Intergenerational effect of maternal childhood maltreatment on next generation's vulnerability to psychopathology: a systematic review with meta-analysis

Yingying Su [1], BMed, MSc, Carl D'Arcy [1, 2], PhD, Xiangfei Meng [3*], BMed, PhD

[1] School of Public Health, University of Saskatchewan, Saskatoon, SK, Canada

[2] Department of Psychiatry, College of Medicine, University of Saskatchewan, Saskatoon, SK, Canada

[3] Department of Psychiatry, McGill, University and the Douglas Mental Health Research Institute, Montreal, Canada

[*]Corresponding author. Department of Psychiatry, Faculty of Medicine, McGill University, 6875 Boulevard LaSalle, Montreal, QC, H4H 1R3, Canada.

E-mail:xiangfei.meng@mcgill.ca

Tel:+ 15147616131 ext. 2352

Fax:+ 15147616131 ext. 3034

This is the accepted manuscript of Su, Y., D'Arcy, C., & Meng, X. (2022). Intergenerational Effect of Maternal Childhood Maltreatment on Next Generation's Vulnerability to Psychopathology: A Systematic Review With Meta-Analysis. Trauma, Violence, & Abuse, 23(1), 152–162. https://doi.org/10.1177/1524838020933870

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

This work was supported by a grant from the Canadian Institute of Health Research (PJT-148845), a discovery grant from the Canada First Excellence Research Fund provided to McGill University for Healthy Brains for Healthy Lives; and a scholar award from the Fonds de recherche du Québec- Sante, Canada awarded to XM.

Abstract

Many studies have identified the multiple negative consequences of childhood maltreatment on subsequent mental health. However, research on the intergenerational effect of maternal childhood maltreatment has not been systematically synthesized. This meta-analysis aimed to provide a quantitative estimate of the intergenerational effect of maternal childhood maltreatment on their offspring's psychopathology. Electronic databases and grey literature were searched for English-language prospective cohort studies. Two reviewers independently extracted data and assessed study quality with the Newcastle-Ottawa Scale. This review only included those studies with, 1) maternal childhood maltreatment occurring prior to 18 years of age, 2) using a clear and reliable assessment for maltreatment exposure, and offspring's mental health problems prior to age 18. Random-effect models were used to calculate the pooled effect size of maternal childhood maltreatment on offspring's psychopathology and meta-regression was used to explore potential confounders. Twelve studies met eligibility criteria. Significant heterogeneity was found across selected studies. Maternal childhood maltreatment was found to have a small but significant effect on the offspring's depression and internalizing behaviors (r=0.14, 95%CI: 0.09-0.19). Two moderators were found, maternal depression and ethnicity. Maternal depression reduced the effect size of maternal maltreatment on offspring's depression and internalizing disorders. The offspring of non-Caucasian mothers who had a history of childhood maltreatment faced a higher risk of mental health problems. There was no evidence of publication bias. This review provides robust evidence to reinforce the need for policies to reduce its occurrence, as it can influence not just one but two or possibly more generations.

Keywords: childhood maltreatment, psychopathology, intergenerational transmission, prospective cohort study, meta-analysis

Introduction

Childhood maltreatment significantly increases the risk of subsequent psychiatric disorders, including depression (Li, D'Arcy, & Meng, 2016; Widom, DuMont, & Czaja, 2007), anxiety (Nanda, Reichert, Jones, & Flannery-Schroeder, 2016), alcohol misuse (Elliott et al., 2014), and emotional and behavioral functioning difficulties (Choi et al., 2019). The World Mental Health Surveys compared data on childhood maltreatment and psychiatric problems in 21 countries and confirmed this association existed across all sociocultural samples (Kessler et al., 2010). The economic and societal implications of both maltreatment and severe psychiatric disorders are considerable (Gilbert et al., 2009; Vigo, Thornicroft, & Atun, 2016). In 2010, the updated WHO report showed that 12% of the global burden of diseases was attributable to mental disorders, and that estimate is expected to reach 15% by 2020 (World Health Organization, 2011). The cumulative economic loss associated with mental disorders is projected to US$ 16.3 trillion worldwide between 2011 and 2030, making the economic loss related to mental disorders higher than that of cancer, chronic respiratory diseases, and diabetes (Trautmann, Rehm, & Wittchen, 2016). The long-term socio-economic effects of childhood maltreatment in later-on life may be due to the occurrence of mental disorders (Barrett, Kamiya, & O'Sullivan, 2014). Those with childhood maltreatment reported lower family incomes and reduced labor force participation (Goodman, Joyce, & Smith, 2011; Stith et al., 2009).

Recent studies of childhood maltreatment have suggested that the deleterious sequela of childhood maltreatment may be transmitted from one generation to the next (Buss et al., 2017). A strong link has been documented between a maternal history of childhood maltreatment and mental health problems in offspring, including depression, anxiety, autism, suicide attempts, and poorer behavioral trajectories across the time (Brent et al., 2004; Brodsky et al., 2008; Collishaw

et al., 2007; Plant, Barker, Waters, Pawlby, & Pariante, 2013; Roberts, Lyall, Rich-Edwards, Ascherio, & Weisskopf, 2013). The offspring of victimized mothers, even without suffering any childhood maltreatment themselves, may experience an increased risk of psychiatric disorders (Plant, Barker, Waters, Pawlby, & Pariante, 2013; Rijlaarsdam et al., 2014). Noteworthy, the association between a history of maternal maltreatment and offspring's mental disorders appears to be particularly pronounced when mothers suffered the abuse during their childhood compared to the later stage of their lives (Thompson, 2007).

Several theoretical frameworks have been proposed to explain the intergenerational transmission of maternal childhood maltreatment to their children's mental illness. One theory explores how the environmental effect of maternal childhood maltreatment could potentially influence the normal development of offspring. Caregiving patterns are the putative mediating mechanism that has been postulated to explain the link (Collishaw et al., 2007; Plant, Pariante, Sharp, & Pawlby, 2015). Mothers, who had a history of maltreatment, are less likely to provide adequate opportunities to observe healthy caregiving behaviors, leading to intrusiveness, hostility towards children, increased use of harsh and intensive discipline and rejection, decreased sensitivity to children's need, decreased mother-children involvement (Bert, Guner, Lanzi, & Centers for Prevention of Child Neglect, 2009; Bosquet Enlow, Englund, & Egeland, 2018; Lomanowska, Boivin, Hertzman, & Fleming, 2017). These negative environmental factors could influence normal fetal programming to produce a less emotionally labile offspring temperament, which may increase the offspring's vulnerability of being maltreated, thus increasing the risk for mental illness (Madigan et al., 2019; Pariante, 2014). From an environmental perspective, disadvantaged caregiving, inability to protect children and aggregated domestic risks may directly put children at higher risk of mental illness (Plant, Pariante, Sharp, & Pawlby, 2015).

Epigenetic vulnerability is also theorized as an explanation of the intergenerational transmission of vulnerability to psychopathology. In animal studies, maternal care (grooming) was found to alter the expression of genes that govern behavior and stress responses (Meaney, 2001). Maternal care has also been shown to affect the subsequent maternal care exhibited by offspring (Meaney, 2001). More recently, in mice studies, Dias and Ressler (2014) demonstrated how a behaviorally induced trauma experience was inherited biologically through the offspring's parental gametes. They observed changes in RNA being passed down through sperm so that the offspring mice inherited what was initially a behavioral trauma fear through their fathers. Subsequent studies showed that with extinction based behavioral strategies this fear could be reversed both behaviorally and biologically in offspring and in the parental germline (Aoued et al., 2019). In human studies, an interdisciplinary framework proposed by Buss and colleagues suggested that the primary model of intergenerational transmission is biological (Buss et al., 2017). Genetic predispositions of the corticotropin-releasing hormone (CRH) receptor 1 Gene and FK506 binding protein 5 (FKBP5) DNA demethylation have been found to render children to be more vulnerable to negative consequences of maternal maltreatment when these genes were passed onto offspring (Buss et al., 2017; Heim et al., 2009; Klengel et al., 2013). Therefore, adverse environmental factors might have more than one pathway linking maternal childhood maltreatment and offspring's mental health.

