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REVIEW



Adverse childhood experiences and substance use among university students: a systematic review

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ABSTRACT

Objective: To perform a critical review of studies examining the relation between adverse childhood experiences (ACEs) and substance use (SU) among university students.

Methods: Observational studies reporting SU of university students for whom ACEs were assessed were identified using PubMed, CINAHL, PsycINFO & ERIC and Web of Science from January 1998 to September of 2021. The study protocol was registered with PROSPERO: CRD42021277882.

Results: Of 450 articles screened, 16 met inclusion criteria, including 53,433 university students with and without ACEs exposure from 17 countries. University students reporting ACEs had an increased risk of alcohol, tobacco, marijuana, prescription-medication, and illicit drug consumption compared to students not reporting ACEs. Having four or more ACEs heightened likelihood of SU. A dose–response relationship between ACEs and SU was reported for each substance. The relationship between ACE type and SU is presented.

Conclusions: University students with higher levels of ACEs have increased probability of SU. The relationship between ACEs and substance type varies, with ACEs having the greatest association with tobacco and illicit drug use. Findings underline that university students may benefit from ACE screening to help identify those at higher risk of SU and engage them in preventive or therapeutic strategies.

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Adverse childhood experiences; Substance-use; college students

Introduction

Substance use (SU), the use of alcohol or drugs, affects over 60% of the world's population (SAMSHA, 2019). SU can have long-term negative effects on life-trajectories in association with risky sexual behaviors, challenged relationships, and mental health decline (Stone et al., 2012). Further, SU can lead to substance use disorders (SUD), the continual use of a substance despite negative effects (Hasin et al., 2013), incurring grave societal, economic, and health costs (Rehm & Shield, 2019).

Emerging adulthood, characterized by rapid shifts into new social environments with less parental supervision and increased substance accessibility, is the population with the highest risk of SU and emerging SUDs (Arnett, 2005; Kessler et al., 2005). Attending college can exacerbate this risk, with 1 in 3 college students reporting recent binge drinking (Krieger et al., 2018). The brain is in a critical stage of development, increasing the severity of long-term consequences of SU (Arnett, 2005). As SU during emerging adulthood is correlated with academic, economic, social, and behavioral challenges, it is important to consider early risk factors (Welsh et al., 2019).

Early life experiences have been related to the risk of SU (Leza et al., 2021). Adverse traumatic or stressful events that occur before age 18, also named adverse childhood experiences (ACEs), are one such risk factor (Centers for Disease Control and Prevention, 2019). ACEs refer to the cumulative exposure

of childhood abuse, neglect, household dysfunction (e.g., parental divorce), and negative environmental experiences (e.g., bullying). Typically, as ACE exposure increases, so does the risk of negative health outcomes (Lee et al., 2021). Worldwide, studies have reported 22–87% of emerging adults have experienced at least one ACE, indicating a high prevalence (Park et al., 2021).

Despite the high prevalence of ACEs and their potential impact, there is limited knowledge of how ACEs influence SU among university students. Two reviews have been conducted on the association between ACEs and emerging adult health outcomes and reported that ACEs were associated with increased SU (Park et al., 2021; Rogers et al., 2022). However, results were not distinct by university students (Park et al., 2021; Rogers et al., 2022) or substance type (Park et al., 2021) thus limiting our understanding. All substances present with differing risk and protective factors (SAMSHA (Producer, 2018), requiring unique social-ecological approaches for prevention, treatment, and recovery. Thus, understanding the relation between ACEs and each specific substance type among university students can aid in identifying and offsetting negative developmental cascades related to SU with a more specified lens. To date, no review has synthesized the available evidence of the relation between ACEs and SU nor the relation between ACEs and substance type among university students specifically. Thus, we performed a systematic review to fill these gaps.

Methods

This systematic review was registered with the PROSPERO International prospective register of systematic reviews (CRD42021277882) and was conducted using an a-priori protocol following PRISMA guidelines (Shamseer et al., 2015).

Eligibility criteria

All studies had to meet the following inclusion criteria: (1) included data about ACE exposure, (2) SU during university attendance, (3) participants with a mean age of 18–30 years, and (4) self-reported or clinical SU outcome. There were no geographical restrictions, and filters for the search included limiting articles to human studies, 18 years or older, and the English language.

Search strategy

A literature search was conducted for studies of SU among university students with a mean age of 18–30 years and ACEs by searching the following electronic databases: CINAHL, PubMed, PsycINFO & ERIC, and Web of Science. The original CDC-Kaiser ACE study was published in 1998, thus the search included published articles starting January 1998 through September 2021 (Felitti et al., 1998). Systematic reviews and meta-analyses were excluded. The final search was run on September 17th, 2021. Relevant studies were identified by the following search terms: (1) adverse childhood experiences, (2) substance use, and (3) university or college students. Medical Subject Headings terms were utilized to increase sensitivity of the search. After removing duplicates, studies were selected by the first author from titles, abstracts, and full texts. Lastly, reference lists of full-text studies were reviewed.

Data extraction

A standardized data extraction excel chart was utilized to provide the following information when available: author, year of publication, study design, country, sample size, mean age of participant, types of ACE exposure, prevalence of ACEs, ACE measurement instrument, mediators, moderators, SU outcomes, and SU instrument.

