#### REVIEW



# The association between adverse childhood experiences and common mental disorders and suicidality: an umbrella review of systematic reviews and meta-analyses

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#### Abstract

Adverse childhood experiences (ACEs) are related to increased risk of common mental disorders. This umbrella review of systematic reviews and meta-analyses aimed to identify the key ACEs that are consistently associated with increased risk of mental disorders and suicidality. We searched PsycINFO, PubMed, and Google Scholar for systematic reviews and meta-analyses on the association between ACEs and common mental disorders or suicidality published from January 1, 2009 until July 11, 2019. The methodological quality of included reviews was evaluated using the AMSTAR2 checklist. The effect sizes reported in each meta-analysis were combined using a random-effects model. Meta-regressions were conducted to investigate whether associations vary by gender or age of exposure to ACEs. This review is registered with PROSPERO (CRD42019146431). We included 68 reviews with moderate (55%), low (28%) or critically low (17%) methodological quality. The median number of included studies in these reviews was 14 (2–277). Across identified reviews, 24 ACEs were associated with increased risk of common mental disorders or suicidality. ACEs were associated with a two-fold higher odds of anxiety disorders (pooled odds ratios (ORs): 1.94; 95% CI 1.82, 2.22), internalizing disorders (OR 1.76; 1.59, 1.87), depression (OR 2.01; 1.86, 2.32) and suicidality (OR 2.33; 2.11, 2.56). These associations did not significantly (P > 0.05) vary by gender or the age of exposure. ACEs are consistently associated with increased risk of common mental disorders and suicidality. Well-designed cohort studies to track the impact of ACEs, and trials of interventions to prevent them or reduce their impact should be global research priorities.

Keywords Adverse childhood experiences · Mental health · Suicide · Evidence synthesis · Umbrella review

## Introduction

Adverse childhood experiences (ACEs) are stressful and potentially traumatic events occurring in childhood or adolescence (0–18 years) that can negatively impact health and well-being. [22, 47] ACEs include exposure to childhood maltreatment, parental mental illness, family dysfunction, violence and socio-economic adversity. [22, 47] ACEs are common across low-, middle- and high-income countries, with two in every five adults having at least one ACE [48, 65] A nationally representative study from the USA found that three in five adults reported at least one ACE, and a quarter of adults had at least three such experiences. [65]

Numerous systematic reviews and meta-analyses have linked ACEs with an increased risk of the common mental disorders throughout the life course. [42, 48, 76] For example, a meta-analysis of observational studies found that compared to individuals with no ACEs, individuals with four or more ACEs have higher odds of anxiety (odds ratio (OR) = 3.70, 95% CI 2.62–5.22), depression (OR = 4.40, 95% CI 3.54–5.46) and suicide attempts (OR = 30.14, 95% CI 14.73–61.67). [42] Consistent with this, about 30% of all mental disorders are attributable to ACEs, [48] including

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30% of cases of anxiety, 40% of cases of depression, [4] and 67% of lifetime suicide attempts [18].

The high prevalence of ACEs (3, 4), coupled with the increasing evidence of their significant contribution to most classes of mental disorders (4, 5), suggests that ACEs could be strategic targets for prevention. However, the strength, quality and consistency of the associations between various ACEs and common mental disorders and suicidality have not been comprehensively assessed, partly because most systematic reviews and meta-analyses to date have focused on the association between a single ACE and a mental disorder. Furthermore, there remain substantial gaps in the evidence base regarding whether the relationship between ACEs and mental disorders vary across populations and developmental stage at exposure to ACEs. Understanding the impact of developmental timing of exposure to ACEs and whether the relationship is more pronounced in certain population groups provides a unique opportunity to identify which populations and sensitive periods in development are best to intervene to reduce the occurrence and impact of ACEs. To reduce the global mental health burden wrought by ACEs, a comprehensive synthesis of the broad evidence base is required, to identify the key ACEs that are consistently associated with increased risk of mental disorders to target in preventive interventions.