Given the importance of childhood maltreatment in the development of psychiatric disorders and the possible link between maternal childhood maltreatment and offspring's psychopathology, it is important to understand to what extent maternal childhood maltreatment may impact upon their children's psychopathology (Miranda, Osa, Granero, & Ezpeleta, 2013; Plant, Jones, Pariante, & Pawlby, 2017). Even though the knowledge about the role of

intergenerational transmission effect of maternal childhood maltreatment on offspring's mental health is increasing (Collishaw et al., 2007), few intergenerational studies have been conducted to explore the consequences of maternal maltreatment on the offspring's physical and mental health outcomes. We were not aware of any systematic review being conducted to summarize the impact of maternal childhood maltreatment on offspring's psychopathology. There is one narrative review conducted by Plant et al. (2018) covering the literature to October 2015 that reported an association of maternal childhood maltreatment with the risk of next generation's psychological wellbeing, in addition to not being a systematic review, the review was not specific to studies on depression/internalizing disorder - common adolescent psychiatric disorders. The epidemiological evidence provided in the review did not provide a basis for a firm conclusion on the intergenerational effect of maternal childhood maltreatment.

This present systematic review and meta-analysis aimed to: 1) quantitatively synthesize the intergenerational effect of maternal childhood maltreatment on offspring's psychopathology; and 2) to improve inferences about the temporal order (cause) and reduce selection bias. The current review only included prospective studies thus dealing with the issue of temporal order. A pooled effect size was calculated to indicate the magnitude and overall strength of the association. We also examined a range of covariates, factors potentially moderating the relationship between maternal childhood maltreatment and offspring's psychopathology.

Methods

This systematic review and meta-analysis are guided by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklists. MOOSE is an evidence-based tool consisting of a checklist of 35 items, which is designed to respond to the issue of increasing diversity and variability of meta-analyses of observational studies by standardizing a reporting checklist thus

improving the usefulness of research (Stroup et al., 2000) (see Appendix A). The MOOSE checklist is one of several guidelines that are part of a larger initiative to improve the reliability and value of published research by using standardized guidelines to promote accurate and transparent reporting of research (see https://www.equator-network.org).

Search Strategy and Inclusion Criteria

Eligible studies were identified by computerized and manual searches. Five bibliographic databases were searched: MEDLINE, PubMed, Web of Science, EMBASE, and Cochrane Library. The literature search comprised articles published between January 1980 and January 2019. The detailed search strategies for each database are fully described in Appendix B. The 'published after 1980' criterion was used because the first research on the impact of childhood adversity on mental health was published during the 1980s. Figure 1 presents a flowchart of the literature search and screening based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (Moher, Liberati, Tetzlaff, & Altman, 2009).

The inclusion criteria were if the study: 1) used a prospective cohort study design; 2) assessed maternal childhood maltreatment exposure prior to the age of 18 with clear information defining the abuse as physical, sexual or emotional abuse, physical or emotional neglect and exposure to domestic violence; 3) had a measure on either depression or internalizing behaviors (which comprise anxious/depressed, withdrawn-depressed, and somatic complaints) among offspring prior to the age of 18; 4) used generally accepted diagnostic criteria for the presence of depression and internalizing behaviors; and, 5) was published in English. Exclusion criteria were if the study:1) only included relatively common punishments (e.g. spanking, or yelling), which may or may not be considered as maltreatment exposures due to cultural variability; 2) did not

provide sufficient information to extract necessary data to calculate the results on any type of childhood maltreatment and the mental health outcomes.

Data Extraction and Quality Assessment

Two reviewers (YS and XM) independently assessed articles to analyze eligible titles, abstracts, and full-text articles, with differences resolved by group discussions. A standardized data extraction sheet was used to collect data from eligible studies. The following study characteristics were extracted from those selected studies: authors(s); year of publication; age of offspring; study site (coded as North America, Europe, and Asia); sample size; source of the study sample (clinical samples vs. community samples); sex of offspring (% of females); ethnicity (% Caucasian); type of abuse (physical abuse, sexual abuse, emotional abuse, and neglect); measures of maternal childhood maltreatment exposures; type of mental health outcomes (diagnoses); psychopathology measures (questionnaires or scales used for offspring's mental health outcomes). To enable a comparison of results from the diverse studies, zero-order correlation coefficients were extracted to indicate the correlation between maternal childhood maltreatment and the offspring's mental outcome. Articles that met the inclusion criteria were then assessed for their methodological quality and potential bias based on the Newcastle-Ottawa Scale (NOS) (Wells, 2001), a widely used scale consisting of eight questions, with a maximum of ten possible points for each type of study. The NOS scores were categorized into two groups based on the mean score of all included studies: above the mean score-high risk of bias, and below the mean score-low risk of bias (Lo, Mertz, & Loeb, 2014).

Meta-analysis

Calculation of effect sizes. To achieve comparable effect sizes for analyses, we used the zero-order correlation coefficient as the common effect size measure in the present study. Effect size coefficients were either directly obtained from studies or first computed and transformed from the reviewed articles (Lipsey & Wilson, 2001). Coefficients (rs) were then converted with Fisher's Z transformation to avoid the standard error skew in correlational analyses. Effect sizes were weighted by their inverse variance, subsequently, the Z-values were converted back to coefficients for the interpretation of results (Fischer, 1944; Hedges & Olkin, 2014; Lipsey & Wilson, 2001). A positive effect size indicates a positive association with r values of 0.10, 0.30 and 0.50 representing small, moderate, and large effects, respectively (Cohen, 1992). Individual studies could generate multiple effect sizes concerning the relationships between different subtypes of maternal maltreatment and outcomes, therefore these within-study effects were dependent on each other. Cheung and Chan have suggested a sample wise approach to handle dependent correlations, simply analyzing them by within-sample mean procedures (Cheung & Chan, 2008). This sample wise method can generate an average effect size based on each set of dependent effect sizes from the same sample (Hunter & Schmidt, 2004).

Statistical analyses and moderators. Random-effect models were performed to synthesize overall effect sizes given the amount of variances produced by differences between and within studies and taking the heterogeneity test results into account. Further, effect sizes could vary across studies as a function of potential moderators. The random variance component was determined by using maximum-likelihood estimation (Lipsey & Wilson, 2001). Cochrane's Q statistic was used to test the heterogeneity (Higgins & Thompson, 2002). Heterogeneity of results was assumed if Q was significant at $p<0.05$, allowing for testing of potential moderators. Categorical factors, including (age of offspring, study site, source of the study sample, type of

maltreatment, measures of maltreatment exposure, and type of outcome), were tested by using procedures analogous to analysis of variance (ANOVA) with a between-group test of homogeneity ($Q_{between}$) (Lipsey & Wilson, 2001). Significant results indicated that effect sizes significantly differed across the categories of the moderator. The impact of continuous variables (publication year, sex, ethnicity, and maternal depression) on results was assessed by meta-regression. We considered the above four variables as continuous due to the availability of data and the feasibility of explanation. A significant slope indicated the moderation effect on the overall effect. Sensitivity analyses were also performed to test the effect of individual studies on overall effect sizes. Finally, publication bias was assessed by funnel plots and quantitatively evaluated by Egger's regression and Begg's correlation (Begg & Mazumdar, 1994; Sterne, Egger, & Smith, 2001). Trim and Fill test was performed to estimate the unbiased pooled effect size while taking publication bias into account (Duval & Tweedie, 2000).

All analyses were conducted using the Comprehensive Meta-Analysis version 2.0 (Biostat, Englewood, NJ, USA) and IBM SPSS Statistical Version 21 (IBM Corp, NY, USA) and the macros statistical program written by Lipsey and Wilson to calculate effect sizes from different measures of statistical association (Lipsey & Wilson, 2001). A p-value less than 0.05 is considered statistically significant.

Results

A total of 12 articles covering 29,682 subjects were included in this meta-analytic review. Figure 1 presents the selection process of the literature search. Table 1 summarizes the study characteristics of these selected studies. All studies were published within the last 20 years. All studies but one were from developed countries with that exception being from China. Overall, the quality of these studies was moderate as assessed by the Newcastle-Ottawa scale with a mean

score of 6.75 (range from 4 to 8) (see Appendix C in supplement). These studies targeted a wide age range of offspring varying from 1 year to 16 years but most of them focused on age from 8 to 14 years of old. The offspring cohort had about half females (50.1%) and Caucasian (48.8%).

