**Modifiable predictors of depression following childhood maltreatment: A Systematic Review and Meta-Analysis**

**Running title: Predictors of depression following maltreatment**

Elizabeth C. Braithwaite Ph.D., 1,2 Robyn M. O’Connor M.Sc., 3 Michelle Degli-Esposti BA,1 Nikki Luke Ph.D4 & Lucy Bowes Ph.D1

1Department of Experimental Psychology, University of Oxford, 9 South Parks Road, Oxford, OX1 3UD

2School of Psychology and Clinical Language Sciences, University of Reading, Earley Gate, Reading, RG6 6AL

3 Department of Social Policy and Intervention, University of Oxford, 32 Wellington Square, Oxford, OX1 2ER

4 Rees Centre for Research in Fostering and Education, Department of Education, University of Oxford, 15 Norham Gardens, Oxford, OX2 6PY

Corresponding author: Professor Lucy Bowes. ADDRESS: Department of Experimental Psychology, University of Oxford, 9 South Parks Road, Oxford, OX1 3UD. TEL: +44 (0)1865 271444 FAX: +44 (0) 1865 310447 EMAIL: Lucy.bowes@psy.ox.ac.uk

**Abstract**

Whilst maltreatment experiences in childhood increase the risk for depression, not all maltreated children become depressed. This review aims to systematically examine the existing literature to identify modifiable factors that increase vulnerability to, or act as a buffer against, depression, and could therefore inform the development of targeted interventions. 13 databases (including Medline, PsychINFO, SCOPUS) were searched (between 1984 and 2014) for prospective, longitudinal studies published in English that included at least 300 participants and assessed associations between childhood maltreatment and later depression. Study quality was assessed using an adapted Newcastle-Ottawa Scale checklist. Meta-analyses (random effects models) were performed on combined data to estimate the effect size of the association between maltreatment and depression. Meta-regressions were used to explore effects of study size and quality. We identified 22 eligible articles (N=12,210 participants), of which 6 examined potential modifiable predictors of depression following maltreatment. No more than two studies examined the same modifiable predictor; therefore it was not possible to examine combined effects of modifiable predictors with meta-regression. It is thus difficult to draw firm conclusions from this study, but initial findings indicate that interpersonal relationships, cognitive vulnerabilities and behavioral difficulties may be modifiable predictors of depression following maltreatment. There is a lack of well-designed, prospective studies on modifiable predictors of depression following maltreatment. A small amount of initial research suggests that modifiable predictors of depression may be specific to maltreatment subtypes and gender. Corroboration and further investigation of causal mechanisms is required to identify novel targets for intervention, and to inform guidelines for the effective treatment of maltreated children.

**Introduction**

Depression is among the most common psychiatric disorders worldwide, with a 12-month prevalence rate estimated between 10-17%, and lifetime prevalence between 17-40% (1, 2). The World Health Organization estimates that depression is the fourth leading cause of Disability-Adjusted Life Years lost, and is ranked first amongst the causes of Years Lived with Disability (3). Further, economic costs of major depression in the USA in 2010 were $210.5 billion, an estimated 21.5% increase since 2000 (4). Given the high prevalence and economic burden, there is a clear impetus to understand depression etiology.

Meta-analyses of cross-sectional and longitudinal studies have consistently found that childhood maltreatment is strongly associated with clinical depression across the life course (5, 6). A meta-analysis of 16 longitudinal studies, totaling 23,544 participants, also found maltreatment was associated with an elevated risk recurrent and persistent depressive episodes, and a lack of response or remission during treatment (7).

Despite the increased risk of depression following maltreatment, not all children who are abused will develop depression symptomatology. Key questions regarding which subgroups of children may be more vulnerable to depression, and the pathways by which maltreatment leads to depression onset within subgroups, remain unanswered. The primary aim of our review is to therefore systematically assess the existing research to increase our understanding of factors that have the potential to be strengthened or changed to reduce the likelihood of depression onset among maltreated children. We defined a ‘modifiable predictor’ of depression as one potentially changeable through lifestyle or existing medical treatment. Given the complex nature of the question, this review includes only the strongest non-experimental studies; those that are longitudinal and prospective. Consideration of study design is vital when addressing questions of causality, and the temporal order of factors that may influence causal pathways, as is the case in this review. This research is of clinical importance, as it has implications for the identification of causal mechanisms in depression onset following maltreatment. A greater understanding of causal mechanisms may result in identification of novel therapeutic targets to prevent depression onset, and to inform guidelines for effective treatment of maltreated children.

