dysfunction	383 (67.79)	195 (68.90)	188 (66.67)
Sexual abuse	109 (19.36)	28 (9.93)	81 (28.83)
Neglect	135 (23.98)	50 (17.67)	85 (30.36)

Some variables missing up to 7 observations; percents are rounded and may not total to 100.

Table 2. Adjusted odds ratios and 95% confidence intervals (CI) from proportional odds model examining ordinal ACE score, substance use, and gender.

Variable	Odds ratio (CI)	*P*-Value
Substance		
Tobacco	REFERENCE	–
Cannabis	1.46 (0.95, 2.24)	.08
Cocaine	1.87 (1.13, 3.09)	.01
Opioids	2.21 (1.27, 3.86)	.01
Gender		
Men	REFERENCE	–
Women	1.49 (1.08, 2.06)	.01

Adjusted for age, race, and education. REFERENCE=reference category.

gender while adjusting for age, race, and education. Three observations (0.5%), all men, were excluded from the analysis due to missing covariates: one each from the opioid, cannabis, and cocaine studies. A score test indicated that the proportional odds assumption was met ($p = .17$). Next, we examined the odds of reporting more ACEs by primary substance used and gender. A 3-df Wald test showed a significant difference in ACE severity by substance used ($p = .02$). Specifically, participants in the cocaine and opioid studies were more likely to report more severe ACEs compared to participants in the tobacco study (cocaine OR = 1.87; 95% CI: 1.13, 3.09; $p = .01$; opioid OR = 2.21; 95% CI: 1.27, 3.86; $p = .01$). Women also had higher odds of reporting more severe ACEs relative to men (OR = 1.49; 95% CI: 1.08, 2.06; $p = .01$).

Table 3 presents adjusted ORs for the four ACE subtypes: emotional/physical abuse, household dysfunction, sexual abuse, and neglect. In terms of emotional/physical abuse, participants in the cocaine study had higher odds of reporting abuse than participants in the

Table 3. Adjusted odds ratios and 95% confidence intervals (CI) from logistic regression model examining ACE subtypes, substance use, and gender.

	Emotional/physical abuse		Household dysfunction		Sexual abuse		Neglect	
Variable	Odds ratio (CI)	*P*-value	Odds ratio (CI)	*P*-Value	Odds ratio (CI)	*P*-Value	Odds ratio (CI)	*P*-Value
Substance								
Tobacco	REFERENCE	–	REFERENCE	–	REFERENCE	–	REFERENCE	–
Cannabis	1.55 (0.95, 2.53)	.08	1.12 (0.68, 1.83)	.66	1.32 (0.73, 2.39)	.37	1.67 (0.96, 2.92)	.07
Cocaine	1.92 (1.10, 3.33)	.02	1.58 (0.89, 2.82)	.12	0.93 (0.47,1.87)	.85	2.46 (1.30, 4.65)	.01
Opioids	1.46 (0.79, 2.69)	.23	2.67 (1.30, 5.49)	.01	1.54 (0.74, 3.20)	.25	1.89 (0.95, 3.75)	.07
Gender								
Men	REFERENCE	–	REFERENCE	–	REFERENCE	–	REFERENCE	–
Women	1.52 (1.06, 2.17)	.02	0.93 (0.64, 1.35)	.69	4.08 (2.51, 6.66)	.04	2.30 (1.52, 3.49)	< .0001

Adjusted for age, race, and education. REFERENCE=reference category.