Overall Effects for Maternal Childhood Maltreatment and Offspring Psychopathology

A composite effect size of maternal childhood maltreatment on offspring's psychopathology was calculated using 12 mean effect sizes weighted by the study's sample sizes. As shown in Figure 2, the pooled effect size from the selected studies was in the small but significant range (r=0.14, 95%CI 0.09-0.19, p<0.001). However, it should be noted that 4 of the 12 studies reported significant moderate effect sizes in the 0.30 range. The heterogeneity test was significant across the studies (Q=117.45, p<0.001). Therefore, a random-effect model was used in the meta-analysis. Sensitivity analyses were used to assess the influence of each study on the pooled effect size by omitting one study at a time. The overall correlation between maternal childhood maltreatment and the offspring's psychopathology was not influenced by the inclusion or exclusion of any specific study (r=0.15, 95%CI 0.04-0.26, p=0.006).

Both funnel plot (Appendix D) and Egger's test (Tau=0.12, p=0.58) and Begg's test (t=0.76, p=0.47) did not show publication bias. In addition, the Trim-and-fill test was conducted to estimate a pooled effect size after adjusting the potential missing publications that might exist in the meta-analysis. After considering the potential missing publications, a small, but significant effect size was found (r=0.12, 95% CI: 0.11-0.14).

Moderator Analyses

Table 2 presents results on the moderation analyses. We found two variables had significant moderation effects: ethnicity (% Caucasian) and maternal depression. Meta-regression analyses

showed that ethnicity significantly moderated the relationship between maternal childhood maltreatment and offspring's psychopathology (p=0.001). The correlation between maternal childhood maltreatment and offspring outcomes was much stronger among studies with higher proportions of non-Caucasians than those with more Caucasians. We also found a significant moderating effect for maternal depression (p=0.001). Maternal depression reduced the correlation between maternal childhood maltreatment and the offspring's disease outcome. No significant moderating effect was found for the rest of the categorical variables (child age, study site, source of study subjects, type of maltreatment, maltreatment assessment, and type of outcome) (p>0.05). Similarly, publication year and sex of offspring did not have a moderating effect in this association (p>0.05).

Discussion

This systematic review and meta-analysis quantitatively summarized the relationship between maternal childhood maltreatment and the offspring's depression and internalizing behaviors. A maternal history of maltreatment in childhood was found to have a small but significant detrimental impact on the offspring's mental health with four of the twelve studies reporting negative impact in the moderate effect size range. Because this systematic review included studies with high heterogeneity, findings of this review should be carefully interpreted. The findings of this current review are generally in line with previous literature, suggesting maternal child maltreatment has a small, but negative consequence on offspring's mental health outcomes (Bosquet Enlow, Englund, & Egeland, 2018; Collishaw et al., 2007; Plant, Pawlby, Pariante, & Jones, 2018).

We found both ethnicity and maternal depression moderated the relationship between maternal childhood maltreatment and offspring's psychopathology. Children of non-Caucasians

were more susceptible to their mother's exposures of child maltreatment. Considering the etiological nature of depression and internalizing disorders, these differences might be caused by multiple factors, including biological factors, environmental exposures and gene-environment interplay. Caucasians and non-Caucasians may have different genetic susceptibilities and psychosocial risk factors. The implication for genotypes is that psychiatric disorders may have varying levels of heritability for different ethnic groups, which determines the offspring's susceptibility to mental health outcomes (Gatt, Burton, Williams, & Schofield, 2015; Hernandez, Plant, Sachs-Ericsson, & Joiner Jr, 2005). Compared to Caucasians, non-Caucasians were more likely to have lower socioeconomic status, higher rates of unemployment and other social stressors (e.g., exposure to crime). All these factors expose offspring to highly stressful and stigmatized environments (Turner & Lloyd, 2004; Ulbrich, Warheit & Zimmerman, 1989). Also, maternal depression moderated the relationship between maternal childhood maltreatment and offspring's psychopathology. As expected, maternal depression reduced the effect size of maternal maltreatment on offspring's depression and internalizing disorders. Clearly, maternal depression and maternal childhood maltreatment were competing risk factors for offspring's psychopathology. The association between maternal depression and adverse child outcomes could be explained by intergenerational epigenetic transmission, effects of environmental mechanisms, and/or gene-environment interactions and the effects of depression treatment interventions (Goodman & Gotlib, 1999; Wilson & Durbin, 2010). The treatment of maternal depression may increase awareness of factors contributing to depression and thus increase awareness of the possibility of the intergenerational transmission of depression and trigger clinical interventions to ameliorate these effects. What this review adds to the literature is that it emphasizes the importance of maternal depression in offspring's mental health outcomes. Meng

et al. in their systematic review alluded to the point that the influence of maltreatment on mental health might become less important as more proximal competing factors come into place (Meng, Fleury, Xiang, Li, & D'Arcy, 2018).

There are several hypotheses proposed to explain the intergenerational transmission of maternal childhood maltreatment on offspring's psychopathology. First, the transmission effect could be inherited through epigenetic alterations in genes encoding for proteins that regulate the process, such as the serotonin-transporter polymorphism (5-HTTLPR), which moderates the effects of environmental factors on the risk of childhood expression of endophenotypes that are associated with depression (Bouvette-Turcot et al., 2015). Second, the transmission may be mediated through gestational biology, with the developing feto-placental unit sensing and responding to biological cues in the maternal compartment (Buss et al., 2017). Third, exposure to negative social/psychological environment may increase the risk of developing mental disorders. Mothers with a history of childhood maltreatment have been found to be more likely to demonstrate depressive behaviors, especially at the earliest two generations intersection points, this may fundamentally contribute to maltreatment in the next generation (Plant, Barker, Waters, Pawlby, & Pariante, 2013). Fourth, maternal childhood maltreatment is often related to marital discord, parenting styles, and tense interpersonal relationships (Dixon, Hamilton-Giachritsis, & Browne, 2005; Fleming, Mullen, Sibthorpe, & Bammer, 1999; Ornduff, 2000). These negative environmental influences may lead to disruptions in stress regulation abilities and change the brain structures and functioning (Bosquet Enlow, Englund, & Egeland, 2018). Fifth, findings from clinical samples indicated that the relationship between parental childhood abuse and offspring psychopathology was mediated by the experience of abuse in the offspring generation (Brent et al., 2004). Children of abused mothers were more likely to experience maltreatment via

mechanisms such as inadequate maternal care, dysfunctional mother-child relationships, and family instability (Collishaw et al., 2007). Intergenerational continuities in offspring abuse combined with these adverse conditions can culminate in elevated vulnerability in offspring to psychiatric illness (Plant, Pariante, Sharp, & Pawlby, 2015). Sixth, offspring with victimized mothers were more likely to be exposed to an accumulation of stressors and psychosocial adversities associated with their mental health problems, for example, unstable housing, acquisition of new friends' figures, which may contribute to the transmission of risk for psychopathology associated with maternal childhood abuse (Wickrama, Conger, & Abraham, 2005). Finally, the intergenerational transmission may also be seen as a result of the complex interplay between genetic and psychosocial environmental factors binding parents to their children (Mason, Chmelka, Trudeau, & Spoth, 2017).

Strengths and Limitations

This systematic review and meta-analysis comprehensively synthesized and provided the first estimation of the negative consequence of maternal childhood maltreatment on the offspring's psychopathology, specifically, depression and internalizing behaviors. The findings of this review suggest that future research and prevention efforts on childhood maltreatment should be extended, if possible, to two generations or more generations.

There are several study limitations to be noted. First, there are a relatively small number of studies in this emerging research field with few studies being eligible for this review. The meta-analysis was limited in terms of its statistical power which may increase the chance of having a false positive effect (Dumas-Mallet, Button, Boraud, Gonon, & Munafò, 2017). The review was also restricted in its ability to explore potential moderators. Second, the generalizability of findings warrants careful interpretation, as most of the included studies measured general

childhood maltreatment rather than individual subtypes of maltreatment. It remains unclear how individual subtype of maltreatment during maternal childhood would predict offspring's psychopathology. Third, the variables in the studies reviewed were limited which in turn limited what characteristics could be examined for their potential roles as moderators. Fourth, this review included mostly studies from developed countries. Findings may not apply to developing countries. Finally, this review had high heterogeneity across studies. These selected studies included a mix of moderators, used both self-report and in-person interviews to collect information on child maltreatment, as well as symptoms and diagnostic measures. Interpretations of these results should be made cautiously.