**Method**

*Search Strategy and Selection Criteria*

We conducted a systematic literature search for studies published in English between 1984 (year the Child Protection Act was introduced in the US) and 2014, to identify primary research studies that investigated relationships between childhood maltreatment and later depression. Our search terms were: ("harsh parenting" OR “abuse\*” OR “neglect\*” OR “maltreat\*” OR "foster care\*" OR "foster famil\*" OR "substitute famil\*" OR “residential care” OR "out-of-home care" OR "out of home care" OR “congregate care” OR “group home” OR “alternative care”) AND (“child\*” OR “youth\*” OR “adolescent\*” OR “infant\*”) AND (“depress\*” OR “Major Depress\*” OR “Dysphoria” OR “Psychopathology” OR “Affective Disorder\*” OR “Dysthym\*” OR “Mood Disorder\*” OR “resilience” OR “internalising” OR “internalizing” OR “suicid\*” OR “self-harm”) AND (“longitudinal” OR “prospective”). As different terms are used to describe modifiable predictors in different disciplines, we did not restrict our search to terms relating to modifiable predictors, but rather used broad search terms, and extracted information regarding factors that would be included in our definition of modifiable predictors of depression along with other study information. 13 databases were searched: ASSIA, Australian Education Index, British Education Index, Cochrane Library, Conference Proceedings Citation Index & Social Sciences Citation Index, ERIC, International Bibliography of Social Sciences, Medline, PsychINFO, SCOPUS, Social Care Online, Social Policy & Practice, Social Services Abstracts. Reference lists were manually checked for studies not retrieved via electronic search.

We identified articles satisfying the following criteria: original, peer-reviewed studies that had a prospective, longitudinal design (over any time period) whereby the measure of maltreatment preceded the measure of depression, and were cohort or case-control studies. Childhood maltreatment or harsh and neglectful parenting was defined as any act or series of acts of commission (physical abuse, sexual abuse, emotional/psychological abuse, or harsh parenting) or omission (neglect) by a parent, caregiver or other person that leads to harm, the potential for harm, or threat of harm to a child (up to 18 years of age). Depression was assessed either as a clinical depression diagnosis or continuous measure of depressive symptoms using scales with reported validity and reliability. Participants were children (10 years or over at outcome measure) or adults in any country and in any setting, including inpatients. We excluded studies if they were cross-sectional, reviews, discussion papers, non-research letters, editorials, case studies or case series, animal studies, qualitative studies without a quantitative element, or articles not published in English. Our goal was to include as many relevant studies as possible. However, analyses based on a small number of small samples can be statistically unstable, a problem exacerbated in models involving multiple covariates and interaction terms. Thus, we required participating studies to have at least 300 individuals to maximize statistical power (8).

*Data Extraction*

EB and RO independently extracted data from eligible articles. Inconsistencies were resolved in consensus meetings and confirmed with the authors of primary studies where necessary. For samples where more than one article was published, we chose one article to include in the review based on A) the inclusion of modifiable predictors, and B) larger total sample size. Missing information was requested from authors.

*Assessing study quality*

Two authors (EB and LB) independently evaluated study quality against criteria devised from the Newcastle Ottowa Scale (NOS), a quality checklist designed to assess the quality of nonrandomized studies in meta-analyses (9). Consensus was evaluated on 20% of ratings and was acceptable. The NOS yields a score from 0 to 9 (one point per item, one item is worth two points), with higher scores indicating higher quality. We rated articles that scored 0-3 ‘lower quality’; 4-6 as ‘moderate quality’, and 7-9 as ‘higher quality’.