This umbrella review of systematic reviews and metaanalyses aimed to synthesize evidence to date on the key ACEs that contribute to the increased risk of anxiety disorders, internalizing disorders, depression or suicidality.

#### Methods

#### Search strategy and selection criteria

To define an ACE, we used the World Mental Health Surveys list of ACEs as a starting point and updated it to include other ACEs reported in the literature. [42, 47, 48] Based on this, the following four categories of ACEs were identified: interpersonal loss (parental separation, parental death, both death and separation), family dysfunction (mental illness, suicidality, substance use disorder, incarceration, domestic violence, inter-parental conflict), maltreatment (physical abuse, sexual abuse, emotional abuse, neglect, felt discrimination, bullying, foster care, and maladaptive parenting (such as harsh discipline, aversiveness, over-involvement or parent–child conflict), [12, 44] and other childhood adversities (child physical illness, parental chronic illness, traumatic experience, economic hardship, neighborhood violence, homelessness).

We searched PsycINFO (Ovid), PubMed (NLM), and Google Scholar for systematic reviews and meta-analyses on the association between ACEs and anxiety disorders, internalizing disorders, depression or suicidality. To identify recent evidence, we limited the search to reviews published between January 2009 and July 11, 2019. A comprehensive search strategy was developed combining three concepts: (1) ACEs, (2) mental disorders or suicidality (anxiety disorders, internalizing disorders, depression or suicidality), and (3) systematic review or meta-analysis. Reference lists of included reviews, additional databases including PROS-PERO, JBI Database of Systematic Reviews and Implementation Reports, and Centers for Disease Control and Prevention were hand-searched for relevant articles.

We included systematic reviews and meta-analyses published in the English language that synthesized data on the associations between ACEs before the age of 18 and the risk of anxiety disorders, internalizing disorders, depression or suicidality before or after the age of 18. Reviews of reviews, and meta-analyses or systematic reviews that include studies on the association between ACEs after the age of 18 years and mental disorders were excluded. The search was not restricted to specific measurement methods for mental disorders (e.g. DSM or ICD diagnostic criteria) or ACEs. Suicidality included suicidal ideation, suicide, suicide attempts or suicidal behaviors. We excluded reviews that searched only one electronic database or did not follow the methodology of systematic reviews.

#### Study selection and data extraction

The titles and abstracts of each review were screened for eligibility by the first author (BWS). Two authors (BWS and WL) independently reviewed the full-text articles to identify reviews meeting our eligibility criteria, and independently evaluated the methodological quality of identified reviews using the AMSTAR2 checklist. This 16-item checklist rates the methodological quality of reviews as high, moderate, low or critically low [77]. Two authors (BWS and WL) independently extracted data on review characteristics, including type of ACE, study design of primary studies, effect sizes, and the number of primary studies reported in each review. Primary studies in each review were not analyzed.

#### **Statistical analysis**

Effect sizes reported as correlation coefficients, [74] regression coefficients, relative risks, [31], and Cohen's ds were converted to odds ratios (OR) to produce comparable estimates. A random-effects model was used to estimate the summary effect and 95% confidence interval (CI) of the log-transformed OR. The random-effects model was preferred due to significant heterogeneity among the included meta-analyses (I<sup>2</sup> > 50%). Subgroup analyses were performed to compare the associations across different groups. We assessed heterogeneity between meta-analyses using the I<sup>2</sup>

statistic [38]. Publication bias was assessed using Begg's adjusted rank correlation test, Egger's regression asymmetry test, and visual inspection of funnel plots [19]. Furthermore, we used meta-regression to investigate whether the associations between ACEs and mental disorders or suicidality vary by type of ACEs, gender or age of exposure to ACEs [34]. Where the included reviews did not provide pooled quantitative estimates, findings from individual systematic reviews were described narratively.