Conclusion

This systematic review demonstrates that the experience of maternal childhood maltreatment has a small but significant impact in increasing the risk of psychopathology among those mothers' children. Improving maternal mental health may help reduce the offspring's risk of depression and internalizing behaviors. This review further informs research examining the long-term consequences of childhood maltreatment and exploring its potential moderators. It is encouraging to know that not all maternal childhood abuse leads to negative mental health outcomes for their children. So, the question arises as to what contributes to the transmission of negative mental health experiences from one generation to the next and conversely what interrupts or mitigates against such transmission? In addition, what is the impact of paternal childhood abuse? How does it affect their children's mental health? Unfortunately, research is scarce on this topic, much more is required. The role of parent-child gender symmetry and asymmetry and type of abuse and how it impacts offsprings' mental health needs further exploration. Finally, a wider range of mental health outcomes needs to be explored.

Critical Review Findings

1. The meta-analytic review of 12 studies showed that maternal childhood maltreatment resulted in a small but significant increased risk of psychopathology (depression & internalizing disorder) among offspring (r=0.14, 95%CI: 0.09-0.19).
2. Meta-regression analyses found that ethnicity played a moderating role in the relationship between maternal childhood maltreatment and offspring's psychopathology, suggesting non-Caucasian children were more vulnerable to their mother's exposures of child maltreatment.
3. Maternal depression acted as a competing factor and moderating factor, reducing the impact of the experience of maternal childhood maltreatment on offspring's depression and internalizing disorders.

Implications for Practice, Policy, and Research

1. Strengthen the capacity of health professionals and specialists to detect childhood maltreatment among mothers and their children and develop effective and timely interventions to reduce the risk of psychopathology and promote positive mental health of the future generations.
2. Intervention strategies should be developed and widely disseminated to ultimately break the cycle by which the consequences of childhood maltreatment are passed down from one generation to the next.
3. Future research and prevention efforts should recognize the potential intergenerational impact of parents' (maternal or paternal) experience of childhood maltreatment and not just focus on the current generation.
4. Future studies exploring the relationship between the subtypes of maternal and paternal maltreatment and offspring's mental health are needed.
5. More research is needed on the impact of parent-child gender symmetry and asymmetry and their effects on parental child abuse and offsprings' mental health relationship.
6. Future studies should also incorporate biological information into studies to complement explaining the process of transmission of maltreatment.

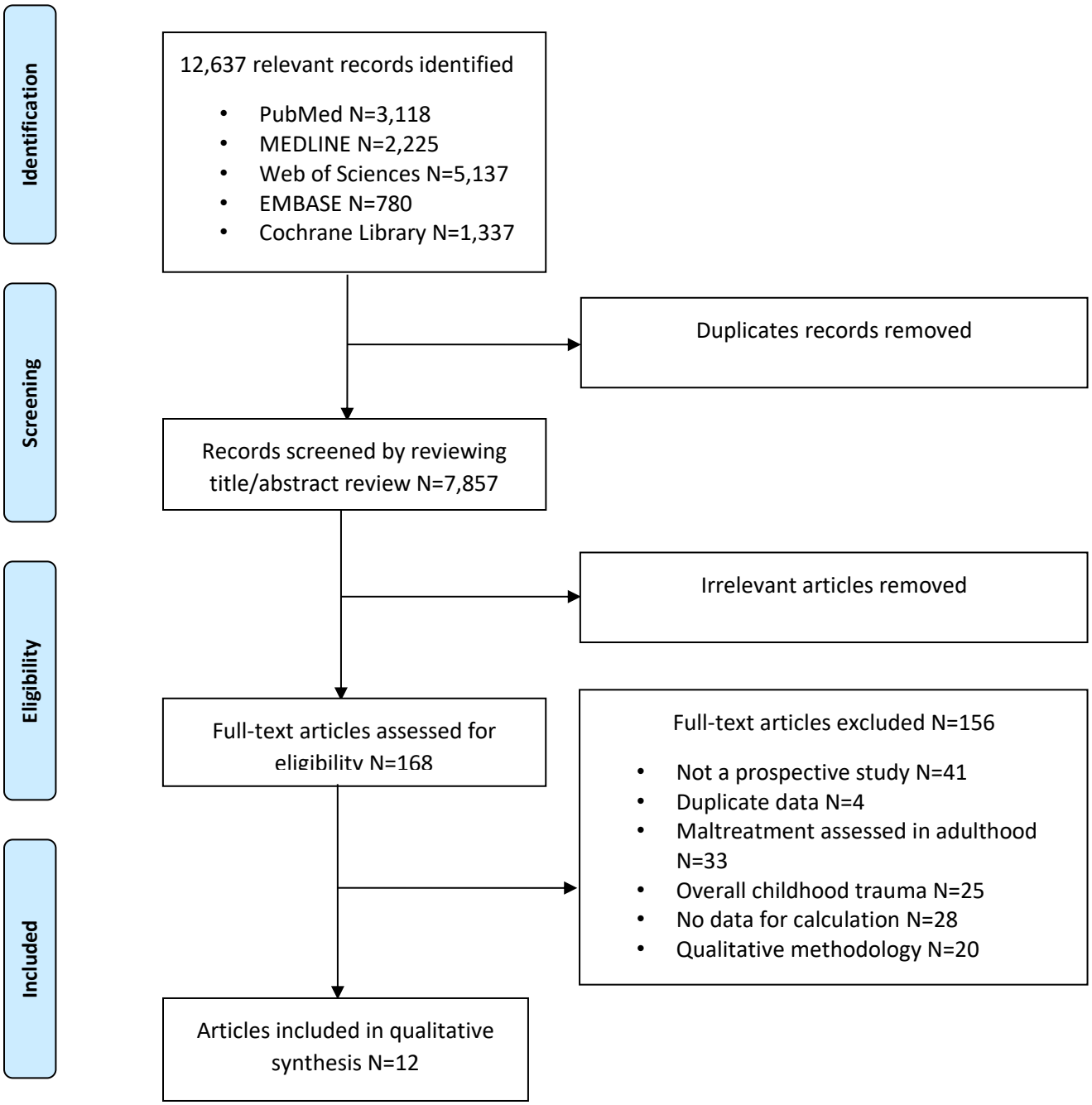


Figure 1. A summary of the literature search in this systematic review.

Study name	Correlation	Lower limit	Upper limit	Z-Value	p-Value
Plant et al, 2013	0.010	-0.166	0.185	0.110	0.912
Roberts et al, 2015	0.090	0.072	0.108	9.635	0.000
Min et al, 2013	0.120	-0.009	0.245	1.821	0.069
Plant et al, 2018	0.110	0.090	0.130	10.705	0.000
Linde-Krieger & Yates, 2018	-0.140	-0.266	-0.009	-2.100	0.036
Rijlaarsdam et al, 2014	0.150	0.121	0.179	10.065	0.000
Koverola et al, 2005	0.420	0.300	0.527	6.331	0.000
Letourneau et al, 2019	0.040	-0.025	0.105	1.203	0.229
Liu et al, 2019	0.053	-0.084	0.188	0.758	0.449
Choi et al, 2019	0.270	0.229	0.310	12.471	0.000
Dubowitz et al, 2001	0.260	0.168	0.347	5.428	0.000
Pereira et al, 2018	0.320	0.128	0.489	3.198	0.001
	0.142	0.093	0.190	5.657	0.000

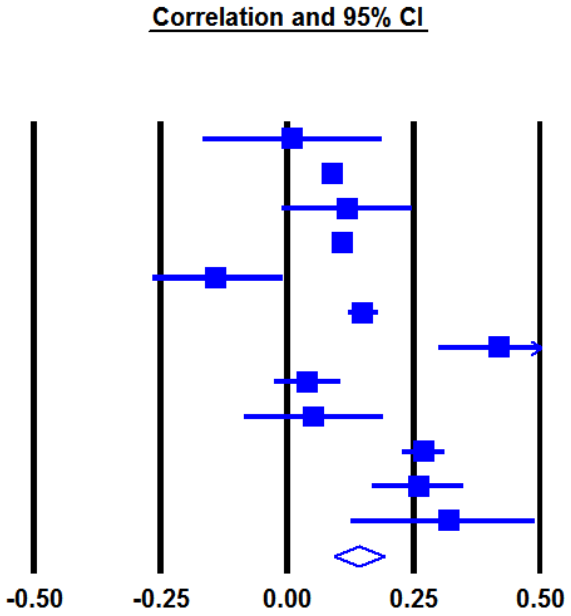


Figure 2. Pooled effect sizes for the association between maternal childhood maltreatment and the offspring's psychopathology.