Quality assessment

The checklist published by the US National Heart, Lung and Blood Institute for observational cohort and cross-sectional studies was used to assess the risk of bias in included studies (National Heart Lung and Blood Institute (Producer), 2019). All studies were assessed by the first author, with the second author reviewing a subsample that resulted in an overall agreement of Cohen's κ equaling 0.87. Disagreements were discussed between the first two authors to reach consensus. The checklist had 14 questions assessing internal validity, of which a final quality rating of good, fair, or poor was given. Articles were excluded if the quality was rated as poor (≤ 4 of the 14 criteria met).

Results

Study selection

Overall, 450 references were found by the algorithms. After removal of 49 duplicates, 401 articles were available for screening. Title and abstract review removed 371 articles and after full-text review, 13 articles were further removed. Methodological quality assessment led to the exclusion of one article that was rated as poor (Brajović et al., 2019). As a result, 16 studies were included (Figure 1).

There were two instances where multiple reports were published on the same cohort with the same outcome variables (Forster et al., 2018, 2019; Kameg et al., 2020; Kameg & Mitchell, 2021). In these cases, only one study per primary outcome was included per cohort to avoid bias by summarizing the same participant more than once. The publication with the highest number of cases for primary outcomes was included (Forster et al., 2019; Kameg et al., 2020).

Study characteristics

Details regarding characteristics of eligible studies are summarized in Tables 1–2. The 16 studies included in total 53,433 university students from 17 countries, whose mean age ranged from 18 to 25. Sample sizes ranged from 292 to 16,370 university students. Over half of the studies were conducted in the United States or Canada ($n = 9$), followed by Africa ($n = 4$), Europe ($n = 2$) and Asia ($n = 1$). Studies were all cross-sectional, with exception to one cohort study (2 years, 6 waves of data) that reported ACEs and SU with just one wave of data for analyses (Windle et al., 2018). All included studies were published in the last 5 years (2015–2021).

ACE instruments, approach, and prevalence

Retrospective self-report measures that asked about early life adversities occurring before 18 years of age, identified ACE exposure (Table 1). The most common instrument utilized was the ACE Questionnaire ($n = 8$), originating from the landmark CDC-Kaiser Permanente study (Felitti et al., 1998). The ACE International Questionnaire ($n = 5$) was also frequently used (World Health Organization, 2012).

ACE instruments captured 5 to 12 ACEs, with a larger focus on exposure to child abuse, neglect, and household dysfunction, and smaller emphasis on the social environment. The most commonly assessed ACE was sexual abuse ($n = 16$), followed by emotional abuse ($n = 15$), physical abuse ($n = 15$), household violence ($n = 14$), parental substance use ($n = 14$), parental mental health ($n = 12$), emotional neglect ($n = 10$), incarceration ($n = 9$), community violence ($n = 9$), physical neglect ($n = 9$), divorce ($n = 7$), homelessness ($n = 1$), financial problems ($n = 1$), bullying ($n = 1$), and caregiver absence ($n = 1$; Table 1). The majority of studies used a cumulative ACE score ($n = 15$), while fewer studies examined the individual ACE type ($n = 7$). The prevalence of having at least 1 ACE ranged from 17.5% to 76.2% and having four or more ACEs ranged from 0.3% to 24.6%.