#### Results

A total of 10,057 systematic reviews and meta-analyses were identified. Following duplicate removal and title and abstract screening, 157 potentially eligible systematic reviews and meta-analyses were reviewed in full text. Of these, we included 68 systematic reviews and meta-analyses on the associations between ACEs and anxiety disorders (n=29), internalizing disorders (n=22), depression (n=43), and suicidality (n = 30) [1-3, 5-7, 9-11, 13, 14, 16, 17, 20, 23-30, 32, 33, 36, 37, 39-43, 46, 49-58, 60, 62-64, 66, 67, 69-73, 75, 78-87, 89-91, 93]; see Fig. 1 for PRISMA flow diagram). The median number of included studies in these reviews was 14 (2-277). Overall, 55%, 28%, and 17% of the reviews were rated as of moderate, low, and critically low quality, respectively (see Appendix Table 1). Summary of important characteristics of included reviews is provided in the Appendix Table 2.

Twenty-four ACEs were significantly associated with increased risk of anxiety disorders, internalizing disorders, depression or suicidality (P < 0.05). The most frequently examined ACEs included childhood maltreatment (including physical abuse, sexual abuse, maladaptive parenting), bullying, parental mental illness, and inter-parental conflict. Low socio-economic status, discrimination, exposure to violence, and parental incarceration were also associated with at least one of the four outcomes. Most ACEs were associated with increased risk of multiple mental disorders or suicidality. The full list of ACEs associated with anxiety disorders, internalizing disorders, depression or suicidality is provided in Table 1.

Meta-analysis of 27 independent effect sizes (11 metaanalyses) [2, 28, 42, 52, 54, 55, 67, 70, 75, 91, 93], showed that exposure to at least one ACE was associated with increased risk of anxiety disorders (OR 1.99; 95%CI 1.76, 2.25; P < 0.001;  $I^2 = 81.8\%$ ). This association was significant both in males (OR 1.52; 1.21, 1.90) and females (OR 1.91; 1.54, 2.36) and across all ages at exposure to ACEs (Table 2). Further meta-regression analyses showed that the associations between ACEs and anxiety disorders did not vary significantly by gender (OR 1.16; 0.93, 1.44, P = 0.157), age at exposure to ACEs (OR 1.06; 0.82, 1.37, P = 0.608) or the study design (OR 0.73; 0.38, 1.36, P = 0.312). Subgroup analyses showed that specific types of ACEs such as sexual abuse, physical abuse, and maladaptive parenting were associated with significantly higher odds of anxiety disorders (Table 3).

The associations between ACEs and anxiety disorders were narratively summarized in 17 systematic reviews. Fifteen of these concluded that ACEs (including: child abuse, separation, racial discrimination, violence, displacement, bullying and parental chronic illness) were associated with significantly higher risk of anxiety disorders. [6, 14, 26, 46, 49–51, 57, 63, 73, 84–87] However, Hoffman et al. [40] found that bereaved children and adolescents showed similar levels of anxiety disorders compared with nonbereaved children or adolescents. In another review, statistically significant associations between vicarious racism and anxiety disorders were found in only one of the three studies included [37].

Meta-analysis of 29 effect sizes from 7 meta-analyses, [3, 11, 24, 72, 78, 83, 93] showed a significant association between ACEs and internalizing disorders (OR 1.76; 1.59, 1.87; P < 0.001;  $I^2 = 74.2\%$ ) (Table 2). Maladaptive parenting was frequently reported and associated with significantly higher odds of internalizing disorders (OR 1.54; 1.47, 1.67) (Table 3). Meta-regressions showed that the associations between ACEs and internalizing disorders did not vary significantly by age at exposure to ACEs (OR 1.08; 0.87, 1.33, P = 0.453) or the study design (OR 1.20; 0.97, 1.48, P = 0.086). Meta-regression was not conducted on gender due to the small number of meta-analyses included. Twenty reviews provided narrative synthesis of the association between ACE and internalizing disorders, and all these studies linked ACEs to internalizing disorders [5–7, 16, 20, 23, 26, 37, 40, 46, 49, 50, 53, 62, 69, 73, 79, 80, 84, 85].