Table 1. Study characteristics of the selected studies in this systematic review.

Authors	Year	Offspring Age	Study site	Sample size	Sample source	Sex No.(% of female)	Ethnicity No.(% of Caucasian)	Type of abuse	Maternal childhood maltreatment measurements	Offspring psychopathology measures	Type of outcome
Plant et al.	2013	11- and 16-year	United Kingdom	125 mother-child dyads	Clinical	68/125 (54.0)	90/125 (72.0)	PA/SA/EN/ PN	Maternal self-report questionnaire	DSM-IV symptoms of depression	Depression
Roberts et al.	2015	9- to 14-year	United States	mothers = 8,882; children = 11,402	Clinical	6,462/11,402 (56.7)	10,645/11,402 (93.4)	PA/EA/SA	Childhood Trauma Questionnaire (CTQ)	Center for Epidemiological Studies Depression Scale–10 (CESD-10)	Depressive Symptoms
Min et al.	2013	9 years	United States	231 mother-child dyads	Clinical	120/231 (51.9)	NA	PA/SA/EA/ EN/PN	Childhood Trauma Questionnaire (CTQ)	Child Behavior Checklist for ages 6-18 (CBCL)	Internalizing behaviors
Plant et al.	2018	11 years	United Kingdom	9,397 mother-child dyads	Community	4,558/9,397 (48.5)	9,087/9,397 (96.7)	PA/SA/EA/ EN/PN	Maternal self-report questionnaire	Strengths and difficulties questionnaire(SDQ); DSM-IV	Internalizing behaviors

Liu et al.	2019	14 months	China	207 mother-child dyads	Clinical	102/207 (49.3)	0/207 (0.0)	PA/EA/SA	Childhood Trauma Questionnaire Short Form (CTQ-SF)	Infant-Toddler Social and Emotional Assessment (ITSEA)	Internalizing behaviors
Linde-Krieger & Yates	2018	4 -and 8-year	United States	225 mother-child dyads	Community	108/225 (48.0)	45/225 (20.0)	SA	A verbal administration of the Early Trauma Inventory	Test Observation Form (TOF)	Internalizing behaviors
Pereira et al.	2018	5 years	Canada	96 mother-child dyads	Community	45/96 (47.0)	79/96 (82.3)	PA/SA/EA/ EN/PN	Childhood Trauma Questionnaire Short Form (CTQ-SF)	Child Behavior Checklist for ages 1.5–5 (CBCL)	Internalizing behaviors
Choi et al.	2019	12 years	United Kingdom	mothers=1,016; children=2,032	Community	1,036/2,032 (51.0)	NA	PA/SA/EA/ EN/PN	Childhood Trauma Questionnaire (CTQ)	Child Behavior Checklist (CBCL)	Internalizing behaviors
Rijlaarsdam et al.	2014	6 years	Netherlands	4,438 mother-child dyads	Community	2,241/4,438 (50.5)	3,333/4,438 (75.1)	PA/SA/EA/ EN/PN	Childhood Trauma Questionnaire (CTQ)	Child Behavior Checklist (CBCL)	Internalizing behaviors
Dubowitz et al.	2001	6- to 7-year	United States	419 mother-child dyads	Clinical	207/419 (49.4)	NA	PA/SA	Study-developed measure	Child Behavior Checklist (CBCL)	Internalizing behaviors
Koverola et al.	2005	8 years	United States	203 mother-child dyads	Clinical	98/203 (48.3)	NA	PA/SA	Study-developed measure	Child Behavior Checklist (CBCL)	Internalizing behaviors

Letourneau et al.	2019	2 years	Canada	907 mother-child dyads	Community	423/907 (46.6)	788/907 (86.9)	PA/SA/EN/ PN	Adverse Childhood Experiences Questionnaire (ACE)	Child Behavior Checklist (CBCL)	Internalizing behaviors

Abbreviations: PA, physical abuse; SA, sexual abuse; EA, emotional abuse; EN, emotional neglect; PN, physical neglect; NA, not available.

Table 2. Potential Moderators of the Meta-Analytic Association between Maternal Childhood Maltreatment and Offspring Psychopathology.

Moderator	k	Number of participants	Fisher's Z	Effect size estimate		Test of homogeneity		Slope(p value)
				r(95%CI)	p value	Cochran's Q	p value	
All studies	12	29,682	5.71	0.14(0.09-0.19)	<0.001	117.45	<0.001	
Categorical moderator								
Age								
0-8 years	7	6,495	2.89	0.15(0.05-0.25)	0.004	0.09	0.76	
9-16 years	5	23,187	2.14	0.13(0.01-0.24)	0.032			
Study site								
North America	7	13,483	2.90	0.15(0.05-0.25)	0.004	0.42	0.81	
Europe	4	15,992	2.27	0.15(0.02-0.27)	0.023			
Asia	1	207	0.38	0.05(-0.22-0.33)	0.703			
Source of sample								
Clinical	5	12,462	3.13	0.18(0.07-0.30)	0.002	0.93	0.23	
Community	7	17,220	2.23	0.11(0.01-0.21)	0.026			
Type of maltreatment								
Abuse only	5	12,456	2.24	0.14(0.02-0.26)	0.025	0.01	0.93	
Abuse and neglect	7	17,226	2.81	0.14(0.04-0.24)	0.005			

Maltreatment assessment								
Self-report	8	15,792	3.46	0.16(0.07-0.26)	<0.001	0.75	0.39	
Interview	4	13,890	1.47	0.09(-0.03-0.22)	0.143			
Type of outcome								
Depression	2	11,527	0.63	0.06(-0.12-0.24)	0.529	0.92	0.34	
Internalizing behavior	10	18,155	3.78	0.16(0.08-2.34)	<0.001			
Continuous moderator								
Publication year	12	29,682	1.51					0.031(0.130)
Gender	12	29,682	0.74					0.004(0.460)
Ethnicity(Caucasian)	9	26,797	-3.33					-0.002(0.001)
Maternal depression	6	23,959	-3.22					-0.006(0.001)

Appendix A. MOOSE checklist for meta-analyses of observational studies

Appendix B. Search strategies

Appendix C. A summary of the Newcastle-Ottawa Scale (NOS) quality assessment for included studies

Appendix D. The publication bias test by the funnel plot (N=12)

Appendix A. MOOSE checklist for meta-analyses of observational studies

Item No	Recommendation	Brief description of how the criteria were handled in the meta-analysis
Reporting of background should include		
1	Problem definition	The importance of the possible link between maternal childhood maltreatment and offspring's psychopathology increased, but no systematic review has been conducted to synthesize findings on this research topic.
2	Hypothesis statement	The maternal experience of childhood maltreatment may pass onto offspring's psychopathology.
3	Description of study outcome(s)	Offspring's psychopathology
4	Type of exposure or intervention used	Maternal experience of childhood maltreatment
5	Type of study designs used	Prospective cohort study
6	Study population	Children who have mothers with childhood maltreatment experience
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	The affiliations of the investigators are provided in the title page.
8	Search strategy, including time period included in the synthesis and key words	MEDLINE, PubMed, Web of Science, EMBASE and Cochrane Library. Articles published between January 1980 and January 2019. Also see eMethods 1 in the supplement.
9	Effort to include all available studies, including contact with authors	Grey literature was also searched to find potentially relevant studies.
10	Databases and registries searched	MEDLINE, PubMed, Web of Science, EMBASE and Cochrane Library
11	Search software used, name and version, including special features used (eg, explosion)	No special search software was used in this study.
12	Use of hand searching (eg, reference lists of obtained articles)	Grey literature was searched for relevant articles.
13	List of citations located and those excluded, including justification	Inclusive and exclusive studies are outlined and detailed in the flow chart (Figure 1) and also in the Methods section.
14	Method of addressing articles published in languages other than English	We only included original empirical studies published in English.
15	Method of handling abstracts and unpublished studies	Abstracts and unpublished studies were excluded.
16	Description of any contact with authors	We contacted all the corresponding authors or first author to request additional data when needed.
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	The inclusion criteria and exclusion criteria are presented in the Methods section.
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	Data extracted and coded were relevant to the study characteristics, exposure, outcome, and potential moderators. Detailed information is listed in the "Coding of Studies and Quality Assessment" section.

