The timing effect of childhood maltreatment in depression: A systematic review and meta-analysis

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Abstract

Although empirical evidence has confirmed the causal relationship between childhood maltreatment and depression, findings are inconsistent on the magnitude of the effect of age of exposure to childhood maltreatment on psychological development. This systematic review with meta-analysis aims to comprehensively synthesize the literature on the relationship between exposure age of maltreatment and depression and to quantitatively compare the magnitude of effect sizes across exposure age groups. Electronic databases and grey literature up to April 6th, 2022, were searched for English-language studies. Studies were included if they: 1) provided the information on exposure age; and 2) provided statistical indicators to examine the relationship between childhood maltreatment and depression. Fifty-eight articles met eligibility criteria and were included in meta-analyses. Subgroup analyses were conducted based on subtypes of maltreatment and measurements of depression. Any kind of maltreatment (correlation coefficient [r]=0.17, 95%CI=0.15~0.18), physical abuse (r=0.13, 95%CI=0.10~0.15), sexual abuse (r=0.18, 95%CI=0.15~0.21), emotional abuse (r=0.17, 95% CI=0.11~0.23), and neglect (r=0.08, 95% CI=0.06~0.11) were associated with an increased risk of depression. Significant differential effects of maltreatment in depression were found across age groups of exposure to maltreatment (Q=34.81, p<0.001). Age of exposure in middle childhood (6-13 years) had the highest risk of depression, followed by late childhood (12-19 years) and early childhood (0-6 years). Implications of the findings provide robust evidence to support targeting victimized children of

all ages and paying closer attention to those in middle childhood to effectively reduce the risk of depression.

Key words: childhood maltreatment, depression, age at maltreatment, sensitivity period, depressive symptom, psychopathology

Introduction

Major depression (MD) is characterized by persistent low mood and reduced interest or pleasure in daily activities along with additional signs and symptoms including lack of joy and reduced energy and self-esteem, impaired ability to think, concentrate, or make decisions, and altered appetite and sleep quality (McIntosh et al., 2019). According to the World Health Organization (WHO), MD is the most common illness worldwide and the leading cause of disability. The WHO estimated that over 350 million (4.4% of the global population) suffered from it and its prevalence increased by more than 18 % between 2005 and 2015, particularly in low- and middle-income countries (Friedrich, 2017; WHO, 2017).

The etiology of MD is not fully understood but is likely caused by a complex combination of genetic, biological, environmental, and psychosocial factors (Uher & Zwicker, 2017). Genetic studies of MD consistently show that MD is polygenic with many genetic variants with small effects and no loci with a major effect can explain its heritable component (Major Depressive Disorder Working Group of the Psychiatric GWAS Consortium et al., 2013). Even though the largest genome-wide meta-analysis of depression including a total of 807,553 individuals identified a total of 102 independent genetic variants, only a small proportion (8.9%) of heritability was captured (Howard et al., 2019). Since the 1960s, adverse social environmental factors have been tested to examine the independent and combined effects of environmental factors in a specific mental disorder (Uher & Zwicker, 2017, Su et al., 2020). Childhood maltreatment, or exposure to abuse or neglect in children under the age of 18, is one of the most

frequently studied environmental factors that has a substantial causal relationship with the occurrence of MD (Kendler et al., 1999; Li et al., 2016; Lippard & Nemeroff, 2019). It is a global problem with serious life-long consequences. The WHO estimates that up to 1 billion children aged 2 to 17 years have experienced physical, sexual, or emotional violence or neglect (Hillis et al., 2016). Statistics on the scale of maltreatment are likely to be underestimated due to most of the abuse and neglect going unreported (Lippard & Nemeroff, 2019). Childhood maltreatment not only increases the risk of psychopathology but also contributes to some of the principal causes of death, disease, and disability, such as heart disease, cancer, and suicide. Childhood maltreatment contributes to a broad range of adverse health and behavioral problems that have high long-term costs over time, for both the child and the society involving various areas of health care and the social systems (Fang et al., 2015; Ferrara et al., 2015; Gilbert et al., 2009).

Although the contribution of child maltreatment is well established for psychopathology (Arseneault, 2017), the evidence is less consistent for whether there are sensitive periods of developmental stages and when the exposure to maltreatment has the most impact on the risk of psychopathology (Dunn et al., 2017; Dunn et al., 2018; Gomez et al., 2017). For MD, several prospective (Keiley et al., 2001; Thornberry et al., 2010) and retrospective studies (Dunn et al., 2013; Dunn et al., 2017; Schalinski et al., 2016) have suggested that the sensitive periods of exposure might exist, and earlier exposure of maltreatment before age of 5 is associated with greater risk of depression. However, other studies have expanded the sensitive period to the age

of 12 (Maercker et al., 2004; Schoedl et al., 2010). In contrast, other studies suggested that later exposure of maltreatment at ages of 10 to 12 (Harpur et al., 2015) and ages of 12 to17 (Thornberry et al., 2001) predict a greater risk of MD. However, other studies, both prospective (Jaffee & Maikovich-Fong, 2011; Oldehinkel et al., 2014) and retrospective (Dunn et al., 2017; Pietrek et al., 2013), fail to find such differential age of exposure impact. These conflicting results on the timing effect of age exposure to maltreatment in MD can be partially explained by the studies' high heterogeneity in terms of sources of study subjects, measurements of childhood maltreatment, measurement of MD, and differences in study designs. For that reason, it is critical to have an objective synthesis of the existing literature to evaluate whether the exposure of maltreatment at different stages of early life leads to the differential risk of psychopathology. We are unaware of any systematic review conducted or published on the timing effect of age of exposure to maltreatment exposure on the development of MD.

To fill this important knowledge gap, this systemic review and meta-analysis aim to examine if age exposure to childhood maltreatment is associated with a disproportional risk of MD. Hopefully, the findings of this systematic review will not only provide robust evidence for the relationship between sensitive periods of maltreatment exposure and the risk of MD but also serve as guidance for prevention and intervention policymaking by showing the critical stage of early life when interventions could have the most impact in preventing the onset of MD.

Methods

Searching strategy and selection criteria

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). The protocol was registered in PROSPERO (CRD42019130724). Both computerized and manual searches were used to retrieve relevant studies. A computerized search of five bibliographic databases (EMBASE, HealthStar, PsychoInfo, Medline, and Cochrane Library) from their inception until April 6, 2022, was conducted for published articles on the exposure of childhood maltreatment factors and MD. Second, a snowball technique was then used to search the reference lists of all relevant studies to identify further studies. We also manually searched the grey literature on the relevant topic. We restricted our search to articles published in English. Appendix A provides a full list of the search strategy.

Authors (YZ, YS, and TG) independently screened the identified records for eligibility from the title, the abstract to the full text. Inconsistent selections were solved by a group discussion with a third author (ML). Studies were included if they met the following criteria: 1) provided the information on the age or age range of the exposure of childhood maltreatment; 2) had clear diagnostic criteria for depression or depressive symptom, specifically Diagnostic and Statistical Manual (DSM) and its updates, International Classification of Diseases (ICD) or other generally accepted criteria; 3) used observational study designs, including case-control, cohort, and cross-sectional studies; 4) had a comparison group of without the exposure of childhood maltreatment; and, 5) provided statistical indicators to examine the relationship between childhood

maltreatment and depression/depressive symptom. Figure 1 presents a flowchart of the study selection process. Appendix B provides a list of the included studies in alphabetical order.

Data extraction and study quality assessment

Data on the first author, year of publication, study setting, sample size, source of study subjects, study designs, measurement of childhood maltreatment, age, and type of exposure to childhood maltreatment, measurement of depression/depressive symptoms, and age of diagnosis were extracted independently by two reviewers (ML and TG). If there were multiple reports of a single study cohort, we selected the one with the largest sample size. Any disagreements among reviewers were solved by group discussions with a third author (XM). In order to gather complete and consistent study information, the reviewers strived to contact the original authors of the studies with missing or discrepant information. We asked them open-ended questions to reduce the risk of bias in responses.

The quality of included studies was assessed based on the Newcastle-Ottawa Quality Assessment Scale (Wells et al., 2021). There were 11 quality characteristics were documented (total score=11), with the assumption of each characteristic equally contributed to overall study quality (Appendix C).

Data synthesis

Data synthesis took into account major sources of heterogeneity, including age exposure to maltreatment, subtypes of maltreatment, and depression measurements. Considering the

variations of different types of maltreatment and measurements of depression (depression diagnosis or depressive symptoms), we grouped the reviewed articles into the following six analyses: (1) any kind of childhood maltreatment and depression in general; (2) physical abuse and depression in general; (3) sexual abuse and depression in general; (4) emotional abuse and depression in general; (5) any kind of childhood maltreatment and depression diagnosis; (6) any kind of childhood maltreatment and depressive symptom. We report the results of each analysis separately.

Meta-analysis

We used the zero-order correlation coefficient (r) as the common effect size measure in this review. Effect size coefficients were either directly obtained from studies or first computed and transformed from data presented in the published articles. Coefficients were then converted with Fisher's Z transformation to avoid the standard error skew in correlational analyses. Once the pooled effect size was available, we then converted Fisher's Z scores back to coefficients to ease the interpretation of results. All the analyses were based on the frequentist framework.

DerSimonian and Laird I^2 statistics. We tested heterogeneity with *DerSimonian* and *Laird* I^2 statistics to determine the proportion of heterogeneity in this systematic review. As suggested, the heterogeneity tests determine whether fixed-effects or random-effects models would be used (Higgins et al., 2003). If these tests show non-significant heterogeneity, we used a fixed-effects

model, whereas a more conservative random-effects model was used when we identified heterogeneity.

Mixed-effects analyses. Mixed-effects analyses (Stram, 1996) were applied to examine whether there are differences in the correlation between exposure age of maltreatment and depression. Mixed-effects analyses applied a random-effects model to combine studies within each subgroup, and a fixed-effect model to combine subgroups and yield the overall effect (Q-value). The study-to-study variance (tau-squared, T^2) was not assumed to be the same for all subgroups. Thus, this value was computed within subgroups but not pooled across subgroups.

Funnel plots and Egger's tests. Funnel plots and Egger's tests were used to test for publication bias. Trim-and-fill methods were performed to estimate the unbiased pooled effect size while taking publication bias into account (Duval & Tweedie, 2000).

Sensitivity analysis. Sensitivity analysis was done by completing a leave-one-out at a time analysis. This test assessed the influence of each study on overall pooled estimates by recalculating correlation coefficients with each study being removed one at a time.

Meta-regression. Multivariate meta-regression was conducted for the overall and subgroup analyses that included at least 40 studies (as suggested by López-López et al., 2014) to explore the effects of the following characteristics: type of childhood maltreatment, type of depression, age of exposure to maltreatment, and quality assessment items based on the Newcastle-Ottawa Quality Assessment Scale (sample size, study design, representativeness, assessment of

childhood maltreatment, assessment of depression, and confounders control). The restricted maximum likelihood and Knapp-Hartung methods were applied to estimate variances (T^2) and standard errors, respectively. Hierarchical regression models were applied to better understand the roles of characteristics: model 1 only included the quality assessment items; model 2 included model 1 and type of childhood maltreatment; model 3 included model 2 and type of depression; and model 4 included model 3 and age of exposure to maltreatment.

All the analyses were conducted using the Comprehensive Meta-Analysis version 2.0 (Biostat, Englewood, NJ, USA).

Results

The initial search produced 40,319 titles, from which 5,839 abstracts were reviewed, and 3,094 articles were fully retrieved for evaluation. A total of 58 articles met the eligibility criteria (Figure 1). All included articles are published articles, and none is from gray literature. This review covers 32,820 study participants, with the sample size of individual studies ranged from 36 to 5,266 (median sample size = 276). Approximately 69.0% (40/58) of the studies were conducted in the United States, with the rest being from Canada, Australia, UK, South Korea, Israel, Spain, German, South Africa, New Zealand, Finland, Mongolia, and Iran. The average score of study quality for selected articles was good at 6.5 (ranged from 4 to 111, see Appendix C). A total of 23 studies (39.7%, 23/58) had above-average quality.

Overall findings on the relationship between childhood maltreatment and depression

All the 58 articles were included in the analysis to examine the overall relationship between the exposure age of childhood maltreatment and depression. Table 1 presents the summarized characteristics of the included articles. Some of the selected articles had information on the different types of childhood maltreatment, age of exposure, relationship with the perpetrator, or type of depression. All this information is included in the specific group analysis. These 58 articles provided information on a total of 111 different research cohorts. Figure 2a presents the individual study, pooled estimates for overall and by exposure age, and funnel plots that were used to visually assess whether the publication bias was present. Table 2 summarizes the pooled estimates and statistics for overall and subgroup analyses and meta-regressions.

The overall pooled coefficient was 0.17 (95% CI 0.15-0.18, $p<0.001$), indicating a significant relationship between childhood maltreatment and depression. The heterogeneity test was significant across the studies ($I^2=88.51\%$, $p<0.001$), indicating that 88.51% of the total variability among effect sizes from individual studies may not cause by sampling error rather by true heterogeneity between studies. A random-effects model was used. As shown in the funnel plot in Figure 2a, not all the observed studies were within the domain which represents 95% CI limits. Asymmetry was evident. There was evidence of publication bias (Egger's test=1.97, p=0.001). The trim-and-fill method was then applied to estimate a pooled effect size after adjusting potential missing publications that might exist in this meta-analysis. After considering the potentially missed publications, the result remains significant (r=0.15, 95% CI=0.12-0.17).

Sensitivity analysis indicated that the overall correlation between childhood maltreatment and depression was not influenced by the inclusion or exclusion of any individual study (r=0.20, 95% CI=0.18-0.23, p<0.001). Meta-regression analyses showed that only age of exposure to maltreatment significantly related to the correlation between childhood maltreatment and depression (F=3.41, p=0.003; k=111, R^2=0.168). Details of meta-regression results can be found in Appendix D.

Figure 2a and Figure 4a show the pooled correlations by exposure age groups. Significant correlations between childhood maltreatment and depression were found in all exposure age groups of maltreatment, with the highest pooled effect of maltreatment being 0.28 (95% CI=0.23-0.32) for age exposure between 0 to 13 years old; and the lowest being 0.09 (95% CI=0.02-0.17) for 0 to 6 years old. Significant and differential effects of maltreatment in depression were also observed in the comparisons across age groups (total between-group difference Q=34.81, p<0.001) (Table 3). The risk of depression with the age exposure to childhood maltreatment between 0 to 13 years was significantly higher than that between 0 to 11 (Q=23.86, p<0.001), 0 to 12 (Q=15.05, p<0.001), 0 to 14 (Q=5.30, p=0.021), 0 to 6 (Q=17.68, p<0.001), and 12 to 19 years (Q=18.99, p<0.001). The correlation between childhood maltreatment and depression was substantially higher for the subjects who exposed to maltreatment between 6 to 12 years of age, compared with those exposed between 0 to 6 years of age (Q=4.45, p=0.035).