No quality checklists exist to assess modifiable predictor variables in longitudinal research. To assess the quality of modifiable predictors, we therefore created three additional criteria. These were:

1. Clear theoretical justification for assessing the modifiable predictor.
2. The modifiable predictor was assessed longitudinally after maltreatment and before depression.
3. The modifiable predictor was assessed using a validated measure.

We assessed the quality of modifiable predictors on a scale of 0-3; each item was scored one point if present.

*Analytic Strategy*

Extracted data were converted into odds ratios (ORs), and we calculated combined OR and 95% confidence intervals (CIs) using random effects models, where weights reflect the inverse variance of each study’s effect estimate. Heterogeneity of effects was assessed using Cochrane Q tests and quantified using I2 tests (10). Forest plots were created to visually examine ORs and CIs of each study, and across studies included in meta-analyses. Publication bias was evaluated by visually investigating funnel plot asymmetry and sensitivity was checked using trim and fill analysis (11).

We conducted analyses in three stages. First, we examined combined OR and CIs in all studies that reported unadjusted associations between maltreatment (of any type) and depression (N=13 studies). We then repeated this to examine adjusted associations (N=7 studies), including studies that accounted for any confounder or covariate. Sensitivity analysis examined unadjusted ORs in the group of studies for which both the unadjusted and adjusted associations were reported (N=7). Due to power constraints, this analysis only included studies where the extracted data *was not* split by maltreatment type. Second, meta-regressions assessed whether unadjusted associations were influenced by study size or quality. The third stage of analysis aimed to use meta-analysis and meta-regression to test effects of modifiable predictors in associations between maltreatment and depression, where data from three or more studies could be combined. Unfortunately, no more than two included studies assessed the same modifiable predictor. Therefore, modifiable predictors of depression are reviewed narratively.

**Results**

*Literature Search*

The literature search yielded 4575 unique articles. 4189 were discarded as irrelevant/ineligible based on titles and abstracts. The remaining 386 articles were assessed for inclusion using the full text, and 364 were excluded. This resulted in 22 articles that met inclusion criteria for the systematic review (see **Figure 1**). Of the 22 articles, 3 did not report associations between maltreatment and depression (12-14), and one reported ORs but not CIs and therefore we were unable to include this in analyses (15). We were unable to contact authors of three articles to request further information, (12-14), and one author no longer had access to data (15). Thus, 18 articles were included in the meta-analysis (N=12,210).

*Study Characteristics*

Characteristics of the 22 included studies are shown in **Table 1.** The study samples ranged from 355 to 4664 participants, and were published between 2001 and 2014. In the majority of studies, participants’ self-reported symptoms of depression on a continuous scale (N=18), and five studies assessed depression via diagnostic interview (14, 16-19). Childhood maltreatment (including harsh parenting) was measured using various methods. Six studies accessed official records (15, 20-24), and the remaining studies used self-reported experiences of maltreatment, where participants reported experiences either as adolescents (13, 19, 25-30) or adults (12, 14, 18, 31, 32).

*Childhood maltreatment and depression*

Our analysis confirmed an association between maltreatment and depression in all studies where maltreatment was not split by type. The combined unadjusted association (N=13 studies) was OR=1.59 (95% CI=1.46-1.75, p<0.001), indicating that maltreated children were more likely than non-maltreated children to develop depression. Significant heterogeneity was observed among these studies (I2=80.1, p<0.001) (**Figure 2A**). The combined adjusted association (N=7 studies) was OR=1.50 (95% CI=1.32-1.70, p<0.001), again indicating that maltreated children were more likely to develop depression than their non-maltreated peers, and significant heterogeneity was observed (I2=92.4, p<0.001) (**Figure 2B**). In sensitivity analyses the unadjusted association was OR=1.71 (95% CI=1.51-1.94) and heterogeneity was evident (I2=48.83%, p<0.001).