19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	Data were extracted and analyzed by two reviewers independently.
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	Because different studies controlled for different confounders, we used zero order effect sizes to make included studies' results more comparable. Zero order effect sizes do not control for confounders.
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	The quality of studies was assessed with Newcastle-Ottawa Scale.
22	Assessment of heterogeneity	Cochrane's Q statistic was used to test the heterogeneity.
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	Random-effect models were used to calculate the overall point estimate. Categorical factors were tested with a between-group test of homogeneity, and the impact of continuous variables on results were assessed by meta-regression. All analyses were conducted using the Comprehensive Meta-Analysis version 2.0 (Biostat, Englewood, NJ, USA) and IBM SPSS Statistical Version 21 (IBM Corp, NY, USA) and the macros statistical program written by Lipsey and Wilson.
24	Provision of appropriate tables and graphics	Two tables and two supplementary tables are provided. PRISMA flow-chart, one Forest Plot and a Funnel Plot are also provided in the main text.
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Figures are appended in the main text. Figure 2-3.
26	Table giving descriptive information for each study included	Table 1.
27	Results of sensitivity testing (eg, subgroup analysis)	Sensitivity analyses were used to assess the influence of each individual study on the pooled effect size.
28	Indication of statistical uncertainty of findings	95% confidence intervals were provided with overall effect estimates.
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	Details on the publication bias are provided in the Result section.
30	Justification for exclusion (eg, exclusion of non-English language citations)	Articles were excluded if: (1) only included relatively common punishments (e.g. spanking, or yelling), which might not be consider as maltreatment exposures due to cultural variability; (2) did not provide sufficient information to extract effect size or data to calculate the results on any type of childhood maltreatment and the psychiatric disorder outcomes.
31	Assessment of quality of included studies	The quality of these studies was moderate as assessed by the Newcastle-Ottawa scale with a mean score of 6.75 (range from 4 to 8) (details see eTable 2 in the Supplement).
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	We fully discussed the possible explanations and mechanisms of the results in the Discussion section.

33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	We discussed the need for future research on this topic among developing countries in the Discussion section.
34	Guidelines for future research	Given that the negative effects of the maternal experience childhood maltreatment is not automatically passed on to the next generation future studies should examine the mechanisms that link maternal childhood maltreatment with offspring's mental health as well as how moderators interrupt this intergenerational transmission.
35	Disclosure of funding source	Disclosed in the relevant section.

Appendix B. Search strategies

PubMed

(((((((depressive disorder[MeSH Terms]) OR major depressive disorder[Text Word]) OR major depression[Text Word]) OR unipolar depression[Text Word]) OR depression[Text Word]) OR depressed[Text Word]) OR depressive[Text Word])) AND (child* AND (abus* OR maltreat* OR neglect OR abandon* OR illtreat* OR ill-treat* OR mal-treat* OR advers* OR trauma* OR ACE*)) AND (maternal* OR parental* OR parents OR intergenerational* OR inter-generational*) Filters: Humans

MEDLINE

(mesh (depressive disorder) OR (major depressive disorder) OR (major depression) OR (unipolar depression) OR depression OR depressed OR depressive) AND (child* AND (abus* OR maltreat* OR neglect OR abandon* OR illtreat* OR ill-treat* OR mal-treat* OR advers* OR trauma* OR ACE*)) AND (maternal* OR parental* OR parent* OR intergenerational* OR inter-generational*)

Web of Sciences

#1 TS= "child*" OR "youth" OR "adolescent*"

#2 TS="abus*" OR "maltreat*" OR "neglect" OR "abandon*" OR "illtreat*" OR "ill-treat*" OR "mal-treat*" OR "advers*" OR "trauma*" OR "ACE*"

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years

#3 TS="depressive disorder" OR TS="major depressive disorder" OR TS="major depression" OR TS="unipolar depression" OR TS=depression OR TS=depressed OR TS=depressive

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years

#4 #2 AND #1

#5 #3 AND #4

#6 TS= "maternal*" OR "parental*" OR "parent*" OR “intergenerational” OR"inter-generational*"

#5 #5 AND #6

EMBASE

#1 TS= "child*" OR "youth" OR "adolescent*"

#2 TS="abus*" OR "maltreat*" OR "neglect" OR "abandon*" OR "illtreat*" OR "ill-treat*" OR "mal-treat*" OR "advers*" OR "trauma*" OR "ACE*"

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years

#3 TS="depressive disorder" OR TS="major depressive disorder" OR TS="major depression" OR TS="unipolar depression" OR TS=depression OR TS=depressed OR TS=depressive

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years

#4 #2 AND #1

#5 #3 AND #4

#6 TS= "maternal*" OR "parental*" OR "parent*" OR “intergenerational” OR"inter-generational*"

#5 #5 AND #6

Cochrane Library

#1 MeSH descriptor: [Depressive Disorder] explode all trees

#2 "major depressive disorder" or "major depression" or "unipolar depression" or "depressed" or "depression" (Word variations have been searched)

#3 #2 or #1 or "depressive" (Word variations have been searched)

#4 MeSH descriptor: [child maltreatment] explode all trees

#5 abus* OR maltreat* OR neglect OR abandon* OR illtreat* OR ill-treat* OR mal-treat* OR advers* OR trauma* OR ACE (Word variations have been searched)

#6 #4 OR #5

#7 #3 AND #6

#8 maternal* OR parental* OR parent* OR intergenerational* OR inter-generational* (Word variations have been searched)

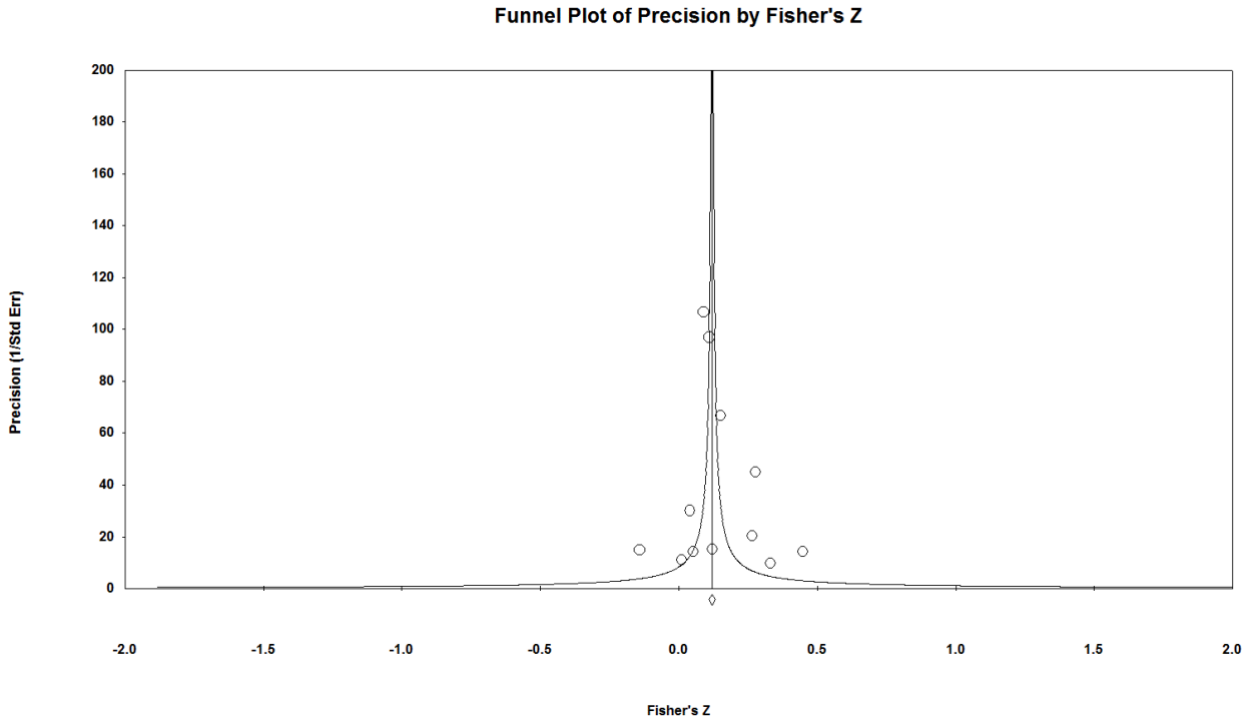
#9 #8 AND #7

Appendix C. A summary of the Newcastle-Ottawa Scale (NOS) quality assessment for included studies