Subgroup analyses by subtypes of childhood maltreatment and depression

We then conducted meta-analyses for different subtypes of maltreatment and different depression measures. Significant pooled correlations were found between physical abuse, sexual abuse, emotional abuse, and neglect, and depression (including the depression diagnosis and the depressive symptoms), respectively. For different depression measures, childhood maltreatment significantly increased the risk of both depression diagnosis and depressive symptoms. Age exposure to maltreatment had differential effects in all subgroup analyses. Sensitivity analyses also supported these findings. Publication bias was only identified in the subgroups of sexual abuse and depressive symptoms. High heterogeneities were found, and random-effects models were used for all subgroup analyses.

Relationships between childhood maltreatment and depression by subtype of maltreatment. Table 2 summarises the overall pooled estimates of the relationships between different subtypes of childhood maltreatment and depression. Figure 2b~2e presents the forest plots and funnel plots of the pooled analyses. Physical abuse (r=0.13, 95% CI=0.10-0.15), sexual abuse (r=0.18, 95% CI=0.15-0.21), emotional abuse (r=0.17, 95% CI=0.11-0.23), and neglect (r=0.08, 95% CI=0.06-0.11), were significantly related to the onset of depression, respectively. In the meta-regression analysis, although the overall age of exposure to maltreatment was not significantly related to the correlation between sexual abuse and depression (F=1.83, p=0.130; k=41, R^2=0.188), individuals who were maltreated between 12 to 19 years of age had a significantly lower risk of depression, compared to those exposed to maltreatment between 0 to 13 years of age (β= -0.11, 95% CI= -0.22 ~ -0.01, p=0.040).

Significant correlations at different ages of exposure to maltreatment were found in all the subtypes of maltreatment (Figure 2b~2e). Figure 4b~4e illustrated the correlations by exposure age group for physical abuse, sexual abuse, emotional abuse, and neglect, respectively. Between-group differences were also found (Table 3) with total between-group difference Q was 22.11 (p=0.001) for physical abuse, 17.99 (p=0.006) for sexual abuse, 11.22 (p=0.047) for emotional abuse, and 18.90 (p=0.002) for neglect, indicating that the correlations between subtypes of maltreatment and depression were significantly affected by age of exposure.

Relationship between childhood maltreatment and depression by depression measures. Figure 3a and 3b present the individual studies, pooled estimates for overall and by age group analyses, and funnel plots for depression diagnosis and depressive symptoms, respectively. Childhood maltreatment was significantly correlated with depression diagnosis (r=0.14, 95% CI=0.11-0.17) and depressive symptoms (r=0.17, 95% CI=0.15-0.19), respectively. Meta-regression analyses showed that age of exposure to maltreatment was significantly associated with the relationship between childhood maltreatment and depressive symptoms (F=3.11, p=0.006; k=94, R^2=0.179).

Significant correlations were found in both depression diagnosis and depressive symptoms for all age groups of exposure to maltreatment (Figure 3a and 3b). Significant between-age-group differences were also found (Q=12.04, p=0.017 for depression diagnosis; and Q=32.35, p<0.001 for depressive symptoms), indicating that age exposure to maltreatment at 0 to13 and 0 to 14 years had higher risks of developing depression diagnosis or depressive symptoms,

compared to those exposed to maltreatment at 0 to 6, 0 to 11, 0 to 12, and 12 to 19 years of age (Table 3 and Figure 4f and 4g).

Discussion

This systematic review and meta-analysis provide the first comprehensive synthesis on differential effects of age exposure to childhood maltreatment in depression. In line with the literature, exposures to any maltreatment and its subtypes during the childhood were associated with an elevated risk of depression (Afifi et al., 2014; Li et al., 2016; Rehan et al., 2017). More importantly, we identified differential effects of age exposure groups in depression, with middle childhood (ages 6 to 13) being the most susceptible period of maltreatment in terms of developing depression. Childhood maltreatment could disrupt the developing neuroendocrine stress response systems in children (Carrion et al., 2002; Cicchetti et al., 2011), and may also result in an increased risk of allostatic load, leading to a wearing down of biological systems, including increasing the risk of inflammation and reducing resistance to illnesses (Danese & McEwen, 2012).

Studies across various scientific domains have suggested differential effects of age exposure to maltreatment in depression but these findings have been inconclusive (Russotti et al. 2021). For instance, studies on chronic stress have found that children's cortisol levels in response to stress vary by age, with children in middle childhood reporting the highest level of cortisol (Bosch et al., 2012). Cortisol is a hormone produced by the adrenal glands and plays an important role in everything from how the body uses glucose (sugar) to the regulation of blood

pressure to the function of the immune system (Schimelpfening, 2020). Short-term cortisol release prepares people for physical and emotional challenges, generates bursts of energy in the face of trauma. However, chronic stress can trigger continuous production of cortisol, and result in various physical and psychological problems, such as diabetes, heart disease, and depression (Dienes et al., 2013; Schimelpfening, 2020). Bosch and his colleagues found that childhood adversities during ages of 6 to 11 were associated with high levels of cortisol, whereas childhood adversities during ages of 12 to 15 were associated with low levels of cortisol, and for the ages 0-5 no associations were detected (Bosch et al., 2012). Differential effects of age exposure to maltreatment in depression could be partially explained by the fact that children in middle childhood are likely to have elevated levels of cortisol, and in turn trigger more risk of developing depression.

The literature on developmental psychopathology has proposed several hypotheses and pathways to illustrate the complex mechanisms of the timing of childhood adversities in psychopathology. Knudsen hypothesised that a “sensitive period” during the developmental stage allows the negative experiences to affect the brain through the processes of neural plasticity, and these changes were then eventually reflected in changes in behaviors (Knudsen, 2004). Childhood neglect and abuse during sensitive periods when hippocampus (Teicher et al., 2018) and amygdala (Demers et al., 2018) were maximally susceptible to trauma (age 7 for boys and age 10 for girls) can result in dysfunction. Dannlowski et al. (2012) has demonstrated a robust effect of childhood maltreatment on amygdala responsiveness to negative facial

expressions and hippocampal volumes in healthy adults without any history of psychiatric disorders, and the impaired hippocampus and amygdala neurogenesis and synaptic dysfunction leading to depression (Duman et al., 2012).

Children between the age of 6 and 13 are in the age period commonly referred to as middle childhood, which is a distinctive period between major developmental transition points. There are distinctive characteristics - physical, behavioral, social, and emotional for the development of children across the age span from 6 to13, for instance, elementary schooling, puberty, transitioning into adolescence. Empirical studies have concluded that physical and emotional changes of puberty give rise to a variety of mental health problems, including depression, anxiety, eating disorders, behavioral disorders, aggression and violence, attention deficit hyperactivity disorder (ADHD), and suicidal ideation and attempts (Goh et al., 2021; Ho et al., 2021; Viner, 2015). The physical maturation process and the fluctuation of hormone levels can affect both body and brain to alter children's needs, interests, and moods (Mental Help, 2021). Children become moodier and irritable during this period. It is common for children to have rapid and unexpected changes in mood which are also symptoms of depression and anxiety disorders. Literature has reported that childhood maltreatment predicted earlier pubertal development which, in turn, was associated with higher levels of internalizing symptoms (Copeland et al., 2010; Mendle et al., 2013; Trickett et al., 2011). Other challenges that children in this age period often have to deal with include transitioning to secondary school, identity development, peer pressure, and family problems. Childhood maltreatment has been identified as

a significant risk factor for heightened reactivity, emotion dysregulation, and poor impulse control (Arens et al., 2012; Dvir et al., 2014; Oshri et al., 2018) and can alter neurocognitive development which could influence the way that children respond to emotional stimuli (Pollak, 2008). When exposed to these multiple stressors, adolescents with poor emotion regulation and impulse control could be more vulnerable to negative emotionality (Duprey et al., 2020). Compared to those who had the exposure in early childhood (0 to 5), maltreatment occurring in middle childhood may have more detrimental effects as these victims have more cognitive capacities that affect their conceptualization and understanding of their adversities, which may have a proximal effect on later-on depression (Newbury et al., 2018). Altogether with previous literature across different scientific domains, this systematic review collectively suggests the highest susceptibility of depression when experiencing middle childhood maltreatment, in contrast to the history of maltreatment during other periods of childhood.

This review also identified that childhood maltreatment was significantly correlated with both depression diagnosis and depressive symptoms, and the correlation with depressive symptoms was stronger than that with depression diagnosis. This could be partially explained by the existence of clinical differences between depression diagnosis and depressive symptoms in terms of severity and clinical manifestations. Previous studies have consistently suggested that depressive symptoms are risk factors for major depression (Horwath et al., 1992; Pine et al., 1999).

Strengths and limitations

This systematic review and meta-analysis comprehensively synthesized all the literature on the research topic, which represents the most updated information on the relationship between the timing effect of maltreatment and depression. Furthermore, it also provided the first synthesis of differential effects of age exposure to childhood maltreatment in depression. This review identified the whole childhood was associated with negative consequences of maltreatment in the development of depression and exposure to maltreatment during middle childhood was the most vulnerable period in the childhood.

There are several study limitations to be noted. First, the meta-analyses were limited in the subgroup analyses due to lack of data for certain age groups, such as 0 to 6 age group for emotional abuse and neglect, and 6 to 12 age group for neglect and depression diagnosis group. Second, all the included studies in this review were from developed countries. Thus, the findings of the review may not be generalized to developing countries. Third, this review had high heterogeneity across studies in each subgroup. These selected studies included a mix of study populations, measurement tools for childhood maltreatment and depression, as well as study designs. The age groups of maltreatment exposures may include both the first onset of maltreatment and chronic maltreated individuals. Depression was a broad category including lifetime depression, past-year depression, recurrent depression, adolescent, and adult depression. All these sources of heterogeneity warrant the cautious interpretation of the results. Finally, retrospective measurements of childhood maltreatment, which are subject to recall bias, were commonly used in cross-sectional studies (35/46). The accuracy of childhood maltreatment

depends largely on the participants' recall and memory, which could be influenced by the depressed state itself (Hardt & Rutter, 2004) and can be experimentally manipulated by mood induction (Cohen et al., 1988).

Implications for practice, policy, and research

This systematic review demonstrates that childhood maltreatment represents a small but significant risk of depression. Children of all ages are vulnerable to the negative effects of maltreatment with the highest risk of depression exposing maltreatment during middle childhood. Prevention and intervention efforts should target children of all ages to effectively minimize the risk of depression among those with a history of maltreatment. Special attention should be paid to victims aged 6 to 13 years. This review makes several recommendations relevant to stakeholders aiming to develop practices or policies to prevent childhood maltreatment, promote resilience, and eventually prevent the occurrence of depression. Future research is also needed to corroborate or contradict the age of exposure to maltreatment in depression. These recommendations are listed in Table 4.

Conclusion

This review not only provides further evidence to support the association between childhood maltreatment and depression but more importantly highlights the differential effects of age exposures to maltreatment in terms of the risk of developing depression. The whole childhood is vulnerable to the negative consequences of maltreatment with middle childhood being the most susceptible timing to maltreatment in developing depression. Implications of the findings suggest

interventions and preventions should target children of all ages with special attention to those aged 6 to 13 years to effectively reduce the risk of depression.

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Table 1

A summary of study characteristics for the articles included in this systematic review

First author	Year	Setting	Sample size	Sample resource/ Cohort	Study design	Measurements of childhood maltreatment	Age of maltreatment exposure	Type of maltreatment	Measurements of depression	Age of outcome	Type of outcome	Statistical indicator
Allen	1989	USA	36	abused: hospital & children's protective services; nonabused: community	cross-sectional	Hospital and County Children's protective services records	7-13	physical abuse	CDI	7-13	depressive symptom	Means, SD's
As-Sanie	2014	USA	273	University hospital	cross-sectional	Sexual and Physical Abuse History Questionnaire	0-13	sexual abuse, physical abuse	CES-D	18+	depressive symptom	Means, t-test
Bhawanie	2017	USA	690	LONGSCAN	cohort	Child protective services records	0-4, 4-8, 0-8	neglect	CBCL, TSC	8, 12, 16	Depression diagnosis	Correlation
Blanchard	2002	USA	71	Patients seeking psychological treatment for irritable bowel syndrome	cross-sectional	Questionnaire that has been used in other surveys	0-13	physical abuse, sexual abuse	BDI	18+	depressive symptom	Cohort numbers in 2×2 table
Briere	1988	USA	278	Female undergraduate students	cross-sectional	Finkelhor's survey of childhood experiences	4-14	sexual abuse	Hopkins Symptom Checklist	18+	chronic & acute depression	Cohen's d, 95% CI
Brock	1997	USA	80	Female university students	cross-sectional	Childhood secsion of Sexual	0-13	sexual abuse	BDI	18+	depressive symptom	Means, SD's

						Experiences Survey						
Brown	2012	UK	273	general population	cross-sectional	CECA	0-8	in general	SCAN	18+	depressive episode	Cohort numbers in 2×2 table
Cerezo	1994	Spain	45	clinical sample & nonclinical control	cross-sectional	clinical records	6-11	any	CDI	8-13	depressive symptoms	Means, SD's
Cicchetti	2010	USA	850	Summer camp students	cross-sectional	official records	0-13	any	CDI	6-13	depressive symptom	Means, SD's
Courtney	2008	USA	195	Adolescent primary care patients	cross-sectional	CTQ	0-13	emotional abuse, physical abuse	BDI	15-18	depressive symptom	Correlation
Duggal	2001	USA	168	previous longitudinal study	cohort	Observations in home, interview, and child protection record	0-5	any	TRF, CBCL, YSR & CDRS	childhood (1-3 grade), adolescence (16/17.5)	Child and adolescent depression diagnosis	Zero-order Correlation
Ensink	2016	Canada	168	abused: clinical sample; control: health & community services	cross-sectional	Referred by health service providers & child protection services	7-12	sexual abuse	CDI	7-12	Depression diagnosis	Correlation
Haapasalo	1999	Finland	89	poison sample	cross-sectional	Abuse Forms	0-14	physical abuse, sexual abuse, emotional abuse, neglect	DICA-R-A	16-22	depressive symptom	Correlation
Haj-Yahia	2001	Israel	652	college students	cross-sectional	Finkelhor's survey of childhood experiences	0-11, 12-16	sexual abuse	BSI	18+	depressive symptom	Means, SD's