We then evaluated the relation of study quality and size with observed risk through meta-regression of study quality ratings and sample size with ORs. The unadjusted association (N=13 studies) between maltreatment and depression, adjusted in meta-regression analysis for study quality was OR=1.48 (95% CI=0.47-4.62), suggesting only a very small influence of quality on effect size. The same analysis adjusted for sample size was OR=2.06 (95% CI=1.06-4.02), and the association was in a negative direction, indicating larger studies reported smaller effects. Publication bias was evident. A funnel plot revealed that smaller studies reporting weak associations had not been published. Correction for bias slightly reduced the unadjusted association (OR=1.30, 95%CI=1.13-1.49).

*Modifiable predictors of depression following maltreatment*

Six studies examined modifiable predictors of depression, and these were categorized as: interpersonal relationships, cognitive vulnerabilities and behavioral difficulties (See **Table 2**).

*Interpersonal relationships*. Two studies, which we rated as higher and moderate quality, examined the role of social support (19, 24). Sperry & Widom (2013) assessed 388 adults with documented histories of maltreatment, and 308 matched controls. Participants self-reported social support at age 39.5 using the Interpersonal Support Evaluation List, which includes 4 items: appraisal, belonging, self-esteem and tangible support. This measure met all three of our quality criteria. Participants reported depression at age 41.2. When adjusting for age, gender and race, maltreated individuals reported significantly lower total social support in adulthood, and also lower sub-types of social support. Total social support, and sub-types, conferred vulnerability to depression following maltreatment, such that maltreatment predicted lower social support and lower social support predicted higher depression. Similarly, Salazar et al*.* (2011) followed 513 youth exiting the foster care system. Participants’ self-reported pre-care and during-care maltreatment at age 17. Perceived social support was self-reported at age 19, and met all quality criteria. This measure was an overall perceived social support composite, calculated by standardizing and taking the mean of two social support measures: The Medical Outcomes Study Social Support Survey and a social network sufficiency measure. Depression was assessed via clinical interview at age 21. Both pre-care and during care maltreatment were associated with depression as a young adult. Maltreated individuals who perceived higher social support were less vulnerable to developing depression compared to maltreated individuals who perceived lower social support. However, buffering effects of social support were stronger for participants with fewer maltreatment experiences, and diminished as maltreatment histories became more complex.

A study that we rated as moderate-quality, analyzed insecure attachment style as a potential modifiable predictor of depression following maltreatment. Hankin *et al.* (2005) examined 652 undergraduate students with a mean age of 18.7, who retrospectively reported experiences of maltreatment during childhood and depressive symptoms at a later time point. They also reported insecure attachment style on the Adult Attachment Questionnaire. However, this measure did not meet all our quality criteria as it was assessed at the same time as depression. Emotional abuse in childhood, but not other abuse sub-types, was associated with an increase in depressive symptoms and insecure attachment styles in young adulthood. Further, it appeared that an insecure attachment increased vulnerability to depression following emotional abuse.

*Cognitive vulnerabilities*. Results presented by Paredes & Calvete (2014), which we rated to be moderate-quality, suggests that a certain cognitive vulnerability, brooding, may be a modifiable predictor of depression. This was a three-phase longitudinal study of 998 adolescents aged 13 to 17. At the first assessment participants retrospectively reported emotional abuse during childhood, and at the second assessment cognitive vulnerabilities were measured using the Children’s Response Style Scales and the Adolescent Cognitive Style Questionnaire. These included two components of rumination (brooding and reflection), and negative inferential styles, and this measure met all three of our quality criteria. Participants’ self-reported depression at all stages. Emotional abuse was associated with increased brooding, which in turn was associated with depression, indicating that increases in brooding may increase vulnerability to depression. However, neither reflection nor negative inferential styles increased vulnerability. Hankin et al. (2005), described above, also assessed negative cognitive style as a modifiable predictor of depression using the Cognitive Style Questionnaire. A negative cognitive style, in part, conferred vulnerability to depression following emotional abuse in univariate analyses. However, in multivariate analyses, which controlled for baseline depression, effects minimized and became non-significant, suggesting a weak relationship.