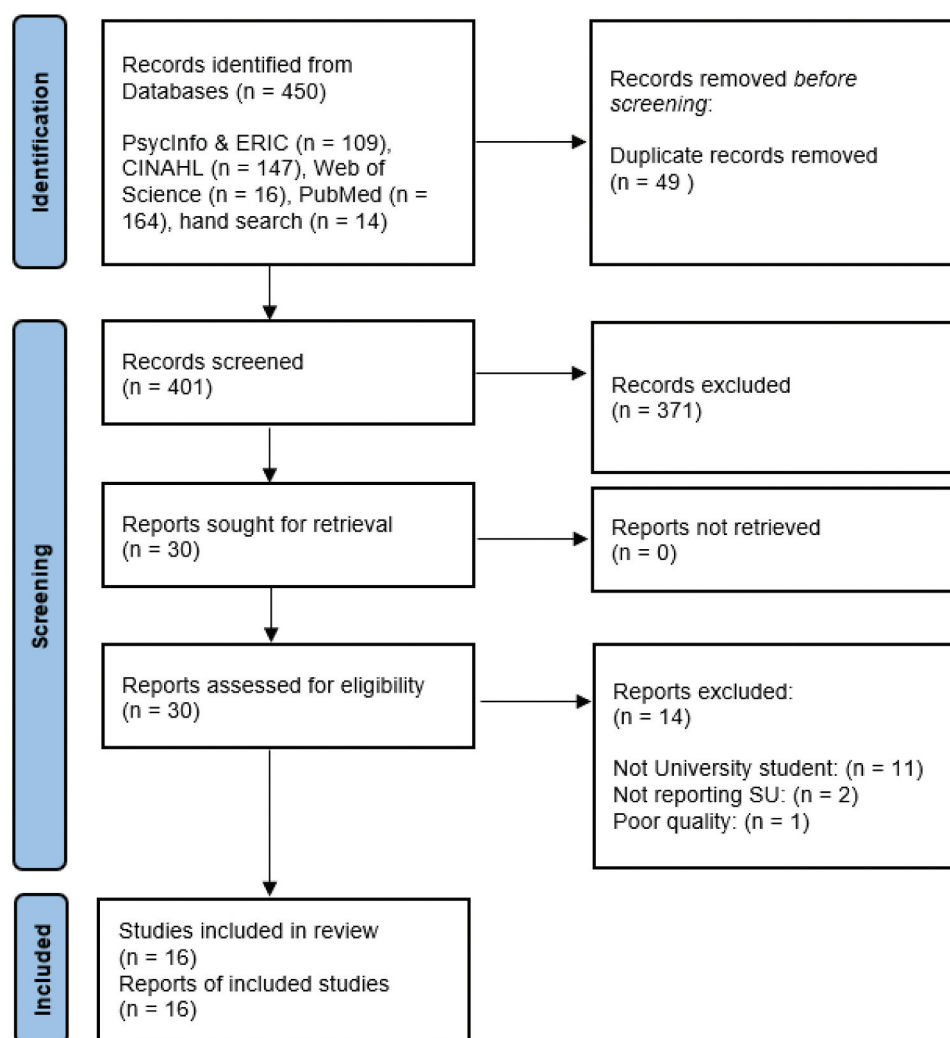


Figure 1. PRISMA flow diagram of literature search.

Substance use

Studies with former references to substance abuse or alcoholism are referred to as problem SU, risky SU, SUD or the appropriate reference term to reduce the use of stigmatizing and outdated terminology (Grigsby, 2021). Among cross-sectional studies, problem SU was utilized to distinguish the negative consequences of SU, whereas risky SU referred to studies investigating the frequency and quantity of SU (Grigsby, 2021). Some studies investigated multiple types of SU outcomes; however, results are presented by substance type for clarification of the relationship between ACEs and specific SU. The most commonly assessed substance was alcohol ($n = 11$), followed by tobacco ($n = 7$), illicit drugs ($n = 7$), marijuana ($n = 2$), and prescription drug misuse ($n = 2$). Due to large heterogeneity, it was not possible to perform a meta-analysis; however, we have provided a graphical description of the association between four or more ACEs and SU (Figure 2).

Alcohol use

Studies used retrospective survey questions about recent alcohol consumption ($n = 7$) or validated measures, such as the

Alcohol Use Disorder Identification Test-Consumption (AUDIT-C; $n = 3$), the Brief Young Adult Alcohol Consequences Questionnaire/Daily Drinking Questionnaire ($n = 1$), and Health Appraisal Questionnaire ($n = 1$); (Table 1).

Most studies found that ACEs were associated with current risky (Brett et al., 2018; Forster et al., 2019; Windle et al., 2018) or problem alcohol use (Hughes et al., 2019; Kameg & Mitchell, 2021; Schafer, 2021; Wiehn et al., 2018). The association between ACEs and risky alcohol use was not supported in one study (Krinner et al., 2020). Students with four or more ACEs were more likely to report lifetime problem alcohol use (Hughes et al., 2019), potentially have alcohol use disorder (Kim, 2017), and report early alcohol initiation (Hughes et al., 2019) (Figure 2). The relationship between ACE type and alcohol outcomes varied, with parental SU, sexual abuse, and physical abuse appearing to be more frequently associated with statistically significant relationships (Table 3).

Three studies assessed the risk of binge drinking. Four or more ACEs were associated with past 2-week binge drinking (Grigsby et al., 2020) (Figure 2). Not all ACE types were significantly associated with binge drinking (Table 3), however, sexual abuse had the strongest relations in two studies (Forster et al., 2019; Zhang et al., 2020).

Table 1. Descriptive characteristics.