Thirty-nine independent effect sizes on the associations between ACEs and depression were reported in 15 metaanalyses [2, 3, 28, 42, 52, 54, 55, 60, 67, 70, 75, 81, 90, 91, 93]. Children with at least one ACE had 2.01 times higher odds of developing depression (95 CI%: 1.86, 2.32;  $P < 0.001; I^2 = 83.4\%$ ) as compared to those with no ACEs (Table 2). Maladaptive parenting behaviours (OR 2.00; 1.76, 2.24), physical abuse (OR 1.55; 1.41, 1.71), sexual abuse (OR 2.02, 1.64, 2.49) and bullying (OR 2.07; 1.07, 2.53) were associated with an increased risk of depression. Metaregressions showed that the associations between ACEs and depression did not vary significantly by age at exposure to ACEs (OR 0.95; 0.77, 1.17 P = 0.662) or the study design (OR 0.96; 0.85, 1.08, P=0.538). Meta-regression was not conducted on gender due to the small number of meta-analyses included.

The associations between ACEs and depression were narratively reported in 30 reviews; 28 found an increased risk of depression associated with ACEs, including: child abuse,



Fig. 1 Flow diagram of selection process

separation, parental mental illness, maladaptive parenting, separation, exposure to violence/displacement, bullying, racial discrimination, and parental chronic illness [5, 6, 13, 14, 17, 20, 23, 26, 33, 37, 39, 40, 46, 50, 53, 56–58, 62, 64, 71, 73, 84, 85, 87, 89]. Two systematic reviews assessed for sex differences in associations between ACEs and depression. Cheng et al. [14] found mixed findings regarding the sex difference in the association between separation (left behind) and depression, with seven studies reporting no sex difference, three studies finding a higher risk in males and Table 1Summary of ACEsassociated to common mentaldisorders or suicidality

| List of ACEs                                 | Number of reviews or meta-analyses reporting associa-<br>tions of ACEs with mental disorders or suicidality <sup>\$</sup> |                         |            |             |  |
|--|---|-------------------------|------------|-------------|--|
|  | Anxiety disorders   | Internalizing disorders | Depression | Suicidality |  |
| Interpersonal loss                           |   |                         |            |             |  |
| Separation/left behind/forced separation     | 2(1)  | _                       | 2          | 1           |  |
| Parent/family dysfunction                    |   |                         |            |             |  |
| Parental mental illness                      | 1   | 3                       | 3          | 2           |  |
| Parental chronic illness                     | 1   | 3                       | 2          |             |  |
| Suicide attempt by parents/friends           |   |                         |            | 4           |  |
| Parental incarceration/immigration detention | 1   | 1                       |            | (1)         |  |
| Divorce                                      | 1   |                         | 2          | 1           |  |
| Inter-parental conflict                      | 3   | _                       | 2(1)       |             |  |
| Child maltreatment                           |   |                         |            |             |  |
| Bullying                                     | 1   | 1                       | 2          | 5           |  |
| Child abuse                                  | 2   | _                       | 2          | -           |  |
| Childhood maltreatment                       | 2   | _                       | 2          | 3           |  |
| Physical or sexual abuse                     |   |                         | 1          | 2           |  |
| Physical abuse                               | 4   | _                       | 5          | 1           |  |
| Sexual abuse                                 | 5   | _                       | 5          | 3           |  |
| Emotional or psychological abuse             | 1   | _                       | 1          | 3           |  |
| Neglect                                      | 1   | 1                       | 2          | 1           |  |
| Maladaptive parenting #                      | 4   | 3                       | 2          | 1           |  |
| Reported racial discrimination               | 2(1)  | 1                       | 4          | -           |  |
| Adoption during childhood                    | 1   | _                       | 1          | -           |  |
| Sexual orientation discrimination            | -   | _                       | 2          | 1           |  |
| Other ACEs                                   |   |                         |            |             |  |
| ACEs (Unspecified)                           | 2   |                         | 2          | 1           |  |
| Military family deployment                   | -   | 2                       | 1          | 1           |  |
| Exposure to violence/war                     | 2   | 1                       | 3          |             |  |
| Family history of sexual abuse               | -   | _                       | _          | 2           |  |
| Homelessness                                 | 2   | 1                       | _          | -           |  |
| Living in refugee camps/displacement         | 1   | 1                       | 1(1)       | (1)         |  |
| Others*                                      | 2   | 2                       | 1          | 3           |  |