*Behavioral Difficulties*. Two studies, that we rated to be moderate quality, investigated aspects of behavior as modifiable predictors. Brensilver et al. (2011) assessed a group of 303 children (aged 9-12) longitudinally over one year, that had documented maltreatment histories, and 151 matched controls. Externalizing behavior was examined using the Youth Self Report, but only met two of our quality criteria as it was not assessed temporally after maltreatment and before depression. Maltreated girls showed a strong relationship between externalizing behavior and depression, such that baseline externalizing problems explained 22% of variance in depressive symptoms. However, this association was not evident among maltreated boys. Brody et al. (2014) examined relationships between self-reported harsh parenting during preadolescence, anger in adolescence measured with the State-Trait Anger Inventory (which met all three of our quality criteria), and late adolescent health (a latent variable composed of C reactive protein, depression and poor health) among 368 African American youth. Harsh parenting was associated with increased anger, which was in turn associated with poor health generally. Unfortunately, the authors did not test whether youth anger increased vulnerability to depressive symptoms specifically. However, harsh parenting and depression was significantly and positively correlated.

**Discussion**

We conducted a systematic review to synthesize existing literature that examined modifiable predictors of depression following maltreatment. We employed stringent inclusion criteria so that only sufficiently powered, longitudinal studies were included. Combined unadjusted and adjusted associations between maltreatment and depression reported here are consistent with effect sizes reported in existing meta-analyses of this association (5-7, 33), demonstrating a clear association when focusing solely on prospective, longitudinal data. Adjusting for study size and quality resulted in only small changes in the effect size. As only 6 of the identified studies examined potential modifiable predictors of depression, it is difficult to draw firm conclusions from this research.

There is some initial evidence that low social support increases vulnerability to depression following maltreatment (19, 24). This may suggest that maltreated children find it more difficult to form relationships from which they gain high levels of support, and therefore are at greater risk of developing depression. Alternatively, other factors relating to maltreatment may make it difficult for children to access social support. Equally, children with existing high social support appear buffered from the detrimental effects of maltreatment on depression, though this appears more effective for children without the co-occurrence of maltreatment subtypes. Similarly, insecure attachment style was associated with depression in later life, which may be because maltreated children with insecure attachment styles find it difficult to form stable and supportive relationships. That being said, a substantial proportion of children in foster care with insecure attachments to birth parents were able to form secure attachments with foster parents (34). This highlights that processes underpinning formation of secure attachment relationships are not biologically or genetically driven, and are malleable under different conditions. Thus, attachment relationships may be modifiable, and therefore a key target for intervention. Indeed, a number of relationship-based interventions already exist for maltreated children, which aim to promote secure attachment, and sensitive and responsive parent-child interactions. Examples of these types of therapies include Attachment Biobehavioral Catchup (ABC), which helps caregivers re-interpret children’s behavioral signals, and Infant Parent Psychotherapy (IPP), which aims to improve the parent-child relationship. Meta-analyses demonstrate that these types of intervention effectively improve attachment security, however effects on externalizing behaviors are minimal (35). It is unknown whether relationship-based interventions promote resilience to depressive and internalizing symptoms, and addressing this theory is a clear future direction for resilience and intervention research.

A wealth of depression research suggests that cognitive biases and vulnerabilities increase risk for depression onset and recurrence (36). Given this existing, extensive field of research, it is surprising that only two studies from the current review investigated cognitive vulnerabilities in susceptibility to depression following maltreatment. One of the main psychological therapies to treat depression, cognitive behavioral therapy (CBT), specifically targets negative patterns of thought about the self and world, in order to alter unwanted behavioral patters and improve mood. CBT is certainly the most well evidenced form of therapy for maltreated children, and has specific adaptations for sexual abuse, physical abuse, and multiple forms of maltreatment (35). In meta-analyses, CBT significantly reduces depression and internalizing symptoms both immediately post-treatment and at 1-year follow up (35), indicating a causal role of cognitive vulnerabilities in associations between maltreatment and depression. The current review also found behavioral difficulties, specifically externalizing behaviors, may also be modifiable predictors of depression following maltreatment, but there are currently few interventions for maltreated children aimed at managing difficult behaviors. As externalizing behaviors are highly comorbid with depression it is, however, unclear whether externalizing problems are on the causal pathway to depression, or are an early manifestation of depression. More research is needed to understand this relationship, but if behavioral difficulties are causal, then interventions aimed at behavior management may be effective for reducing depression.