Study and Country	Types ACEs	ACE instrument/ cumulative or individual ACEs	Prevalence (%)		Male (%)	Mean Age (SD)	Outcome/Measure
			1 ACE	4 + ACE			
Brett et al., 2018, USA	EA, PA, SA, EN, VH, SU, MH, IN	ACES-SF/ cumulative	19.2	8.4	385	20.09 (3.01)	Alcohol consumption and consequences/ Daily Drinking Questionnaire.
El Mhamdi et al., 2018, Tunisia	VC, PN, EN, PA, SA, EA, PR, CV	ACE-IQ/ cumulative and individual	76.2	NR	1200	22.00 (2.1)	Brief Young Adult Alcohol Consequences Questionnaire/ Current tobacco smoking/
El Mhamdi et al., 2017, Tunisia	VC, PN, EN, PA, SA, EA, PR, CV	ACE-IQ/ cumulative and individual	74.8	9.8	1200	22.00 (2.1)	Fagerstrom Test for Nicotine Dependence/ SU (tobacco, alcohol, and street drugs)/ Health Appraisal Questionnaire
Forster et al., 2019, USA	SU, EA, PA, VH, SA	Items from org. ACE/ cumulative and individual	45.0	NR	7148	22.27 (4.06)	Alcohol, marijuana, tobacco, binge drinking, illicit drugs, polysubstance/Survey
Grigsby et al., 2020, USA	EA, PA, SA, VH, IN, SU, MH	Items from org. ACE/ cumulative	51.7	8.62	16370	21.52 (2.83)	Recent tobacco smoking, binge drinking, and e-cigarette use/ Survey
Hughes et al., 2019, Europe	PA, EA, SA, DIV, VH, MH, SU, IN	Family health questionnaire/ cumulative	46.2	5.6	14661	18–25	Early alcohol initiation, problematic alcohol use, smoking, drug use/ Survey
Kameg et al., 2020, USA	PA, EA, SA, EN, PN, MH, SU, IN, DIV, VH	Org. ACE/ cumulative	56.2	NR	616	18–21	Risky alcohol use and risky drug use/ AUDIT-C; DAST-10
Kim, 2017, South Korea	PA, EA, SA, EN, PN, MH, SU, IN, DIV, VC, BU	ACE-IQ/ cumulative and individual	49.9	7.8	939	21.83 (NR)	Alcohol use disorder (problem alcohol use and potential alcohol use disorder)/ AUDIT-K
Krinner et al., 2020, USA	PN, PA, EN, EA, SA, SU, MH, VH	ACE-IQ/ cumulative	NR	NR	568	21.00 (NR)	Risky alcohol use/Survey
Onu et al., 2021, Nigeria	PA, SA, EA, EN, PN, SU, MH, VH, DIV, IN	Org. ACE/cumulative	NR	NR	301	22.60 (NR)	Risky tramadol use/ Tramadol Abuse Scale
Pakdaman et al., 2021, USA	SU, MH, PA, EA, HOM, SA	Org. ACE/cumulative	17.5	9.1	3899	24.55 (7.65)	Risky prescription use (opiates, antidepressants, sedatives, and stimulants)/ Survey
Ramakrishnan et al., 2019, Canada	EA, PA, SA, MH, VH, DIV, IN, SU, EN, PN	Org. ACE/ cumulative	NR	NR	292	18.85(2.23)	Substance use disorder (excluding alcohol and tobacco)/DAST-10
Schafer, 2021, USA	SA, MH, VH, SU	CPICS/ cumulative and individual	24.0	0.3	795	18.56 (0.51)	Risky alcohol use/ Survey
Wiehn et al., 2018, Germany	EA, PA, SA, MH, VH, DIV, IN, SU, EN, PN, FP, CA, BU	ACE-IQ/ cumulative and individual	22.9	24.6	1466	24.09 (4.49)	Risky alcohol use, tobacco use, illegal drugs/ AUDIT-C; Survey
Windle et al., 2018, USA	PA, EA, SA, EN, PN, DIV, MH, SU, IN, VH	Org. ACE/cumulative	21.3	12.4	2969	18–25	Alcohol, tobacco, marijuana/ Survey
Zhang et al., 2020, Zambia	PA, EA, SU, SA, VH	Org. ACE/ individual	27.6	NR	624	22.90 (2.2)	Tobacco, binge drinking, and illicit drug/ Survey

Abbreviations: EU = European Union; USA = United States of America; PN = physical neglect; EN = emotional neglect; PA = physical abuse; EA = emotional abuse; SA = sexual abuse; SU = household or parental SU; MH = household or parental mental health; IN = incarceration; CV = collective violence; VH = violence household; VC = violence community; DIV = divorce; BU = bullying; HOM = homelessness; FP = financial problems; CA = caregiver absence; PR = parental/caregiver relationship; PS = parental separation/divorce; PD = parental death; NR = not reported; The Adverse Childhood Experiences Questionnaire– Short Form = ACES-SF; Adverse Childhood Experiences–International Questionnaire = ACE-IQ; Children's Perception of Interparental Conflict Scale = CPICS; Original ACE Scale = Org. ACE; Drug Abuse Screening Tool = DAST-10; AUDIT = Alcohol Use Disorder Identification Test Consumption

Table 2. Mediators, moderators, and SU outcomes.

Study	Mediators/Moderators	Covariates in Adjusted Models	Substance Type	Main Findings (related to SU)
Brett et al., 2018	Mindfulness	Sex and age	Alcohol	-Higher ACE score and lower levels of mindfulness predict risky alcohol use. -Mindfulness mediates the relationship between ACEs and problem alcohol use.
El Mhamdi et al., 2018	Gender	Anxiety, depression, and intrafamilial ELA	Tobacco	-Prevalence of current smoking is higher among emerging adults who report early life adversities
El Mhamdi et al., 2017	Gender	Age, marital status, edu., and anxiety, depression	Tobacco, alcohol, and street drugs	-Students with ≥1 ACE had significantly higher odds of SU compared to counterparts without ACE exposure.
Forster et al., 2019	Ethnicity	Age, sex, state, and depressive symptoms	Alcohol, marijuana, tobacco, and illicit drugs	-The odds of SU increased with increased ACE exposure. -Every additional ACE was associated with a corresponding increase in odds of alcohol, binge drinking, tobacco, marijuana, illicit drugs, and polysubstance use. -Significant ethnic variation of the dose-response relationship between ACEs and tobacco, marijuana, and binge drinking existed.
Grigsby et al., 2020	NA	Sex, age, race/ethnicity, and site	Tobacco and alcohol	-Graded relationship between ACE exposure and cigarette use, and e-cigarette use. -ACEs did not yield gender-specific SU trajectories.
Hughes et al., 2019	Supportive childhood relationships	Age, gender, and childhood SES	Alcohol, smoking, and drug use	-Strong association between ACE and SU outcomes. -Supportive childhood relationships were associated with moderating risk of smoking and problem alcohol use.
Kameg et al., 2020	NA	NA	Alcohol and drugs	-No significant association between ACE score and risky alcohol use, however a statistically significant association between ACEs and risky drug use.
Kim, 2017	NA	Sex, region, parental edu., and family income	Alcohol	-Significant correlation between ACEs and alcohol use disorder
Krinner et al., 2020	NA	Age, sex, race/ethnicity, and health behaviors,	Alcohol and tobacco	-Graded associations of cumulative ACE exposure and alcohol use disorder. - ACE exposure was not associated with risky alcohol use.
Onu et al., 2021	Sociosexual behavior	Age	Tramadol use	-ACEs were positively associated with tramadol use.
Pakdaman et al., 2021	NA	School year, sex, race/ethnicity	Prescription drugs	-The relationship between ACEs and tramadol use was mediated by sociosexual behaviors and desires. -ACEs were significantly related to increased opiate, antidepressant, sedative, and stimulant use.
Ramakrishnan et al., 2019	Positive urgency	NA	Substance use disorder	-Race/ethnicity interaction was significant in prediction of stimulant misuse. -Positive urgency partially mediated the relationship between ACEs and substance use disorders.
Schafer, 2021	NA	NA	Alcohol	- A dose-response relationship between ACEs and risky alcohol use emerged.
Wiehn et al., 2018	NA	Sex, age, parental age and edu., migration bkgd, and family SES	Alcohol, tobacco, and illegal drugs	-Household substance use was significantly associated with risky alcohol use. -Experiencing four or more ACEs was associated with current smoking and substance use disorders.
Windle et al., 2018	NA	Age, sex, and race/ethnicity	Alcohol, tobacco, and marijuana	-A dose response relationship between ACEs and health risk behaviors was found. -Higher ACE scores significantly predicted risky cigarette, alcohol, and marijuana use.
Zhang et al., 2020	NA	Age, sex, and maternal edu.	Tobacco, alcohol and illicit drugs	-ACEs were associated with increased risk of smoking, binge drinking, and illicit drug use