<sup>\$</sup>Number of studies reporting positive associations (number of studies that did not find positive associations)

<sup>#</sup>Includes harsh or hostile parenting such as harsh parenting, aversiveness, over-involvement or parentchild conflict

\*Includes loneliness, perceived socio-economic status

two, a higher risk in females. A review by Fazel et al. [23] found that exposure to violence was associated with higher risk of depression in females. Conversely, two other systematic reviews found no statistically significant associations between displacement (living in refugee camps) [85], or household dysfunction [87], and depression.

In the meta-analysis of 33 independent associations from 9 meta-analyses [2, 29, 41–43, 60, 67, 70, 82], ACEs were associated with a two-fold increased odds of suicidality (OR 2.33; 2.11, 2.56; P < 0.001;  $l^2 = 88.6\%$ ). The association was significant both in males (OR 2.14; 1.81, 2.53) and females (OR 2.28; 2.03, 2.56) (Table 2). Bullying (both traditional

and cyberbullying) was the most frequently reported ACE (28 effect sizes from 6 meta-analyses) associated with suicidality (OR 2.27; 2.06, 2.49) (Table 3). Meta-regressions showed that the associations between ACEs and suicidality did not vary significantly by age at exposure to ACEs (OR 0.88; 0.64, 1.20, P = 0.418) or the study design (OR 1.17; 0.90, 1.53, P = 0.216). Meta-regression was not conducted on gender due to the small number of meta-analyses included.

The associations between ACEs and suicidality were narratively summarized in 16 systematic reviews. Fourteen linked ACEs (such as parental mental illness, child abuse, Table 2Random effects meta-<br/>analysis of the association<br/>between ACEs and mental<br/>disorders and suicidality