Assessment item	Study											
	Plant et al. (2013)	Roberts et al. (2015)	Min et al. (2013)	Plant et al. (2018)	Liu et al. (2019)	Linde-Krieger & Yates (2018)	Pereira et al. (2018)	Choi et al. (2019)	Rijlaarsdam et al. (2014)	Dubowitz et al. (2001)	Koverrola et al. (2005)	Letourneau et al. (2019)
Selection												
1. Representativeness of the intervention cohort												
a) truly representative of the average, elderly, community-dwelling resident	0	0	0	1	0	0	0	0	1	0	0	0
b) somewhat representative of the average, elderly, community-dwelling resident	1	1	0	0	1	1	1	1	0	0	0	1
c) selected group of patients, e.g. only certain socio-economic groups/areas	0	0	0	0	0	0	0	0	0	0	0	0
d) no description of the derivation of the cohort	0	0	0	0	0	0	0	0	0	0	0	0
2. Selection of the non-intervention cohort												
a) drawn from the same community as the intervention cohort	1	1	1	1	1	1	1	1	1	1	0	1
b) drawn from a different source	0	0	0	0	0	0	0	0	0	0	0	0
c) no description of the derivation of the non-intervention cohort	0	0	0	0	0	0	0	0	0	0	0	0
3. Ascertainment of intervention (exposure)												
a) secure record (e.g. health care record)	0	0	0	0	0	0	0	0	0	0	0	0

b) structured interview	0	1	1	0	0	1	0	1	1	0	0	0
c) written self-report	0	0	0	0	0	0	0	0	0	0	0	0
d) other / no description	0	0	0	0	0	0	0	0	0	0	0	0
4. Demonstration that outcome of interest was not present at start of study												
a) yes	1	1	1	1	1	1	1	0	1	0	0	1
b) no	0	0	0	0	0	0	0	0	0	0	0	0
Comparability												
1. Comparability of cohorts on the basis of the design or analysis												
a) study controls for age, sex, marital status	0	0	0	0	0	0	0	0	0	0	0	0
b) study controls for any additional factors (e.g. socio-economic status, education)	1	1	1	1	0	1	1	1	1	1	1	1
Outcome												
1. Assessment of outcome												
a) independent blind assessment	1	1	1	1	1	1	1	1	1	1	1	1
b) record linkage	0	0	0	0	0	0	0	0	0	0	0	0
c) self-report	0	0	0	0	0	0	0	0	0	0	0	0

d) other / no description	0	0	0	0	0	0	0	0	0	0	0	0
2. Was follow up long enough for outcomes to occur												
a) yes, if median duration of follow-up >= 6 month	1	1	1	1	1	1	1	1	1	1	1	1
b) no, if median duration of follow-up < 6 months	0	0	0	0	0	0	0	0	0	0	0	0
3. Adequacy of follow up of cohorts												
a) complete follow up: all subjects accounted for	1	1	1	1	1	0	0	0	0	1	1	1
b) subjects lost to follow up unlikely to introduce bias: number lost <= 20%, or description of those lost suggesting no different from those followed	0	0	0	0	0	1	1	1	1	0	0	0
c) follow up rate < 80% (select an adequate %) and no description of those lost	0	0	0	0	0	0	0	0	0	0	0	0
d) no statement	0	0	0	0	0	0	0	0	0	0	0	0
Overall	7	8	7	7	6	8	7	7	8	5	4	7



Appendix D. The publication bias test by the funnel plot (N=12)

References

Aoued, H.S., Sannigrahi, S., Doshi, N., Morrison, F.G., Linsen baum, H., Hunter, S., …Dias, B.G. (2019). Reversing behaviral, neuroantomical, and germline influences of intergenerational stress. *Biological Psychiatry, 85*, 248-256.

Barrett, A., Kamiya, Y., O'Sullivan, V. (2014). Childhood sexual abuse and later-life economic consequences. *Journal of Behavioral and Experimental Economics*, *53*, 10-16.

Begg, C. B., Mazumdar, M. (1994). Operating characteristics of a rank correlation test for publication bias. *Biometrics*, 1088-1101.

Bert, S. C., Guner, B. M., Lanzi, R. G., Centers for Prevention of Child Neglect. (2009). The influence of maternal history of abuse on parenting knowledge and behavior. *Family Relations, 58*, 176-187.

Bosquet Enlow, M., Englund, M. M., Egeland, B. (2018). Maternal childhood maltreatment history and child mental health: Mechanisms in intergenerational effects. *Journal of Clinical Child & Adolescent Psychology*, *47*, S47-S62.

Bouvette-Turcot, A. A., Fleming, A. S., Wazana, A., Sokolowski, M. B., Gaudreau, H., Gonzalez, A., …Meaney, M. (2015). Maternal childhood adversity and child temperament: An association moderated by child 5-HTTLPR genotype. *Genes, Brain and Behavior*, *14*, 229-237.

Brent, D. A., Oquendo, M., Birmaher, B., Greenhill, L., Kolko, D., Stanley, B., …Mann, J. J. (2004). Familial transmission of mood disorders: convergence and divergence with transmission of suicidal behavior. *Journal of the American Academy of Child & Adolescent Psychiatry*, *43*, 1259-1266.

Brodsky, B. S., Mann, J. J., Stanley, B., Tin, A., Oquendo, M., Birmaher, B., …Melhem, N. (2008). Familial transmission of suicidal behavior: factors mediating the relationship between childhood abuse and offspring suicide attempts. *The Journal of Clinical Psychiatry*, *69*, 584.

Buss, C., Entringer, S., Moog, N. K., Toepfer, P., Fair, D. A., Simhan, H. N., …Wadhwa, P. D. (2017). Intergenerational transmission of maternal childhood maltreatment exposure: implications for fetal brain development. *Journal of the American Academy of Child & Adolescent Psychiatry*, *56*, 373-382.

Cheung, S. F., Chan, D. K. S. (2008). Dependent correlations in meta-analysis: The case of heterogeneous dependence. *Educational and Psychological Measurement*, *68*, 760-777.

Choi, K. W., Houts, R., Arseneault, L., Pariante, C., Sikkema, K. J., Moffitt, T. E. (2019). Maternal depression in the intergenerational transmission of childhood maltreatment and its sequelae: Testing postpartum effects in a longitudinal birth cohort. *Development and Psychopathology*, *31*, 143-156.

Cohen, J. (1992). Quantitative methods in psychology: A power primer. *Psychological Bulletin*, *112*, 1155-1159.

Collishaw, S., Dunn, J., O'CONNOR, T. G., Golding, J., Avon Longitudinal Study of Parents and Children Study Team. (2007). Maternal childhood abuse and offspring adjustment over time. *Development and Psychopathology*, *19*, 367-383.

Dias, B.G., Ressler, K.J. (2014). Parental olfactory experience behavior and neural structure in subsequent generations. *Nature Neuroscience, 17,* 89-96.

Dixon, L., Hamilton-Giachritsis, C., Browne, K. (2005). Attributions and behaviours of parents abused as children: A mediational analysis of the intergenerational continuity of child maltreatment (Part II). *Journal of Child Psychology and Psychiatry, 46,* 58-68.

Dumas-Mallet, E., Button, K. S., Boraud, T., Gonon, F., Munafò, M. R. (2017). Low statistical power in biomedical science: a review of three human research domains. *Royal Society Open Science*, *4*, 160254.

Duval, S., Tweedie, R. (2000). Trim and fill: a simple funnel-plot–based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*, *56*, 455-463.

Elliott, J. C., Stohl, M., Wall, M. M., Keyes, K. M., Goodwin, R. D., Skodol, A. E., …Hasin, D. S. (2014). The risk for persistent adult alcohol and nicotine dependence: the role of childhood maltreatment. *Addiction, 109*, 842-850.

Fischer, R. (1944). Statistical methods for research workers, 1925. Edinburgh: Oliver and Boyd.

Fleming, J., Mullen, P. E., Sibthorpe, B., Bammer, G. (1999). The long-term impact of childhood sexual abuse in Australian women. *Child Abuse & Neglect*, *23*, 145-159.

Gatt, J. M., Burton, K. L., Williams, L. M., Schofield, P. R. (2015). Specific and common genes implicated across major mental disorders: a review of meta-analysis studies. *Journal of Psychiatric Research*, *60*, 1-13.

Gilbert, R., Widom, C. S., Browne, K., Fergusson, D., Webb, E., Janson, S. (2009). Burden and consequences of child maltreatment in high-income countries. *The Lancet*, *373*, 68-81.