Limitations of this systematic review, and the individual studies, should be considered. Our inclusion criteria were strict so only well-powered longitudinal studies were included, however there was great variability in measures of maltreatment and depression. Whilst all included studies were prospective in design, many included retrospective reports of maltreatment, which is likely to result in recall bias. Accessing official records may be more reliable; however restricting measures to official records identifies only a small proportion of cases, which may be a biased, unrepresentative subset. Further, many studies assessed depression via clinical interview, but a significant number assessed depression via self-report, which is subject to current mood. It is also important to note that there may be inherent bias in participants with symptoms depression who are willing to take part in prospective, longitudinal research compared with their counterparts who are not willing to partake in research, and therefore results may not be wholly generalizable to the population. However, this is of course somewhat unavoidable in observational research. Of the six studies to examine modifiable predictors of depression, two utilized official records (20, 24), and four assessed maltreatment via youth report (19, 25, 27, 37). Just one study assessed depression via clinical interview (19) and the remaining used a self-report measure (20, 24, 25, 27, 37).

We assessed study quality using the Newcastle-Ottowa Scale. However, there are no existing checklists specifically designed to assess the quality of risk factors in longitudinal research, which may be on causal pathways between exposure and outcome. We thus created three quality criteria for assessing modifiable risk factors, but this has not been validated. The lack of quality checklists is a limitation for any scientific field focused on assessing mechanisms in health and disease. The development and validation of such checklists is of academic and clinical importance. Another limitation is that we focused on depression as an outcome, and therefore studies where depression and other psychiatric and physical conditions were comorbid were not included, as these were beyond the scope of this review. For example, there have been reports of poor physical and psychological outcomes, including substance abuse, for those who experienced childhood abuse (38). Thus, potentially higher risk groups with co-morbidity were not included in the review. We also did not search the grey literature for unpublished data, as we included only peer-reviewed studies published in journal articles.

Many questions remain regarding future research. Well-designed longitudinal, prospective research investigating and characterizing modifiable predictors in associations between maltreatment and depression are lacking. The design of such studies requires careful consideration to elucidate causal mechanisms and identify targets for intervention. For example, measuring and statistically controlling for baseline symptoms is important to understand cyclical relationships and causal links between variables, and to tease apart correlates of exposure and outcome. A critical question concerns the underlying biological processes that may lead to depression onset following maltreatment exposure, and future studies should seek to ameliorate the biological mechanisms underlying potential modifiable predictors, such as cognitive processes and behavior, using physiological and neuroimaging techniques. It is also currently unclear whether different modifiable predictors may be important for subtypes of abuse, and whether modifiable predictors are gender-specific. Just one of the included studies in our review tested for gender differences, and reported that for maltreated girls there was a strong association between externalizing symptoms and depression, but this association was not evident in boys. No other studies reported effects by gender, thus we were unable to test overall effects of gender in meta-analyses. However, given the higher prevalence of depression in females, and the emerging idea that mechanisms leading of psychopathology in the context of early-life stress may be sex-specific (39), it is possible that modifiable predictors of depression following maltreatment may also be gender specific.

There is an underdeveloped profile of research regarding modifiable predictors of depression following maltreatment from high quality, sufficiently powered studies. There is initial evidence to suggest interpersonal relationships, cognitive vulnerabilities and behavioral difficulties may act as modifiable predictors of this association. Identifying and understanding mechanisms of modifiable predictors of depression among maltreated children may help us to better understand what works, for which children and why. Such research will enhance the development of targeted interventions for maltreated children.

**Conflict of Interest**

The authors declare no conflict of interest.

**References**

1. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003;289(23):3095-105.