|                        | Anxiety disorders | Depression        | Suicidality       | Internalizing disorders |
|------------------------|-------------------|-------------------|-------------------|-------------------------|
| At least one ACE       |                   |                   |                   |                         |
| Effect sizes (studies) | 27 (11)           | 39 (15)           | 33 (9)            | 29 (7)                  |
| Pooled OR (95% CI)     | 1.99 (1.76, 2.25) | 2.01 (1.86, 2.32) | 2.33 (2.11, 2.56) | 1.76 (1.59, 1.87)       |
| P value                | < 0.001           | < 0.001           | < 0.001           | < 0.001                 |
| <sup>2</sup>           | 81.8%             | 83.4%             | 88.6%             | 74.2%                   |
| Sex                    |                   |                   |                   |                         |
| Males                  | 3 (2)             |                   | 5 (2)             |                         |
| Pooled OR (95% CI)     | 1.52 (1.21, 1.90) |                   | 2.14 (1.81, 2.53) |                         |
| [ <sup>2</sup>         | 23.1%             | _                 | < 0.001           | -                       |
| P value                | < 0.001           |                   | 15.7%             |                         |
| Females                | 3 (2)             |                   | 5 (2)             |                         |
| Pooled OR (95% CI)     | 1.91 (1.54, 2.36) | _                 | 2.28 (2.03, 2.56) |                         |
| P value                | < 0.001           |                   | < 0.001           | -                       |
| [2]                    | 33.2%             |                   | 0.00%             |                         |
| Study design           |                   |                   |                   |                         |
| Cohort                 | 4 (2)             | 14 (5)            | 5 (2)             | 13 (2)                  |
| Pooled OR (95% CI)     | 2.05 (1.62, 2.59) | 2.16 (1.89, 2.47) | 1.82 (1.61, 2.05) | 1.52 (1.37, 1.69)       |
| P value                | < 0.001           | < 0.001           | < 0.001           | < 0.001                 |
| [2]                    | 64.8%             | 65.4%             | 0.00%             | 47.7%                   |
| Multiple study designs | 14 (8)            | 25 (10)           | 36 (8)            | 10 (5)                  |
| Pooled OR (95% CI)     | 1.83 (1.57, 2.12) | 2.03 (1.80, 2.33) | 2.25 (2.05, 2.47) | 1.93 (1.66, 2.24)       |
| P-value                | < 0.001           | < 0.001           | < 0.001           | < 0.001                 |
| [2]                    | 82.6%             | 85.7%             | 88.4%             | 87.8%                   |
| Cross-sectional        |                   | 8 (3)             |                   |                         |
| Pooled OR (95% CI)     |                   | 1.87 (1.52, 2.30) |                   |                         |
| P-value                | -                 | < 0.001           | -                 | -                       |
| [ <sup>2</sup>         |                   | 70.7%             |                   |                         |
| Age*                   |                   |                   |                   |                         |
| Childhood              | 12 (7)            | 23 (7)            | 12 (5)            | 9 (4)                   |
| Pooled OR (95% CI)     | 1.92 (1.67, 2.22) | 2.09 (1.79, 2.45) | 2.56 (2.07, 3.16) | 1.73 (1.59, 1.87)       |
| P value                | < 0.001           | < 0.001           | < 0.001           | < 0.001                 |
| [ <sup>2</sup>         | 74.2%             | 84.5%             | 88.8%             | 77.6%                   |
| Other age groups*      | 9 (4)             | 24 (8)            | 21 (5)            | 20 (4)                  |
| Pooled OR (95% CI)     | 2.05 (1.69, 2.50) | 1.98 (1.78, 2.20) | 2.24 (2.00, 2.51) | 1.74 (1.60, 1.94)       |
| P-value                | < 0.001           | < 0.001           | < 0.001           | < 0.001                 |
| [2]                    | 81.8%             | 73.4%             | 89.0%             | 77.6%                   |

<sup>\*</sup>Includes: before 16, <13, 5–12, 12–18, adolescent and children, offspring, under 18 years Note: A meta-analysis was not conducted if the total number of associations available were <2

and family dysfunction) to increased risk of suicidality [2, 6, 10, 20, 27, 30, 32, 36, 39, 51, 58, 66, 70, 73]. However, two reviews did not find a significant association between suicidality and parental incarceration [7], or displacement due to violence [23].

There was no evidence of publication bias for the associations between ACEs and anxiety disorders, internalizing disorders, depression and suicidality as assessed using the Egger and Begg's tests and visual inspection of funnel plots (Figs 1, 2, 3 4 in the Appendix). Sensitivity analyses using meta-regressions showed that the associations between ACEs and mental disorders or suicidality did not significantly vary according to the methodological quality of included meta-analyses. Because of the small number of reviews, we could not perform analyses on assessment methods for ACEs (self-report, health records, parental report), the outcomes (anxiety disorders, internalizing disorders, depression or suicidality), or exposure to multiple ACEs.

| Table 3 | Random effects meta-analysis of | the association between | types of ACEs and mental | disorders and suicidality |
|---------|---------------------------------|-------------------------|--------------------------|---------------------------|
|---------|---------------------------------|-------------------------|--------------------------|---------------------------|