Harpur	2015	USA	1,354	risky children in the LONGSCAN	cohort	official records	0-4, 6-8, 10-12	any	CES-D	14	depressive symptoms	Spearman's rho Correlation
Harrop-Griffiths	1988	USA	55	hospital patients	cross-sectional	a structured interview being developed for previous study	0-14	sexual abuse	SCL-90	18+	depression	Cohort numbers in 2×2 table
Hauer	2008	UK	133	volunteer via newspaper advertisement	cross-sectional	a standard semistructured interview	0-11	sexual abuse	BDI-II	18+	depressive symptom	Means, SD's
Huang	2020	USA	1,690	FFCWS	cohort	Parent-Child CTS	5	physical abuse	CES-D	15	depressive symptoms	Pearson's Correlation
Hughes	1988	USA	58	cases from shelter; controls from local media	cross-sectional	multiple records	7-12	physical abuse, emotional abuse	CDI	7-12	depressive symptoms	Means, SD's
Jaschek	2016	USA	1,041	The Boricua Youth Study (BYS) data	cohort	modified TEQ	0-13	neglect, physical abuse, sexual abuse, multiple abuse	DISC-IV	10-13	depressive symptom	Means, SD's
Jones	2013	Australia	307	two previous population-based cohort	cross-sectional	valid self-report questions	0-13	any	CIDI	18+	depressive symptom	Pearson's Correlation
Kazdin	1985	USA	79	inpatients of a psychiatric facility	cross-sectional	interviews with parents/guardians and child, and legal documentation	0-12, 6-13, 0-13	physical abuse	CDI	6-13	depressive symptom	Means, SD's

Koci	2004	USA	568	community volunteers	cross-sectional	Women's Health History Form	0-12, 13-19	any	MMPI-2	18+	depressive symptoms	Spearman's rho Correlation
Kohrt	2004	Mongolia	99	population-based sample (boys)	cross-sectional	official records	0-10	physical abuse, emotional abuse	MFQ	3-10	depressive symptom	Spearman's Correlation
Lee	2012	USA	849	two cohorts from Pittsburgh Youth Study	cohort	official records	0-11	any	Recent Moods and Feelings Questionnaire	12-17 & 24/25	depressive symptom	Means, SD's
Lizardi	1995	USA	90	hospital patients and community controls	cross-sectional	EHEI & modified PBI	0-14	physical abuse, sexual abuse	DSM-III-R	18+	depression	Cohort numbers in 2×2 table
Luterek	2004	USA	355	University students	cross-sectional	LEQ	0-13	sexual abuse	BDI	18+	depressive symptom	Zero-order Correlation
Maciejewski	2006	USA	50	clinical-based samples and matched controls for depression	case-control	ETI	0-11	physical abuse, sexual abuse, emotional abuse	SCID, HRSD	18+	depression	Cohort numbers in 2×2 table
Mannarino	1991	USA	169	Referral abused cases and similar control group from schools	cross-sectional	Regional rape crisis centers	6-12	sexual abuse	CDI	6-12	depressive symptoms	Means, SD's
Marse	2002	USA	128	hospital patients	cross-sectional	Child PARQ	7-12	physical abuse, emotional abuse, neglect, and any	CDI	7-12	depressive symptoms	Pearson's Correlation

McCutcheon	2009	Australia	5,266	Australian Twin Register	cross-sectional	NCS	0-12, 13-17	physical abuse, sexual abuse	DIS, CIDI, SCID	1-12, 13-17, 18+	Depression diagnosis	Cohort numbers in 2×2 table
Mehta	2017	Canada	229	clinical sample	cross-sectional	SPAHQ	0-13	sexual abuse	DASS-21	18+	depressive symptom	Pearson's Correlation
Meyerson	2002	USA	130	US Department of Labor Job Corps facility	cross-sectional	SEQ	0-12	sexual abuse	BDI-II	16-18	depressive symptom	Correlation
Mikaeili	2013	Iran	893	school-based sample	cross-sectional	CTQ	0-14	physical abuse, emotional abuse, emotional neglect, physical neglect, any	SCL-90-R	12-14	depressive symptom	Means, SD's
Miller	2014	USA	884	risky children in the LONGSCAN	cohort	self-report and offical reports	0-12	physical abuse, emotional abuse, sexual abuse	TSCC, TSI	16 & 18	depressive symptom	Zero-order Correlation
Min	2015	South Korea	1,198	school-based sample	cross-sectional	CAS	0-13	physical abuse, emotional abuse, neglect	CES-D	12-13	depressive symptom	Pearson's Correlation
Miron	2014	USA	1,043	Female university students	cross-sectional	FEQ, CHQ, TLEQ	0-14, 0-12, 13-17	physical abuse, emotional abuse, sexual abuse	DASS-21	18+	depressive symptoms	Correlation

Miron	2016	USA	377	university students	cross-sectional	TLEQ	0-12	sexual abuse	DASS-21	18+	depressive symptom	Correlation
Morais	2016	USA	498	Male adolescents sexually offensed and received treatment	cross-sectional	clinical interview and official records	0-11	sexual abuse	K-SADS-PL	adolescence (mean age = 15)	depression	Cohort numbers in 2×2 table
Morokoff	2009	USA	473	Patients in substance abuse treatment facilities and an STI clinic	cross-sectional	Questionnaire that has been used previously	0-14	sexual abuse	short form of the CES-D	18-46	depressive symptom	Zero-order Correlation
Mueller-Pfeiffer	2013	German	287	psychiatric services	cross-sectional	TEC	0-6, 7-12, 13-18	any	HADS	17+	depressive symptoms	Correlation
Palosaari	2013	Israel	197	school-based sample	cross-sectional	Questions selected based on the American Professional Society on the Abuse of Children	0-12	emotional abuse & neglect	Depression Self-Rating Scale for Children	0-12	depressive symptom	Pearson's Correlation
Park	2018	South Korea	1,796	Participants from Korean Children and Youth Panel Study (KCYPS)	cohort	Validated questions	0-9	physical abuse, neglect	SCL-90-R	11	depressive symptom	Correlation
Polanczyk	2009	New Zealand	899	Dunedin study	cohort	self-report, behavioral observations, parental reports, multiple changes	3-11	any	DSM-III-R, DSM-IV	18-21, 26-32	depression	Cohort numbers in 2×2 table

						of primary caregiver						
Quevedo	2008	USA	170	Participants' mothers from public health clinics	cohort	Home observations, interviews, legal records	0-5, 4-17	physical abuse, sexual abuse, emotional abuse	SCL-90-R, YASR, SCID-I	18+	depressive symptoms	Zero-order Correlation
Rabinovitch	2015	USA	166	Participants from a RCT project	cohort	CSEQ	0-13	sexual abuse	CES-D	14-20	depressive symptom	Correlation
Rich	2005	USA	551	Female college students	cross-sectional	CTS, SES, CSVQ	0-13, 14-18/19	verbal abuse, physical abuse, sexual abuse	BDI-II	18-19	depressive symptoms	Correlation
Roatta	2000	USA	92	inner city couples	cross-sectional	Sexual Abuse Experience Questionnaire	0-13	sexual abuse	BDI	18+	depressive symptom	Correlation
Shanahan	2011	USA	1,004	population-based sample	cross-sectional	CAPA/YAPA	9-12, 13-16	any	CAPA/YAPA	9-12, 13-16, 19/21+	Depression diagnosis	Odds ratio
Skeen	2016	South Africa	989	community-based program	cross-sectional	UNICEF survey	0-13	harsh physical discipline, harsh psychological discipline	CDI-Short Form & TSCC	4-13	depressive symptom	Means, SD's
Thomas	2011	USA	110	Patients in a health care center	cross-sectional	WSHQ	0-13	sexual abuse	BDI-II	22-65	depressive symptom	Correlation
Turner	2004	USA	649	University students	cross-sectional	a list of acts recommended by previous study	13	physical abuse	CES-D	18+	depressive symptoms	Zero-order Correlation

Ullman	2014	USA	1,863	volunteer	cross-sectional	modified SES	0-13	sexual abuse	CES-D	18+	depressive symptom	Correlation
Walker	1988	USA	55	hosptical patients	cross-sectional	Questionnaire that has been used in other surveys	0-14	sexual abuse	NIMH-DIS	18+	depression	Chi-squared
Warmingham	2019	USA	620	cases: official records; controls: matched from community	cross-sectional	official records	0-12	neglect	CDI	10-12	depressive symptom	Cohen's d, 95% CI
Whiffen	2000	Canada	192	Volunteer in community	cross-sectional	Questionnaire that has been used in other surveys	0-13	sexual abuse	BDI	18+	depressive symptom	Correlation
Widom	2007	USA	1,196	cases: official records; controls: matched from community	cross-sectional	official records	0-11	physical abuse, sexual abuse, neglect, any	NIMH DIS-III-R	18+	depression, & depressive symptom	Means, SD's
Zelikovsky	2002	USA	100	university students	cross-sectional	PsyMQ, PhyMQ, CSVQ	0-13	emotional abuse, combined	BDI	18+	depressive symptom	Means, SD's

Note:

BDI, Beck Depression Inventory; BSI, Brief Symptom Inventory; CAPA, Child and Adolescent Psychiatric Assessment; CAS, Childhood Abuse Scale; CBCL, Child Behavior Checklist; CDI, Children's Depression Inventory; CDRS, Children's Depression Rating Scale; CES-D, Center for Epidemiological Studies Depression; CHQ, Childhood History Questionnaire; CIDI, Composite International Diagnostic Interview; CSEQ, Childhood Sexual Experiences Question; CSVQ, Sexual Child Victimization Questionnaires; CTQ, Childhood Trauma Questionnaire; CTS, Conflict Tactics Scale; DASS, Depression Anxiety Stress Scale; DIC-R-A, Diagnostic Interview for Children and Adolescents-Adolescent version; DIS, Diagnostic Interview Schedule; DISC-IV, Diagnostic Interview Schedule for Children; EHEI, Early Home Environment Interview; ETI, Early Trauma Inventory; FEQ, Family Experiences Questionnaire; FFCWS, Fragile Families and Child Well-being Study; HADS, Hospital Anxiety and Depression Scale; HRSD, Hamilton Rating Scale for Depression; IDAS-II, Inventory of Depression and Anxiety Scale-Second Version; K-SADS-PL, Kafman Schedule for Affective

Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version; LEQ, Life Experiences Questionnaire; LONGSCAN, Longitudinal Studies of Child Abuse and Neglect; MACE, Maltreatment and Abuse Chronology of Exposure scale; MFQ, Mood and Feelings Questionnaire; MMPI, Minnesota Multiphasic Personality Inventory; NCS, National Comorbidity Survey; NIMH, National Institute of Mental Health; PARQ, Parental Acceptance-Rejection Questionnaire; PBI, Parental Bonding Instrument; PhyMQ, Physical Child Maltreatment Questionnaire; PsyMQ, Psychological Child Maltreatment Questionnaire; SCAN, Schedule for Clinical Assessment in Neuropsychiatry; SCID, Structured Clinical Interview for DSM Disorders; SCL-90, Symptom Checklist–90; SCL-90-R, Symptom Checklist–90–Revised; SEQ, Sexual Experiences Questionnaire; SES, Sexual Experiences Survey; SPAHQ, Sexual-Physical Abuse History Questionnaire; TEC, Traumatic Experiences Checklist; TEQ, Traumatic Experience Questionnaire; TLEQ, Traumatic Life Events Questionnaire; TRF, Teacher's Report Form; TSC, Trauma Symptom Checklist; TSCC, Trama Symptom Checklist for Children; TSI, Trama Symptom Inventory; WSHQ, Wyatt Sex History Questionnaire; YAPA, Young Adult Psychiatric Assessment; YASR, Young Adult Self-Report; YSR, Youth Self Report; SD, Standard Deviation.

Table 2

Correlations (r) between childhood maltreatment and depression by exposure age

	Number of articles	Number of study cohorts	Pooled estimates				Meta regression[1]													
							Model 1				Model 2				Model 3				Model 4			
			Overall r (95% CI)	Heterogeneity I^2	Egger's test	Sensitivity analysis (r [95% CI])	Tau^2	R^2	Q	Significant moderator	Tau^2	R^2	Q	Significant moderator	Tau^2	R^2	Q	Significant moderator	Tau^2	R^2	Q	Significant moderator
Overall	58	111	0.17*** (0.15~0.18)	88.51***	1.97**	0.20 *** (0.18~0.23)	0.014	0.021	882.44***	None	0.015	0.000	859.81***	None	0.015	0.000	836.40***	None	0.012	0.168	565.50***	Age of exposure
By type of child maltreatment																						
Physical abuse	24	29	0.13*** (0.10~0.15)	89.05***	2.09	0.19*** (0.14~0.24)																
Sexual abuse	30	41	0.18*** (0.15~0.21)	77.74***	1.59*	0.19*** (0.16~0.22)	0.008	0.089	133.11***	None					0.008	0.046	133.06***	None	0.007	0.188	91.49***	Age of exposure
Emotional abuse	15	21	0.17*** (0.11~0.23)	89.69***	0.53	0.22*** (0.15~0.29)																
Neglect	9	11	0.08*** (0.06~0.11)	94.44***	2.19	0.17** (0.07~0.26)																
By depression measure																						
Diagnosis of depression	8	18	0.14*** (0.11~0.17)	66.84***	1.05	0.14*** (0.10~0.18)																
Depressive symptoms	51	94	0.17*** (0.15~0.19)	89.47***	1.91**	0.21*** (0.18~0.23)	0.015	0.035	769.84***	None	0.016	0.000	750.89***	None					0.013	0.179	470.06***	Age of exposure

[1] Model 1 = quality assessment items only; Model 2 = Model 1 + type of childhood maltreatment; Model 3 = Model 2 + type of depression; Model 4 = Model 3 + age of exposure.