2. Moffitt TE, Caspi A, Taylor A, Kokaua J, Milne BJ, Polanczyk G, et al. How common are common mental disorders? Evidence that lifetime prevalence rates are doubled by prospective versus retrospective ascertainment. Psychol Med. 2010;40(6):899-909.

3. WHO. The world health report 2001 - mental health: new understanding, new hope. Geneva: 2001.

4. Greenberg PE, Fournier AA, Sisitsky T, Pike CT, Kessler RC. The economic burden of adults with major depressive disorder in the United States (2005 and 2010). J Clin Psychiatry. 2015;76(2):155-62.

5. Lindert J, von Ehrenstein OS, Grashow R, Gal G, Braehler E, Weisskopf MG. Sexual and physical abuse in childhood is associated with depression and anxiety over the life course: systematic review and meta-analysis. Int J Public Health. 2014;59(2):359-72.

6. Infurna MR, Reichl C, Parzer P, Schimmenti A, Bifulco A, Kaess M. Associations between depression and specific childhood experiences of abuse and neglect: A meta-analysis. J Affect Disord. 2016;190:47-55.

7. Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. Am J Psychiatry. 2012;169(2):141-51.

8. Smith PG, Day NE. The design of case-control studies: the influence of confounding and interaction effects. Int J Epidemiol. 1984;13(3):356-65.

9. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottowa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses 2013. Available from: <http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp>.

10. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539-58.

11. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics. 2000;56(2):455-63.

12. Lev-Wiesel R, Daphna-Tekoah S. The role of peripartum dissociation as a predictor of posttraumatic stress symptoms following childbirth in Israeli Jewish women. J Trauma Dissociation. 2010;11(3):266-83.

13. Munson MR, McMillen C. Trajectories of Depression Symptoms among Older Youths Exiting Foster Care. Soc Work Res. 2010;34(4):235-49.

14. Smit F, Beekman A, Cuijpers P, de Graaf R, Vollebergh W. Selecting key variables for depression prevention: results from a population-based prospective epidemiological study. J Affect Disord. 2004;81(3):241-9.

15. Thornberry TP, Ireland TO, Smith CA. The importance of timing: the varying impact of childhood and adolescent maltreatment on multiple problem outcomes. Dev Psychopathol. 2001;13(4):957-79.

16. Danese A, Moffitt TE, Harrington H, et al. Adverse childhood experiences and adult risk factors for age-related disease: Depression, inflammation, and clustering of metabolic risk markers. Archives of Pediatrics & Adolescent Medicine. 2009;163(12):1135-43.

17. Fergusson DM, Horwood LJ, Miller AL, Kennedy MA. Life stress, 5-HTTLPR and mental disorder: findings from a 30-year longitudinal study. The British Journal of Psychiatry. 2011;198(2):129-35.

18. Robertson-Blackmore E, Putnam FW, Rubinow DR, Matthieu M, Hunn JE, Putnam KT, et al. Antecedent trauma exposure and risk of depression in the perinatal period. J Clin Psychiatry. 2013;74(10):e942-8.

19. Salazar AM, Keller TE, Courtney ME. Understanding social support's role in the relationship between maltreatment and depression in youth with foster care experience. Child Maltreat. 2011;16(2):102-13.

20. Brensilver M, Negriff S, Mennen FE, Trickett PK. Longitudinal relations between depressive symptoms and externalizing behavior in adolescence: moderating effects of maltreatment experience and gender. J Clin Child Adolesc Psychol. 2011;40(4):607-17.

21. Herrenkohl TI, Hong S, Klika JB, Herrenkohl RC, Russo MJ. Developmental Impacts of Child Abuse and Neglect Related to Adult Mental Health, Substance Use, and Physical Health. Journal of family violence. 2013;28(2).

22. Lee C, Cronley C, White HR, Mun E-Y, Stouthamer-Loeber M, Loeber R. Racial Differences in the Consequences of Childhood Maltreatment for Adolescent and Young Adult Depression, Heavy Drinking, and Violence. Journal of Adolescent Health. 2012;50(5):443-9.

23. Mersky JP, Topitzes J. Comparing early adult outcomes of maltreated and non-maltreated children: A prospective longitudinal investigation. Children and Youth Services Review. 2010;32(8):1086-96.