|                                     | Anxiety disorders          | Depression        | Suicidality       | Internalizing disorders |
|-------------------------------------|----------------------------|-------------------|-------------------|-------------------------|
| Childhood Maltreatment <sup>+</sup> |                            |                   |                   |                         |
| Effect sizes (studies)              | 12 (6)                     | 20 (8)            | 28 (6)            | _                       |
| Pooled OR (95% CI)                  | 1.86 (1.62, 2.14)          | 2.02 (1.79, 2.29) | 2.27 (2.06, 2.49) |                         |
| P value                             | < 0.001                    | < 0.001           | < 0.001           | _                       |
| $I^2$                               | 72.1%                      | 82.0%             | 87.7%             |                         |
| Bullying                            |                            | 5(5)              | 25 (5)            |                         |
| Pooled OR (95% CI)                  | -                          | 2.07 (1.70, 2.53) | 2.25 (2.03, 2.50) |                         |
| P value                             |                            | < 0.001           | < 0.001           | _                       |
| $I^2$                               |                            | 75.8%             | 88.5%             |                         |
| Physical abuse                      | 4 effect sizes (3 studies) | 5 (4)             |                   |                         |
| Pooled OR (95% CI)                  | 1.60 (1.40, 1.78)          | 1.55 (1.41, 1.71) | -                 | _                       |
| P value                             | < 0.001                    | < 0.001           |                   |                         |
| $I^2$                               | 85.0%                      | 0.0%              |                   |                         |
| Sexual abuse                        | 3 (2)                      | 5 (4)             |                   |                         |
| Pooled OR (95% CI)                  | 1.77 (1.14, 2.74)          | 2.02 (1.64, 2.49) | -                 | _                       |
| P value                             | 0.011                      | < 0.001           |                   |                         |
| $I^2$                               | 83.1%                      | 70.0%             |                   |                         |
| Maladaptive parenting               | 12 (2)                     | 14 (7)            |                   | 17 (2)                  |
| Pooled OR (95% CI)                  | 2.21 (1.86, 2.63)          | 2.00 (1.76, 2.24) |                   | 1.54 (1.47, 1.67)       |
| P-value                             | < 0.001                    | < 0.001           |                   | < 0.001                 |
| $I^2$                               | 66.7%                      | 40.0%             |                   | 31.3%                   |
| Other ACEs #                        |                            | 5 (5)             | 8 (5)             |                         |
| Pooled OR (95% CI)                  | -                          | 1.93 (1.20, 3.11) | 2.71 (1.95, 3.76) | _                       |
| P-value                             |                            | 0.007             | < 0.001           |                         |
| $I^2$                               |                            | 96.1%             | 89.2%             |                         |

<sup>+</sup>Includes sexual abuse, physical abuse, emotional abuse or neglect

<sup>#</sup>Includes: separation, parental illness, exposure to violence, ACEs(unspecified), or family separation

Note: A meta-analysis was not conducted if the total number of associations available < 2

## Discussion

The novelty of this umbrella review is that it summarizes evidence of the strength, quality and consistency of the associations between a comprehensive list of ACEs and the risk of common mental disorders and suicidality. We summarized both quantitative and narrative evidence of the associations between ACEs and mental disorders. We included 68 systematic reviews and meta-analyses and found robust evidence that ACEs are associated with increased risk of mental disorders and suicidality in both males and females. Exposure to at least one ACE in general, and to specific types of ACEs such as child maltreatment, bullying, and maladaptive parenting behaviours, were associated with a two-fold increased risk of anxiety disorders, internalizing disorders, depression or suicidality. These associations were evident across different age groups at exposure to ACEs (e.g. under 5 years, under 18 years).

This umbrella review has three key findings. First, we identified a comprehensive list of ACEs associated with

increased risk of common mental disorders and suicidality. Given the high prevalence of ACEs in the community, [21, 48, 61, 65, 68, 88] and their association with increased risk of multiple mental disorders and suicidality, preventive interventions targeting ACEs may reduce the substantial burden of mental disorders and suicidality. Multicomponent interventions focusing on improving parenting, strengthening economic support to families, providing quality care and education in early life, mental health counselling, and social service referrals could reduce the occurrence of ACEs and ameliorate their impacts on mental health [45, 59, 94].