tobacco study (OR = 1.92; 95% CI: 1.10, 3.33; $p = .02$), and women had higher odds than men (OR = 1.52; 95% CI: 1.06, 2.17; $p = .02$). Primary opioid use was associated with higher odds of reporting household dysfunction compared to tobacco use (OR = 2.67; 95% CI: 1.30, 5.49; $p = .01$). Specifically, a greater proportion of opioid study participants endorsed items regarding divorce, familial alcohol and drug use, and mental illness/suicide attempts in the home relative to participants in other studies. Women had over four times higher odds of reporting sexual abuse compared to men (OR = 4.08; 95% CI: 2.51, 6.66; $p = .04$) without evidence of differences by primary substance used. Finally, the odds of neglect were higher among cocaine users (OR = 2.46; 95% CI: 1.30, 4.65; $p = .01$) and women (OR = 2.30; 95% CI: 1.52, 3.49; $p < .01$) compared to primary tobacco users and men, respectively. Specifically, women were more likely to endorse the subscale item "Did you often feel that no one in your family loved you or thought you were important or special, or your family didn't look out for each other, feel close to each other, or support each other?"

Discussion

Results from the present study suggest differences in the prevalence of ACEs by primary substance used and gender in individuals engaged in SUD research, without an interaction between variables. Women reported a higher number of ACEs relative to men and were more likely to report emotional or physical abuse, sexual abuse, and neglect, but not household dysfunction. Individuals enrolled in the cocaine and opioid, but not cannabis, studies were more likely to report severe ACEs relative to participants in the tobacco study, despite a higher proportion of women in the latter trial. Similarly, participants in the cocaine study were more likely to report emotional or physical abuse and neglect, and participants in the opioid trial were more likely to report household dysfunction, relative to the tobacco group. Taken together, these findings suggest that individuals with high levels of childhood adversity, particularly women, may be overrepresented in studies of SUDs and that this prevalence may differ by substance. As ACEs have previously been associated with worse outcomes in addiction treatment (13,18), the high prevalence of ACEs among individuals presenting for SUD research may influence outcomes in addiction clinical trials. As such, ACEs should be included as covariates in trial analyses and considered in the development of novel prevention strategies and treatments for SUDs.

Our results generally align with those obtained from larger epidemiological work. Most participants in our studies reported having experienced at least one ACE, and more participants had experienced four or more ACEs, indicating "severe" childhood adversity, than had experienced no ACEs at all. This is consistent with the notion that ACEs dose-dependently predispose individuals to SUDs (9,10). Similarly, women with SUDs were more often in the severe adversity group relative to men, consistent with previous work (9). While the average total number of years of substance use was fairly high in this sample for both genders assessed (approximately 13 years), it is possible that some of this overrepresentation of women with a high number of ACEs is due to telescoping in women who have experienced severe adversity (17). Women were also four times as likely as men to report having experienced sexual abuse, which has been associated with co-occurrence of other ACEs (19). Importantly, increased childhood trauma severity has been positively associated with both SUD severity and with the likelihood and intensity of relapse, particularly for women (14,39,40). Individuals who have experienced more ACEs may require more trauma-focused interventions or support both during and following completion of treatment in order to prevent relapse.

Similar to the gender findings, we observed a higher prevalence of ACEs in individuals enrolled in cocaine and opioid use disorder studies, but not cannabis use disorder study, relative to tobacco trial. Greater ACE exposure has been associated with reduced emotional regulation and specifically with an increase in rash behavior when experiencing negative emotions (negative urgency) (41). The lack of difference between cannabis and tobacco users may therefore be related to a comparable perceived risk profile between these substances. In contrast, individuals who have experienced severe childhood adversity may be more tolerant to the enhanced risk profiles inherent in obtaining and using cocaine or opioids, including risks associated with overdose, substance contamination, and injection as a route of administration. This hypothesis is consistent with previous work indicating a strong, graded relationship between ACEs and risky sexual behavior (4,42,43) and may relate to findings indicating a dose-dependent effect of ACEs on the likelihood of engaging in injection drug use (4,10,11). However, it cannot be discerned from the present study whether ACEs reduce aversion associated with perceived risk of a given behavior, including using certain substances, or if ACEs contribute to increased rewarding effects of opioids or cocaine specifically. Further mechanistic exploration into the association between ACEs and perceived risk/reward may be of value in developing treatment strategies for individuals with ACEs and SUDs.

