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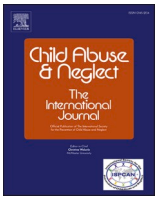

Associations between adverse childhood experiences and substance use: A meta-analysis

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ABSTRACT

Background: Adverse childhood experiences (ACEs) can be associated with negative health outcomes such as substance use. However, extant literature assessing this association is mixed.
Objective: The present meta-analysis was conducted to obtain a pooled effect size for the association between ACEs and substance use (i.e., smoking, problematic alcohol use, heavy alcohol use, illicit drug use, and cannabis use).
Participants and setting: The present meta-analyses included 102 studies (N = 901,864), where 42.32 % of participants were male, and the mean age was 30.91 years.
Methods: Searches were conducted in MEDLINE, Embase, and PsycINFO in August 2021 and moderators were examined. Inclusion criteria included studies that measured ACEs prior to age 18 and substance use, and were published in English. All analyses were completed in Comprehensive Meta-Analysis Software, Version 3.0 (Borenstein et al., 2009).
Results: Pooled effect sizes between ACEs and smoking [OR = 1.803 (95 % CI 1.588, 2.048)], problematic alcohol use [OR = 1.812 (95 % CI 1.606, 2.044)], heavy alcohol use [OR = 1.537 (95 % CI 1.344, 1.758)], cannabis use [OR = 1.453 (95 % CI 1.184, 1.786)] and illicit drug use [OR = 1.695 (95 % CI 1.530, 1.878)] were significant. Significant moderators contribute to the understanding of the association between ACEs and substance use, and are discussed extensively.
Conclusions: ACEs confer risk for substance use and trauma-informed approaches to substance use treatment should be considered. Study limitations and implications are discussed.

1. Introduction

Substance use may be associated with a range of negative and far-reaching implications that impact both the individual and society broadly. Extant literature suggests that substance use is associated with both physical and mental health concerns throughout the lifespan (Schulte & Hser, 2014) and is estimated to cost over $400 billion in the US annually, making it one of the costliest health expenditures (National Drug Intelligence Center, 2011; Sacks et al., 2015). Thus, elucidation of risk factors for substance use has the potential to inform prevention and intervention strategies and reduce its effects on individuals and society.

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Engagement in various types of substance use is multi-determined, and it is important to note that substance use is not inherently harmful, nor is it assumed that all substance use leads to impairment and distress. However, existing literature suggests that higher levels of alcohol consumption, compared to low levels or abstinence, and use of tobacco and illicit drugs have been associated both directly and indirectly with leading causes of mortality in the United States (Mokdad et al., 2005). Previous literature has suggested that exposure to adverse childhood experiences (ACEs; Felitti et al., 1998) including abuse, neglect, and maltreatment prior to the age of 18 years, may be one precipitant of various types of substance use across the lifespan (e.g., Leza et al., 2021).

1.1. Adverse childhood experiences: Risk factor for substance use

ACEs are common, with pooled prevalence estimates suggesting that 60 % of the population has experienced at least one ACEs, with 16.1 % experiencing four or more ACEs (Madigan et al., in press). Experiences in childhood, particularly relational experiences with caregivers, provide the context for either adaptive or maladaptive emotional, behavioural, and social development (Sroufe et al., 1999). Thus, exposure to ACEs, which most often occur in the context of relationships with adults, have been identified as a potent risk factor for various types of substance use, including alcohol use, illicit drug use, and smoking (e.g., Hughes et al., 2017; Petruccelli et al., 2019).

Mechanistically, it has been broadly proposed that exposure to ACEs may lead to alterations in an individual's affect regulation systems and stress responses (Buss et al., 2017), which are implicated in the development of mental health concerns (Baumeister et al., 2014). Past research has demonstrated that exposure to child maltreatment is associated with elevated allostatic load, defined as the cumulative toll of stress on the body's physical systems (McEwen, 1998). Elevated allostatic load may play a role in the association between ACEs and substance use given that exposure to stress may increase likelihood of substance use via a reduction in self-regulatory abilities (Schwabe et al., 2011). Below we review the empirical literature supporting the association between ACEs and various substance use outcomes.

1.1.1. Smoking

Existing literature examining the association between ACEs and smoking has demonstrated mixed results. For example, among two studies both utilizing samples of college students, one study did not find a significant difference in tobacco use based on ACEs exposure, while the other found that ACEs significantly predicted cigarette smoking (Windle et al., 2018; Young-Wolff et al., 2019). A longitudinal birth cohort from 1958 found that ACEs were associated with smoking initiation in adolescence, smoking heavily at age 16, and continuing to be a smoker across the lifespan in a dose-response manner (Joannès et al., 2022). However, this study found that the association between ACEs and smoking across the lifespan was attenuated when accounting for covariates including low levels of education, being unemployed, and having a child prior to being 23 years old.

1.1.2. Problematic and heavy alcohol use

There exists considerable research on the association between ACEs exposure and alcohol use, in which some research found a significant positive association (e.g., Dube et al., 2002) while others did not (e.g., Boughner & Frewen, 2016). These associations may vary based on the multitude of ways alcohol use can be categorized. For example, Brett et al. (2018) found that total ACEs score was significantly associated with alcohol-related consequences but not number of drinks consumed per week. It has been previously mentioned that not all substance use is inherently problematic, and such is also the case for alcohol use. However, past research has indicated that ACEs exposure was associated with a progression from alcohol use with no problems to moderate and severe alcohol use problems, characterized by low, moderate, and severe risk of meeting the alcohol use disorder criteria, respectively (Alvanzo et al., 2020).

1.1.3. Illicit drug use

The association between ACEs and drug use has presented mixed findings. For example, past research has identified illicit drug use to possess the highest risk ratios associated with ACEs compared to several other risk factors for poor health (Bellis et al., 2019). In contrast, other research did not find a significant association between ACEs and illicit drug use in a sample of males recruited from a hospital emergency department (Cunradi et al., 2020).

1.1.4. Cannabis use

Some past research has considered cannabis use to be synonymous with illicit drug use (e.g., Hughes et al., 2017) and therefore has not been examined separately from other drugs. However, research has found cannabis use to be less harmful in terms of social harms (e.g., healthcare costs), physical harms, and risk for dependence (Taylor et al., 2012).

1.2. Previous meta-analyses and limitations

To our knowledge there have been two meta-analyses examining the broad implications of ACEs for health outcomes among global general population samples, including sub-analyses between ACEs and problematic substance use (Hughes et al., 2017; Petruccelli et al., 2019). Overall, these meta-analyses demonstrated a small to medium association between ACEs and substance use outcomes in addition to a ballooning of research in this area within recent years. Thus, the present meta-analysis will be important to capture up-to-date pooled prevalence rates of the association between ACEs and several substance use outcomes.