24. Sperry DM, Widom CS. Child abuse and neglect, social support, and psychopathology in adulthood: a prospective investigation. Child Abuse Negl. 2013;37(6):415-25.

25. Brody GH, Yu T, Beach SRH, Kogan SM, Windle M, Philibert RA. Harsh parenting and adolescent health: A longitudinal analysis with genetic moderation. Health Psychology. 2014;33(5):401-9.

26. Clark DB, De Bellis MD, Lynch KG, Cornelius JR, Martin CS. Physical and sexual abuse, depression and alcohol use disorders in adolescents: onsets and outcomes. Drug Alcohol Depend. 2003;69(1):51-60.

27. Hankin BL. Childhood Maltreatment and Psychopathology: Prospective Tests of Attachment, Cognitive Vulnerability, and Stress and Mediating Processes. Cognitive therapy and Research. 2005;29(6):645-71.

28. O'Connor RC, Rasmussen S, Hawton K. Predicting deliberate self-harm in adolescents: a six month prospective study. Suicide Life Threat Behav. 2009;39(4):364-75.

29. Schilling EA, Aseltine RH, Jr., Gore S. Adverse childhood experiences and mental health in young adults: a longitudinal survey. BMC Public Health. 2007;7:30.

30. Wu C-I. The Interlocking Trajectories between Negative Parenting Practices and Adolescent Depressive Symptoms. Current Sociology. 2007;55(4):579-97.

31. Rich CL, Gidycz CA, Warkentin JB, Loh C, Weiland P. Child and adolescent abuse and subsequent victimization: a prospective study. Child Abuse Negl. 2005;29(12):1373-94.

32. Seng JS, Sperlich M, Low LK, Ronis DL, Muzik M, Liberzon I. Childhood abuse history, posttraumatic stress disorder, postpartum mental health, and bonding: a prospective cohort study. J Midwifery Womens Health. 2013;58(1):57-68.

33. Li M, D'Arcy C, Meng X. Maltreatment in childhood substantially increases the risk of adult depression and anxiety in prospective cohort studies: systematic review, meta-analysis, and proportional attributable fractions. Psychol Med. 2016;46(4):717-30.

34. Joseph MA, O'Connor TG, Briskman JA, Maughan B, Scott S. The formation of secure new attachments by children who were maltreated: an observational study of adolescents in foster care. Dev Psychopathol. 2014;26(1):67-80.

35. Macdonald G, Livingstone N, Hanratty J, McCartan C, Cotmore R, Cary M, et al. The effectiveness, acceptability and cost-effectiveness of psychosocial interventions for maltreated children and adolescents: an evidence synthesis. Health Technol Assess. 2016;20(69):1-508.

36. Everaert J, Koster EH, Derakshan N. The combined cognitive bias hypothesis in depression. Clinical psychology review. 2012;32(5):413-24.

37. Paredes P, Calvete E. Cognitive vulnerabilities as mediators between emotional abuse and depressive symptoms. J Abnorm Child Psychol. 2014;42(5):743-53.

38. Springer KW, Sheridan J, Kuo D, Carnes M. The long-term health outcomes of childhood abuse. An overview and a call to action. J Gen Intern Med. 2003;18(10):864-70.

39. Glover V, Hill J. Sex differences in the programming effects of prenatal stress on psychopathology and stress responses: an evolutionary perspective. Physiol Behav. 2012;106(5):736-40.

**Figure Legends**

**Figure 1** Study selection procedure for a systematic review of the association between childhood maltreatment and later depression, examined in prospective, longitudinal studies.

**Figure 2.** Forest plots of individual and pooled odds ratios (OR) and 95% confidence intervals (CI) for childhood maltreatment and depression. The size of the shaded box around the individual study ORs represent the weight of that study in the pooled analysis. A) The unadjusted association between maltreatment of any type and depression, N=13 studies. B) The adjusted (for any confounder, covariate or modifiable predictor) association between maltreatment of any type and depression, N=7 studies.