With regard to specific associations between ACE subtypes and substance used, we observed increased household dysfunction in the opioid study and increased emotional/physical abuse and neglect in the cocaine study relative to the tobacco trial. No differences were observed between cannabis and tobacco users, in line with the comparable number of ACEs reported by these groups, nor were differences seen across substances for sexual abuse. Previous research indicates that childhood sexual abuse may increase incidence of SUDs nonspecifically (15), which may explain the latter finding. The association between household dysfunction and opioid, but not cocaine or cannabis use disorders, is consistent with prior research examining parental suicide attempt specifically (31). In contrast, elevated prevalence of emotional/physical abuse and neglect in participants with cocaine, but not other, use disorders is unique to this study. Notably, these ACE subtypes are also associated with aberrant alcohol use, including earlier initiation of use (15,30,39), and age of first alcohol use has been shown to predict age of first cocaine use (39). Additionally, given the high prevalence of cocaine and alcohol co-use (44), the cocaine study had the least stringent exclusion criteria pertaining to alcohol use, in that only the need for medically supervised detoxification was exclusionary. It is therefore possible that our cocaine results reflect a higher rate of alcohol co-use within our study population than in other work. Finally, in contrast to some (29,30), but not other (31), prior work, we did not observe an interaction between gender and ACE subtype on substance used. This may be the result of a sample size limitation, as those studies that did find significant outcomes were several orders of magnitude larger than the present work.

Other limitations of this study include a reliance on retrospective self-report and participant inclusion being limited to non-treatment SUD studies. Considered together, it is likely that the present study underestimates the prevalence of ACEs in the overall population of individuals with SUDs. Previous work indicates underreporting of ACEs when assessed retrospectively relative to prospective measures (45), and underreporting is especially pronounced with respect to childhood sexual abuse in men (46). Interestingly, however, it is retrospective – not prospective – reporting of ACEs that is associated with the prevalence of SUDs (47), suggesting individual perception of the experience may be what leads that person to subsequent substance use. Therefore, while ACEs may be underreported in this study, what has been reported may be a valuable proxy for an unknown latent variable. With respect to the sample used, exclusion of individuals with polysubstance use disorders or significant untreated psychiatric illnesses likely reduced the prevalence of ACEs relative to the overall population of individuals with SUDs. Indeed, ACEs have been shown to be dose-dependently associated with polysubstance use disorder (9) as well as schizophrenia, bipolar disorder, and major depression (48). The tobacco and cocaine studies also specifically excluded individuals with current post-traumatic stress disorder (PTSD). As PTSD may be a direct consequence of exposure to severe childhood adversity, excluding these individuals could potentially have impacted results for these studies. However, PTSD prevalence was low in the cannabis (5/169; 3%) and opioid (3/78; 4%) studies, and was equally distributed across genders, suggesting skew was likely marginal. Finally, individuals not seeking treatment for SUDs may differ in their experience of ACEs relative to treatment-seekers. A study of individuals seeking opioid detoxification reported a mean ACE score of 3.64 (49), compared to our observed score of 2.72 in participants with opioid use disorder. Number of ACEs may therefore be positively associated with a greater perceived need for SUD treatment; however, more research is needed to explore this potential correlation.

Taken together, results from the present study indicate an increased prevalence of ACEs in women and individuals with cocaine and opioid use disorders relative to other groups enrolled in clinical SUD research. Greater prevalence of ACEs may be associated with higher rates of substance-associated consequences observed in these groups (50). Given the high prevalence of ACEs and their differential impact on treatment outcomes (13,18), ACEs should be considered as an important covariate in SUD research. In addition, future research is needed to clarify the mechanism(s) through which ACEs impact SUD presentation, and interventions that target potential mechanisms, such as emotional dysregulation, deserve further evaluation for efficacy in SUD treatment (51). More attention must be given to ACEs in substance use treatment settings to counteract their negative impact on treatment outcomes, with special consideration given to those in most at-risk populations.

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Disclosure statement

KMG has provided consultation to Jazz Pharmaceuticals. The remaining authors report no relevant disclosures.

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