A central limitation of existing meta-analyses is that they have examined ACEs categorically versus continuously. In studies that

examine ACEs categorically, individuals with 1, 2, 3, or 4+ ACEs are compared to the referent group of 0 ACEs in terms of their likelihood for substance use, with most studies focusing on the arbitrary comparison of 4+ vs 0 ACEs. However, when including only participants with 0 or 4+ ACEs, this exclusion sacrifices a substantial number of studies, and accordingly, precision in meta-analytic estimates. Therefore, the present study provides a comparison of the aggregate effect size between ACEs and each of the measured substance use variables categorically and continuously to investigate any differences based on measurement.

Another notable limitation of existing meta-analyses is that potential moderators have not been examined. Given that existing literature has presented mixed findings on the association between ACEs and substance use, it is critical to explore whether sample and study-level factors may explain between-study variability. The results of moderator analyses can be informative for understanding the circumstances for which associations are strengthened or attenuated, which can in turn inform future prevention and intervention strategies used to mitigate the risk and sequalae of substance use.

1.3. Potential moderators of the association between ACEs and substance use

1.3.1. Sex

Past literature has highlighted differences in both substance use and exposure to adversity by sex. Kessler et al. (1994) found that males and females tend to differ in their patterns of substance use, such that males reported higher rates of dependence on alcohol and illicit drugs compared to females, however more recent research suggests the sex gap is narrowing (McHugh et al., 2018). It has also been argued that subgroups of females may experience unique risks that can increase likelihood of substance use, including ethnic or sexual minoritization and trauma histories (Hemsing et al., 2016). Sex differences in ACEs exposure have also varied, where some research has found females were more likely than males to experience sexual abuse, but sex differences in other ACEs categories have not consistently been found (Dong et al., 2003; Dube et al., 2005). Thus, differences in the prevalence of substance use and ACEs based on sex highlight the importance of investigating sex as a moderating variable in the association between exposure to ACEs and substance use.

1.3.2. Age

Previous research has found that rates of substance use vary across the lifespan. For example, Vasilenko et al. (2017) demonstrated that substance use disorders generally decline with age. For example, emerging adulthood is a period where executive functioning and decision-making skills are still developing and individuals may experience social settings in which substance use is encouraged (Chadi et al., 2018). However, research assessing the impact of substance use across the adult lifespan is limited. As such, exploration of the role of age as a moderator may inform trajectories of substance use across the developmental spectrum.

1.3.3. Race and ethnicity

The distribution of ACEs is not equal across racial and ethnic groups. Specifically, ACEs are more common among groups exposed to systemic oppression and disadvantage. Past research has found that Black and Latinx individuals experience greater ACEs exposure compared to White individuals (Maguire-Jack et al., 2020). Given that higher levels of ACEs confer greater risk for negative health outcomes, it will be important to examine the role of racial and ethnic minoritization in the relationship between ACEs and substance use.

1.3.4. Measurement

The method in which ACEs are examined (i.e., continuously or categorically) may explain variability across study findings (Reidy et al., 2021). When studies examine the association between substance use and ACEs as a continuous variable, statistical power is maximized as all participants are included in one analysis. However, many studies compare individuals with each of 1, 2, 3, or 4+ ACEs to the referent of 0 ACEs. Thus, the current meta-analyses will test whether the methodological approach for examining ACEs explains between-study heterogeneity.

1.3.5. Informant

The informant of substance use may also explain between-study variability. Existing research that explores the association between ACEs and substance use typically utilizes either self-report methodology, such as the completion of questionnaires by the participant, diagnostic interviews, or the use of case records, such as a review of hospital records. While past research has suggested that clinical interviews represent the most valid method of assessing substance use, there is also support for the validity of self-report measures (Denis et al., 2012). However, social desirability effects may bias substance use reporting, possibly leading individuals to provide lower reports of substance use when measured using an interview compared to self-report measures (Richman et al., 1999). Thus, we examine informant of substance use as a moderator in our meta-analysis.

1.3.6. Year of publication

Rates of substance use and attitudes towards substance use (e.g., disapproval of substance use, perceived risk associated with use) have changed over time (Keyes et al., 2012). Further, the implementation of ACEs screening in routine care (e.g., van Roessel et al., 2021) may be associated with increased knowledge and awareness of ACEs both among healthcare providers and laypeople (Bryant & VanGraafeiland, 2020) possibly leading to more frequent routine screening and a willingness for patients to disclose ACEs exposure. Overall, changes in trends in substance use across cohorts and changes in the reporting and knowledge of ACEs may influence the magnitude of associations. As such, year of publication was examined as a moderator in the association between ACEs and substance

use.

1.4. The current study

The objective of the present meta-analysis was to test the overall effect size of the association between ACEs exposure and substance use (i.e., smoking, problematic alcohol use, heavy alcohol use, cannabis use, and illicit drug use) in all studies amassed to date. A secondary aim was to test between-study moderators of the association between ACEs and substance use, as this can inform for which individuals and under what circumstances that substance use following ACEs exposure is greater.

The categories of substance use in the present study are consistent with previous meta-analyses (Hughes et al., 2017; Petruccelli et al., 2019) to allow for direct comparisons to existing literature. The present meta-analysis will address existing gaps in literature by examining the association between ACEs and substance use via continuous (i.e., sum of ACEs experienced), as well as categorical (e.g., 4 vs 0 ACEs) methods. Lastly, to determine whether effect sizes when ACEs are measured categorically differ as the number of ACEs increases, we also conduct a sub-analysis where we compare effect sizes for substance use across the ACEs continuum (i.e., 0 versus 1 ACE, 0 versus 2 ACEs, 0 versus 3 ACEs, and 0 versus 4+ ACEs).

2. Methods

2.1. Definition of constructs

Adverse Childhood Experiences (ACEs) were assessed using cumulative retrospective self-reports or file review from child abuse records. Exposure to child adversity included maltreatment and household dysfunction experienced prior to age 18. Child adversity was measured using either the original 8-item ACEs (Felitti et al., 1998), which included physical abuse, sexual abuse, emotional abuse, parent substance use, parent mental health issues, parent divorce or separation, parent incarceration, and exposure to domestic violence; the 10-item measure, which included additional items assessing physical and emotional neglect; or an alternative composite measure of ACEs. *Substance use* was measured using either a self-report questionnaire or diagnosis by a clinician. For the purposes of consistency, the present study used the construct definitions for smoking, problematic alcohol use, heavy alcohol use, illicit drug use, and smoking, used by Hughes et al. (2017; see Supplemental Table 1).

2.2. Search strategy

The present meta-analysis used the updated PRISMA 2020 guidelines (Page et al., 2021) and searches were conducted using MEDLINE, Embase, and PsychINFO by a health sciences librarian and included articles up to August 2021 (see Supplemental Table 2 for an example search strategy and Supplemental Table 3 for the PRISMA 2020 Checklist). Articles included in the present meta-analysis were drawn from the ACEs Data Catalogue, developed in the Determinants of Child Development Lab at the University of Calgary, and as a result, the outcome terms were not restricted or included as search terms. The search used in the present meta-analysis included the acronym ACEs and “adverse childhood event or experiences”. The year of publication was limited to 1998, the year that the original ACEs study was published (Felitti et al., 1998), and onwards. Language and date restrictions were not applied. References for all full-text studies meeting inclusion criteria were reviewed, and the references in relevant meta-analyses were searched. Together, these search strategies revealed a total of 11,926 non-duplicate articles that underwent review for inclusion in the current meta-analysis (see Supplemental Fig. 1). The present meta-analysis and associated protocol was not registered.