*p<0.05; **p<0.01; ***p<0.001

Table 3

Comparisons between age groups of exposure by subgroup analyses[1]

Comparisons	**Any childhood maltreatment vs. any depression**	**Physical abuse vs. any depression**	**Sexual abuse vs. any depression**	**Emotional abuse vs. any depression**	**Neglect vs. any depression**	**Any childhood maltreatment vs. depression diagnosis**	**Any childhood maltreatment vs. depressive symptoms**
0-11 vs. 0-12	0.130 vs. 0.156	0.085 vs. 0.175**	0.128 vs. 0.139	NA	NA	0.131 vs. 0.164	0.122 vs. 0.154
0-11 vs. 0-13	0.130 vs. 0.278***	0.085 vs. 0.281***	0.128 vs. 0.250**	NA	NA	NA	0.122 vs. 0.278***
0-11 vs. 0-14	0.130 vs. 0.178	0.085 vs. 0.131	0.128 vs. 0.259**	NA	NA	0.131 vs. 0.304	0.122 vs. 0.159
0-11 vs. 0-6	0.130 vs. 0.094	NA	NA	NA	NA	NA	0.122 vs. 0.094
0-11 vs. 6-12	0.130 vs. 0.218	NA	NA	NA	NA	NA	0.122 vs. 0.194
0-11 vs. 12-19	0.130 vs. 0.130	0.085 vs. 0.082	0.128 vs. 0.129	NA	NA	0.131 vs. 0.076	0.122 vs. 0.151
0-12 vs. 0-13	0.156 vs. 0.278***	0.175 vs. 0.281*	0.139 vs. 0.250*	NA	NA	NA	0.154 vs. 0.278***
0-12 vs. 0-14	0.156 vs. 0.178	0.175 vs. 0.131	0.139 vs. 0.259*	NA	NA	0.164 vs. 0.304	0.154 vs. 0.159
0-12 vs. 0-6	0.156 vs. 0.094	NA	NA	NA	NA	NA	0.154 vs. 0.094
0-12 vs. 6-12	0.156 vs. 0.218	NA	NA	NA	NA	NA	0.154 vs. 0.194
0-12 vs. 12-19	0.156 vs. 0.130	0.175 vs. 0.082*	0.139 vs. 0.129	NA	NA	0.164 vs. 0.076*	0.154 vs. 0.151
0-13 vs. 0-14	0.278 vs. 0.178*	0.281 vs. 0.131	0.250 vs. 0.259	0.275 vs. 0.113	0.347 vs. 0.041**	NA	0.278 vs. 0.159*
0-13 vs. 0-6	0.278 vs. 0.094***	NA	NA	NA	NA	NA	0.278 vs. 0.094***
0-13 vs. 6-12	0.278 vs. 0.218	NA	NA	0.275 vs. 0.178	NA	NA	0.278 vs. 0.194
0-13 vs. 12-19	0.278 vs. 0.130***	0.281 vs. 0.082	0.250 vs. 0.129**	NA	NA	NA	0.278 vs. 0.151***
0-14 vs. 0-6	0.178 vs. 0.094	NA	NA	NA	NA	NA	0.159 vs. 0.094
0-14 vs. 6-12	0.178 vs. 0.218	NA	NA	0.113 vs. 0.178	NA	NA	0.159 vs. 0.194
0-14 vs. 12-19	0.178 vs. 0.130	0.131 vs. 0.082	0.259 vs. 0.129*	NA	NA	0.304 vs. 0.076*	0.159 vs. 0.151
0-6 vs. 6-12	0.094 vs. 0.218*	NA	NA	NA	NA	NA	0.094 vs. 0.194
0-6 vs. 12-19	0.094 vs. 0.130	NA	NA	NA	NA	NA	0.094 vs. 0.151
6-12 vs. 12-19	0.218 vs. 0.130	NA	NA	NA	NA	NA	0.194 vs. 0.151

Note:

[1]Between-age-group differences were examined by mixed-effects analyses. Age group 4-17 was not included in any comparison because of insufficient data (only 2 study cohorts in the overall analysis).

NA, comparisons were not available due to insufficient data (2 study cohorts or less) in at least one of the age groups of exposure to childhood maltreatment.

*p<0.05; **p<0.01; ***p<0.001

Table 4
Implications of this review for practice, policy, and future research

Practice & policy	1. In conjunction with the WHO Global status report on violence prevention (World Health Organization, 2014), preventing childhood maltreatment should utilize a multisectoral approach including both risk reductions and the promotion of protective factors, such as strengthening income and economic positions, providing positive parenting skills, teaching positive coping and problem-solving skills, making community and health services available, constructing safe environments for children, implementing laws ending maltreatment, and improving education and life skills (World Health Organization, 2016). 2. For health professionals, targeted education and training on the impact of childhood maltreatment should facilitate the early identification of childhood maltreatment and thus reducing the risk of psychopathology. 3. Middle childhood (6 to 13 years) should be the core target among the whole childhood. Collaborations with schools (especially elementary schools and junior high schools), parents, local communities, and teachers can be helpful to prevent and identify the occurrence of maltreatment. Educational projects for children and their families can raise awareness of maltreated behaviors and promote resilience. Factors at individual, familial, and societal levels play a significant role in promoting psychological wellbeing and reduced the risk of negative consequences of childhood maltreatment (Meng et al., 2018).
Future research	Future research is needed by: 1. Strengthening the research on the early life exposures, especially before age of 6 years, specific types of maltreatment (emotional abuse and neglect), and studies conducted in low- and middle-income countries. 2. Encouraging prospective cohort studies when possible. 3. Applying multiple measurements of childhood maltreatment as well as depression to increase the accuracy of the research findings.

References:

Meng, X., Fleury, M. J., Xiang, Y. T., Li, M., & D'Arcy, C. (2018). Resilience and protective factors among people with a history of child maltreatment: a systematic review. *Soc Psychiatry Psychiatr Epidemiol, 53*(5), 453-475. doi:10.1007/s00127-018-1485-2

World Health Organization. (2014). *Global status report on violence prevention 2014*. Retrieved from: www.who.int/violence_injury_prevention/violence/status_report/2014

World Health Organization. (2016). *INSPIRE: seven strategies for ending violence against children*. Retrieved from: https://www.who.int/violence_injury_prevention/violence/inspire-package/en/

Figure 1 PRISMA flow diagram

Note: Eligible studies could be included in multiple subgroup analyses as their available data permitted.

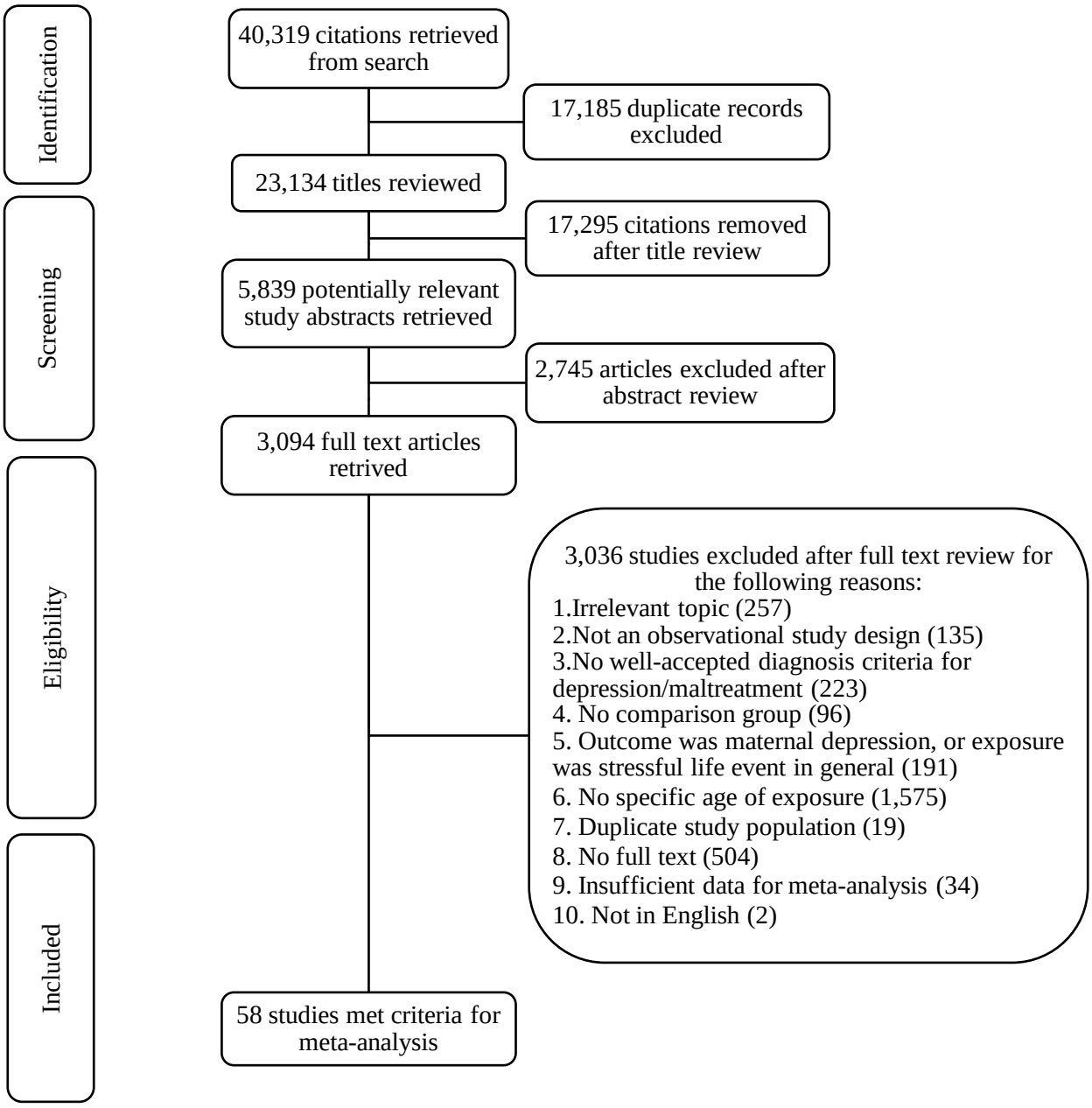
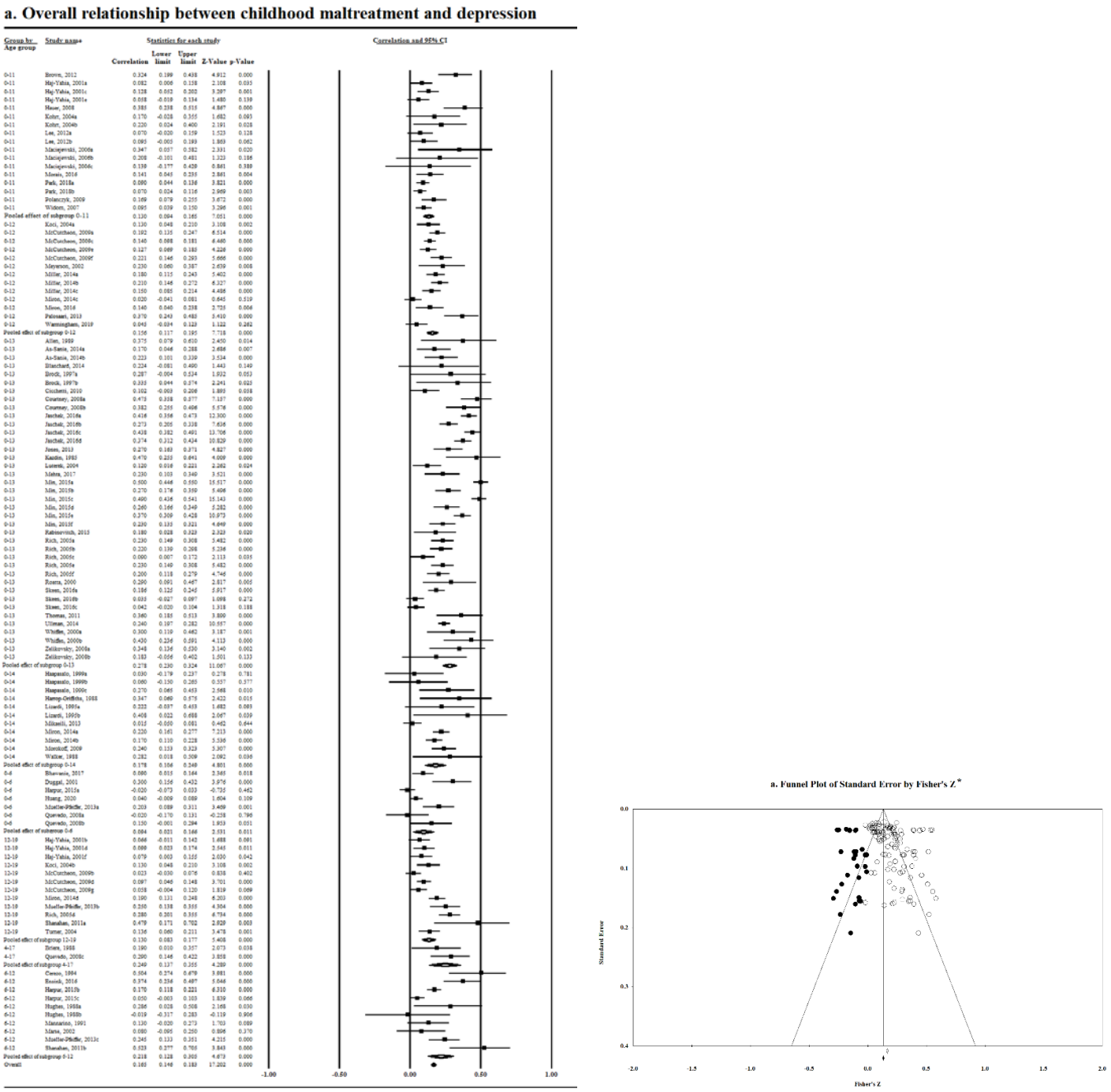


Figure 2 Forest plots and funnel plots for the relationship between childhood maltreatment and depression by subtypes of childhood maltreatment.

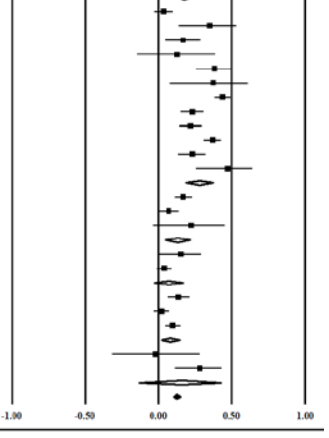
In the funnel plots, the x-axis shows the Fisher's Z estimate for each study and y-axis is standard error of the Fisher's Z estimate. The dashed line represents the 95% confidence interval (CI) and the point estimate of the Fisher's Z illustrates as the solid line.