Second, although most ACE research has focused on child maltreatment, especially sexual and physical abuse in high-income countries [42], other adversities such as maladaptive parenting behaviours were as important as child maltreatment in predicting mental disorders. These data are consistent with previous research suggesting that the effects of maladaptive parenting behaviors on children's mental health outcomes are strong but are largely overlooked [48, 93]. One possible explanation for the strong relationship between maladaptive parenting and negative mental health outcomes is that ACEs tend to cluster within families, and most children with ACEs are exposed to multiple ACEs. [48, 65] Parents with mental illness [44], low socio-economic status, substance use disorders or a history of maltreatment [8, 15] are more likely to use maladaptive parenting strategies which, in turn, increase offspring risk for mental disorders. Fortunately, preventive parenting interventions have demonstrated robust, sustained benefits for children's internalizing outcomes [94], and should be implemented more widely to reduce maladaptive parenting and buffer against the impact of other ACEs (e.g. socio-economic disadvantage) [92].

Third, broad social and family-related factors, such as discrimination, inter-parental conflict, parental mental and chronic illnesses, parental incarceration, and exposure to violence or war were also associated with increased risk of mental disorders. Although the association between these ACEs and our outcomes of interest are not as quantifiably robust as the other ACEs, their prominence in narrative reviews indicate that these ACEs are important broader factors that likely also impact on internalizing and suicidality outcomes, in part because they tend to co-occur with the other ACEs (e.g. maladaptive parenting, child maltreatment). This suggests the need for more robust evidence of the associations between these ACEs and internalizing and suicidality outcomes.

The multidimensional and overlapping nature of ACEs [48, 65] and their negative impact on common mental disorders and suicidality has implications for clinical and policy interventions. Interventions to prevent ACEs and mitigate their negative impacts might focus on promoting positive parenting behaviours and the prevention of bullying and child abuse. From a public health perspective, the overlapping nature of ACEs and their associations with multiple mental disorders and suicidality suggest that effective interventions to address ACEs require collaboration between various sectors and stakeholders across different areas of adversity. Well-designed cohort studies are required to explore the trajectories after exposure to ACEs, including the developmental periods when preventive interventions could be optimally effective. Future research should also focus on identifying interventions effective for reducing ACEs and their impact on mental health while employing standardized assessment of ACEs and associated mental disorders.

There are several limitations to this review. Almost half of the included systematic reviews and meta-analyses had low or critically low methodological quality, mostly due to the absence of double screening for study selection and data extraction and infrequent declaration of funding sources. Whether the effect of ACEs varies by age of exposure or age at which the mental disorder is measured could not be sufficiently explored due to limited data. Most of the included reviews were based on cross-sectional studies that are unable to discern the temporal relationship of ACEs and mental health outcomes. ACEs were assessed retrospectively in all studies included in this review, which might have introduced recall or reporting biases. Longitudinal studies with repeated measurements of exposure to ACEs and subsequent onset of mental disorders are likely to be most informative. However, retrospective reports by adults of their own ACEs in childhood have been found to have acceptable validity [35]. The absence of a standardized measurement of ACEs and their effects on mental health may have contributed to the considerable heterogeneity between the systematic reviews and meta-analyses. Most of the ACEs found to be associated with increased risk of mental disorders pertained to high-income countries owing to the lack of data from lowand middle-income countries, therefore suggesting the need for further evidence in low- and middle-income countries. We also need a better understanding of the trajectories from exposure to ACEs to mental disorders, including the time when preventive interventions could be optimally effective.

## Conclusion

This is the first study to comprehensively re-analyze systematic reviews and meta-analyses of ACEs associated with common mental disorders or suicidality. Our findings demonstrate that ACEs, including the commonest types such as childhood maltreatment (sexual, physical, or emotional abuse), maladaptive parenting, and bullying, are associated with a two-fold increase in the risk of common mental disorders or suicidality in later life. To prevent a substantial burden of mental disorders in the population, the development, evaluation and implementation of interventions to prevent ACEs or reduce their impact need to be global research priorities.

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**Availability of data and materials** The authors declare that the data supporting the findings of this study are available within the article and its supplementary information files.

### **Compliance with ethical standards**

**Conflicts of interest** The authors declare that there are no conflict of interests.

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