2.3. Study inclusion and exclusion criteria

All titles and abstracts yielded from the search strategy were reviewed by three independent coders. All full text articles of studies that potentially met inclusion criteria were examined.

2.3.1. Inclusion criteria

Studies were deemed to have met inclusion criteria if they (1) included a measure of ACEs exposure that was measured using self-report, interviews, or official child protection records; (2) included an outcome measure of substance use that was measured using self-report, interviews, or official child protection records; (3) sufficient information was provided for the calculation of an effect size; (4) published in English.

2.3.2. Exclusion criteria

Articles were excluded on the basis of: (1) non-empirical publications, including descriptive reports, case studies, or book and narrative reviews; (2) did not include a measure of ACEs or substance use; or (3) utilized a qualitative study design.

Based on the present inclusion and exclusion criteria, 11,926 studies met the initial inclusion criteria, and 597 full text articles were reviewed. Of these, 495 articles were deemed to have met exclusion criteria and were subsequently excluded. As such, 102 studies were included in the present meta-analysis.

2.4. Data extraction

Effect sizes for the association between ACEs and substance use and moderator variables were extracted from all studies that met inclusion criteria. The extracted moderators included: (1) mean participant age, (2) sex (% male), (3) race and ethnicity, (4) measurement methodology, (5) effect sizes for the association between continuous and categorical ACEs and substance use outcomes, (6) year of publication. All data were extracted by the first author and one additional coder. Discrepancies in data extraction were resolved via consensus. Interrater reliability ranged from $\kappa = 0.77–1.00$ and intraclass correlation (ICC) = 0.99–1.00.

An 8-item study quality tool was adapted from the National Institute of Health Quality Assessment Tool for Observation Cohort and Cross-Sectional Studies (NHLBI, n.d.). Studies were scored either 0 (no) or 1 (yes) for each of the 7 items (see Supplemental Table 4) and summed to give a total score out of 7. When information was unclear or not provided by the study authors, it was marked as 0 (no).

2.5. Data synthesis

The present meta-analysis included one effect size per study for each outcome (i.e., problematic alcohol use, heavy alcohol use, smoking, cannabis use, illicit drug use). Whenever possible, the present meta-analysis included unadjusted statistics over adjusted statistics to increase homogeneity across measurements. For studies that measured more than one type of substance use, effect sizes were extracted and included in separate meta-analyses on these outcomes. To ensure independent samples were only represented once within each meta-analysis, we selected the study with the largest sample size and most comprehensive data collection information when multiple publications were available for the same sample (e.g., NESARC).

2.6. Data analysis

2.6.1. Effect size estimation

Meta-analyses were conducted to determine the pooled effect size for the associations between ACEs and each outcome via Comprehensive Meta-Analysis Software, Version 3.0 (Bornstein, 2009). In the overall pooled effect size estimations, ACEs measured continuously and categorically were included. Included studies provided various effect size metrics, including correlations (r), odds ratios (OR), and chi-squares, all of which were used to derive pooled estimates. Studies using correlations examined ACEs as a continuous variable, whereas chi-square and OR examined ACEs most often as a comparison between 4 or more ACEs (4+ ACEs) against the reference group of 0 ACEs.[1] Some studies also reported non-significant findings without the provision of effect sizes ($n = 3$), in which case a p-value of .50 was used, following the recommendations made by Rosenthal (1995). All pooled effect sizes are represented as OR with 95 % confidence intervals. All analyses were performed using random effect models due to the variability in population parameters across included studies.

2.6.2. Publication bias testing

The process by which research studies are selected for publication is not random and can favor studies with positive effects (Scheel et al., 2021). Thus, there is the potential for publication bias in systematic reviews of the literature. Accordingly, funnel plots inspection was used to assess for publication bias (Peters et al., 2007).

2.6.3. Moderator analyses

In keeping with up-to-date practice, we report the overall level of heterogeneity (τ^2) and the score dispersion in the prediction interval, in addition to the I^2 statistic (Borenstein, 2022). In instances where heterogeneity was observed, each moderator was separately examined. Further, significance of categorical and continuous moderators was determined by the Q statistic and by mixed-effects model meta-regressions, respectively (Thompson & Higgins, 2001). Categorical moderators with more than 3 studies per cell were examined (Borenstein et al., 2009).

2.6.4. Sub-analyses

The pooled estimates derived for each meta-analysis herein included only one effect size per sample. However, many studies reporting on ACEs do so by comparing the contrast of 0 [reference group] vs 1 ACEs, 0 vs 2 ACEs, 0 vs 3 ACEs, and 0 vs 4 ACEs and find that a unit increase in ACE score is associated with greater risk compared to no ACEs. Therefore, we conducted sub-analyses on studies presenting ACEs data in a gradient relation to determine if pooled associations differentiate between 0 vs 1 ACEs, 0 vs 2 ACEs, or 0 vs 3 ACEs on the substance use outcomes. As these comparisons include overlapping participants (i.e., those with 0 ACEs are in every comparison), 85 % confidence intervals are used as a more conservative significance test (Goldstein & Healy, 1995). A difference between effect sizes is identified if the 85 % confidence intervals do not overlap.

[1] When multiple contrasts were provided, we defaulted to selecting the 4+ ACEs versus 0 ACEs contrast for effect size calculations. In the event a study only presented analyses for 1+ ACEs versus the reference group of 0, or 2+ versus 0 ACEs, or 3+ ACEs versus 0, these studies were also included. In such cases, we defaulted to selecting the highest ACE+ vs 0 OR provided within a study.

3. Results

3.1. Studies selected

The initial search yielded 11,926 non-duplicate records and 597 full text articles were reviewed (see Supplemental Fig. 1). A total of 102 studies were included in the meta-analysis. Study characteristics can be found in Supplemental Table 5. A total of $k = 51$ studies reported on smoking, $k = 37$ reported on problematic alcohol use, $k = 17$ reported on heavy alcohol use, $k = 16$ reported on cannabis use, and $k = 43$ reported on illicit drug use.