Abbreviations: education = edu.; early life adversities = ELA; background = bkgd; NA = not assessed; significant = statistical significance

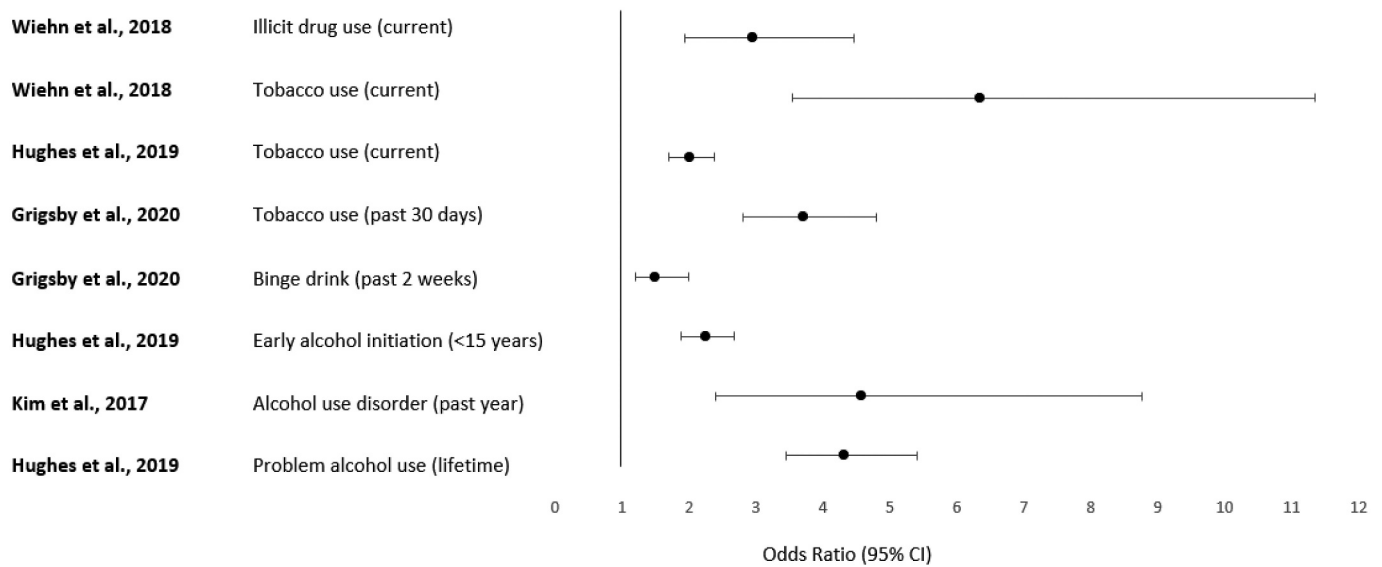


Figure 2. Strength of association of exposure to 4+ ACEs and SU.

Tobacco use

Seven studies analyzed the risk of tobacco consumption following ACE exposure. Most studies used retrospective survey questions to identify recent cigarette smoking and one study utilized the Fagerstorm Test for Nicotine Dependence (Table 1). In all studies, ACEs increased the likelihood of current cigarette smoking (Forster et al., 2019; Grigsby et al., 2020; Hughes et al., 2019; Wiehn et al., 2018; Windle et al., 2018). When measured by ACE type, the association wasn't always statistically significant (Table 3), however sexual abuse, parental SU, and collective and peer violence had the strongest relations (El Mhamdi et al., 2018; Zhang et al., 2020). Having four or more ACEs was found to increase odds of current or past 30-day tobacco use (Grigsby et al., 2020; Hughes et al., 2019; Wiehn et al., 2018) (Figure 2).

Marijuana use

Two studies measured the relation between ACEs and past 30-day marijuana use utilizing self-report retrospective survey questions (Table 1). Cumulated ACEs predicted risky past 30-day marijuana use (Windle et al., 2018) and were associated with past 30-day marijuana use (Forster et al., 2019). Parental SU, sexual abuse, and physical abuse were statistically significantly related to marijuana use (Table 3).