Goodman, S. H., Gotlib, I. H. (1999). Risk for psychopathology in the children of depressed mothers: a developmental model for understanding mechanisms of transmission. *Psychological Review*, *106*, 458.

Goodman, A., Joyce, R., Smith, J. P. (2011). The long shadow cast by childhood physical and mental problems on adult life. *Proceedings of the National Academy of Sciences, 108,* 6032-6037.

Hedges, L. V., Olkin, I. (2014). Statistical methods for meta-analysis: Academic Press.

Heim, C., Bradley, B., Mletzko, T., Deveau, T. C., Musselmann, D. L., Nemeroff, C. B., …Binder, E. B. (2009). Effect of childhood trauma on adult depression and neuroendocrine function: sex-specific moderation by CRH receptor 1 gene. *Frontiers in Behavioral Neuroscience, 3*, 41.

Hernandez, A., Plant, E. A., Sachs-Ericsson, N., Joiner Jr, T. E. (2005). Mental health among Hispanics and Caucasians: Risk and protective factors contributing to prevalence rates of psychiatric disorders. *Journal of Anxiety Disorders*, *19*, 844-860.

Higgins, J. P., Thompson, S. G. (2002). Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine, 21*, 1539-1558.

Hunter, J. E., Schmidt, F. L. (2004). Methods of meta-analysis: Correcting error and bias in research findings: Thousands Oaks, Calif., Sage Publications.

Kessler, R. C., McLaughlin, K. A., Green, J. G., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., …Benjet, C. (2010). Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *The British Journal of Psychiatry*, *197*, 378-385.

Klengel, T., Mehta, D., Anacker, C., Rex-Haffner, M., Pruessner, J. C., Pariante, C. M., …Nemeroff, C. B. (2013). Allele-specific FKBP5 DNA demethylation mediates gene–childhood trauma interactions. *Nature Neuroscience, 16*, 33.

Li, M., D'Arcy, C., Meng, X. (2016). Maltreatment in childhood substantially increases the risk of adult depression and anxiety in prospective cohort studies: systematic review, meta-analysis, and proportional attributable fractions. *Psychological Medicine. 46,* 717-730.

Lipsey, M. W., Wilson, D. B. (2001). Practical meta-analysis: Thousands Oaks, Calif., Sage Publications.

Lo, C. K. L., Mertz, D., Loeb, M. (2014). Newcastle-Ottawa Scale: comparing reviewers' to authors' assessments. *BMC Medical Research Methodology, 14*, 45.

Lomanowska, A., Boivin, M., Hertzman, C., Fleming, A. S. (2017). Parenting begets parenting: A neurobiological perspective on early adversity and the transmission of parenting styles across generations. *Neuroscience, 342,* 120-139.

Madigan, S., Cyr, C., Eirich, R., Fearon, R. P., Ly, A., Rash, C., …Alink, L. R. (2019). Testing the cycle of maltreatment hypothesis: Meta-analytic evidence of the intergenerational transmission of child maltreatment. *Development and Psychopathology, 31,* 23-51.

Mason, W. A., Chmelka, M. B., Trudeau, L., Spoth, R. L. (2017). Gender moderation of the intergenerational transmission and stability of depressive symptoms from early adolescence to early adulthood. *Journal of Youth and Adolescence, 46,* 248-260.

Meaney, M. J. (2001). Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. *Annual Review of Neuroscience, 24,* 1161-1192.

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. *Social Psychiatry and Psychiatric Epidemiology, 53,* 453-475.

Miranda, J. K., de la Osa, N., Granero, R., Ezpeleta, L. (2013). Multiple mediators of the relationships among maternal childhood abuse, intimate partner violence, and offspring psychopathology. *Journal of Interpersonal Violence, 28*, 2941-2965.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Annals of Internal Medicine, 151*, 264-269.

Nanda, M. M., Reichert, E., Jones, U. J., Flannery-Schroeder, E. (2016). Childhood maltreatment and symptoms of social anxiety: Exploring the role of emotional abuse, neglect, and cumulative trauma. *Journal of Child & Adolescent Trauma, 9*, 201-207.

Ornduff, S. R. (2000). Childhood maltreatment and malevolence: Quantitative research findings. *Clinical Psychology Review, 20*, 997-1018.

Pariante, C. M. (2014). Depression during pregnancy: molecular regulations of mothers' and children's behaviour. *Biochemical Society Transactions, 42*, 582-586.

Plant, D., Barker, E. D., Waters, C., Pawlby, S., Pariante, C. (2013). Intergenerational transmission of maltreatment and psychopathology: the role of antenatal depression. *Psychological Medicine, 43*, 519-528.

Plant, D. T., Jones, F. W., Pariante, C. M., Pawlby, S. (2017). Association between maternal childhood trauma and offspring childhood psychopathology: mediation analysis from the ALSPAC cohort. *The British Journal of Psychiatry, 211*, 144-150.

Plant, D. T., Pariante, C. M., Sharp, D., Pawlby, S. (2015). Maternal depression during pregnancy and offspring depression in adulthood: role of child maltreatment. *The British Journal of Psychiatry, 207*, 213-220.

Plant, D. T., Pawlby, S., Pariante, C. M., Jones, F. W. (2018). When one childhood meets another–maternal childhood trauma and offspring child psychopathology: A systematic review. *Clinical Child Psychology and Psychiatry*, *23*, 483-500.

Rijlaarsdam, J., Stevens, G. W., Jansen, P. W., Ringoot, A. P., Jaddoe, V. W., Hofman, A., … Tiemeier, H. (2014). Maternal childhood maltreatment and offspring emotional and behavioral problems: Maternal and paternal mechanisms of risk transmission. *Child Maltreatment*, *19*, 67-78.

Roberts, A. L., Lyall, K., Rich-Edwards, J. W., Ascherio, A., Weisskopf, M. G. (2013). Association of maternal exposure to childhood abuse with elevated risk for autism in offspring. *JAMA Psychiatry*, *70*, 508-515.

Sterne, J. A., Egger, M., Smith, G. D. (2001). Investigating and dealing with publication and other biases in meta-analysis. *BMJ*, *323*, 101-105.

Stith, S. M., Liu, T., Davies, L. C., Boykin, E. L., Alder, M. C., Harris, J. M., …Dees, J. E. M. E. G. (2009). Risk factors in child maltreatment: A meta-analytic review of the literature. *Aggression and Violent Behavior*, *14*, 13-29.

Stroup, D. F., Berlin, J. A., Morton, S. C., Olkin, I., Williamson, G. D., Rennie, D., …Thacker, S. B. (2000). Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA*, *283*, 2008-2012.

Thompson, R. (2007). Mothers' violence victimization and child behavior problems: Examining the link. *American Journal of Orthopsychiatry*, *77*, 306-315.

Trautmann, S., Rehm, J., Wittchen, H. U. (2016). The economic costs of mental disorders: Do our societies react appropriately to the burden of mental disorders? *EMBO Reports*, *17*, 1245-1249.

Turner, R. J., Lloyd, D. A. (2004). Stress Burden and the Lifetime Incidence of Psychiatric Disorder inYoung Adults: Racial and Ethnic Contrasts. *Archives of General Psychiatry, 61*, 481-488.

Ulbrich, P. M., Warheit, G. J., Zimmerman, R. S. (1989). Race, socioeconomic status, and psychological distress: An examination of differential vulnerability. *Journal of Health and Social Behavior*, 131-146.

Vigo, D., Thornicroft, G., Atun, R. (2016). Estimating the true global burden of mental illness. *The Lancet Psychiatry*, *3*, 171-178.

Wells, G. (2001). The Newcastle-Ottawa Scale (NOS) for assessing the quality of non randomised studies in meta-analyses. Retrieved from *http://www. ohri.ca/programs/clinical_epidemiology/oxford. Asp*.

Wickrama, K. A. S., Conger, R. D., Abraham, W. T. (2005). Early adversity and later health: The intergenerational transmission of adversity through mental disorder and physical illness. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *60*, S125-S129.

Widom, C. S., DuMont, K., Czaja, S. J. (2007). A prospective investigation of major depressive disorder and comorbidity in abused and neglected children grown up. *Archives of General Psychiatry*, *64*, 49-56.

Wilson, S., Durbin, C. E. (2010). Effects of paternal depression on fathers' parenting behaviors: A meta-analytic review. *Clinical Psychology Review*, *30*, 167-180.

World Health Organization. (2008). The global burden of disease: 2010 update. *Geneva: World Health Organization*.