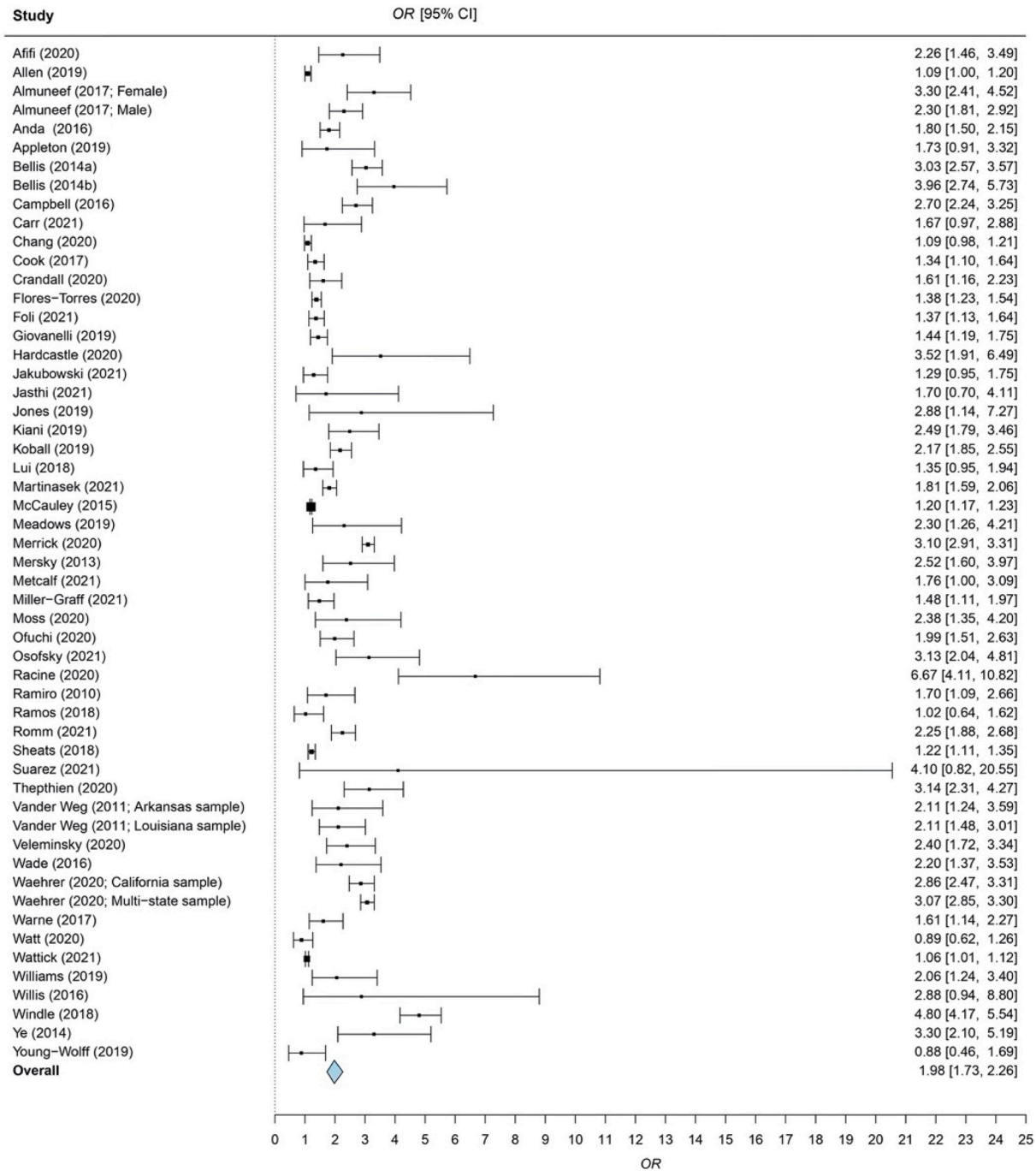

Fig. 1. Forest plot of effect sizes for the association between ACEs and smoking outcomes.

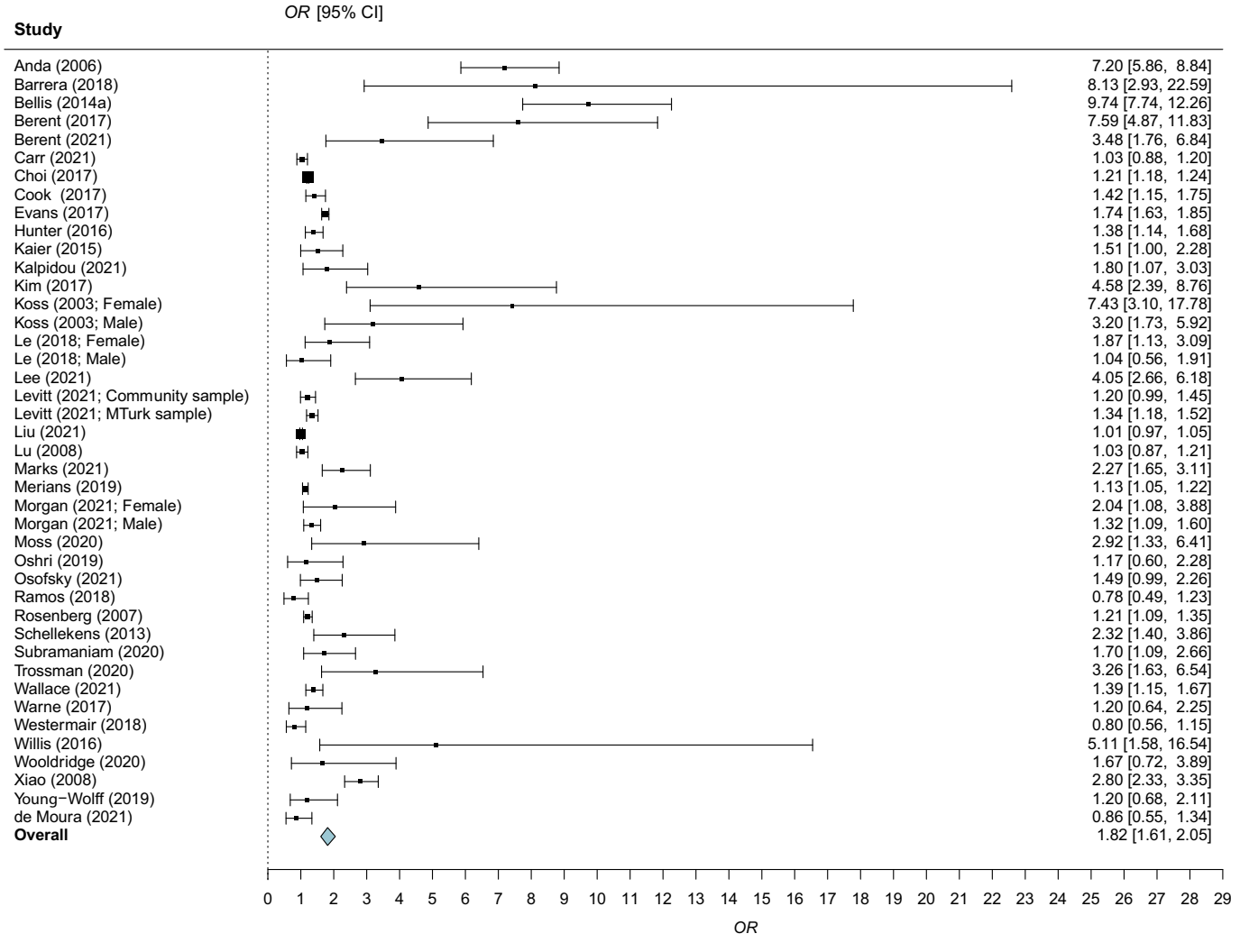

Fig. 2. Forest plot of effect sizes for the association between ACEs and problematic alcohol use outcomes.