Prescription drug misuse

The relation between ACEs and prescription drug misuse was assessed by two studies; one utilized a self-report retrospective survey question and the other used the Tramadol Abuse Scale

Table 3. ACE type and SU.

	ACE TYPE	Outcome																
		Alcohol use	Potential alcohol use disorder	Risky alcohol use				Binge drink				Tobacco use				Marijuana use		Illicit drug use
Household dysfunction	Parental substance use	*	*			*	*			#2	#1	*		*	*	*	*	
	Parental interpersonal violence									#2	#1							
	Parental relationship	NA	NA	NA	NA	NA	NA	NA	NA	#2	#1	NA	NA	NA	NA	NA	NA	
	Divorce	NA	*			NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	*
	Incarcerated parent	NA	*			NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Parental mental illness	NA				*	NA	NA	NA	#2	#1	NA	NA			NA	NA	*
	Parental problems	NA	NA	NA	*	NA	NA	NA	NA	NA	NA	NA	NA			NA	NA	
Parental death	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA			NA	NA	*	
Neglect	Physical neglect	NA			*	NA	NA	NA		#1	NA	NA			NA	NA		
	Emotional neglect	NA				NA	NA	NA	NA	NA	NA	NA	*		NA	NA		
Abuse	Sexual abuse	*	*			*	*	*	#2	#1	*	*			*	*	*	
	Emotional abuse		*			NA				NA	NA	*			*		*	
	Physical abuse	*	*			NA	*		#2						*			
Violence	Bullying/peer violence	NA				NA	NA	NA	#2	#1	NA	NA			NA	NA	*	
	Violence community	NA				NA	NA	NA	#2	#1	NA	NA	NA	NA	NA	NA	NA	
	Collective violence	NA	NA	NA	NA	NA	NA	NA	#2	#1	NA	NA	NA	NA	NA	NA	NA	

Abbreviations: Statistically significant odds ratio = *; statistically non-significant odds ratio = blue color; NA = not assessed; female = 1; male = 2; Data presented from the following studies: (Forster et al., 2019; Kim, 2017; El Mhamdi et al., 2018, 2017; Schafer, 2021; Wiehn et al., 2018; Zhang et al., 2020)

(Table 1). Results indicated that ACEs were associated with risky tramadol use among male university students (Onu et al., 2021) and past year prescription drug use, including stimulant, antidepressant, opiate, and sedative use (Pakdaman et al., 2021) (Figure 3).

Illicit drug use

Seven studies reported the link between ACEs and illicit drug use other than cannabis (e.g., cocaine, heroin, ecstasy). Four studies utilized survey questions to assess illicit drug use, two studies used the Drug Abuse Screening Test (DAST-10), and one utilized the Health Appraisal Questionnaire (Table 1). ACEs were associated with increased likelihood of lifetime and last year illicit drug use (Forster et al., 2019; Hughes et al., 2019), risky drug use, and SUDs (Kameg & Mitchell, 2021; Ramakrishnan et al., 2019). The association of ACEs with addictive behaviors, SUDs, and illicit drug use varied by ACE type, with parental SU, sexual abuse, and physical abuse having the most statistically significant relationships (El Mhamdi et al., 2017; Wiehn et al., 2018; Zhang et al., 2020) (Table 3). Exposure to multiple ACEs was related to current illicit drug use (Figure 2) (Wiehn et al., 2018) and increased risk of having a lifetime addictive behavior by eightfold in females and 16-fold in males (El Mhamdi et al., 2017).

Quality rating

Overall, all included studies were rated with good or fair quality (Table 4). Studies of lower quality typically did not recruit all subjects from the same population nor uniformly apply inclusion and exclusion criteria. This may have resulted in findings being less representative of university students. All measurement of ACEs relied on retrospective self-report measures. While utilized frequently in the literature, this design introduces recall bias that may impact the association estimate.

Most studies utilized 1–6 covariates in their statistical analyses (81%) to adjust for potential confounding factors (Table 2).

Strength of association between substances

When studies measured the strength of relations between ACEs and more than one substance type, differences in effect size emerged in diverging patterns. For example, among students who experienced four or more ACEs, there was a stronger association with problem alcohol use than tobacco use (Hughes et al., 2019), whereas the opposite pattern was also demonstrated (Grigsby et al., 2020). Wiehn et al. (2018) indicating higher odds for cigarette use compared to illicit drug use among students with four or more ACEs. Reviewed together, persons with four or more ACEs have increased risk of binge drinking (adjusted odds ratio (aOR) (95%CI):1.5 (1.2,2.0)), problem alcohol use (aOR (95%CI) range: 4.32–4.57 (2.39,8.76)), illicit drug use (aOR (95%CI): 2.95 (1.94, 4.47)), and tobacco use (aOR (95%CI) range: 2.01–6.34 (1.7, 11.34)) (Figure 2). Two studies reported the dose response relationship between ACE exposure and SU (Forster et al., 2019; Pakdaman et al., 2021), demonstrating for every additional ACE experienced, there was a subsequent increase in odds of SU (Figure 3), with illicit drug use having the largest increase per additional ACE.