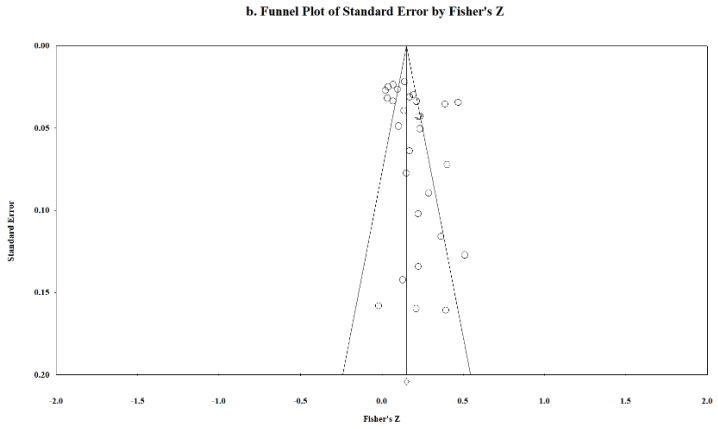
*Funnel plots present the findings after applying the trim-and-fill method. The open dots and diamond indicate the observed studies, and the closed dots and diamond indicate the missing studies imputed by the trim-and-fill method.



b. Physical abuse

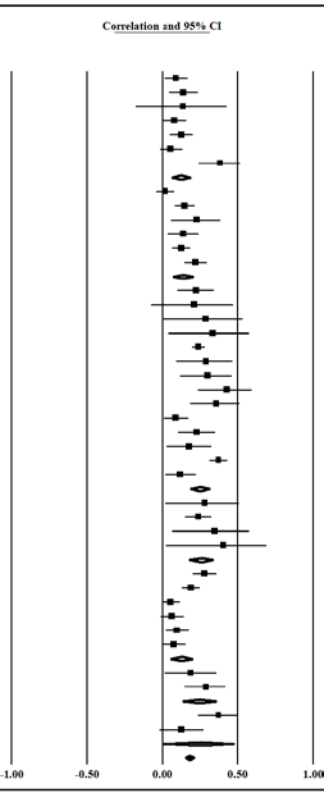
Group by Time point	Study name	Correlation	Lower limit	Upper limit	Z-Value	p-Value
0-11	Widom, 2007	0.103	0.008	0.197	2.114	0.034
0-11	Maciejewski, 2006b	0.208	-0.101	0.481	1.323	0.186
0-11	Park, 2018b	0.070	0.024	0.116	2.969	0.003
0-11	Kohrt, 2004b	0.220	0.024	0.400	2.191	0.028
Pooled effect of subgroup 0-11		0.085	0.044	0.125	4.082	0.000
0-12	Miller, 2014b	0.210	0.146	0.272	6.327	0.000
0-12	McCutcheon, 2009a	0.192	0.135	0.247	6.514	0.000
0-12	McCutcheon, 2009c	0.140	0.098	0.181	6.460	0.000
Pooled effect of subgroup 0-12		0.175	0.131	0.219	7.623	0.000
0-13	Skeen, 2016	0.035	-0.027	0.097	1.098	0.272
0-13	Zelikovsky, 2008a	0.348	0.136	0.530	3.140	0.002
0-13	As-Sanie, 2014a	0.170	0.046	0.288	2.686	0.007
0-13	Blanchard, 2014	0.127	-0.150	0.386	0.900	0.368
0-13	Courtney, 2008b	0.382	0.255	0.496	5.576	0.000
0-13	Allen, 1989	0.375	0.079	0.610	2.450	0.014
0-13	Jaschek, 2016c	0.438	0.382	0.491	13.706	0.000
0-13	Rich, 2005a	0.230	0.149	0.308	5.482	0.000
0-13	Rich, 2005b	0.220	0.139	0.298	5.236	0.000
0-13	Min, 2015e	0.370	0.309	0.428	10.973	0.000
0-13	Min, 2015f	0.230	0.135	0.321	4.649	0.000
0-13	Kardin, 1985	0.470	0.255	0.641	4.009	0.000
Pooled effect of subgroup 0-13		0.281	0.187	0.370	5.675	0.000
0-14	Miron, 2014b	0.170	0.110	0.228	5.536	0.000
0-14	Mikaeili, 2013	0.070	0.004	0.135	2.092	0.036
0-14	Lizardi, 1995a	0.222	-0.037	0.453	1.682	0.093
Pooled effect of subgroup 0-14		0.131	0.044	0.216	2.945	0.003
0-6	Quevedo, 2008b	0.150	-0.001	0.294	1.953	0.051
0-6	Huang, 2020	0.040	-0.009	0.089	1.604	0.109
Pooled effect of subgroup 0-6		0.071	-0.027	0.168	1.428	0.153
12-19	Turner, 2004	0.136	0.060	0.211	3.478	0.001
12-19	McCutcheon, 2009b	0.023	-0.030	0.076	0.838	0.402
12-19	McCutcheon, 2009d	0.097	0.046	0.148	3.701	0.000
Pooled effect of subgroup 12-19		0.082	0.018	0.145	2.512	0.012
6-12	Hughes, 1988b	-0.019	-0.317	0.283	-0.119	0.906
6-12	Marse, 2002	0.280	0.112	0.433	3.216	0.001
Pooled effect of subgroup 6-12		0.161	-0.132	0.428	1.076	0.282
Overall		0.126	0.102	0.150	10.151	0.000

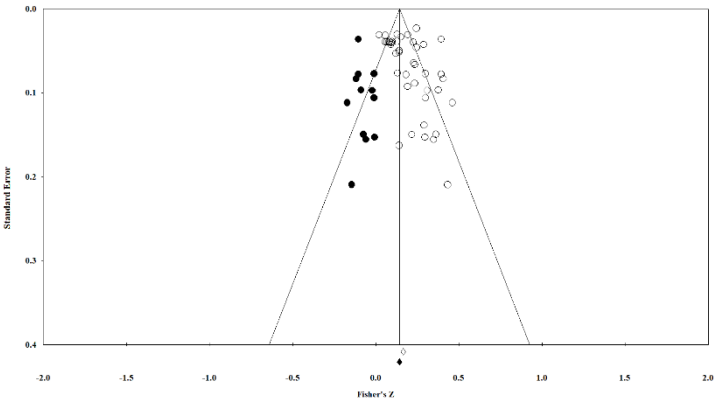




c. Sexual abuse

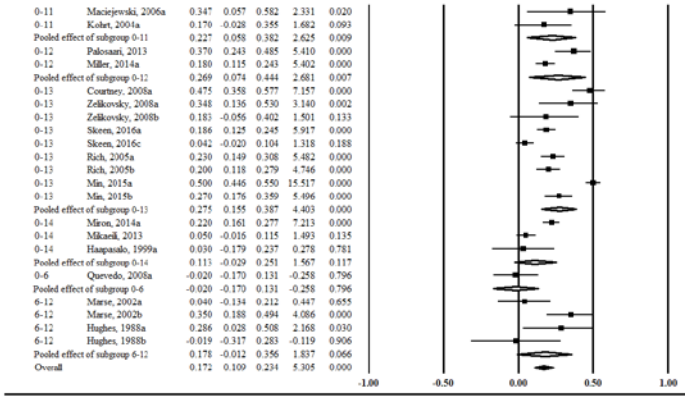
Group by Age group	Study name	Correlation	Lower limit	Upper limit	Z-Value	p-Value
0-11	Widom, 2007	0.092	0.014	0.170	2.299	0.021
0-11	Morais, 2016	0.141	0.045	0.235	2.861	0.004
0-11	Maciejewski, 2006c	0.139	-0.177	0.429	0.861	0.389
0-11	Haj-Yahia, 2001a	0.082	0.006	0.158	2.108	0.035
0-11	Haj-Yahia, 2001c	0.128	0.052	0.202	3.297	0.001
0-11	Haj-Yahia, 2001e	0.058	-0.019	0.134	1.480	0.139
0-11	Hauer, 2008	0.385	0.238	0.515	4.867	0.000
Pooled effect of subgroup 0-11		0.128	0.067	0.187	4.135	0.000
0-12	Miron, 2014c	0.020	-0.041	0.081	0.645	0.519
0-12	Miller, 2014c	0.150	0.085	0.214	4.486	0.000
0-12	Meyerson, 2002	0.230	0.060	0.387	2.639	0.008
0-12	Miron, 2016	0.140	0.040	0.238	2.725	0.006
0-12	McCutcheon, 2009e	0.127	0.069	0.185	4.226	0.000
0-12	McCutcheon, 2009f	0.221	0.146	0.293	5.666	0.000
Pooled effect of subgroup 0-12		0.139	0.075	0.201	4.229	0.000
0-13	As-Sanie, 2014b	0.223	0.101	0.339	3.534	0.000
0-13	Blanchard, 2014	0.214	-0.077	0.471	1.447	0.148
0-13	Brock, 1997a	0.287	-0.004	0.534	1.932	0.053
0-13	Brock, 1997b	0.335	0.044	0.574	2.241	0.025
0-13	Ullman, 2014	0.240	0.197	0.282	10.557	0.000
0-13	Roatta, 2000	0.290	0.091	0.467	2.817	0.005
0-13	Whiffen, 2000a	0.300	0.119	0.462	3.187	0.001
0-13	Whiffen, 2000b	0.430	0.236	0.591	4.113	0.000
0-13	Thomas, 2011	0.360	0.185	0.513	3.899	0.000
0-13	Rich, 2005c	0.090	0.007	0.172	2.113	0.035
0-13	Mehta, 2017	0.230	0.103	0.349	3.521	0.000
0-13	Rabinovitch, 2015	0.180	0.028	0.323	2.323	0.020
0-13	Jaschek, 2016d	0.374	0.312	0.434	10.829	0.000
0-13	Luterek, 2004	0.120	0.016	0.221	2.262	0.024
Pooled effect of subgroup 0-13		0.250	0.190	0.309	7.898	0.000
0-14	Walker, 1988	0.282	0.018	0.509	2.092	0.036
0-14	Morokoff, 2009	0.240	0.153	0.323	5.307	0.000
0-14	Harrop-Griffiths, 1988	0.347	0.069	0.575	2.422	0.015
0-14	Lizardi, 1995b	0.408	0.022	0.688	2.067	0.039
Pooled effect of subgroup 0-14		0.259	0.182	0.333	6.433	0.000
12-19	Rich, 2005d	0.280	0.201	0.355	6.734	0.000
12-19	Miron, 2014d	0.190	0.131	0.248	6.203	0.000
12-19	McCutcheon, 2009g	0.058	-0.004	0.120	1.819	0.069
12-19	Haj-Yahia, 2001b	0.066	-0.011	0.142	1.688	0.091
12-19	Haj-Yahia, 2001d	0.099	0.023	0.174	2.545	0.011
12-19	Haj-Yahia, 2001f	0.079	0.003	0.155	2.030	0.042
Pooled effect of subgroup 12-19		0.129	0.060	0.196	3.669	0.000
4-17	Briere, 1988	0.190	0.010	0.357	2.073	0.038
4-17	Quevedo, 2008c	0.290	0.146	0.422	3.858	0.000
Pooled effect of subgroup 4-17		0.249	0.137	0.355	4.289	0.000
6-12	Ensink, 2016	0.374	0.236	0.497	5.046	0.000
6-12	Mannarino, 1991	0.130	-0.020	0.273	1.703	0.089
Pooled effect of subgroup 6-12		0.255	0.004	0.476	1.991	0.046
Overall		0.182	0.154	0.209	12.513	0.000

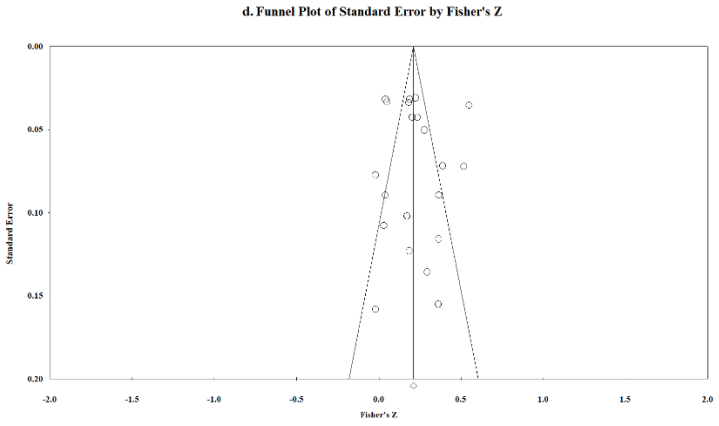




d. Emotional abuse

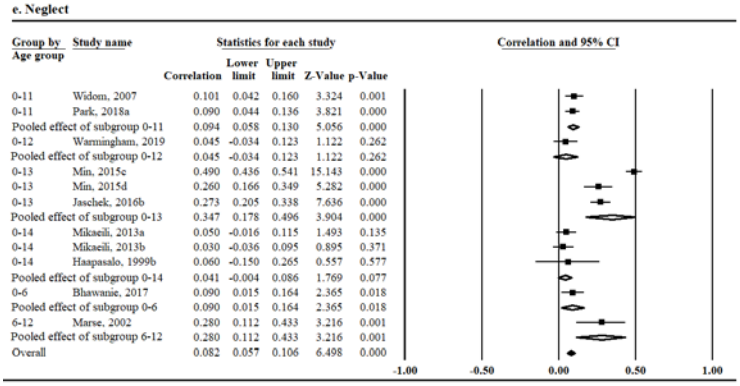
Group by Age group	Study name	Correlation	Lower limit	Upper limit	Z-Value	p-Value
0-11	Maciejewski, 2006a	0.347	0.057	0.582	2.331	0.020
0-11	Kohrt, 2004a	0.170	-0.028	0.355	1.682	0.093
Pooled effect of subgroup 0-11		0.227	0.058	0.382	2.625	0.009
0-12	Palosaari, 2013	0.370	0.243	0.485	5.410	0.000
0-12	Miller, 2014a	0.180	0.115	0.243	5.402	0.000
Pooled effect of subgroup 0-12		0.269	0.074	0.444	2.681	0.007
0-13	Courtney, 2008a	0.475	0.358	0.577	7.157	0.000
0-13	Zelikovsky, 2008a	0.348	0.136	0.530	3.140	0.002
0-13	Zelikovsky, 2008b	0.183	-0.056	0.402	1.501	0.133
0-13	Skeen, 2016a	0.186	0.125	0.245	5.917	0.000
0-13	Skeen, 2016c	0.042	-0.020	0.104	1.318	0.188
0-13	Rich, 2005a	0.230	0.149	0.308	5.482	0.000
0-13	Rich, 2005b	0.200	0.118	0.279	4.746	0.000
0-13	Min, 2015a	0.500	0.446	0.550	15.517	0.000
0-13	Min, 2015b	0.270	0.176	0.359	5.496	0.000
Pooled effect of subgroup 0-13		0.275	0.155	0.387	4.403	0.000
0-14	Miron, 2014a	0.220	0.161	0.277	7.213	0.000
0-14	Mikaeili, 2013	0.050	-0.016	0.115	1.493	0.135
0-14	Haapasalo, 1999a	0.030	-0.179	0.237	0.278	0.781
Pooled effect of subgroup 0-14		0.113	-0.029	0.251	1.567	0.117
0-6	Quevedo, 2008a	-0.020	-0.170	0.131	-0.258	0.796
Pooled effect of subgroup 0-6		-0.020	-0.170	0.131	-0.258	0.796
6-12	Marse, 2002a	0.040	-0.134	0.212	0.447	0.655
6-12	Marse, 2002b	0.350	0.188	0.494	4.086	0.000
6-12	Hughes, 1988a	0.286	0.028	0.508	2.168	0.030
6-12	Hughes, 1988b	-0.019	-0.317	0.283	-0.119	0.906
Pooled effect of subgroup 6-12		0.178	-0.012	0.356	1.837	0.066
Overall		0.172	0.109	0.234	5.305	0.000