3.2. Sample characteristics

The present meta-analysis included 186 samples. Across all 102 studies, 901,864 participants were included, with 42.32 % being male and a mean age of 30.91 years (age range, 15–62; Supplemental Table 5). Ten studies (9.8 %) were from Asia, eleven (10.78 %) from Europe, seventy-six (74.51 %) from North America, one (0.98 %) from Oceania, one (0.98 %) from Africa, two (1.96 %) from the Middle East, and one (0.98 %) multi-country study that included more than one continent. With regards to race and ethnicity, 67 of the included studies reported having racial or ethnic minority participants, with the mean across studies as follows: White (62.47 %), Black (31.35 %), Latinx (18.85 %), Asian (20.71 %), Indigenous (18.95 %), and Other race (i.e., studies that included the categories “other”, “biracial”, “multiracial”; 11.03 %). The mean study quality score was 4.66 (range, 3–6; see Supplemental Table 6).

3.3. Meta-analytic results for ACEs and smoking

3.3.1. Pooled effect size

A total of 55 samples were available for this random-effects meta-analysis, which produced a significant pooled effect size (OR = 1.979, 95 % CI [1.734, 2.259]; Fig. 1). The funnel plot inspection revealed asymmetry (see Supplemental Fig. 2) and when results were adjusted by adding seven imputed studies using Duval and Tweedie’s trim and fill technique (Peters et al., 2007), the adjusted effect size was OR = 1.803 (95 % CI 1.588, 2.048).

3.3.2. Moderator analyses

Between study heterogeneity was indicated (Q = 2136.766, $p < .001$; $I^2 = 97.473$; $\tau^2 = 0.016$). The prediction interval ranged from

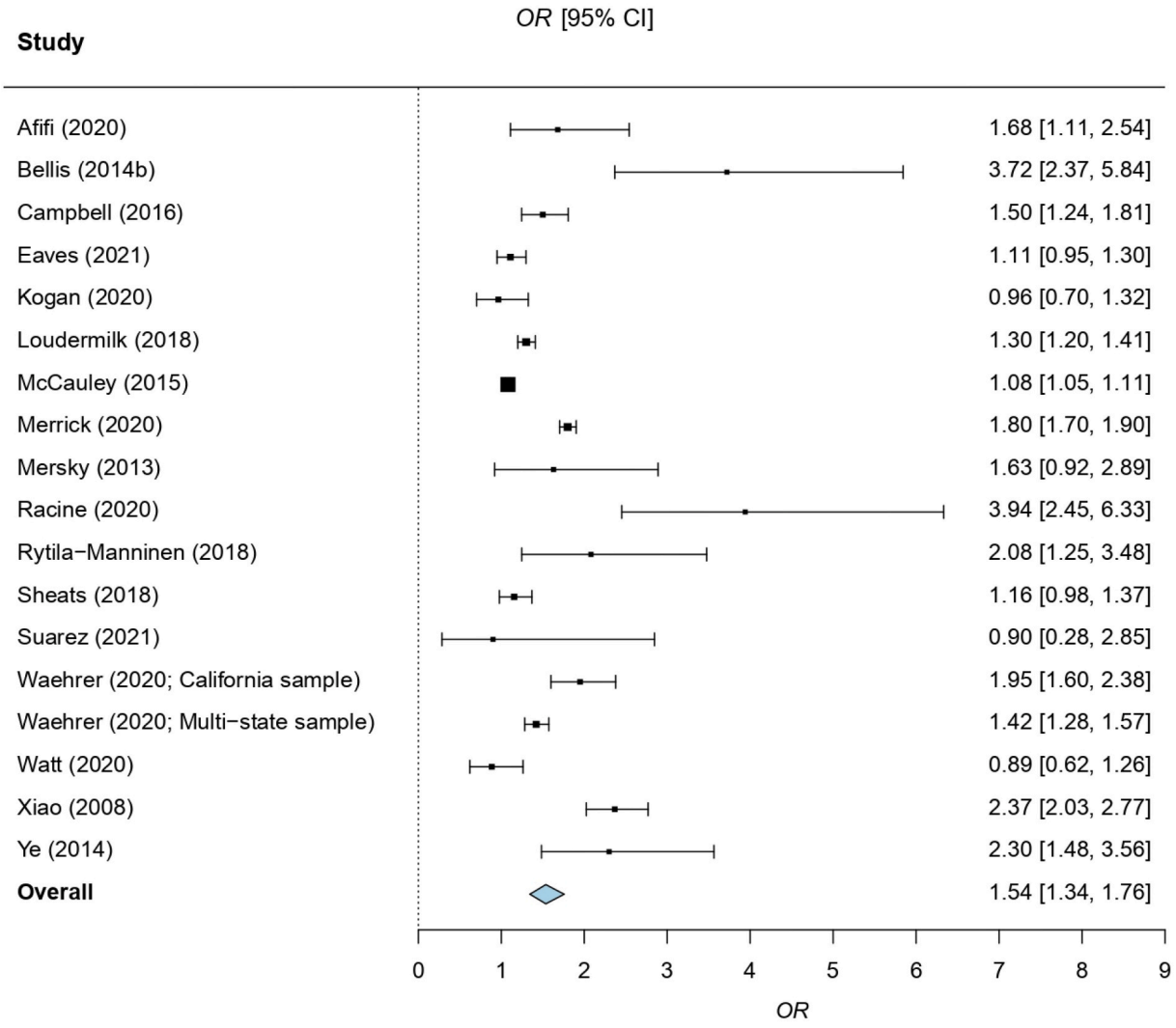

Fig. 3. Forest plot of effect sizes for the association between ACEs and heavy alcohol use outcomes.

$r = -0.07$ to 0.42. This indicates that the true effect size may range from null to large effects and thus heterogeneity between studies exists and moderators were explored (see Supplemental Table 7). Two moderators were identified to be significant. Effect sizes were stronger in samples where smoking was assessed via self-report OR = 2.01 (95 % CI 1.72, 2.35) versus interview methods OR = 1.66 (95 % CI 1.15, 2.41). Effect sizes were stronger in samples where ACEs were treated categorically (i.e., 4+ versus 0 [referent] ACEs; OR = 2.524 (95 % CI 2.204, 2.889)) compared to continuously (i.e., accumulation of ACEs; OR = 1.786 (95 % CI 1.552, 2.057)). Age, sex, race and ethnicity, and year of publication were not significant moderators.