Mediators and moderators

Fewer than half of the included studies ($n = 7$) assessed mediators and moderators of the relationship between ACEs and SU. Mindfulness and sociosexual behaviors were identified as mediators of the association of ACEs with past 30-day problem alcohol use (Brett et al., 2018) and tramadol use (Onu et al., 2021), respectively. Positive urgency, a facet of impulsivity, was found to partially mediate ACEs and SUDs (Ramakrishnan et al., 2019). Moderators of the relation between ACEs and SUDs were also identified, including supportive childhood

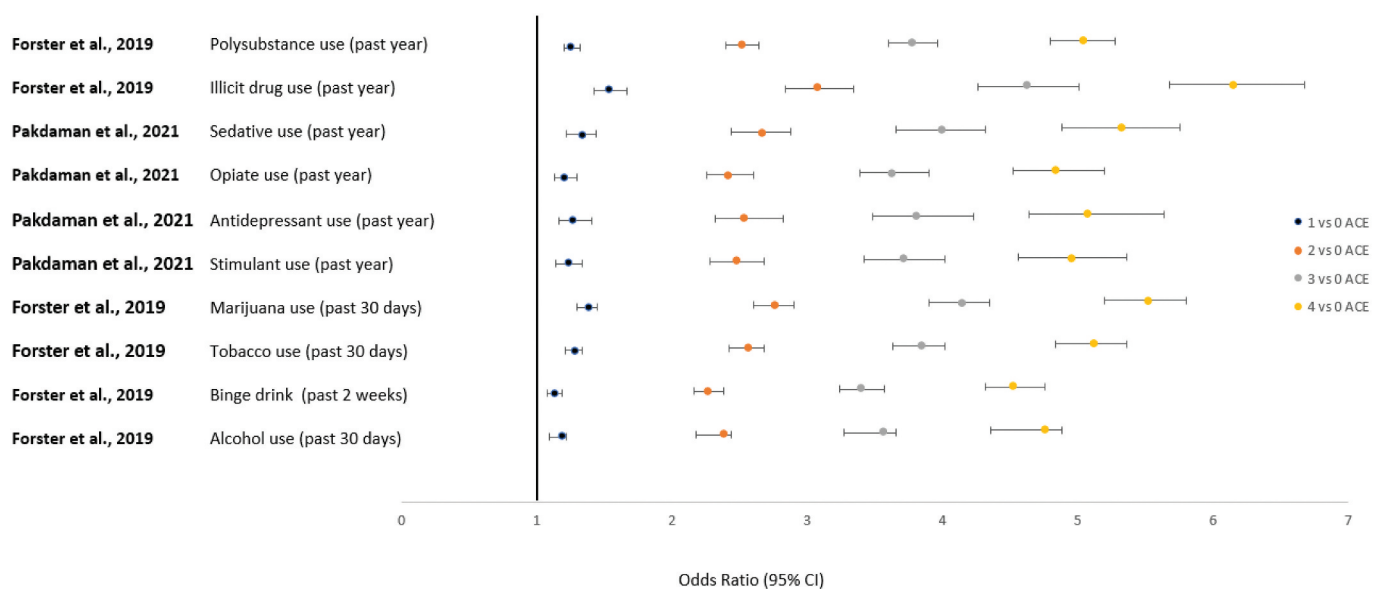


Figure 3. Dose response relationship between ACEs and SU.

Table 4. Risk of bias. Based on selected items of the US National Heart, Lung and Blood Institute for observational cohort and cross-sectional studies. 1: Research question clearly stated, 2: Study population clearly specified/defined, 3: Subjects selected from same/similar populations, 4: Sample size justification provided, 5: Exposure interest measured prior to outcomes being measured, 6: Timeframe sufficient to see association between exposure and outcome, 7: Multiple levels of exposure examined, 8: Exposures measured clearly defined, valid, and reliable, 9: Exposure assessed more than once, 10: Outcome measures clearly defined, valid, and reliable, 11: Key potential confounding variables measured /adjusted statistically.

First author (year)	1-Research question	2-Study pop	3-Subject pop	4-Sample size	5-Temporality	6-Timeframe	7-Exposure assess	8-Exposure variable	9- Repeated measurement of exposure	10-Outcome variable	11-Confounders
Brett et al., 2018	+	+	+	-	+	+	+	-	-	+	+
El Mhamdi et al., 2018	+	+	+	-	+	+	+	-	-	+	+
El Mhamdi et al., 2017	+	+	+	-	+	+	+	-	-	+	+
Forster et al., 2019	+	+	-	-	+	+	+	-	-	+	+
Grigsby et al., 2020	+	+	+	-	+	+	+	-	-	+	+
Hughes et al., 2019	+	+	-	-	-	+	+	-	-	-	+
Kameg et al., 2020	+	+	+	-	+	+	+	-	-	+	-
Kim, 2017	+	-	-	-	+	+	+	-	-	+	+
Krinner et al., 2020	+	+	+	-	+	+	+	-	-	+	+
Onu et al., 2021	+	+	+	-	+	+	-	-	-	+	+
Pakdaman et al., 2021	+	+	+	-	+	+	+	-	-	+	+
Ramakrishnan et al., 2019	+	+	+	-	+	+	+	-	-	+	+
Schafer, 2021	+	+	+	-	+	+	+	-	-	-	-
Wiehn et al., 2018	+	+	+	-	+	+	+	-	-	+	+
Windle et al., 2018	+	+	+	-	+	+	+	-	-	+	+
Zhang et al., 2020	+	+	-	+	-	-	+	-	-	+	+