e. Neglect

Group by Age group	Study name	Correlation	Lower limit	Upper limit	Z-Value	p-Value
0-11	Widom, 2007	0.101	0.042	0.160	3.324	0.001
0-11	Park, 2018a	0.090	0.044	0.136	3.821	0.000
Pooled effect of subgroup 0-11		0.094	0.058	0.130	5.056	0.000
0-12	Warmingham, 2019	0.045	-0.034	0.123	1.122	0.262
Pooled effect of subgroup 0-12		0.045	-0.034	0.123	1.122	0.262
0-13	Min, 2015c	0.490	0.436	0.541	15.143	0.000
0-13	Min, 2015d	0.260	0.166	0.349	5.282	0.000
0-13	Jaschek, 2016b	0.273	0.205	0.338	7.636	0.000
Pooled effect of subgroup 0-13		0.347	0.178	0.496	3.904	0.000
0-14	Mikaeili, 2013a	0.050	-0.016	0.115	1.493	0.135
0-14	Mikaeili, 2013b	0.030	-0.036	0.095	0.895	0.371
0-14	Haapasalo, 1999b	0.060	-0.150	0.265	0.557	0.577
Pooled effect of subgroup 0-14		0.041	-0.004	0.086	1.769	0.077
0-6	Bhawanie, 2017	0.090	0.015	0.164	2.365	0.018
Pooled effect of subgroup 0-6		0.090	0.015	0.164	2.365	0.018
6-12	Marse, 2002	0.280	0.112	0.433	3.216	0.001
Pooled effect of subgroup 6-12		0.280	0.112	0.433	3.216	0.001
Overall		0.082	0.057	0.106	6.498	0.000



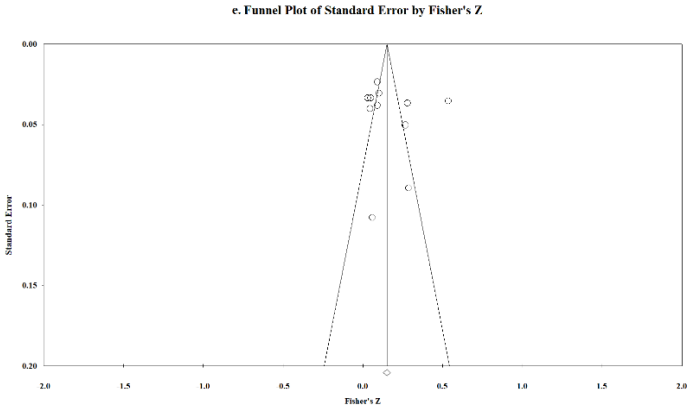
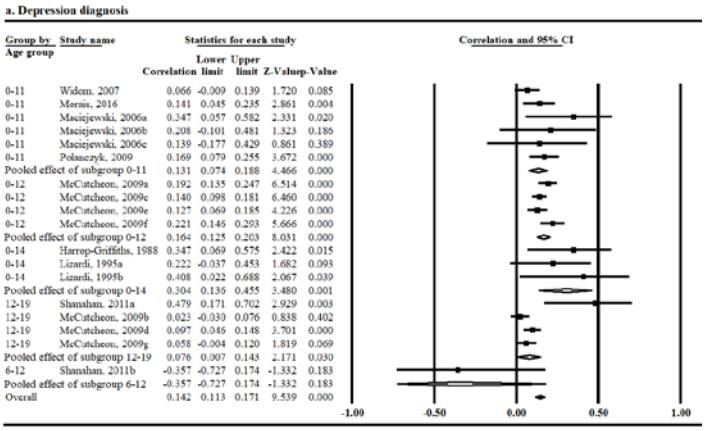
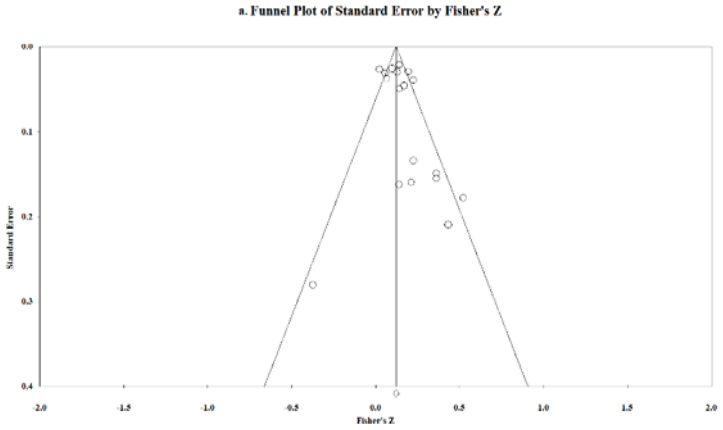


Figure 3 Forest plots and funnel plots for the relationship between childhood maltreatment and depression by different measures of depression.

In the funnel plots, the x-axis shows the Fisher's Z estimate for each study and y-axis is standard error of the Fisher's Z estimate. The dashed line represents the 95% confidence interval (CI) and the point estimate of the Fisher's Z illustrates as the solid line.

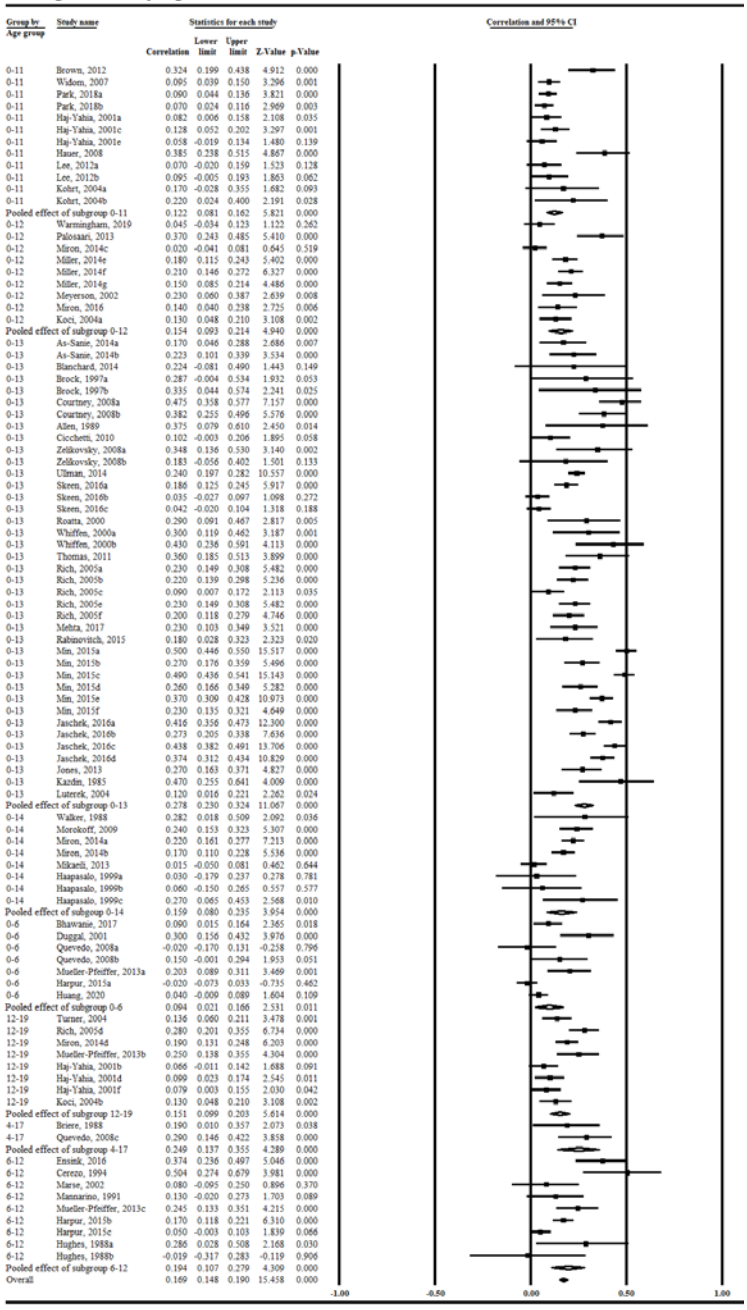
*Funnel plots present the findings after applying the trim-and-fill method. The open dots and diamond indicate the observed studies, and the closed dots and diamond indicate the missing studies imputed by the trim-and-fill method.





b. Depressive symptoms

Group by Age group	Study name	Correlation	Lower limit	Upper limit	Z-Value	p-Value
0-11	Brown, 2012	0.324	0.199	0.438	4.912	0.000
0-11	Widom, 2007	0.095	0.039	0.150	3.296	0.001
0-11	Park, 2018a	0.090	0.044	0.136	3.821	0.000
0-11	Park, 2018b	0.070	0.024	0.116	2.969	0.003
0-11	Haj-Yahia, 2001a	0.082	0.006	0.158	2.108	0.035
0-11	Haj-Yahia, 2001c	0.128	0.052	0.202	3.297	0.001
0-11	Haj-Yahia, 2001e	0.058	-0.019	0.134	1.480	0.139
0-11	Hauser, 2008	0.385	0.258	0.515	4.867	0.000
0-11	Lee, 2012a	0.070	-0.020	0.159	1.523	0.128
0-11	Lee, 2012b	0.095	-0.005	0.193	1.863	0.062
0-11	Kohrt, 2004a	0.170	-0.028	0.355	1.682	0.093
0-11	Kohrt, 2004b	0.220	0.024	0.400	2.191	0.028
Pooled effect of subgroup 0-11		0.122	0.081	0.162	5.821	0.000
0-12	Warmingham, 2019	0.045	-0.034	0.123	1.122	0.262
0-12	Palosaari, 2013	0.370	0.243	0.485	5.410	0.000
0-12	Miron, 2014c	0.020	-0.041	0.081	0.645	0.519
0-12	Miller, 2014e	0.180	0.115	0.243	5.402	0.000
0-12	Miller, 2014f	0.210	0.146	0.272	6.327	0.000
0-12	Miller, 2014g	0.150	0.085	0.214	4.486	0.000
0-12	Meyerson, 2002	0.230	0.060	0.387	2.639	0.008
0-12	Miron, 2016	0.140	0.040	0.238	2.725	0.006
0-12	Koci, 2004a	0.130	0.048	0.210	3.108	0.002
Pooled effect of subgroup 0-12		0.154	0.093	0.214	4.940	0.000
0-13	As-Sanie, 2014a	0.170	0.046	0.288	2.686	0.007
0-13	As-Sanie, 2014b	0.223	0.101	0.339	3.534	0.000
0-13	Blanchard, 2014	0.224	-0.081	0.490	1.443	0.149
0-13	Brock, 1997a	0.287	-0.004	0.534	1.932	0.053
0-13	Brock, 1997b	0.335	0.044	0.574	2.241	0.025
0-13	Courtney, 2008a	0.475	0.358	0.577	7.157	0.000
0-13	Courtney, 2008b	0.382	0.255	0.496	5.576	0.000
0-13	Allen, 1989	0.375	0.079	0.610	2.450	0.014
0-13	Cicchetti, 2010	0.102	-0.003	0.206	1.895	0.058
0-13	Zelikovsky, 2008a	0.348	0.136	0.530	3.140	0.002
0-13	Zelikovsky, 2008b	0.183	-0.056	0.402	1.501	0.133
0-13	Ullman, 2014	0.240	0.197	0.282	10.557	0.000
0-13	Skeen, 2016a	0.186	0.125	0.245	5.917	0.000
0-13	Skeen, 2016b	0.035	-0.027	0.097	1.098	0.272
0-13	Skeen, 2016c	0.042	-0.020	0.104	1.318	0.188
0-13	Roatta, 2000	0.290	0.091	0.467	2.817	0.005
0-13	Whiffen, 2000a	0.300	0.119	0.462	3.187	0.001
0-13	Whiffen, 2000b	0.430	0.236	0.591	4.113	0.000
0-13	Thomas, 2011	0.360	0.185	0.513	3.899	0.000
0-13	Rich, 2005a	0.230	0.149	0.308	5.482	0.000
0-13	Rich, 2005b	0.220	0.139	0.298	5.236	0.000
0-13	Rich, 2005c	0.090	0.007	0.172	2.113	0.035
0-13	Rich, 2005e	0.230	0.149	0.308	5.482	0.000
0-13	Rich, 2005f	0.200	0.118	0.279	4.746	0.000
0-13	Mehta, 2017	0.230	0.103	0.349	3.521	0.000
0-13	Rabinovitch, 2015	0.180	0.028	0.323	2.323	0.020
0-13	Min, 2015a	0.500	0.446	0.550	15.517	0.000
0-13	Min, 2015b	0.270	0.176	0.359	5.496	0.000
0-13	Min, 2015c	0.490	0.436	0.541	15.143	0.000
0-13	Min, 2015d	0.260	0.166	0.349	5.282	0.000
0-13	Min, 2015e	0.370	0.309	0.428	10.973	0.000
0-13	Min, 2015f	0.230	0.135	0.321	4.649	0.000
0-13	Jaschek, 2016a	0.416	0.356	0.473	12.300	0.000
0-13	Jaschek, 2016b	0.273	0.205	0.338	7.636	0.000
0-13	Jaschek, 2016c	0.438	0.382	0.491	13.706	0.000
0-13	Jaschek, 2016d	0.374	0.312	0.434	10.829	0.000
0-13	Jones, 2013	0.270	0.163	0.371	4.827	0.000
0-13	Kazdin, 1985	0.470	0.255	0.641	4.009	0.000
0-13	Luterek, 2004	0.120	0.016	0.221	2.262	0.024
Pooled effect of subgroup 0-13		0.278	0.230	0.324	11.067	0.000
0-14	Walker, 1988	0.282	0.018	0.509	2.092	0.036
0-14	Morokoff, 2009	0.240	0.153	0.323	5.307	0.000
0-14	Miron, 2014a	0.220	0.161	0.277	7.213	0.000
0-14	Miron, 2014b	0.170	0.110	0.228	5.536	0.000
0-14	Mikaeili, 2013	0.015	-0.050	0.081	0.462	0.644
0-14	Haapasalo, 1999a	0.030	-0.179	0.237	0.278	0.781
0-14	Haapasalo, 1999b	0.060	-0.150	0.265	0.557	0.577
0-14	Haapasalo, 1999c	0.270	0.065	0.453	2.568	0.010
Pooled effect of subgoup 0-14		0.159	0.080	0.235	3.954	0.000
0-6	Bhawsine, 2017	0.090	0.015	0.164	2.365	0.018
0-6	Duggal, 2001	0.300	0.156	0.432	3.976	0.000
0-6	Quevedo, 2008a	-0.020	-0.170	0.131	-0.258	0.796
0-6	Quevedo, 2008b	0.150	-0.001	0.294	1.953	0.051
0-6	Mueller-Pfeiffer, 2013a	0.203	0.089	0.311	3.469	0.001
0-6	Harpur, 2015a	-0.020	-0.073	0.033	-0.735	0.462
0-6	Huang, 2020	0.040	-0.009	0.089	1.604	0.109
Pooled effect of subgroup 0-6		0.094	0.021	0.166	2.531	0.011
12-19	Turner, 2004	0.136	0.060	0.211	3.478	0.001
12-19	Rich, 2005d	0.280	0.201	0.355	6.734	0.000
12-19	Miron, 2014d	0.190	0.131	0.248	6.203	0.000
12-19	Mueller-Pfeiffer, 2013b	0.250	0.138	0.355	4.304	0.000
12-19	Haj-Yahia, 2001b	0.066	-0.011	0.142	1.688	0.091
12-19	Haj-Yahia, 2001d	0.099	0.023	0.174	2.545	0.011
12-19	Haj-Yahia, 2001f	0.079	0.003	0.155	2.030	0.042
12-19	Koci, 2004b	0.130	0.048	0.210	3.108	0.002
Pooled effect of subgroup 12-19		0.151	0.099	0.203	5.614	0.000
4-17	Briere, 1988	0.190	0.010	0.357	2.073	0.038
4-17	Quevedo, 2008c	0.290	0.146	0.422	3.858	0.000
Pooled effect of subgroup 4-17		0.249	0.137	0.355	4.280	0.000
6-12	Ensink, 2016	0.374	0.236	0.497	5.046	0.000
6-12	Cerezo, 1994	0.504	0.274	0.679	3.981	0.000
6-12	Marse, 2002	0.080	-0.095	0.250	0.896	0.370
6-12	Mannarino, 1991	0.130	-0.020	0.273	1.703	0.089
6-12	Mueller-Pfeiffer, 2013c	0.245	0.133	0.351	4.215	0.000
6-12	Harpur, 2015b	0.170	0.118	0.221	6.310	0.000
6-12	Harpur, 2015c	0.050	-0.003	0.103	1.839	0.066
6-12	Hughes, 1988a	0.286	0.028	0.508	2.168	0.030
6-12	Hughes, 1988b	-0.019	-0.317	0.283	-0.119	0.906
Pooled effect of subgroup 6-12		0.194	0.107	0.279	4.309	0.000
Overall		0.169	0.148	0.190	15.458	0.000