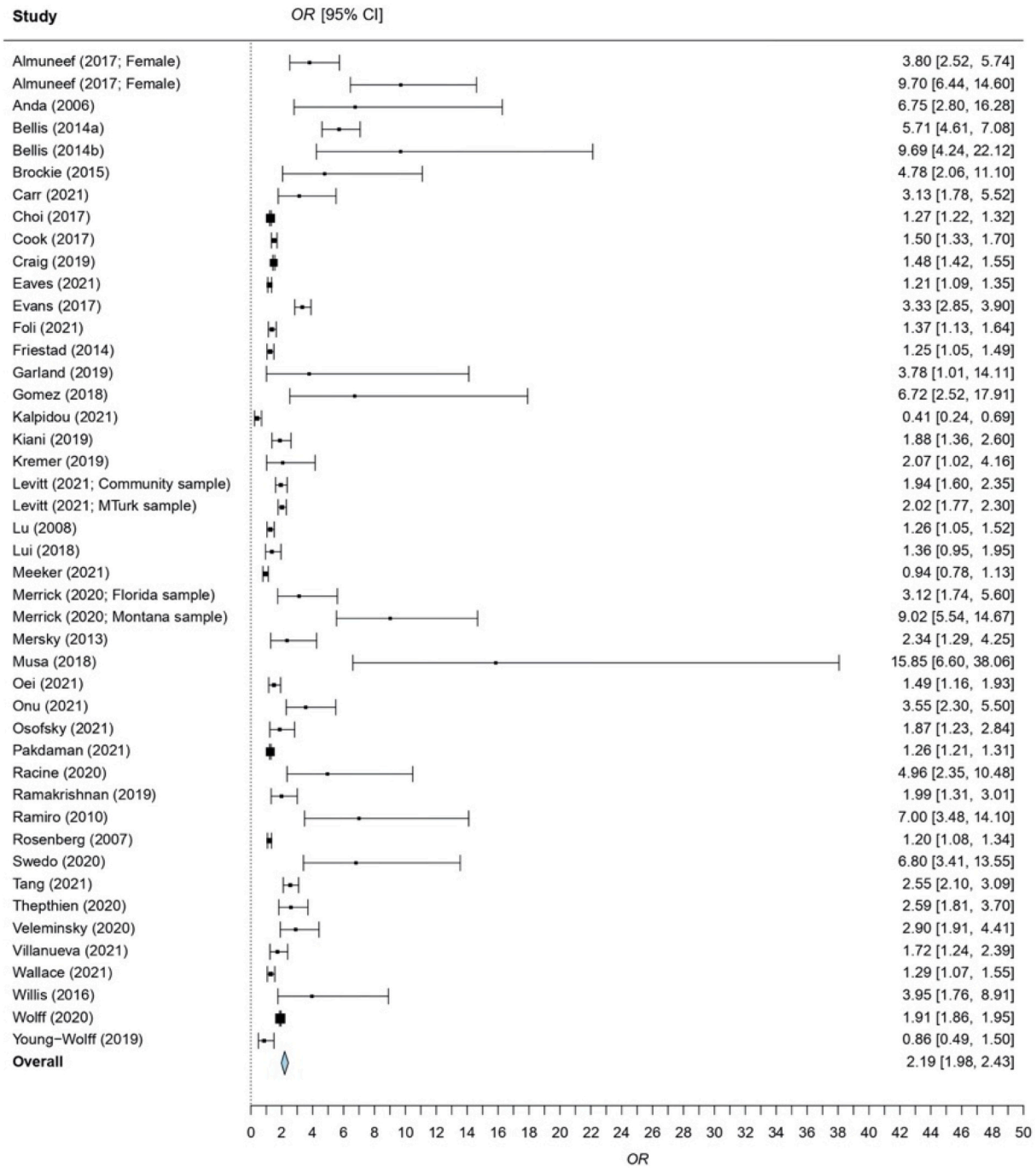

Fig. 4. Forest plot of effect sizes for the association between ACEs and illicit drug use outcome.

3.4. Meta-analytic results for ACEs and problematic alcohol use

3.4.1. Pooled effect size

A total of 46 samples produced a significant pooled effect size (OR = 1.812, 95 % CI [1.606, 2.044]; see Fig. 2). Examination of the funnel plot revealed symmetry, suggesting no publication bias.

3.4.2. Moderator analyses

Between study heterogeneity was indicated (Q = 1134.153, $p < .001$; $I^2 = 96.032$; $\tau^2 = 0.011$). The prediction interval ranged from $r = -0.05$ to 0.36 (see Supplemental Table 7). Three moderators emerged as significant. First, the problematic alcohol use informant was a significant moderator. Specifically, effect sizes were stronger in samples where problematic alcohol use was assessed via self-report OR = 2.01 (95 % CI 1.657, 2.442) versus interview methods OR = 1.279 (95 % CI 1.057, 1.549). Second, effect sizes were also stronger in samples where ACEs were treated categorically (i.e., 4+ versus 0 [referent] ACEs; OR = 4.002 (95 % CI 2.341, 6.842)) compared to continuously (i.e., accumulation of ACEs; OR = 1.410 [95 % CI 1.297, 1.532]). Lastly, publication year was a significant moderator, such that the association between ACEs and problematic alcohol use was stronger among older studies $b = -0.045$ (95 % CI −0.069, −0.021). Age, race and ethnicity, and sex were not significant moderators.

3.5. Meta-analytic results for ACEs and heavy alcohol use

3.5.1. Pooled effect size

A total of 19 samples produced a significant pooled effect size (OR = 1.537, 95 % CI [1.344, 1.758]; see Fig. 3). Examination of the funnel plot revealed symmetry, suggesting no publication bias.