relationships (Hughes et al., 2019), gender (El Mhamdi et al., 2018, 2017), and ethnicity (Forster et al., 2018). Supportive childhood relationships moderated the risk of current smoking and lifetime problem alcohol use as related to ACEs (Hughes et al., 2019). Gender and the type of adversity modified the relationship between ACEs and past year and 30-day risky alcohol use (Schafer, 2021; Wiehn et al., 2018), past 30-day binge drinking (Zhang et al., 2020) past 30-day tobacco use (El Mhamdi et al., 2018; Zhang et al., 2020), lifetime addictive behaviors (El Mhamdi et al., 2018, 2017), and lifetime illicit drug use (Zhang et al., 2020). Statistically significant ethnic variation of the dose–response relationship between ACEs and SU existed, whereby Asian/Pacific Islanders had greater risk of past year stimulant and marijuana use and non-Hispanic White persons had greater likelihood of past year marijuana, sedative, and antidepressant use (Forster et al., 2019; Pakdaman et al., 2021).

Discussion

To our knowledge, this is the first systematic review summarizing the existing evidence and study characteristics about the relationship between ACEs and specific SU types among university students. This review identified 16 relevant articles, all published within the last 5 years, indicating an emerging research focus. Nearly all studies reported a positive relation between ACEs and SU or risky SU, including alcohol, tobacco, marijuana, prescription-medication, and illicit drug use. The strength of association between ACEs and SU differed by substance, with the greatest strength for tobacco and illicit drug use. The relationship between ACE type and SU differed by substance and study, however, childhood sexual abuse and parental SU appeared to have the greatest number of statistically significant associations. A dose–response relationship emerged for every substance, whereby, as ACEs accumulate, there is a corresponding increased risk for SU. The findings demonstrated are similar to a review on the relation

between ACEs and SU during emerging adulthood, however, add a unique perspective by focusing on university students and discussing the strength of association between ACEs and SU (Rogers et al., 2022). Further, these results are consistent with the research that has analyzed the association of ACEs and SU in older adults and the general population (Hughes et al., 2017; Kalmakis & Chandler, 2015; Petruccioli et al., 2019). The majority of studies came from economically developed nations; thus, future research should be conducted globally to determine if this relationship is consistent across other cultural and economic contexts.

While strong associations of ACEs with SU were demonstrated, it is important to view these results with caution as there is heterogeneity in the classification of ACEs. Included studies ranged from assessing 5 to 12 ACEs from both household and social environments, which contributed to the diverse prevalence of ACEs reported across studies. Since 1998, ACEs have encompassed childhood abuse, neglect, and household dysfunction. In the last decade, researchers have widened the spectrum of childhood adversities to also reflect traumas, such as community violence and bullying (Finkelhor et al., 2013). A consensus about the definition of ACEs would be beneficial, as well as standardization when measuring SU outcomes.

Several limitations within the literature and review exist. First, there was heterogeneity in the classification of ACEs and SU (e.g., time frame of SU, frequency of SU) among studies. Second, only manuscripts that used cumulative ACE measures were included for the review, thus, manuscripts that investigated the impact of single adverse events could be excluded. Nevertheless, this methodology has been commonly used to look at the relation between cumulative childhood trauma and SU (Kalmakis & Chandler, 2015; Leza et al., 2021; Park et al., 2021). Third, included studies utilized retrospective self-report measures of ACEs, potentially affected by recall bias. However, prospective ACE records have confirmed similar findings of negative life outcomes utilizing retrospective ACE measures (Reuben et al., 2016). Fourth, confounding

variables were inconsistently included and reported. Fifth, the selection and extraction of information was made by a single reviewer. Despite this limitation, a subsample of quality reviews was completed by two reviewers and obtained high reliability. Further, this study adhered to PRISMA guidelines and is the first to systematically review and summarize studies that examined the relation between ACEs and specific SU types among university students.

Regardless of these methodological issues, there is convincing evidence that ACEs increase risk of SU among university students and this relation is complex. As such, resilience models that emphasize mediators and moderators in promoting healthy development regardless of ACE exposure should be explored. One identified mediator, mindfulness, is supported by a growing body of literature demonstrating its role with resilience building and better behavioral health among persons with ACEs (Robin Ortiz & Sibinga, 2017; Whitaker et al., 2014). Among university students, mindfulness has been found to mediate the association between ACEs and SU and mental health outcomes (Brett et al., 2018; McKeen et al., 2021). Thus, interventions among university students that promote mindfulness may protect against future SU despite prior ACE trauma (Robin Ortiz & Sibinga, 2017).

Early screening of ACE exposure among university students, if feasible, might identify students at higher risk of SU and SUD and engage them in preventive or therapeutic strategies. As individuals with a history of ACEs are more likely to fail treatment for SUDs (López-Castro et al., 2015; Najavits et al., 2016), the challenges associated with treatment may be due to a lack of individualized and specific treatment. Thus, screening for ACEs and protective factors (The Positive and Adverse Childhood Events Survey (PACES)), combined with a nonjudgmental, trauma informed, person-centered screening approach may be well suited for university students (Chandler et al., 2018; Leitch, 2015). While previously used among adult populations, this method intends to promote mindfulness and is believed to decrease the potential for further traumatization while providing education and self-reflection on the link between ACEs and SU (Leitch, 2015). This knowledge may introduce self-awareness to university students regarding the pathway between ACEs and SU and build resilience and self-acceptance (Chandler et al., 2018; R. Ortiz, 2019).

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