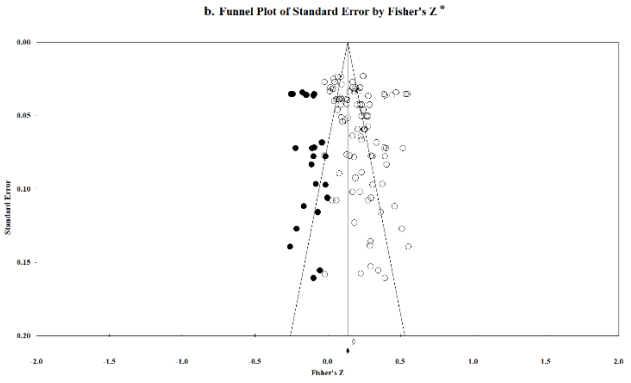
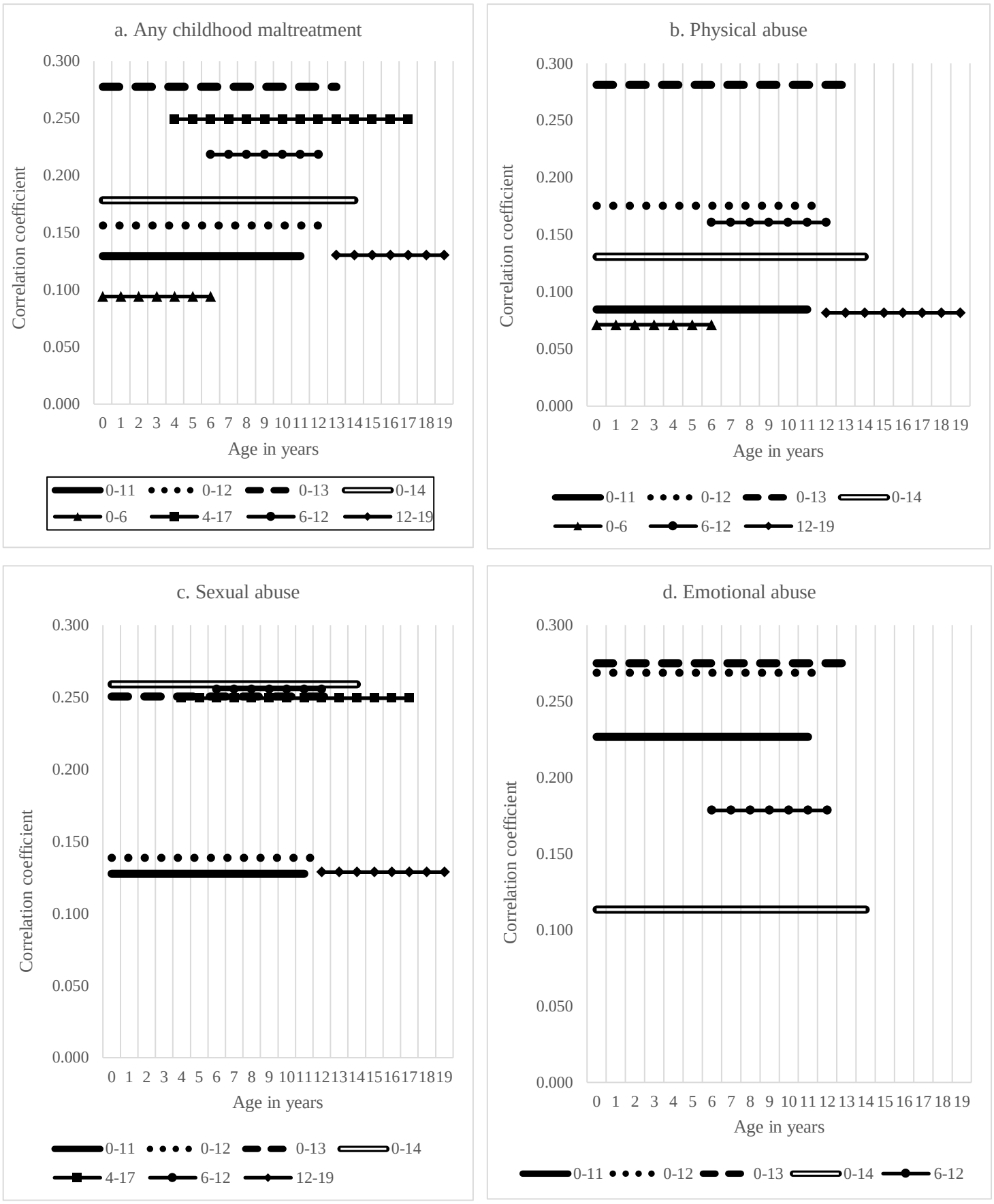
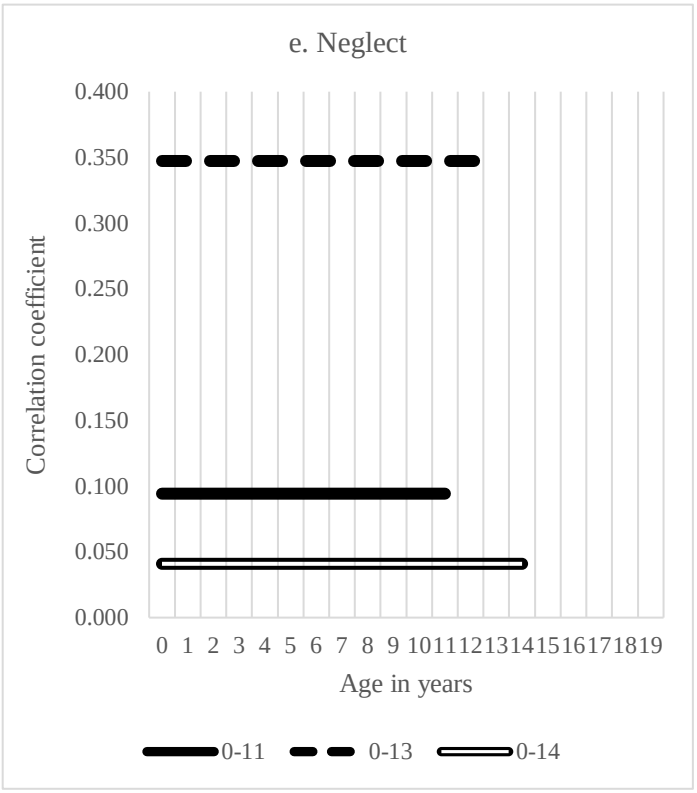
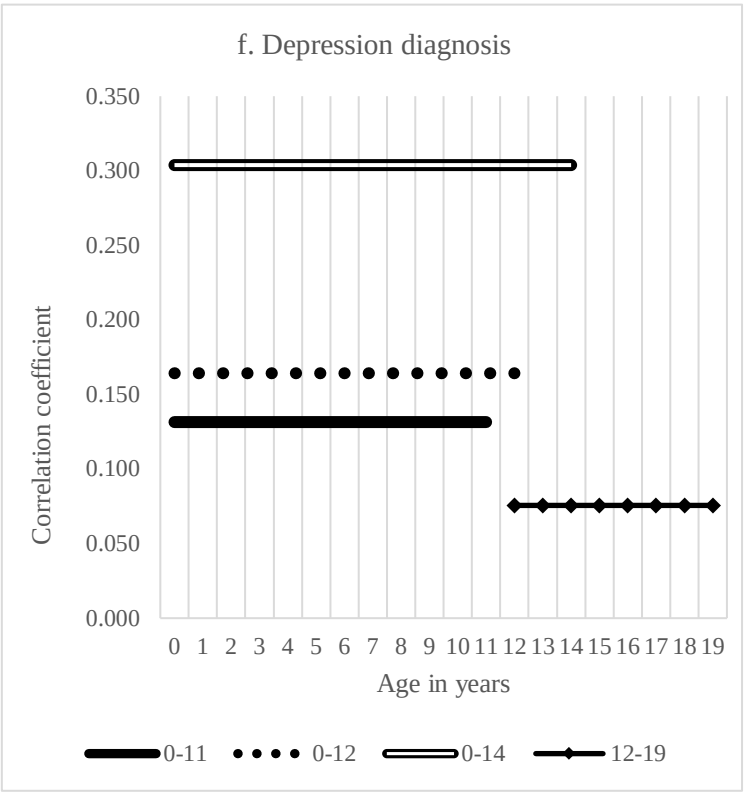
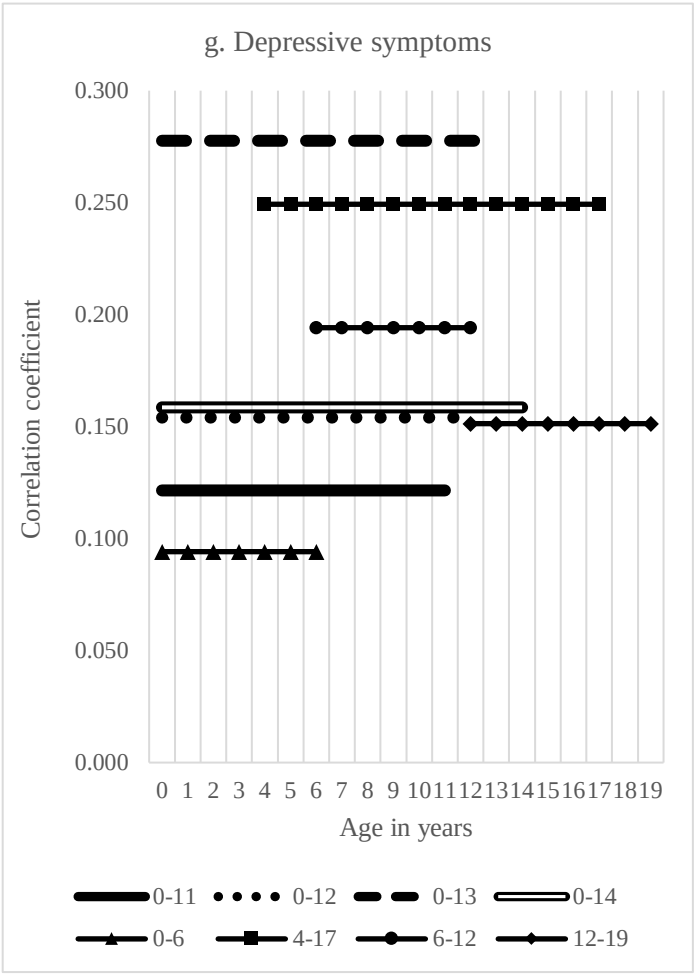