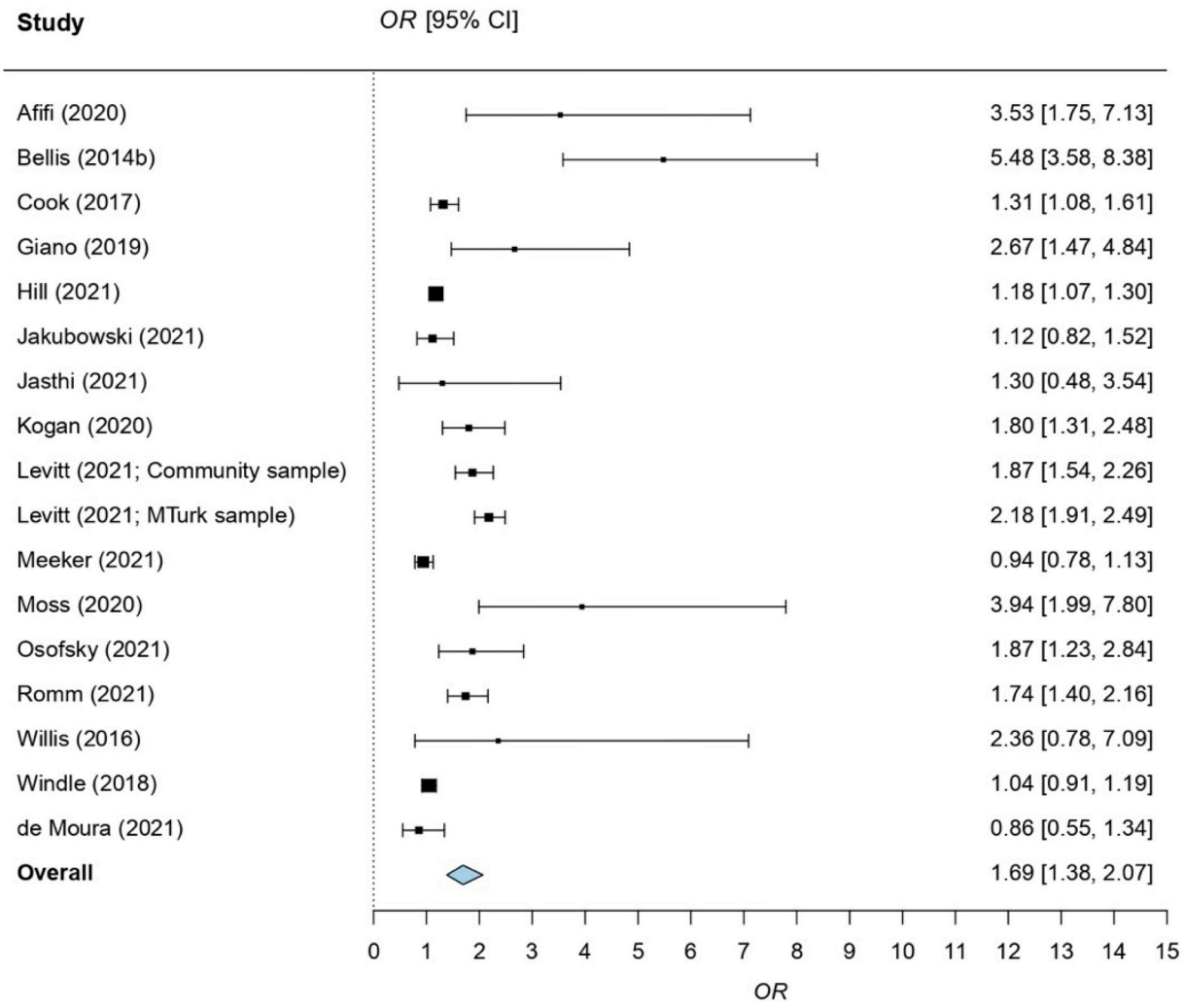

Fig. 5. Forest plot of effect sizes for the association between ACEs and cannabis use outcomes.

3.5.2. Moderator analyses

Between study heterogeneity was indicated (Q = 463.983, $p < .001$; $I^2 = 96.121$; $\tau^2 = 0.005$). The prediction interval ranged from $r = -0.04$ to 0.27 and moderators were explored (see Supplemental Table 7). The informant of heavy alcohol use was a significant moderator. Specifically, effect sizes were stronger in samples where problematic alcohol use was assessed via self-report OR = 1.483 (95 % CI 1.268, 1.734) versus interview methods OR = 1.667 (95 % CI 0.933, 2.978). Second, effect sizes were also stronger in samples where ACEs were treated categorically (i.e., 4+ versus 0 [referent] ACEs; OR = 2.034, [95 % CI 1.673, 2.474]) compared to continuously (i.e., accumulation of ACEs; OR = 1.308 [95 % CI 1.179, 1.450]). Finally, year of publication was a significant moderator. That is, the association between ACEs and heavy alcohol use was stronger among older studies, $b = -0.45$ (95 % CI −0.089, −0.0001). Age, race and ethnicity, and sex were not significant moderators.

3.6. Meta-analytic results for ACEs and illicit drug use

3.6.1. Pooled effect size

A total of 49 samples produced a significant pooled effect size (OR = 2.191 [95 % CI 1.976, 2.428]; see Fig. 4). Funnel plot inspection revealed asymmetry (Supplemental Fig. 3) and when results were adjusted by adding 14 imputed studies using Duval and Tweedie's trim and fill technique (Peters et al., 2007), the adjusted effect size was OR = 1.695 (95 % CI 1.530, 1.878).

3.6.2. Moderator analyses

Between study heterogeneity was indicated (Q = 1224.339, $p < .001$; $I^2 = 96.080$; $\tau^2 = 0.007$). The prediction interval ranged from $r = 0.05$ to 0.37 and moderators were explored (see Supplemental Table 7). Four significant moderators emerged. First, effect sizes were stronger among studies that examined illicit drug use via self-report OR = 2.314 (95 % CI 2.029, 2.639) compared to interview OR = 1.51 (95 % CI 1.12, 2.04). Effect sizes were stronger in samples where ACEs were treated categorically (i.e., 4+ versus 0 [referent] ACEs; OR = 4.482 [95 % CI 3.357, 5.984]) compared to continuously (i.e., accumulation of ACEs; OR = 1.661 [95 % CI 1.499, 1.841]). Year of publication was also a significant moderator, $b = -0.019$ (95 % CI −0.042, 0.004), indicating that effect sizes between ACEs and illicit drug use were larger among older studies. Finally, minority was a significant moderator, such that the association between ACEs and illicit drug use was stronger among studies that included fewer participants that identified as minorities, $b = -0.006$ (95 % CI −0.010, −0.0009). Age and sex were not significant moderators.

3.7. Meta-analytic results for ACEs and cannabis use

3.7.1. Pooled effect size

A total of 17 samples produced a significant pooled effect size (OR = 1.692, 95 % CI [1.385, 2.068]; see Fig. 5). The funnel plot inspection revealed asymmetry (see Supplemental Fig. 4). When results were adjusted by adding three imputed studies using Duval and Tweedie's trim and fill technique (Peters et al., 2007), the adjusted effect size was OR = 1.453 (95 % CI 1.184, 1.786).

3.7.2. Moderator analyses

Between study heterogeneity was indicated (Q = 177.521, $p < .001$; $I^2 = 90.987$; $\tau^2 = 0.010$). The prediction interval ranged from $r = -0.08$ to 0.35 and moderators were explored (see Supplemental Table 7). Year of publication emerged as a significant moderator, $b = -0.117$ (95 % CI -0.224, −0.009), indicating that the association between ACEs and cannabis use was stronger among older studies. Type of informant and categorical vs. continuous were not able to be examined as moderators due to too few studies providing this information. Age, sex, and minority status were not significant moderators.

3.8. Sub-analyses of studies examining ACEs categorically

To examine the gradient relation between ACEs and substance use, we derived pooled effect sizes in studies that included associations specifically as 0 [reference group] vs 1 ACEs, 0 vs 2 ACEs, 0 vs 3 ACEs, and 0 vs 4 ACEs. A difference between effect sizes is identified if the 85 % confidence intervals do not overlap. With this subset of studies, there is some support for the gradient relation suggesting that as the number of ACEs increases, so too does the magnitude of risk (see Supplemental Table 8).

4. Discussion

It has been proposed that cumulative risk is associated with cumulative outcomes through a mediated net of adversity, whereby negative childhood events and disadvantage cluster together, and lead to risk-taking and poor outcomes across the lifespan (Atkinson et al., 2015). The results of the present meta-analysis demonstrate that the accumulation of ACEs prior to the age of 18 confers risk for multiple outcomes that may either directly or indirectly increase health risks, including problematic alcohol use, heavy drinking, illicit drug use, cannabis use, and smoking.