Figure 4. Correlations between childhood maltreatment and depression by age of exposure




e. Neglect
Correlation coefficient
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
Age in years
0-11
0-13
0-14


f. Depression diagnosis
Correlation coefficient
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
Age in years
0-11
0-12
0-14
12-19


g. Depressive symptoms
Correlation coefficient
0.300
0.250
0.200
0.150
0.100
0.050
0.000
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
Age in years
0-11
0-12
0-13
0-14
0-6
4-17
6-12
12-19

Appendix A Search Strategy

OVID (EMBASE, HealthStar, PsychoInfo, and Medline)

#1 (childhood or early life or infan* or child).tw.
#2 (maltreat* or neglect).mh. or abus*.tw. or mistreat*.tw. or illtreat*.tw. or ill-treat*.tw. or mal-treat*.tw. or advers*.tw. or trauma*.tw. or ACE.tw.
#3 depression*.mh. or depress*.tw. or mood*.tw.
#4 #1 and #2 and #3
#5 limit #4 to English language
#6 limit #5 to human

Cochrane Library

#1 (childhood OR early life OR infan* OR child):ti,ab,kw (Word variations have been searched)
#2 MeSH descriptor: [Child Abuse] explode all trees
#3 (abus* OR mistreat* OR illtreat* OR ill-treat* OR mal-treat* OR advers* OR trauma* OR ACE):ti,ab,kw
#4 #2 OR #3
#5 MeSH descriptor: [Depression] this term only
#6 (depress* OR mood*):ti,ab,kw
#7 #5 OR #6
#8 #1 AND #4 AND #7 in Cochrane Reviews, Trials

Appendix B Data References

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Appendix C

Assessment of studies quality characteristics

First author	Year	Design				Measurement				Analysis		Result	Total
		Sample size[1]	Study design[2]	Appropriate study conduction[3]	Representativeness[4]	Selection of control[5]	Ascertainment of exposure[6]	Assessment of exposure[7]	Assessment of outcome[8]	Appropriate analysis[9]	Appropriate confounding control[10]	Appropriate result interpretation[11]	
Allen	1989	1	0	1	0	0	1	1	0	1	1	1	7
As-Sanie	2014	1	0	1	0	1	0	0	0	1	1	1	6
Bhawanie	2017	1	1	1	1	1	1	1	0	1	1	1	10
Blanchard	2002	0	0	1	0	1	0	0	0	1	0	1	4
Briere	1988	1	0	1	0	1	0	0	0	1	0	1	5
Brock	1997	1	0	1	0	1	0	0	0	1	0	1	5
Brown	2012	1	0	1	1	1	0	0	1	1	0	1	7
Cerezo	1994	0	0	1	0	0	1	1	0	1	1	1	6
Cicchetti	2010	1	0	1	0	1	1	1	0	1	1	1	8
Courtney	2008	1	0	1	0	1	0	0	0	1	0	1	5
Duggal	2001	1	1	1	1	1	1	1	0	1	0	1	9
Ensink	2016	1	0	1	0	0	1	1	0	1	1	1	7
Haapasalo	1999	1	0	1	1	1	0	0	1	1	0	1	7
Haj-Yahia	2001	1	0	1	0	1	0	0	0	1	0	1	5
Harpur	2015	1	1	1	0	1	1	1	0	1	0	1	8
Harrop-Griffiths	1988	0	0	1	0	1	0	0	0	1	0	1	4
Hauer	2008	1	0	1	0	1	0	0	0	1	1	1	6
Huang	2020	1	1	1	0	1	0	0	0	1	0	1	6
Hughes	1988	0	0	1	0	1	0	1	0	1	0	1	5
Jascheck	2016	1	1	1	1	1	0	0	1	1	1	1	9
Jones	2013	1	0	1	1	1	0	0	1	1	0	1	7
Kazdin	1985	1	0	1	0	1	1	1	0	1	0	1	7
Koci	2004	1	0	1	0	1	0	0	0	1	1	1	6
Kohrt	2004	1	0	1	1	1	1	1	0	1	1	1	9

Lee	2012	1	1	1	0	1	1	1	1	1	1	1	10
Lizardi	1995	1	0	1	0	1	0	0	1	1	0	1	6
Luterek	2004	1	0	1	0	1	0	0	0	1	0	1	5
Maciejewski	2006	0	0	1	0	1	0	0	1	1	1	1	6
Mannarino	1991	1	0	1	0	1	1	1	0	1	0	1	7
Marse	2002	1	0	1	0	1	0	0	0	1	0	1	5
McCutcheon	2009	1	0	1	0	0	0	0	1	1	1	1	6
Mehta	2017	1	0	1	0	1	0	0	0	1	0	1	5
Meyerson	2002	1	0	1	0	1	0	0	0	1	1	1	6
Mikaeili	2013	1	0	1	0	1	0	0	0	1	0	1	5
Miller	2014	1	1	1	0	1	1	1	0	1	1	1	9
Min	2015	1	0	1	0	1	0	0	0	1	1	1	6
Miron	2014	1	0	1	0	1	0	0	0	1	1	1	6
Miron	2016	1	0	1	0	1	0	0	0	1	1	1	6
Morais	2016	1	0	1	0	1	1	1	0	1	0	1	7
Morokoff	2009	1	0	1	0	1	0	0	0	1	1	1	6
Mueller-Pfeiffer	2013	1	0	1	0	1	0	0	0	1	1	1	6
Palosaari	2013	1	0	1	0	1	0	0	0	1	0	1	5
Park	2018	1	1	1	1	1	0	0	1	1	1	1	9
Polanczyk	2009	1	1	1	1	1	1	1	1	1	1	1	11
Quevedo	2008	1	1	1	0	1	1	1	1	1	0	1	9
Rabinovitch	2015	1	1	1	0	1	0	0	0	1	1	1	7
Rich	2005	1	0	1	0	1	0	0	0	1	0	1	5
Roatta	2000	1	0	1	0	1	0	0	0	1	0	1	5
Shanahan	2011	1	0	1	1	1	0	0	0	1	0	1	6
Skeen	2016	1	0	1	1	1	0	0	0	1	1	1	7
Thomas	2011	1	0	1	0	1	0	0	0	1	1	1	6
Turner	2004	1	0	1	0	1	0	0	0	1	1	1	6
Ullman	2014	1	0	1	0	1	0	0	0	1	0	1	5
Walker	1988	0	0	1	0	0	0	0	1	1	0	1	4

Warmingham	2019	1	0	1	0	1	1	1	0	1	0	1	7
Whiffen	2000	1	0	1	0	1	0	0	0	1	0	1	5
Widom	2007	1	0	1	0	1	1	1	1	1	1	1	9
Zelikovsky	2002	1	0	1	0	1	0	0	0	1	0	1	5

[1]Sample size provides enough power for analysis: yes=1; no=0.

[2]Study design: cohort study=1; case control or cross-sectional study=0.

[3]Whether the study being conducted appropriately considering the nature of study design: yes=1; no=0.

[4]Representativeness of the population: population-based representative=1; Not representative, selected group, volunteers, or no description=0.

[5]Selection of the non-exposed cohort/control: drawn from the same population=1; drawn from a different source or no description=0.

[6]Ascertainment of exposure to childhood maltreatment: data on exposure collected prospectively or collected retrospectively although the official reports were generated in real-time=1; data on exposure collected retrospectively=0.

[7]Assessment of exposure: all cases from secure official record (court-substantiated abuse) =1; self-reported or structured interview or self-administered questionnaire=0.

[8]Assessment of outcome: use of structured clinical interview for DSM-III/IV (DIS, DISC, CIDI)=1; questions from published health surveys/screening instruments, own system, symptoms described, no system, not specified, or self-reported=0.

[9]Appropriate statistical analysis: yes=1; no=0.

[10]Appropriate methods to control confounding: yes (multivariable adjusted OR including SES, education, or family dysfunction in models)=1; no (univariate analysis or controls for age/sex only)=0.

[11]Analysis results were appropriately interpreted, neither over- nor under-interpreted from findings: yes=1; no=0.

Appendix D

Meta regression analyses in overall and subgroup meta analyses[1]

	Any childhood maltreatment (k=111)				Sexual abuse (k=41)			Depressive symptoms (k=94)		
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 3	Model 4	Model 1	Model 2	Model 4
Sample size										
Not enough power for analysis	1	1	1	1	1	1	1	1	1	1
Enough power for analysis	-0.098 (-0.231, 0.036)	-0.094 (-0.23, 0.042)	-0.097 (-0.234, 0.040)	-0.092 (-0.228, 0.045)	-0.095 (-0.284, 0.093)	-0.097 (-0.288, 0.094)	-0.033 (-0.240, 0.173)	-0.099 (-0.277, 0.079)	-0.101 (-0.282, 0.08)	-0.083 (-0.264, 0.097)
Study design										
Cross-sectional/case-control	1	1	1	1	1	1	1	1	1	1
Cohort study	-0.009 (-0.089, 0.072)	-0.008 (-0.09, 0.074)	-0.012 (-0.099, 0.074)	0.000 (-0.086, 0.086)	0.018 (-0.132, 0.169)	0.013 (-0.143, 0.170)	-0.010 (-0.190, 0.170)	-0.028 (-0.116, 0.059)	-0.030 (-0.120, 0.061)	-0.027 (-0.120, 0.067)
Representativeness										
Not representative/no description	1	1	1	1	1	1	1	1	1	1
Population-based representative	0.048 (-0.026, 0.122)	0.045 (-0.036, 0.125)	0.043 (-0.038, 0.124)	0.023 (-0.055, 0.101)	0.221 (-0.040, 0.482)	0.212 (-0.060, 0.483)	0.164 (-0.124, 0.453)	-0.008 (-0.096, 0.079)	-0.012 (-0.106, 0.081)	-0.023 (-0.110, 0.065)
Assessment of exposure										
Self-report/structured interview	1	1	1	1	1	1	1	1	1	1
Official record	-0.052 (-0.124, 0.021)	-0.055 (-0.131, 0.022)	-0.053 (-0.13, 0.024)	-0.021 (-0.100, 0.057)	0.009 (-0.101, 0.120)	0.009 (-0.103, 0.122)	0.007 (-0.145, 0.159)	-0.054 (-0.132, 0.024)	-0.051 (-0.133, 0.032)	-0.015 (-0.101, 0.070)
Assessment of outcome										
Instrument/survey/self-reported	1	1	1	1	1	1	1	1	1	1
Structured clinical interview	-0.041 (-0.107, 0.025)	-0.040 (-0.108, 0.029)	-0.032 (-0.114, 0.05)	-0.017 (-0.098, 0.064)	-0.036 (-0.139, 0.066)	-0.024 (-0.153, 0.105)	-0.033 (-0.166, 0.100)	0.025 (-0.068, 0.119)	0.031 (-0.066, 0.128)	0.054 (-0.049, 0.158)
Confounding control										
No	1	1	1	1	1	1	1	1	1	1
Yes	0.016 (-0.038, 0.069)	0.015 (-0.040, 0.071)	0.017 (-0.04, 0.073)	0.026 (-0.03, 0.082)	0.014 (-0.065, 0.093)	0.015 (-0.066, 0.096)	0.048 (-0.045, 0.141)	0.044 (-0.015, 0.102)	0.042 (-0.019, 0.103)	0.050 (-0.010, 0.109)
Type of maltreatment		F=0.05, df=4	F=0.05, df=4	F=0.20, df=4					F=0.14, df=4	F=0.02, df=4
Any maltreatment		1	1	1					1	1
Emotional abuse		0.007 (-0.086, 0.099)	0.007 (-0.086, 0.099)	-0.031 (-0.122, 0.059)					0.028 (-0.07, 0.126)	-0.009 (-0.104, 0.087)
Neglect		-0.013 (-0.129, 0.103)	-0.014 (-0.130, 0.103)	-0.028 (-0.137, 0.080)					0.009 (-0.113, 0.130)	-0.009 (-0.123, 0.104)
Physical abuse		-0.009 (-0.091, 0.073)	-0.006 (-0.090, 0.077)	-0.032 (-0.112, 0.048)					0.029 (-0.062, 0.121)	-0.002 (-0.090, 0.087)
Sexual abuse		-0.011 (-0.086, 0.065)	-0.009 (-0.085, 0.068)	-0.020 (-0.094, 0.055)					0.011 (-0.072, 0.093)	0.001 (-0.079, 0.081)
Type of outcome										
Depression diagnosis			1	1		1	1			
Depressive symptoms			0.018 (-0.083, 0.118)	-0.033 (-0.132, 0.066)		0.021 (-0.112, 0.155)	-0.025 (-0.158, 0.107)			

Age of maltreatment				F=3.41**, df=7			F=1.83, df=6			F=3.11**, df=7
0-13				1			1			1
0-11				-0.146** (-0.233, -0.059)			-0.108 (-0.227, 0.011)			-0.157** (-0.252, -0.063)
0-12				-0.126** (-0.216, -0.036)			-0.128 (-0.256, 0.000)			-0.122* (-0.225, -0.018)
0-14				-0.109* (-0.208, -0.011)			0.032 (-0.144, 0.208)			-0.140* (-0.247, -0.032)
0-6				-0.169** (-0.290, -0.048)						-0.146* (-0.274, -0.017)
12-19				-0.155*** (-0.243, -			-0.111* (-0.216, -0.006)			-0.131* (-0.231, -0.031)
4-17				0.067)			0.045 (-0.171, 0.261)			-0.020 (-0.238, 0.198)
6-12				-0.001 (-0.214, 0.211)			0.005 (-0.237, 0.247)			-0.075 (-0.206, 0.056)
				-0.077 (-0.197, 0.042)						
Tau^2	0.014	0.015	0.015	0.012	0.008	0.008	0.007	0.015	0.016	0.013
Q	882.44***	859.81***	836.40***	565.50***	133.11***	133.06***	91.49***	769.84***	750.89***	470.06***
R^2	0.021	0.000	0.000	0.168	0.089	0.046	0.188	0.035	0.000	0.179

Notes:

[1] Model 1 = quality assessment items only; Model 2 = Model 1 + type of childhood maltreatment; Model 3 = Model 2 + type of depression; Model 4 = Model 3 + age of exposure.

*p<0.05; **p<0.01; ***p<0.001