There are several reasons to expect an association between ACEs and substance use. Broadly, cumulative or prolonged exposure to stress may lead to physiological and emotional dysregulation, which can increase proclivity for substance use (Stellern et al., 2023). Given that exposure to parental substance use is an ACE, the relationship between ACEs and substance use in adulthood may be accounted for by the transmission of substance use across generations. Indeed, a longitudinal study consisting of a nationally representative sample demonstrated that substance use in a previous generation predicts substance use in the current generation (Knight

et al., 2014). Future research may wish to compare the association between ACEs and substance use, including and excluding parental substance use, to strengthen our understanding of the intergenerational transmission of substance use.

A unique component of the current meta-analysis was the examination of moderators. Our findings showed that effect sizes were higher in studies where ACEs were measured categorically, as opposed to continuously. One reason for this finding is that statistically, categorical analyses such as Odd Ratios provide an estimate of two extremes of the measurement spectrum (i.e., 0 versus 4). When analyses compare 0 versus 4+ ACEs, a comparison is being made between opposite ends of the ACEs distribution, which includes 40 % vs 16.1 % of the population, respectively (Madigan et al., in press). As such, the disproportionately smaller sample of individuals who had experienced 4+ ACEs compared to those without ACEs exposure may inflate the effect size. Thus, previous meta-analyses examining ACEs and negative health outcomes that only compare 4+ versus 0 ACEs are likely overestimating the true effect across the entire population. Also, Reidy et al. (2021) demonstrated that more variance in negative outcomes was accounted for when the ACEs measurement considered the frequency of occurrence rather than a simple count score. Thus, there is growing evidence suggesting that how ACEs are measured and the types of statistical models used may influence our understanding of the magnitude of association with negative outcomes. Practically speaking, the research approach of measuring ACEs in a categorical manner is inconsistent with clinical practice. That is, clinicians may choose to follow up with all endorsement of ACEs exposure, rather than only inquiring among individuals who have experienced 4+ ACEs.

The finding that effect sizes for the association between ACEs and smoking, heavy alcohol use, problematic alcohol use, and illicit drug use were stronger among studies that utilized self-report measures of substance use compared to clinician interview may be due to single-informant bias, which has demonstrated greater effect sizes in past research (Bauer et al., 2013). The present finding may also be attributed to social desirability, such that a past meta-analysis demonstrated that less social desirability in responding occurred when participants responded to sensitive items (e.g., mental health, illegal drug use) via computer compared to face-to-face interviews (Richman et al., 1999). Future research should explore the differences in effect size of the association between ACEs and substance use based on measurement methodology to better understand factors that may impact the validity of self-report substance use measures.

The associations between ACEs and problematic alcohol use, heavy alcohol use, illicit drug use, and cannabis use were stronger among older studies. These findings may reflect the “decline effect”, whereby the strength of the association between variables have been found to weaken over time, possibly due to studies with null results being previously less likely to be published (Schooler, 2011). These results may also be attributed to cohort effects, such that existing literature has found that rates of binge drinking were higher among birth cohorts that held more approving attitudes towards binge drinking (Keyes et al., 2012). A prominent change among recent years is the legalization of cannabis in Canada and many US states. Past research has found that legalization of cannabis has been associated with increased cannabis use, more accepting attitudes towards use, and lower perceived risk associated with cannabis (Miech et al., 2015).

Finally, the association between ACEs and illicit drug use was moderated by minority status, such that the association was stronger among studies that included a smaller proportion of racialized or ethnic minority individuals. While ACEs are more common among groups exposed to greater disadvantage and systemic oppression, including racialized or ethnic minority individuals (Maguire-Jack et al., 2020), this finding may be interpreted using challenge models of resiliency. That is, exposure to hardship and stressors related to racism and systemic oppression may serve to build resilience against future stressors (Zimmerman, 2013). In contrast, it is possible that individuals who do not belong to a racial or ethnic minority group have less experience with many of these stressors, and thus may be less prepared to deal with future stressors.

4.1. Study implications

Results from this meta-analysis point to the importance of developing and utilizing trauma-informed approaches for substance use treatment (SAMHSA and Center for Behavioral Health Statistics and Quality, 2019). For example, assessment of ACEs can provide valuable information to help contextualize an individual’s substance use concerns or diagnoses. Additionally, ACEs screening has been implemented in routine healthcare with a high degree of acceptability among clients (van Roessel et al., 2021). Further, the results of this study suggest that individuals who have experienced ACEs should be provided with early prevention efforts to protect against potentially problematic substance use. For example, past qualitative research has suggested that prevention efforts for trauma-affected youth should focus on psychoeducation regarding trauma and substance use, building skills for coping, and peer support (Shin et al., 2022). Lastly, results signal the critical need to go upstream and build effective mitigation strategies that support children exposed to ACEs.

Of note, ACEs are not necessarily deterministic of problematic outcomes. Several studies have shown that social support from family, partners, and community can serve as important protective factors. For example, Madigan et al. (2016) found that mothers who experienced a high number of ACEs had lower levels of marital conflict when they also reported high levels of feelings of security, trust, order, and connectedness in their neighborhood environment. Thus, future research may wish to extend upon these findings by identifying factors that can be fostered to attenuate the association between ACEs and substance use.

4.2. Limitations

The present research is not without limitations. First, the meta-analyses, which were correlational in nature, conceptualized substance use consistent with existing literature (e.g., Hughes et al., 2017) to allow for direct comparison of results in light of an influx in research on this topic in recent years. Future research may wish to examine both problematic use and non-problematic use for all outcomes and compare results. Second, all studies included in the present meta-analysis were cross-sectional, and as such, study design

could not be evaluated as a moderator. Given the limited research assessing the association between ACEs and substance use across the lifespan, longitudinal research is needed to better understand patterns of association over time. Relatedly, all studies used retrospective reports to measure ACEs. While this is standard in the field, reports may be biased by the respondents' personality traits and memory inaccuracies associated with recall of childhood events (Reuben et al., 2016). Third, we could not examine several important moderators, such as socioeconomic status and education level, due to a low number of studies reporting on these variables. Future research should encourage the reporting of demographic variables during the publication process to improve transparency and allow for important moderator variables to be tested in meta-analyses. Finally, the ACEs score is a frequency count which fails to capture important contextual information, including the perpetrator, severity, timing, and chronicity of maltreatment experiences.

5. Conclusions

Findings from the current study provide support for the notion that exposure to ACEs confers risk for substance use across the lifespan. The findings show that exposure to ACEs is associated with greater smoking, problematic alcohol use, heavy alcohol use, illicit drug use, and cannabis use. An important take-away from the current study is that the method in which ACEs are measured has implications for the magnitude of association between ACEs and substance use. From a clinical perspective, using trauma-informed approaches to prevent substance use from becoming problematic, or for treatment of problematic substance use, with or without the use of the ACEs measure (see Racine et al., 2020) is warranted.

Declaration of competing interest

None.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chiabu.2023.106431.

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